FUSED HETEROCYCLES : SYNTHESIS OF SOME NEW IMIDAZOTHIAZOLES

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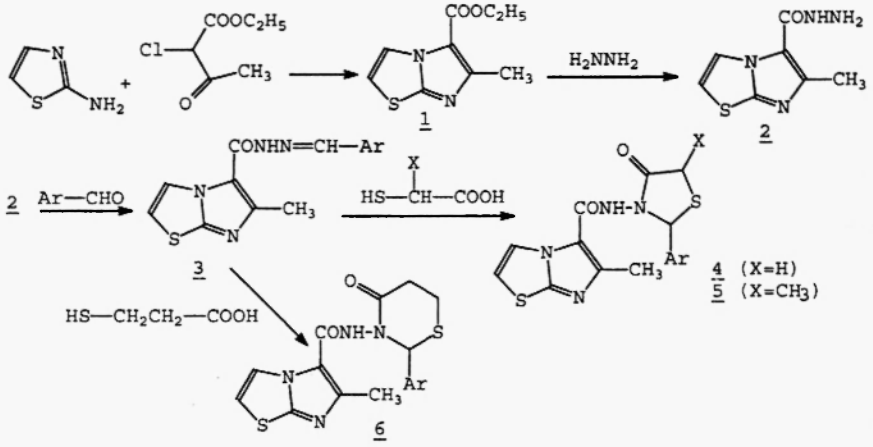
Abstract- Reaction of aldehyde-hydrazones or semicarbazones bearing an imidazo[2,1-*b*][1,3]thiazole ring system with mercaptoalkanoic acids were investigated. Antimycobacterial activities of compounds thus obtained were evaluated against *Mycobacterium tuberculosis* $H_{37}R_v$ using rifampine as standard.

Treatment of tuberculosis is still one of the major problems due to the rise of multidrug resistant tuberculosis in clinical practice. Since many years, isonicotinic acid hydrazide (isoniazide) has been used as a principal drug for the treatment of the desease. The effects of substituents and bioisosteric replacements on its antituberculous activity are still under investigation (1).

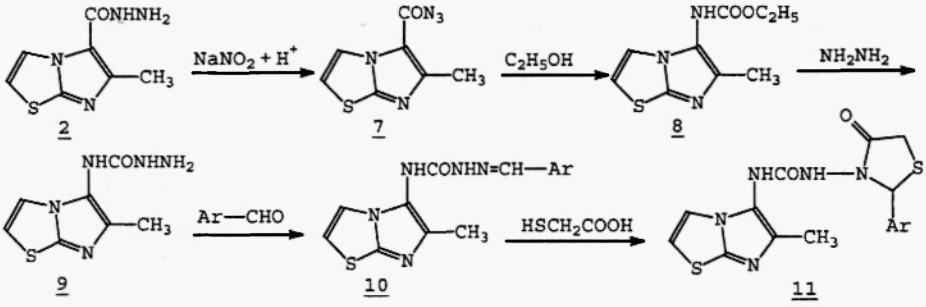
This prompted us to synthesize 6-methylimidazo[2,1-*b*][1,3]thiazole-5-carbohydrazide 2, a structural analog of isoniazide, and its hitherto unreported derivatives to screen their antituberculous properties.



Ar: a,C_6H_5; b,C_6H_4F(4); c,C_6H_4Cl(4); d,C_6H_4Br(4); e,$C_6H_4CH_3$(4); f,$C_6H_4OCH_3$(4); g,$C_6H_4NO_2$(2)

6-Methylimidazo[2,1-*b*][1,3]thiazole-5-carbohydrazide was synthesized by the reaction of hydrazine with ethyl 6-methylimidazo[2,1-*b*][1,3]thiazole-5-carboxylate (2). 2 reacted with aromatic aldehydes to afford hydrazide-hydrazones 3 which furnished N-(2-aryl-

4-oxo-1,3-thiazolidin-3-yl)-6-methylimidazo[2,1-*b*][1,3]thiazole-5-carboxamide 4,5 on cyclodehydration with mercaptoacetic acids. Reacting hydrazide-hydrazones with 3-mercaptopropanoic acid, 4-oxo-1,3-thiazinanes 6 were also obtained. On the other hand 6-methylimidazo[2,1-*b*][1,3]thiazole-5-carbohydrazide on treatment with sodium nitrit gave 6-methylimidazo[2,1-*b*][1,3]thiazole-5-carbonyl azide 7 (3) which on refluxing with ethanol was converted into the corresponding carbamate, 8.



