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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL 2-CHLORO-4-(METHYLSULFONYL) PHENYL CONTAINING ACYLTHIOUREA AND 1,3-THIAZOLIDIN-4-ONE AS PROMISING ANTIMICROBIAL AGENTS

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Abstract
A series of acylthiourea derivatives, 2-chloro-4-(methylsulfonyl)-N-(arylcarbamothioyl) benzamides were synthesized by reaction of 2-chloro-4-(methylsulfonyl) benzoyl chloride with ammonium thiocyanate and substituted aromatic amines. Cyclocondensation of acylthiourea derivatives, 2-chloro-4-(methylsulfonyl)-N-(arylcarbamothioyl) benzamides with tert-butyl chloroacetate yielded thiazolidinone derivatives, 3-{[2-chloro-4-(methylsulfonyl) phenyl]carbonyl}-2-(imino)-1,3-thiazolidin-4-one. Structure elucidation of the synthesized compounds has been accomplished on the basis of elemental analysis, mass, IR, ^{1}H-NMR and ^{13}C-NMR data. Synthesized compounds were screened for their antimicrobial activity against gram-positive, gram-negative bacteria and some selected fungal stains.

Keywords: 1,3-thiazolidin-4-one, acylthiourea, cyclocondensation, antimicrobial activity.

Introduction

4-Thiazolidinones (1,3-thiazolidin-4-one) have been known for a long time, [I] and a large number of heterocyclic compounds possessing 4-oxo-thiazolidine moiety, exhibit valuable biological properties, such as antibacterial, [II-IV] antimicrobial, [V-VI] anticancer, [VII-IX] anticonvulsant, [X] antiviral [XI-XII] and anti-HIV activity, [XIII] etc. There are many available methods for the synthesis of thiazolidinones, but the treatment of schiff bases with thioglycolic acid and treatment of thiourea derivatives with monochloroacetic acid are the most commonly used methods.

The present work describes the synthesis of acylthiourea derivatives by reacting 2-chloro-4-(methylsulfonyl) benzoyl chloride with ammonium thiocyanate and substituted aromatic amines followed by conversion of thiourea derivatives to 4-thiazolidinones by cyclocondensation of thiourea derivatives with tert-butyl chloroacetate.

Experimental section

All reagents and solvents used for the preparation of the compounds were of laboratory reagent grade quality and were obtained from s d fine chem., rankem and Spectrochem. Melting points

were determined by open capillary tubes on a Veego melting point apparatus and are uncorrected. IR spectra of the all synthesized compounds were recorded on Perkin Elmer spectrophotometer. Mass spectra were recorded on a Waters Q-Tof Premier spectrometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker 500 MHz instrument operating at 500 MHz for ^{1}H and 75 MHz for ^{13}C-NMR using DMSO-d_6 or $CDCl_3$ as solvents. Chemical shifts were given as δ values in parts per million (ppm) relative to tetramethylsilane as internal standard

Synthesis of 2-chloro-4-(methylsulfonyl) benzoyl chloride (1)
2-chloro-4-(methylsulfonyl) benzoic acid (10g, 0.0426mol) was added to thionyl chloride (40ml), resulting suspension was heated to reflux and refluxed till a clear solution was observed which indicate the completion of reaction, Unreacted thionyl chloride was distilled off under reduced pressure and traces of thionyl chloride were further removed by stripping with dry toluene to get 2-chloro-4-(methylsulfonyl) benzoyl chloride **(1)**.

Synthesis of acylthioureas (3) via 2-chloro-4-(methylsulfonyl) benzoyl isothiocyanate (2)
To a solution of 2-chloro-4-(methylsulfonyl) benzoyl chloride (corresponding to 10g of 2-chloro-4-(methylsulfonyl)benzoic acid, 0.0426mol) in chloroform (50ml) was added ammonium thiocyanate (3.24g, 0.0426mol). The reaction mixture was heated to reflux and refluxed for 1 hour to form 2-chloro-4-(methylsulfonyl) benzoyl isothiocyanate **(2)** *in situ*. A solution of substituted aromatic amine (0.0426mol) in chloroform (20 ml) was added drop wise to the reaction mixture under reflux and refluxing continued for 4-8 h. depending upon the completion of reaction. Completion of the reaction was monitored on silica gel TLC plate using hexane-ethyl acetate (1:1) as mobile phase. After the completion of reaction separated ammonium chloride was removed by filtration, chloroform layer was recovered under reduced pressure and obtained residue was purified by crystallization from ethanol to obtained acylthiourea derivatives **(3)**.

