Supporting Information

Discovery of Newer Antitubercular Oxazolyl thiosemicarbazones

Dharmarajan Sriram,* Perumal Yogeeswari, Rathinasababathy Thirumurugan, Roheet Kumar Pavana

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Experimental Section

Melting points were taken on an electrothermal melting point apparatus (Buchi BM530) in open capillary tubes and are uncorrected ^{1}H-NMR spectra were scanned on a JEOL Fx 400MHz NMR spectrometer using $CDCl_3$, DMSO-d_6 as solvent. Chemical shifts are expressed in δ (ppm) relative to tertamethylsilane. Elemental analyses (C, H, and N) were performed on Perkin Elmer model 240C analyzer and the data were within ± 0.4% of the theoretical values

Synthesis of Cyclobutylacetonitrile

24.6gm of sodium cyanide (0.503 mole), 180 mL dimethylsulfoxide were charged in 500 mL two necked round bottom flask fitted with magnetic bar at 60^{o}C. The reaction mixture was stirred at 60^{o}C followed by drp wise addition of 37.5 mL (0.335 mole) bromomethylcyclobutane. The reaction mixture was stirred at 70^{o}C for 3 h. TLC was checked inferencing the complete conversion of reactant to product. The reactin mixture was cooled to room temperature and poured it in 1200 mL of crushed ice. Stirred the reaction mixture in ice for 30 min and product was extracted with diethylether (3X500 mL). The organic layer was washed with 6N HCl (700 mL), saturated sodium bicarbonate solution (700 mL) and brine (700 mL). After drying organic layer over anhydrous sodium sulphate, the solvent was evaporated under reduced pressure (150 torr) at 40^{o}C to yield product as colorless liquid of 23.9g (75%).^{1}H-NMR ($CDCl_3$) δ (ppm): 1.78-2.22 (m, 6H ($3CH_2$), Cyclobutyl protons); 2.42 (d, 2H, CH_2, J=6.8); 2.64 (Sep, 1H, Aycolbutyl proton, J=7.2).

Synthesis of Cyclobutylacetaldehyde

24.84g of (0.282) Cyclobutylactonitrile, 200 mL dichloromethane were charged in 1000 mL round bottom flask equipped with magnetic bar at -75 ^{o}C under nitrogen atmosphere. The reaction mixture was stirred at -75 ^{o}C followed by drop wise addition of 200 mL DIBAL-H (20% weight solution in toluene). The reaction mixture was stirred at -75 ^{o}C for 15 min. The reaction mixture was allowed to heat to 0^{o}C and stirred for 3 h. TLC was checked inferencing the complete conversion of reactant to product. The reaction mixture was quenched with drop wise addition of saturated ammonium chloride solution (600 mL) at -20 ^{o}C and stirred at -20 ^{o}C for 30 min. Acidified the reaction mixture with 2n HCl (700 mL) at -20 ^{o}C and stirred it for 30 min (pH=1). The organic layer was separated out and aqueous layer was extracted with diethylether (3X600 mL). The combined organic layer was washed with brine (500 mL). After drying organic layer over anhydrous sodium sulphate, the solvent was evaporated under reduced pressure to yield product (58.7 g) as yellow solution with toluene and it was used for the next transformation assuming 70% yield.

Synthesis of 5-cyclobutyloxazol-2-amine

19.38g (0.197 mole) of Cyclobutylactaldehyde was charged in 500 mL two-necked round bottom flas equipped with magnetic bar at 0 ^{o}C under nitrogen atmosphere followed by drop wise addition of bromine (11.2 mL, 0.217 mole) at 0 ^{o}C. The reaction mixture was stirred at 5-10^{o}C for 3 h. The reaction mixture was added in a slow stream to a preheated solution of 30.06 g (0.394 mole) of urea in 150 mL of DMF at 90 ^{o}C and was heated for 3 h. TLC was checked inferencing the complete conversion of reactant to product. Then the reaction mixture was stirred at room temperature for 12 h. The whole reaction mixture

was concentrated under vacuum to remove DMF and basified with 30% sodium hydroxide solution (pH=14) that was extracted with diethylether (2X600mL). The organic layer was washed 700mL of brine. After drying organic layer over anhydrous sodium sulphate, the solvent was evaporated under reduced pressure to yield product (20.06g). ^{1}H-NMR (DMSO-d_6) δ (ppm): 1.75-2.28 (m, 6H ($3CH_2$), Cyclobutyl protons); 3.47 (quintet, 1H, cycolbutyl proton, J=7.2); 6.69 (s, 1H, 4-H); 7.5 (s, 2H, NH_2).

Synthesis of 4-(5-cyclobutyloxazol-2-yl)thiosemicarbazide

To a solution of 5-cyclobutyloxazol-2-amine (0.01 mol) in THF (10 ml) was added sodium hydroxide (0.01 mol) and carbon disulphide (0.75 ml). The mixture was stirred at 15–20^{o}C for 1 h, to the stirred mixture was added hydrazine hydrate (0.01 mol) and stirring continued at 60 ^{o}C for 1 h more. On adding water, a pale yellow solid separated out which is recrystallized from DMF-ethanol afforded pale yellow crystals. Yield: 90%;

General procedure for the preparation of 4-(5-cyclobutyloxazol-2-yl)thiosemicarbazones

Equimolar quantities (0.02 mol) of appropriate carbonyl compound and 4-(5-cyclobutyloxazol-2-yl)thiosemicarbazide were dissolved in warm ethanol containing 1 ml of glacial acetic acid. The reaction mixture was refluxed for 1-2 h and set aside. The resultant solid was washed with dilute ethanol dried and recrystallized from ethanol–chloroform mixture. Yield: 62-86%.