Ar: a, C_6H_5; b, $C_6H_4F(4)$

The carbamate 8 on reaction with hydrazine in ethanol yielded the respective hydrazinecarboxamide 9. Similarly, 9 was also converted into the corresponding semicarbazones 10 and 4-oxo-1,3-thiazolidines 11 by the above sequenced reaction. The compounds 2-11 were found to be inactive against *Mycobacterium tuberculosis* $H_{37}R_v$.

EXPERIMENTAL

Chemistry

Melting points were determined on a Büchi 530 apparatus in open capillary tubes and are uncorrected. IR spectra were recorded on KBr discs, using a Perkin Elmer 1600 FT-IR spectrophotometer. ^{1}H NMR spectra were obtained in DMSO-d_6 on a Bruker AC 200 or Varian LX-300 spectrophotometer using TMS as the internal standard. EIMS were performed on a VG Zab Spec(70 eV) instrument. CIMS(CH_4) were run at Sittingbourne Research Center, UK. Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer. All new compounds gave satisfactory elemental analysis. The starting materials were either commercially available or synthesized according to the references cited.

Ethyl 6-methylimidazo[2,1-b][1,3]thiazole-5-carboxylate 1: 1 was obtained according to the literature method (4) and used without any purification. mp 98°C; yield: 35%.

6-Methylimidazo[2,1-b][1,3]thiazole-5-carbohydrazide 2: 2 was prepared by the reaction of 1 with hydrazine according to the literature method (2) and recrystallized from C_2H_5OH(96%). mp 183-185°C; yield: 80%.

Benzylidene 6-methylimidazo[2,1-b][1,3]thiazole-5-carboxylic acid hydrazides 3:

General procedure

A solution of 0.005 mol 2 in C_2H_5OH(96%)(25 ml) and 0.0055 mol of an appropriate aromatic aldehyde was heated under reflux for one hour. The precipitate obtained was recrystallized from C_2H_5OH(96%).

6-Methyl-N-(phenylmethylidene)imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3a: ($C_{14}H_{12}N_4OS$) (284.33); mp 237-239 °C; yield: 31%; IR, ν: 3225, 3096 (NH), 1641 (CO) cm^{-1}; ^{1}H NMR, δ: 11.32 (1H, s, NH), 8.30 (1H, d, 3-H), 8.00 (1H, d, 2-H), 7.66-7.34(6H, m, N=CH and C_6H_5), 2.49 (3H, s, 6-CH_3) ppm; CIMS(CH_4)(m/z)= 285 (M+H, 100).

6-Methyl-N-[(4-fluorophenyl)methylidene]imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3b: ($C_{14}H_{11}FN_4OS.H_2O$) (320.34); mp 252-254 °C; yield: 83%; IR, ν: 3196, 3115(NH), 1634 (CO) cm^{-1}; ^{1}H NMR, δ: 11.36 (1H, s, NH), 8.33 (1H, s, N=CH),8.03 (1H, d, 3-H), 7.76 (2H, t, H-3,5), 7.38 (1H, d, 2-H), 7.30 (2H, t, H-2,6), 2.51 (3H, s, 6-CH_3) ppm.