Synthesis of 1,3-thiazolidin-4-one derivatives (4)
Tert-butyl chloroacetate (0.011mol) was added to a solution of acylthiourea (0.01mol) in acetic acid (25 ml). The reaction mixture was heated to reflux and refluxed for 8-12 h. depending upon the completion of reaction. Completion of the reaction was monitored on silica gel TLC plate using hexane- ethyl acetate (1:1) as mobile phase. After the completion of reaction, the reaction mixture was poured into a mixture of ice and water, obtained solid was filtered washed with water, dried and purified by crystallization from ethanol obtained 1,3-thiazolidin-4-one derivatives **(4)**.

Spectral data of acylthiourea derivatives
2-chloro-4-(methylsulfonyl)-N-(phenylcarbamothioyl) benzamide (3a); Yield 60%, m. p. 213°C, IR (KBr, cm^{-1}): 3209 (NH), 1682 (C=O, amide), 1537 (C=S), 1305 (S=O); ^{1}H NMR (DMSO-d6, δ ppm): 12.16-12.19 (d,2H, NH-CS-NH), 7.28-8.12 (m, 8H, Ar-H), 3.39 (s, 3H, S-CH_3); ^{13}CNMR (DMSO-d6, δ ppm): 178.80 (C=S), 166.79 (C=O), 144.08-124.89 (arom. C), 43.49 (SCH_3); MS: *m/z* = 368.9; Anal. Calcd. for $C_{15}H_{13}ClN_2O_3S_2$: C, 48.84; H, 3.55; N,7.59. Found: C, 48.44; H, 3.51; N, 7.54.

2-chloro-N-[(4-methylphenyl)carbamothioyl]-4-(methylsulfonyl)benzamide (3b); Yield 62%, m. p. 190°C, IR (KBr, cm^{-1}): 3200 (NH), 1684 (C=O, amide), 1533 (C=S), 1301 (S=O); ^{1}H NMR (DMSO-d6, δ ppm): 12.11-12.21 (d,2H, NH-CS-NH), 7.21-8.12 (m, 7H, Ar-H), 3.39 (s, 3H, S-CH_3), 2.38 (s, 3H, CH_3) ; $^{13}CNMR$ (DMSO-d6, δ ppm): 179.40 (C=S), 170.79 (C=O), 143.78-123.80 (arom. C), 44.39 (SCH_3), 25.45 (CH_3); MS: *m/z* = 383 [M+·]; Anal. Calcd. for $C_{16}H_{15}ClN_2O_3S_2$: C, 50.19; H, 3.95; N,7.32. Found: C, 50.23; H, 3.86; N, 7.33.

2-chloro-N-[(4-methoxyphenyl)carbamothioyl]-4-(methylsulfonyl)benzamide (3c); Yield 56%, m. p. 188°C, IR (KBr, cm^{-1}): 3207 (NH), 1682 (C=O, amide), 1540 (C=S), 1306 (S=O); ^{1}H NMR (DMSO-d6, δ ppm): 12.21-12.23 (d, 2H, NH-CS-NH), 7.24-8.11 (m, 7H, Ar-H), 3.78 (s, 3H, OCH_3), 3.31 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 169.10 (C=S), 169.55 (C=O), 144.00-124.19 (arom. C), 55.98 (OCH_3), 44.40 (SCH_3); MS: *m/z* = 399 [M+·]; Anal. Calcd. for $C_{16}H_{15}ClN_2O_4S_2$: C, 48.18; H, 3.79; N,7.02. Found: C, 48.21; H, 3.79; N, 6.98.

2-chloro-N-[(4-chlorophenyl)carbamothioyl]-4-(methylsulfonyl)benzamide (3d); Yield 62%, m. p. 228°C, IR (KBr, cm^{-1}): 3212 (NH), 1688 (C=O, amide), 1531 (C=S), 1305 (S=O); ^{1}H NMR (DMSO-d6, δ ppm): 12.21-12.24 (d, 2H, NH-CS-NH), 7.31-8.18 (m, 7H, Ar-H), 3.30 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 181.00 (C=S), 167.70 (C=O), 144.40-124.12 (arom. C), 44.87 (SCH_3); MS: *m/z* = 404 [M+·]; Anal. Calcd. for $C_{15}H_{12}Cl_2N_2O_3S_2$: C, 44.67; H, 3.00; N, 6.95. Found: C, 44.71; H, 3.03; N, 7.00.