2-hydroxybenzaldehyde *N*-(5-cyclobutyl-1,3-oxazol-2-yl)thiosemicarbazone (6a)

1.75-2.28 (m, 6H ($3CH_2$), Cyclobutyl protons); 3.47 (quintet, 1H, cycolbutyl proton, J=7.2); 5.88 (s, 1H, Carbimino-H); 6.69 (s, 1H, 4-H); 7.1 (s, 2H, 2XNH); 7.2-7.6 (m, 4H, Ar-H); 8.2 (s, 1H, OH).

(1*Z*)-1-(2-hydroxyphenyl)ethan-1-one*N*-(5-cyclobutyl-1,3-oxazol-2-yl)thiosemicarbazone (6k)

1.76-2.28 (m, 6H ($3CH_2$), Cyclobutyl protons); 2.44 (s, 3H, CH_3), 3.48 (quintet, 1H, cycolbutyl proton, J=7.2); 6.69 (s, 1H, 4-H); 7.0 (s, 2H, 2XNH); 7.2-7.68 (m, 4H, Ar-H); 8.12 (s, 1H, OH).

(*Z*)-(3-bromophenyl)(phenyl)methanone*N*-(5-cyclobutyl-1,3-oxazol-2-yl)thiosemicarbazone (6q)

1.76-2.28 (m, 6H ($3CH_2$), Cyclobutyl protons); 3.48 (quintet, 1H, cycolbutyl proton, J=7.2); 6.69 (s, 1H, 4-H); 7.1 (s, 2H, 2XNH); 7.5-7.88 (m, 9H, Ar-H).

1,3-diphenylacetone *N*-(5-cyclobutyl-1,3-oxazol-2-yl)thiosemicarbazone (6r)

1.76-2.26 (m, 6H ($3CH_2$), Cyclobutyl protons); 2.6 (s, 4H, $2XCH_2$); 3.5 (quintet, 1H, cycolbutyl proton, J=7.2); 6.68 (s, 1H, 4-H); 7.0 (s, 2H, 2XNH); 7.06-7.14 (m, 10H, Ar-H).

(3*Z*)-1*H*-indole-2,3-dione 3-[*N*-(5-cyclopropyl-1,3-oxazol-2-yl)thiosemicarbazone] (6s)

1.76-2.26 (m, 6H ($3CH_2$), Cyclobutyl protons); 3.5 (quintet, 1H, cycolbutyl proton, J=7.2); 6.68 (s, 1H, 4-H); 7.0 (s, 2H, 2XNH); 7.07-7.17 (m, 4H, Ar-H); 10.7 (s, 1H, NH).

Elemental analysis (C,H, and N) of compounds 6a-6t

Compound	Calculated	Found
6a	C: 56.94; H: 5.10; N: 17.71.	C: 56.90; H: 5.02; N: 17.74.
6b	C: 52.16; H: 4.38; N: 20.28.	C: 52.11; H: 4.42; N: 20.26.

6c	C: 52.16; H: 4.38; N: 20.28.	C: 52.1; H: 4.38; N: 20.22.
6d	C: 52.16; H: 4.38; N: 20.28.	C: 52.15; H: 4.39; N: 20.24.
6e	C: 61.12; H: 5.77; N: 17.82.	C: 61.07; H: 5.82; N: 17.81.
6f	C: 53.81; H: 4.52; N: 16.73.	C: 53.87; H: 4.49; N: 16.73.
6g	C: 59.45; H: 6.16; N: 20.39.	C: 59.4; H: 6.12; N: 20.42.
6h	C: 58.16; H: 5.49; N: 16.96.	C: 58.18; H: 5.52; N: 16.95.
6i	C: 55.48; H: 5.24; N: 16.17.	C: 55.5; H: 5.26; N: 16.16.
6j	C: 61.12; H: 5.77; N: 17.82.	C: 61.11; H: 5.80; N: 17.83.
6k	C: 58.16; H: 5.49; N: 16.96.	C: 58.15; H: 5.46; N: 17.0.
6l	C: 58.16; H: 5.49; N: 16.96.	C: 58.12; H: 5.49; N: 16.98.
6m	C: 62.17; H: 6.14; N: 17.06.	C: 62.17; H: 6.12; N: 17.11.
6n	C: 58.34; H: 5.81; N: 21.26.	C: 58.3; H: 5.86; N: 21.20.
6o	C: 53.47; H: 4.77; N: 19.49.	C: 53.46; H: 4.76; N: 19.53.
6p	C: 67.0; H: 5.35; N: 14.88.	C: 67.09; H: 5.3; N: 14.91.
6q	C: 55.39; H: 4.21; N: 12.30.	C: 55.28; H: 4.22; N: 12.29.
6r	C: 68.29; H: 5.98; N: 13.85.	C: 68.28; H: 6.02; N: 13.79.
6s	C: 56.29; H: 4.43; N: 20.51.	C: 56.31; H: 4.42; N: 20.49.
6t	C: 53.47; H: 3.93; N: 19.49.	C: 53.46; H: 3.90; N: 19.42.