6-Methyl-N-[(4-chlorophenyl)methylidene]imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3c: ($C_{14}H_{11}ClN_4OS$) (318.77); mp 261-263 °C; yield: 98%; IR, ν: 3191, 3112 (NH), 1635 (CO) cm^{-1}; ^1H NMR, δ: 11.43 (1H, s, NH), 8.32 (1H, s, N=CH), 8.02 (1H, d, 3-H), 7.72 (2H, d, H-3,5), 7.52 (2H, d, H-2,6), 7.37 (1H, d, 2-H), 2.51 (3H, s, 6-CH_3) ppm; CIMS(CH_4) (m/z)= 319 (M+H, 74).
6-Methyl-N-[(4-bromophenyl)methylidene]imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3d: ($C_{14}H_{11}BrN_4OS$) (363.22); mp 256-258 °C ; yield: 95%; IR, ν: 3191, 3113 (NH), 1631 (CO) cm^{-1}; ^1H NMR, δ: 11.40 (1H, s, NH), 8.30 (1H, s, N=CH), 8.01 (1H, d, 3-H), 7.66 (4H, m, H-2,3,5,6), 7.36 (1H, d, 2-H), 2.50 (3H, s, 6-CH_3) ppm.
6-Methyl-N-[(4-methylphenyl)methylidene]imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3e: ($C_{15}H_{14}N_4OS$) (298.35); mp 222-224 °C; yield: 84%; IR, ν: 3151, 3115 (NH), 1635 (CO) cm^{-1}; ^1H NMR, δ: 11.25 (1H, s, NH), 8.26 (1H, s, N=CH), 7.98 (1H, d, 3-H), 7.56 (2H, d, H-2,6), 7.35 (1H, d, 2-H), 7.25 (2H, d, H-3,5), 2.49 (3H, s, 6-CH_3), 2.32 (3H, s, CH_3) ppm.
6-Methyl-N-[(4-methoxyphenyl)methylidene]imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3f: ($C_{15}H_{14}N_4O_2S.3H_2O$) (368.40); mp 190-192 °C; yield: 98%; IR, ν: 3151, 3115 (NH), 1641 (CO) cm^{-1}; ^1H NMR, δ: 11.25 (1H, s, NH), 8.28 (1H, s, N=CH), 8.03 (1H, d, 3-H), 7.65 (2H, d, H-2,6), 7.38 (1H, d, 2-H), 7.02 (2H, d, H-3,5), 3.32 (3H, s, OCH_3), 2.50 (3H, s, 6-CH_3) ppm; CIMS(CH_4) (m/z)= 315 (M+H, 52).
6-Methyl-N-[(2-nitrophenyl)methylidene]imidazo[2,1-b][1,3]thiazole-5-carbohydrazide 3g: ($C_{15}H_{14}N_5O_3S.H_2O$) (347.35): mp 241-243 °C; yield: 92%; IR,ν:3345,3134 (NH),1680(CO)cm^{-1};^1H NMR,δ:11.22(1H,s,NH),8.75(1H,s,N=CH),8.10(2H,d,H-3,6),8.03(1H,d,3-H), 7.81(1H,t,H-5),7.69 (1H, t, H-4), 7.40 (1H, d, 2-H), 2.50 (3H, s, 6-CH_3) ppm; CIMS (CH_4) (m/z)= 330 (M+H, 50).

N-(2-Aryl-4-oxo-1,3-thiazolidin-3-yl)-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 4 5; *N-(2-Aryl-4-oxo-1,3-thiazinan-3-yl)-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide* 6
General procedure
A mixture of hydrazide-hydrazone 3 (0.005 mol) and mercaptoalkanoic acid (30 ml) (mercaptoacetic acid , 2-mercaptopropanoic acid or 3-mercaptopropanoic acid) was refluxed in 30 ml dry benzene using a *Dean-Stark* water trap. Excess benzene was evaporated *in vacuo*. The residue was triturated with saturated $NaHCO_3$ aqueous solution until CO_2 evaluation ceased and was allowed to stand overnight. The solid thus obtained was washed with water and recrystallized from C_2H_5OH-H_2O. In the case of 4b and 4c which could not be solidified by $NaHCO_3$ the crude products were converted into their HCl salts by passing dry HCl through their ethanolic-aetheral solution. The salts thus obtained were recrystallized from C_2H_5OH(96%).