5-[({[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}carbamothioyl)amino]-1H-imidazole-4-carboxamide (3e); Yield 55%, m. p. 238°C, IR (KBr, cm^{-1}): 3210 (NH), 1685 (C=O, amide), 1533 (C=S), 1305 (S=O); ^{1}H NMR (DMSO-d6, δ ppm): 13.06-12.10 (m, 5H, NH-CS-NH, NH2 and Nh of imidazole), 7.54-7.60 (m, 3H, Ar-H), 3.38 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 181.10 (C=S), 167.65 (C=O), 161.32 (C=O of amide), 144.00-114.66 (ring. C), 43.22 (SCH_3); MS: *m/z* = 402 [M+·]; Anal. Calcd. for $C_{13}H_{12}ClN_5O_4S_2$: C, 38.86; H, 3.01; N, 17.43. Found: C, 38.89; H, 3.11; N, 17.44.

N-(1-azabicyclo[2.2.2]oct-3-ylcarbamothioyl)-2-chloro-4-(methylsulfonyl)benzamide (3f); Yield 54%, m. p. 222°C, IR (KBr, cm^{-1}): 3216 (NH), 1690 (C=O, amide), 1530 (C=S), 1302 (S=O); ^{1}H NMR (DMSO-d6, δ ppm): 12.13-12.16 (d,2H, NH-CS-NH), 7.20-8.10 (m, 3H, Ar-H), 3.33 (s, 3H, CH_3), 2.59-1.67 (m, 12H, quiniclidine ring-H); $^{13}CNMR$ (DMSO-d6, δ ppm): 177.98 (C=S), 168.55 (C=O), 144.08-124.37 (arom. C), 58.73-43.21 (SCH_3 and quiniclidine ring); MS: *m/z* = 402 [M+·]; Anal. Calcd. for $C_{16}H_{20}ClN_3O_3S_2$: C, 47.81; H, 5.02; N, 10.45. Found: C, 47.80; H, 5.00; N, 10.44.

Spectral data of 1,3-thiazolidin-4-one derivatives

3-{[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}-2-(phenylimino)-1,3-thiazolidin-4-one (4a); Yield 58%, m. p. 199°C, IR (KBr, cm^{-1}): 1737 (C=O), 1646 (C=N), 1306 (S=O), 1187 (C-S); ^{1}H NMR (DMSO-d6, δ ppm): 7.99-7.39 (m, 8H, Ar-H), 4.22 (s, 2H, CH_2 of thiazolidinone ring), 3.28 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 176.79 (C=O), 175.90 (C=O of thiazolidinone ring), 144.13-126.15 (arom. C), 43.45 (SCH_3), 34.24 (CH_2 of thiazolidinone ring); MS: *m/z* = 409 [M+·]; Anal. Calcd. for $C_{17}H_{13}ClN_2O_4S_2$: C, 49.94; H, 3.20; N, 6.85. Found: C, 49.99; H, 3.21; N, 6.80.

3-{[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}-2-[(4-methylphenyl)imino]-1,3-thiazolidin-4-one (4b); Yield 56%, m. p. 181°C, IR (KBr, cm^{-1}): 1732 (C=O), 1640 (C=N), 1306 (S=O), 1180 (C-S); ^{1}H NMR (DMSO-d6, δ ppm): 8.08-7.47 (m, 7H, Ar-H), 4.17 (s, 2H, CH_2 of thiazolidinone ring), 3.21 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 176.22 (C=O), 175.10 (C=O of thiazolidinone ring), 145.53-124.13 (arom. C), 44.41 (SCH_3), 32.28 (CH_2 of thiazolidinone ring); MS: *m/z* = 423 [M+·]; Anal. Calcd. for $C_{18}H_{15}ClN_2O_4S_2$: C, 51.12; H, 3.58; N, 6.62. Found: C, 51.10; H, 3.50; N, 6.69.