N-(2-Phenyl-4-oxo-1,3-thiazolidin-3-yl)-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 4a: ($C_{16}H_{14}N_4O_2S_2.0.5\ H_2O$) (367.35); mp 111-116 °C; yield: 84%; IR, ν: 3280, 3095, 3050 (NH), 1680 (CO, thiazolidine), 1640 (CO) cm^{-1}; ^1H NMR ($CDCl_3$), δ: 8.06 (1H, d, 3-H), 7.68 (1H, s, NH), 7.45-7.36 (5H, m, C_6H_5), 6.87 (1H, d, 2-H), 5.96 (1H, s, N-CH-S), 3.97, 3.75 (1H, 1H, 2d, J=16 Hz, CH_2-S), 2.18 (3H, s, 6-CH_3) ppm; EIMS(70eV) (m/z)= 358 (M^+, 80).
N-[2-(4-Fluorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 4b: ($C_{16}H_{13}FN_4O_2S_2$.HCl) (412.87); mp 225-226 °C; yield : 86%; IR, ν: 3151, 3115 (NH), 1684 (CO, thiazolidine), 1627 (CO) cm^{-1}; ^1H NMR, δ: 10.48 (1H, s, NH), 8.03 (1H, d, 3-H), 7.60 (2H, t, H-3,5), 7.25 (2H, t, H-2,6), 6.15 (1H, s, N^+H), 5.95 (1H, s, N-CH-S), 4.00,3.85(1H,1H,2d,J=16Hz,CH_2-S),2.25(3H,s,6-CH_3)ppm.
N-[2-(4-Chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide.HCl 4c: ($C_{16}H_{13}ClN_4O_2S_2$.HCl) (429.33); mp 231-233 °C; yield: 91%; IR, ν: 3154, 3084 (NH), 1711 (CO, thiazolidine), 1669 (CO) cm^{-1}; ^1H NMR, δ: 10.36 (1H, s, NH), 7.98 (1H, d, 3-H), 7.58 (2H, d, H-3,5), 7.50 (1H, d, 2-H), 7.48 (2H, d, H-2,6) 5.93 (1H, s, N-CH-S), 5.37 (1H, s, N^+H), 4.00, 3.50 (1H, 1H, 2d, J=16 Hz, CH_2-S), 2.50 (3H, s, 6-CH_3) ppm; EIMS(70eV) (m/z)= 394 (M^++2-HCl, 0.6), 392 (M^+-HCl, 1).
N-[2-(4-Bromophenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 4d: ($C_{16}H_{13}BrN_4O_2S_2$) (437.31); mp 151-153 °C; yield: 95%; IR, ν: 3305, 3044(NH), 1702 (CO, thiazolidine), 1648 (CO) cm^{-1}; ^1H NMR, δ: 10.09 (1H, s, NH), 7.90 (1H, d, 3-H), 7.61 (2H, d, H-3,5), 7.50 (2H, d, H-2,6),7.36 (1H,d, 2-H), 5.90 (1H, s, N-CH-S), 3.96, 3.86 (1H, 1H, 2d, J=16 Hz, CH_2-S), 2.20 (3H, s, 6-CH_3) ppm.
N-[2-(4-Methylphenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 4e: ($C_{17}H_{16}N_4O_2S_2.2H_2O$) (408.49); mp 232-234°C; yield: 67%; IR, ν: 3277, 3117 (NH), 1701 (CO, thiazolidine), 1652 (CO) cm^{-1}; ^1H NMR, δ: 10.29 (1H, s, NH), 7.92 (1H, d, 3-H), 7.49 (1H,d, 2-H) ,7.40 (2H, d, H-3,5), 7.19 (2H, d, H-2,6), 5.89 (1H, s, N-CH-S), 3.92, 3.80 (1H, 1H, 2d, J=16 Hz, CH_2-S), 2.30 (3H, s, CH_3) ,2.24 (3H, s, 6-CH_3) ppm.
N-[2-(2-Nitrophenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 4g : ($C_{16}H_{13}N_5O_4S_2$) (403.42); mp 184-187°C; yield: 97%; IR, ν: 3235 (NH), 1702

(CO, thiazolidine), 1664 (CO) cm^{-1}; ^1H NMR, δ: 10.15 (1H, s, NH), 8.10 (1H, d, 3-H), 7.94 (2H, d, H-3,5), 7.89 (1H, d, H-4) , 7.65 (1H, t ,H-3), 7.37 (1H, d ,2-H), 6.28 (1H, s, N-CH-S), 4.00, 3.78 (1H, 1H, 2d, J=16 Hz, CH_2-S), 2.25 (3H, s, 6-CH_3) ppm.