3-{[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}-2-[(4-methoxyphenyl)imino]-1,3-thiazolidin-4-one (4c); Yield 62%, m. p. 177°C, IR (KBr, cm^{-1}): 1735 (C=O), 1641 (C=N), 1300 (S=O), 1208 (C-S); ^{1}H NMR (DMSO-d6, δ ppm): 7.91-7.31 (m, 7H, Ar-H), 4.22 (s, 2H, CH_2 of thiazolidinone ring), 3.77 (s, 3H, O-CH_3), 3.31 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 175.58 (C=O), 175.35 (C=O of thiazolidinone ring), 144.13-126.15 (arom. C), 53.87 (OCH_3), 43.45 (SCH_3), 34.24 (CH_2 of thiazolidinone ring); MS: *m/z* = 439 [M+·]; Anal. Calcd. for $C_{18}H_{15}ClN_2O_5S_2$: C, 49.26; H, 3.44; N, 6.38. Found: C, 49.35; H, 3.40; N, 6.40.

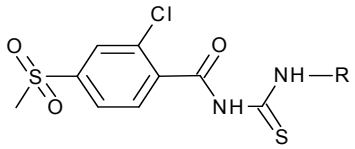
3-{[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}-2-[(4-chlorophenyl)imino]-1,3-thiazolidin-4-one (4d); Yield 60%, m. p. 210°C, IR (KBr, cm^{-1}): 1731 (C=O), 1650 (C=N), 1315 (S=O), 1190 (C-S); ^{1}H NMR (DMSO-d6, δ ppm): 7.81-7.34 (m, 7H, Ar-H), 4.15 (s, 2H, CH_2 of thiazolidinone ring), 3.23 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 177.71 (C=O), 176.91 (C=O of thiazolidinone ring), 144.78-124.45 (arom. C), 44.14 (SCH_3), 34.58 (CH_2 of thiazolidinone ring); MS: *m/z* = 444 [M+·]; Anal. Calcd. for $C_{17}H_{12}ClN_2O_4S_2$: C, 46.06; H, 2.73; N, 6.32. Found: C, 46.10; H, 2.74; N, 6.16.

3-{[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}-4-oxo-1,3-thiazolidin-2-ylidene]amino}-1H-imidazole-4-carboxamide (4e); Yield 46%, m. p. 217°C, IR (KBr, cm^{-1}): 1741 (C=O), 1636 (C=N), 1304 (S=O), 1192 (C-S); ^{1}H NMR (DMSO-d6, δ ppm): 8.02-7.94 (m, 3H, Ar-H), 4.20 (s, 2H, CH_2 of thiazolidinone ring), 3.20 (s, 3H, CH_3); $^{13}CNMR$ (DMSO-d6, δ ppm): 177.22 (C=O), 176.40 (C=O of thiazolidinone ring), 144.13-126.11 (arom. C), 44.45 (SCH_3), 34.22 (CH_2 of thiazolidinone ring); MS: *m/z* = 442 [M+·]; Anal. Calcd. for $C_{15}H_{12}ClN_5O_5S_2$: C, 40.77; H, 2.74; N, 15.85. Found: C, 40.61; H, 2.75; N, 15.80.

3-{[2-chloro-4-(methylsulfonyl)phenyl]carbonyl}-2-(1-azabicyclo[2.2.2]oct-3-ylimino)-1,3-thiazolidin-4-one (4f); Yield 55%, m. p. 204°C, IR (KBr, cm^{-1}): 1743 (C=O), 1637 (C=N), 1300 (S=O), 1202 (C-S); ^{1}H NMR (DMSO-d6, δ ppm): 8.12-7.99 (m, 3H, Ar-H), 4.18 (s, 2H, CH_2 of thiazolidinone ring), 3.26 (s, 3H, CH_3), 2.59-1.67-(m, 12H, quiniclidine ring-H); $^{13}CNMR$ (DMSO-d6, δ ppm): 176.79 (C=O), 175.90 (C=O of thiazolidinone ring), 144.13-126.15 (arom. C), 43.45 (SCH_3), 34.24 (CH_2 of thiazolidinone ring); MS: *m/z* = 442 [M+·]; Anal. Calcd. for $C_{18}H_{20}ClN_3O_4S_2$: C, 48.92; H, 4.56; N, 9.51. Found: C, 48.90; H, 4.50; N, 9.50.

Table-I

Physical constants of acylthiourea derivatives (3a-f)



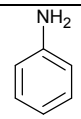
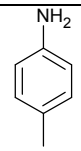
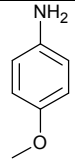
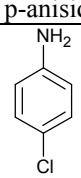
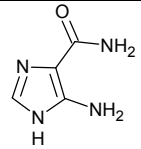
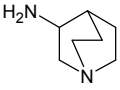
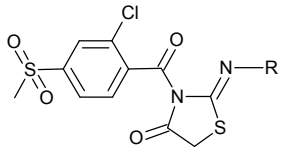
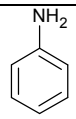
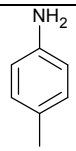
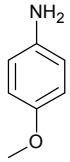
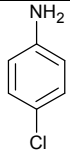
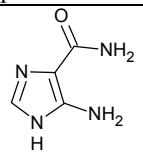
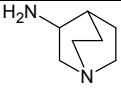
Sr. No.	Substitution (-R)	Molecular Formula/ Molecular Weight	M. P. (°C)	Yield (%)	% Composition Calculated / Found		
					C	H	N
3a	 Aniline	$C_{15}H_{13}ClN_2O_3S_2$ 368.85	213	60	48.84 (48.44)	3.55 (3.51)	7.59 (7.54)
3b	 p-Toluedine	$C_{16}H_{15}ClN_2O_3S_2$ 382.88	190	62	50.19 (50.23)	3.95 (3.86)	7.32 (7.33)
3c	 p-anisidine	$C_{16}H_{15}ClN_2O_4S_2$ 398.88	188	56	48.18 (48.21)	3.79 (3.79)	7.02 (6.98)
3d	 p-chloroaniline	$C_{15}H_{12}Cl_2N_2O_3S_2$ 403.30	228	62	44.67 (44.71)	3.00 (3.03)	6.95 (7.00)
3e	 5-amino-1*H*-imidazole-4-carboxamide	$C_{13}H_{12}ClN_5O_4S_2$ 401.84	238	55	38.86 (38.89)	3.01 (3.11)	17.43 (17.44)
3f	 3-amino quiniclidine	$C_{16}H_{20}ClN_3O_3S_2$ 401.93	222	54	47.81 (47.80)	5.02 (5.00)	10.45 (10.44)

Table-II

Physical constants of 1,3-thiazolidin-4-one derivatives (4a-f)