N-(5-methyl-2-phenyl-4-oxo-1,3-thiazolidin-3-yl)-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 5a: ($C_{17}H_{16}N_4O_2S_2.0.5H_2O$) (381.46); mp 120-125 °C; yield: 70%; IR, ν: 3125, 3085 (NH), 1705 (CO, thiazolidine), 1652 (CO) cm^{-1}; ^1H NMR, δ: 10.30 (1H, s, NH), 7.88 (1H, d, 3-H), 7.53-7.32 (6H, m, C_6H_5 and 2-H), 5.89 (1H, s, N-CH-S), 4.15 (1H, q, J=6.91 Hz, CO-CH-S), 2.13 (3H, s, 6-CH_3), 1.58 (3H, d, CH_3) ppm; EIMS(70eV)(m/z)= 372 (M^+, 30).

N-[2-(4-Fluorophenyl)-5-methyl-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 5b: ($C_{17}H_{15}FN_4O_2S_2$) (390.44): mp 199 °C; yield: 87%; IR, ν: 3233 (NH), 1705 (CO, thiazolidine), 1658 (CO) cm^{-1}; ^1H NMR, δ: 10.00 (1H, s, NH), 7.86 (1H, d, 3-H),7.76 (2H, t, H-3,5), 7.56 (1H, d, 2-H), 7.22 (2H, t, H-2,6) ,5.89 (1H, s, N-CH-S), 4.15 (1H, q, J=6.88 Hz, CO-CH-S), 2.16 (3H, s, 6-CH_3), 1.58 (3H, d, CH_3) ppm.

N-[5-Methyl-2-(4-methylphenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 5e: ($C_{18}H_{18}N_4O_2S_2.2H_2O$) (422.52): mp 115-117 °C; yield: 60%; IR, ν: 3260, 3154, 3114 (NH), 1709 (CO, thiazolidine), 1651(CO) cm^{-1}; ^1H NMR, δ: 10.02 (1H, s, NH), 7.85 (1H, d, 3-H), 7.40-7.33 (3H, m, 2-H and H-2,6), 7.19 (2H, d, J= 8 Hz, H-3,5), 5.84 (1H, s, N-CH-S), 4.11 (1H, q, J=7.01Hz, CO-CH-S), 2.30 (3H, s, CH_3-4) 2.18 (3H, s, 6-CH_3), 1.58 (3H, d, CH_3 thiazolidine) ppm.

N-[5-Methyl-2-(2-nitrophenyl)-4-oxo-1,3-thiazolidin-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 5g: ($C_{17}H_{15}N_5O_4S_2.1.5H_2O$) (444.50); mp 238 °C; yield: 51%; IR, ν: 3233, 3121 (NH), 1705 (CO, thiazolidine), 1663 (CO) cm^{-1}; ^1H NMR, δ: 10.07 (1H, s, NH), 8.09-7.80 (4H, m, 3-H and H-3,5,6), 7.63 (1H, t, H-4), 7.34 (1H, d, 2-H), 6.25 (1H, s, N-CH-S),4.20(1H,q,J=6.94Hz,CO-CH-S),2.27(3H,s,6-CH_3),1.55 (3H, d, CH_3 thiazolidine)ppm.

N-(4-oxo-2-phenyl-1,3-thiazinan-3-yl)-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 6a: ($C_{17}H_{16}N_4O_2S_2$) (372.45); mp 148-149 °C; yield: 52%; IR, ν: 3126, 3084 (NH), 1670, 1635(CO) cm^{-1}; ^1H NMR, δ: 9.84 (1H, s, NH), 7.73 (1H, d, 3-H), 7.74-7.27 (6H, m, C_6H_5 and 2-H), 6.01 (1H, s, N-CH-S), 3.17-2.84 (4H, m, CH_2-CH_2-S), 2.00 (3H, s, 6-CH_3) ppm.

N-[2-(4-Methylphenyl)-4-oxo-1,3-thiazinan-3-yl]-6-methylimidazo[2,1-b][1,3]thiazole-5-carboxamide 6e: ($C_{18}H_{18}N_4O_2S_2.H_2O$) (404.47); mp 188 °C; yield: 70%; IR, ν: 3119 (NH), 1657, 1624 (CO) cm^{-1}; ^1H NMR, δ: 9.89 (1H, s, NH), 7.71 (1H, d, 3-H), 7.31-7.28 (3H, m, 2-H and H-3,5), 7.15 (2H, d, H-2,6), 5.95 (1H, s, N-CH-S), 3.16-2.85 (4H, m, CH_2-CH_2-S), 2.27 (3H, s, 6-CH_3), 1.97 (3H, s, CH_3) ppm; EIMS(70 eV)(m/z)= 386 (M^+, 100).

6-Methylimidazo[2,1-b][1,3]thiazole-5-carbonyl azide 7 (3): To a suspension of 2 (0.005 mol) in 25 ml of water, 5 ml of HCl(20%) was added. The solution was cooled on ice while stirring was treated dropwise with aqueous $NaNO_2$ (0.006 mol in 4 ml of water). After the reaction was completed, the precipitate was collected by filtration, washed with cold water and dried. mp 116 °C; yield: 95%; IR, ν: 2245 (CON_3) cm^{-1}; ^1H NMR, δ: 8.17(1H,d,3-H), 7.50 (1H, d, 2-H), 2.53 (3H, s, 6-CH_3) ppm. The product was used for further reactions without purifications.

Ethyl 6-methylimidazo[2,1-b][1,3]thiazol-5-ylcarbamate 8: 0.005 Mol of 7 in 40 ml of absolute C_2H_5OH was refluxed for 5 hours then C_2H_5OH was removed *in vacuo*. The product thus obtained was recrystallized from C_2H_5OH(96%).($C_9H_{11}N_3O_2S$) (225.27); mp 161-162 °C; yield: 62%; IR, ν: 3146, 3122 (NH), 1721 (CO) cm^{-1}; ^1H NMR, δ: 9.03 (1H, s, NH), 7.53 (1H, d, 3-H), 7.13 (1H, d, 2-H), 4.14 (2H, q, CH_2), 2.00 (3H, s, 6-CH_3), 1.21 (3H, t, CH_3) ppm; EIMS(70 eV)(m/z)= 225 (M^+, 45).

N-(6-Methylimidazo[2,1-b][1,3]thiazol-5-yl)hydrazinecarboxamide 9: 0.005 Mol of 8 in 0.025 mol of hydrazine was refluxed for 6 hours. The precipitate formed after cooling was filtered, washed with water, dried and recrystallized from C_2H_5OH (96%).($C_7H_9N_5OS$)(211.24); mp 209-210 °C; yield: 62%; IR, ν: 3311-3092 (NH, broad), 1627 (CO) cm^{-1}; ^1H NMR, δ: 9.34 (1H, s, CONH), 8.05 (1H, d, 3-H), 7.94 (1H, s, NH), 7.35 (1H, d, 2-H), 6.06 (2H, s, NH_2), 2.52 (3H, s, 6-CH_3) ppm; EIMS(70 eV)(m/z)= 211 (M^+, 1)

Aldehyde N-(6-methylimidazo[2,1-b][1,3]thiazol-5-yl)semicarbazones 10: 10a,b were obtained according to the general method given under 3 using 0.0025 mol of 9 and 0.003 mol of the appropriate aldehyde.

Benzaldehyde N-(6-methylimidazo[2,1-b][1,3]thiazol-5-yl)semicarbazone 10a: ($C_{14}H_{13}N_5OS$) (299.34); mp 206-207 °C; yield: 78%; IR, ν: 3375, 3197 (NH), 1686 (CO) cm^{-1}; ^1H NMR, δ: 10.90 (1H, s, NH), 9.00 (1H, s, NH), 7.98 (1H, s, N=CH), 7.90-7.80 (2H, m, H-2,6), 7.60 (1H, d, 3-H), 7.50-7.35 (3H, m, H-3,4,5), 7.15 (1H, d, 2-H), 2.15 (3H, s, 6-CH_3) ppm.