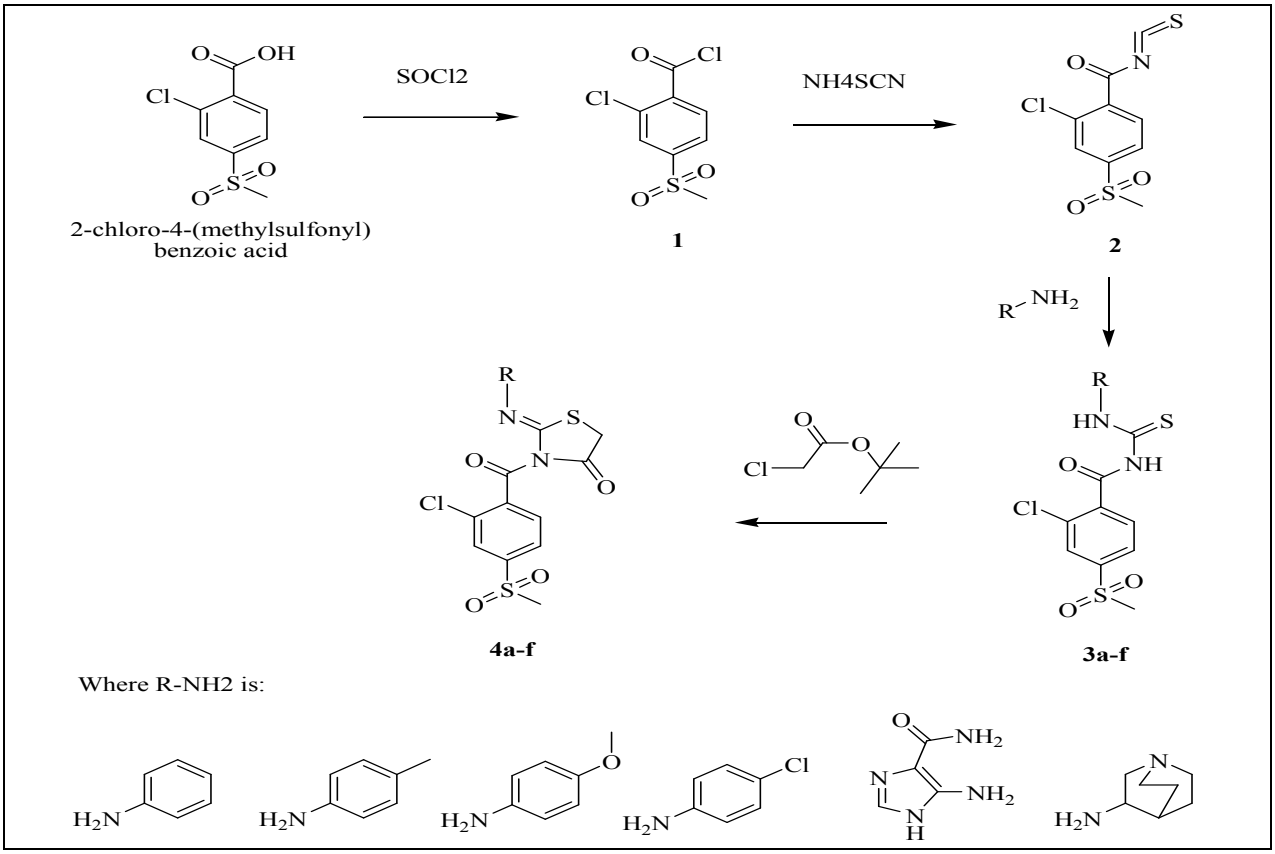
Sr. No.	Substitution (-R)	Molecular Formula/ Molecular Weight	M. P. (°C)	Yield (%)	% Composition Calculated / Found		
					C	H	N
4a	 Aniline	$C_{17}H_{13}ClN_2O_4S_2$ 408.87	199	58	49.94 (49.99)	3.20 (3.21)	6.85 (6.80)
4b	 p-Toluedine	$C_{18}H_{15}ClN_2O_4S_2$ 422.90	181	56	51.12 (51.10)	3.58 (3.50)	6.62 (6.69)
4c	 p-anisidine	$C_{18}H_{15}ClN_2O_5S_2$ 438.90	177	62	49.26 (49.35)	3.44 (3.40)	6.38 (6.40)
4d	 p-chloroaniline	$C_{17}H_{12}Cl_2N_2O_4S_2$ 443.32	210	60	46.06 (46.10)	2.73 (2.74)	6.32 (6.16)
4e	 5-amino-1*H*-imidazole-4-carboxamide	$C_{15}H_{12}ClN_5O_5S_2$ 441.86	217	46	40.77 (40.61)	2.74 (2.75)	15.85 (15.80)
4f	 3-amino quiniclidine	$C_{18}H_{20}ClN_3O_4S_2$ 441.95	204	55	48.92 (48.90)	4.56 (4.50)	9.51 (9.50)

Results and discussion

The acylthiourea derivatives (**3a-f)** were synthesized by following the reaction scheme-I. 2-chloro-4-(methylsulfonyl) benzoic acid was converted into 2-chloro-4-(methylsulfonyl) benzoyl chloride (**1)** by refluxing in thionyl chloride in anhydrous conditions, after removing unreacted thionyl chloride by distillation under reduced pressure solid 2-chloro-4-(methylsulfonyl) benzoyl chloride was then treated with a ammonium thiocyanate in anhydrous chloroform under reflux conditions to afford 2-chloro-4-(methylsulfonyl) benzoyl isothiocyanate **(2)** *in situ*, followed by treatment with aromatic amines in the media of anhydrous chloroform under reflux to afford acylthiourea derivatives **(3a-f)** as residue, the residue was purified by crystallization from ethanol.

All acylthiourea derivatives have been characterized by their melting point, elemental analysis, IR, mass and NMR spectral studies. All spectroscopic and elemental analyses data confirm the proposed structures synthesized compounds.