4-Fluorobenzaldehyde N-(6-methylimidazo[2,1-b][1,3]thiazol-5-yl)semicarbazone 10b: ($C_{14}H_{12}FN_5OS$) (317.34); mp 216-219 °C; yield: 68%; IR,ν: 3300-3200 (NH, broad), 1678 (CO) cm^{-1}; ^1H NMR, δ: 10.87 (1H, s, NH), 8.97 (1H, s, NH), 7.93 (1H, s, N=CH), 7.90-7.88 (2H, m, H-2,6), 7.55 (1H, d, 3-H), 7.23 (2H, t, H-3,5), 7.11 (1H, d, 2-H), 2.52 (3H, s, 6-CH_3) ppm; EIMS(70eV)(m/z)= 317 (M^+, 2).

N-(6-Methylimidazo[2,1-b][1,3]thiazol-5-yl)-N'-(2-aryl-4-oxo-1,3-thiazolidin-3-yl)ureas 11: The compounds 11a,b were obtained according to the general method given under 4-6 using 0.0025 mol of appropriate semicarbazone and 3-5 ml of mercaptoacetic acid.

N-(6-Methylimidazo[2,1-b][1,3]thiazol-5-yl)-N'-(4-oxo-2-phenyl-1,3-thiazolidin-3-yl)urea 11a: ($C_{16}H_{15}N_5O_2S_2$)(373.44); mp 254-259 °C; yield: 78%; IR, ν: 3375, 3267, 3199 (NH), 1690 (CO thiazolidine), 1670 (CO) cm^{-1}; ^1H NMR, δ: 8.70 (1H, s, NH), 8.30 (1H, s, NH), 7.50-7.19 (6H, m, 3-H and C_6H_5), 7.05 (1H, d, 2-H), 5.80 (1H, s, N-CH-S), 3.83, 3.72 (1H,1H 2d, J=16Hz, CH_2S), 1.98 (3H, s, 6-CH_3) ppm; EIMS(70eV)(m/z)= 373 (M^+, 20).
N-(6-Methylimidazo[2,1-b][1,3]thiazol-5-yl)-N'-[2-(4-fluorophenyl)-4-oxo-1,3-thiazolidin-3-yl]urea 11b: ($C_{16}H_{14}FN_5O_2S_2.H_2O$) (409.45); mp 280-282 °C; yield: 72%; IR, ν: 3267, 3109(NH), 1690 (CO thiazolidine), 1670 (CO) cm^{-1}; ^1H NMR, δ: 8.80 (1H, s, NH), 8.40 (1H, s, NH), 7.60-7.50 (2H, m, H-2,6), 7.24-7.19 (3H, m, 3-H and H-3,5), 7.12 (1H, d, 2-H), 5.81 (1H, s, N-CH-S), 3.83, 3.72 (1H, 1H, 2d, J=16Hz, CH_2S), 1.97 (3H, s, 6-CH_3) ppm; EIMS(70eV) (m/z)= 391(M^+, 1).

Antimycobacterial activity
Antimycobacterial screen was conducted at 12.5 μg/ml against *Mycobacterium tuberculosis* $H_{37}R_v$ in BACTEC 12B medium using the BACTEC 460 radiometric system at National Institute of Allergy and Infectious Diseases, USA. Rifampine (minimal inhibitory concentration 0.025 μg/ml) was used as the standard. All the compounds were inactive against *M.tuberculosis* $H_{37}R_v$ at 12.5 μg/ml and not selected for further evaluation at higher concentration to determine their actual MIC (5).

RESULTS AND DISCUSSION

Ethyl 6-methylimidazo[2,1-*b*][1,3]thiazole-5-carboxylate 1 was reacted with hydrazine hydrate to give 2. Condensation of 2 with appropriate aromatic aldehydes yielded the corresponding hydrazones 3a-g which on condensation with mercaptoacetic acid, 2-mercaptopropanoic acid or 3-mercaptopropanoic acid afforded the 4-oxo-1,3-thiazolidines 4a-e,g,5a,b,e,g and 4-oxo-1,3-thiazinanes 6a,e respectively. The IR spectra of compounds 4 and 5 showed CO bands at 1711-1680 cm^{-1} providing confirmatory evidence for ring closure. ^1H NMR spectra of compounds 4,5 displayed two doublets at about 4.00-3.50 ppm and a quartet at about 4.20-4.11 ppm, respectively, due to the inequivalence of the protons (SCH_2 and SCH) (6). The singlet of N=CH at about 8.75-8.26 ppm in the spectra of 3 was shifted upfield to 6.28-5.84 ppm by the loss of the sp^2 character of the involved C atom. From the reaction of arylidene 6-methylimidazo[2,1-*b*][1,3]thiazol-5-carbohydrazides with 3-mercaptopropanoic acid only two compounds, 6a and 6e could be obtained. Our attempts to prepare the others failed. The IR spectra of 6a and 6e showed two carbonyl bands at about 1670-1657 cm^{-1} and 1635-1624 cm^{-1}. In the ^1H NMR spectra of 4-oxo-1,3-thiazinanes, multiplets at about 3.17-2.84 ppm due to endocyclic CH_2CH_2 protons provided firm support for the structures. Further support was the resonance of the C-H proton at position 2 of the 1,3-thiazinane ring in the spectra of 6a (6.01 ppm) and 6e (5.95 ppm). The upfield shifts observed here again are consistent with the change in the hybridization state of the involved carbon atom. CI mass spectra of 3a,c,f,g and EI mass spectra of 4a,c,5a,6e displayed quasi-molecular and molecular ions,respectively. On the other hand reaction of 2 with $NaNO_2/H^+$ yielded 6-methylimidazo[2,1-*b*][1,3]thiazole-5-

carbonyl azide 7. The IR spectrum of 7 displayed a strong band at 2245 cm^{-1} due to azide stretching (3). Heating 7 with absolute ethanol led to ethyl N-(6-methylimidazo[2,1-*b*][1,3]thiazole-5-yl)carbamate 8 via Curtius reaction. 8 showed characteristic peaks at 3146, 3122 and 1721 cm^{-1} due to NH and C=O groups. The absence of azide peak at 2245 cm^{-1} also supported the formation of 8. Hydrazinolysis of 8 gave N-(6-methylimidazo[2,1-*b*][1,3]thiazol-5-yl)hydrazinecarboxamide 9. The NH and C=O absorption peaks were observed at 3311-3092 and 1627 cm^{-1} respectively, in the IR spectrum of 9. In the ^{1}H-NMR spectrum, NH_2, NH and CONH protons appeared at 6.06, 7.94 and 9.34 ppm, respectively. EI mass spectra of 8 and 9 showed molecular ions. 9 was condensed with aromatic aldehydes to afford aldehyde N-(6-methylimidazo[2,1-*b*][1,3]thiazol-5-yl)semicarbazones 10a,b which were cyclized to give N-(6-methylimidazo[2,1-*b*][1,3]thiazol-5-yl)-N'-(2-aryl-4-oxo-1,3-thiazolidin-3-yl)urea 11a,b. The IR spectra of 10 and 11 showed two separate bands resulting from the NH and C=O bands of amide function at about 3375-3109 and 1686-1670 cm^{-1}, respectively. A new C=O band at 1690 cm^{-1} in the spectra of 11a,b provided evidence for the 4-oxo-1,3-thiazolidine structure. On the other hand the singlet of N=CH at about 7.98-7.93 ppm in the spectra of 10a,b were shifted upfield to 5.81-5.80 ppm in the spectra of 11a,b. EI mass spectra of 10b and 11a,b displayed molecular ions which confirmed molecular weights.

All compounds were evaluated for *in vitro* antimycobacterial activity against *M. tuberculosis* $H_{37}R_v$ at the concentration of 12.5 μg ml^{-1} and were found to be ineffective against the microorganism at this concentration.

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