Reaction scheme-I



1,3-thiazolidin-4-one derivatives **(4a-f)** were synthesized from acylthiourea derivatives **(3a-f)** by following the reaction scheme-I. Acylthiourea derivatives undergoes cyclocondensation with tert-butyl chloroacetate in the media of acetic acid under reflux conditions to afford 1,3-thiazolidin-4-one derivatives **(4a-f)**, conventional work-up method was applied, 1,3-thiazolidin-4-one derivatives were further purified by crystallization from ethanol. Progress of the reaction

and purity of isolated and purified compounds was monitored on silica gel TLC plate using hexane- ethyl acetate (1:1) as mobile phase.

All 1,3-thiazolidin-4-one derivatives have been characterized by their melting point, elemental analysis, IR, mass and NMR spectral studies. All spectroscopic and elemental analyses data confirm the proposed structures synthesized compounds.

Conversion of acylthiourea derivatives in to 1,3-thiazolidin-4-one derivatives have been confirmed by thin layer chromatography and as well as by spectral analysis. Peak of C=S at around 1540-1530 cm^{-1} of acylthiourea derivatives disappeared in 1,3-thiazolidin-4-one derivatives while peak of C=N at around 1650-1630 cm^{-1} and a peak of C-S at around 1210-1180 cm^{-1} were observed confirming the formation of thiazolidinone ring. Similarly the peak at around 4.2 δ ppm (s, 2H, CH_2 of thiazolidinone ring) in ^{1}H-NMR and the peak at around 34 δ ppm (CH_2 of thiazolidinone ring) in ^{13}C-NMR indicate the formation of thiazolidine ring. Molecilar mass and fragmentation pattern of all synthesized compounds were determined by mass spectroscopy.

Antimicrobial activity

The antimicrobial activity of both categories of compounds was determined by the disc diffusion method [XIV], zone inhibition was measured in mm and the activity of synthesized compounds was compared with standard drugs. The *in vitro* antimicrobial activity was carried out in two gram positive bacteria, two gram negative bacteria and two fungi against 24 h culture. The gram positive bacteria used were *Staphylococcus aureus* and *Bacillus subtilis*, gram negative bacteria used were *Escherichia coli* and *Klebsiella pneumonia,* while the fungi used were *Aspergillus niger* and *Candida albicans*. The compounds were tested at a concentration of 100µg/ml in Dimethylformamide. The zone of inhibition was compared after 24 h of incubation at 37° against Ciprofloxacin (100µg/ml) as standards for comparison of antibacterial activity and 72 h at 25° against Ciclopirox olamine (100µg/ml) as standards for comparison of antifungal activity. In general, all synthesized compounds exhibited good inhibitory activity against tested pathogenic microorganism (table-III). 1,3-thiazolidin-4-one derivatives (**4a-f)** showed higher activity in comparison to that of acylthiourea derivatives **(3a-f)**.

Table-III

Antimicrobial activity of synthesized compounds

Compounds	Zone of inhibition (mm)					
	Gram positive bacteria		Gram negative bacteria		Fungi	
	S. aureus	*B. subtilis*	*E. coli*,	*K. pneumonia*	*A. niger*	*C. albicans*
3a	5.0	5.0	6.5	6.0	5.0	5.5
3b	6.0	5.5	6.0	5.0	6.0	5.0
3c	6.0	5.5	6.5	5.0	5.5	5.5
3d	5.0	5.0	6.0	6.5	6.0	5.5
3e	5.5	5.0	5.5	5.5	5.0	5.5
3f	5.0	5.5	6.0	6.0	5.0	6.0
4a	7.5	7.0	8.0	7.5	8.0	8.0
4b	7.5	8.0	7.5	7.0	7.0	7.0
4c	7.5	7.0	7.5	7.5	8.5	8.5
4d	7.0	8.5	8.0	8.0	8.0	8.5
4e	7.0	8.0	7.5	8.0	8.0	8.5
4f	7.5	8.0	7.5	75	8.0	8.5
Ciprofloxacin	10.0	10.0	9.5	9.5	NA	NA
Ciclopirox olamine	NA	NA	NA	NA	10.0	10.0

Conclusion

The present study reports the successful synthesis of some novel acylthiourea derivatives **(3a-f)** and 1,3-thiazolidin-4-one derivatives (**4a-f)** containing 2-chloro-4-(methylsulfonyl) phenyl moiety with several structural variations. Biological evaluation of synthesized compounds exhibited good inhibitory activity against tested pathogenic microorganism. 1,3-thiazolidin-4-one derivatives (**4a-f)** showed higher activity than acylthiourea derivatives **(3a-f)**.

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