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NOTE

Synthesis and Biological Screening of Some New 3[2-Methyl-1,2-dihydropyrimido[1,2c]benzimidazole-1-thionyl]-6,8-dibromo-2-substituted-3*H*-quinazolin-4-one

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In this paper, the synthesis and characterization of substituted quinazolin-4-ones from 3-amino-2-methyl-1,2-dihydropyrimido-(1,2-c)- benzimidazole-1-thione are reported. The synthesized compounds were also screened for their analgesics and antiinflammatory and diuretic activity.

Key Words: Biological screening, Quinazoline-4-ones.

Quinazolin-4-(3*H*)-one and pyrimido (1,2-c) benzimidazole derivatives are versatile molecules for designing potential bioactive agents and these derivatives have been evaluated for a wide spectrum of biological activities such as anticonvulsants[1], anti-HIV[2], anticancer[3], antiinflammatory[4], anti-rheumatic and antiallergic[5] properties. We hereby report the synthesis of title compounds from 3-amino-2-methyl-1, 2dihydropyrimido-(1,2-c)-benzimidazole-1-thione and screened for their analgesic and antiinflammatory and diuretic activity.

Anthranilic acid/3,5-dibromoanthranilic acid reacts with acetic anhydride, propionic anhydride and benzoyl chloride to form corresponding 2-methyl/-ethyl/-phenyl benzoxazin-4-one by N-acylation followed by dehydrative cyclization mechanism[6] 2-substituted/6,8-dibromo derivatives of benzoxazin-4-ones where condensed with 3-amino-2-methyl-1, 2-dihydropyrimido-(1,2-c)-benzimidazole-1-thione[7] IR and NMR spectra of the compounds were consistent with the assigned structure.

Analgesic activity: Some selected compounds were evaluated for their analgesic activity by tail flick method[8]. Analgin was used as standard. Among the compounds tested, compounds NB4, NB5 displayed moderate analgesic activity.

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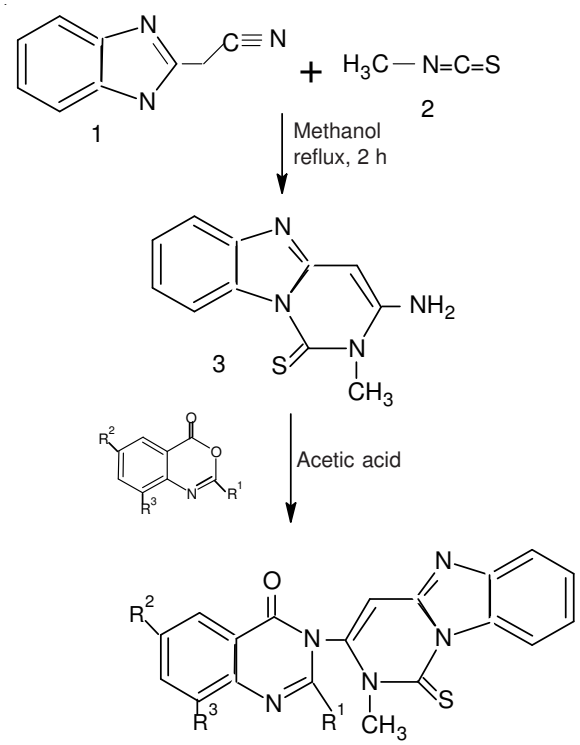
Antiinflammatory activity: Antiinflammatory carrageennan induced rat paw oedema method was adapted to evaluate antiinflammatory activity of some synthesized compounds. Phenylbutazone was used as a standard drug. Compounds NB2, NB3, NB5 have been shown moderate antiinflammatory activity against the standard drug.

Diuretic activity: Albino rats of either sex weighing between 140-200 g were used to evaluate diuretic activity of some selected compounds hydrochlorothiazide was used as a standard drug at a dose of 5 mg/kg body weight of albino rats. The test compounds were given at two dose levels (50 and 100 mg/kg body weight) orally. Compounds NB1 and NB6 shown moderate diuretic activity.



Scheme

3-Amino-2-methyl-1, 2-dihydropyrimido-[1,2-C] benzimidazole-2-thione (3): 1*H*-benzimidazole-2-acetonitrile (**1**) (1.57g, 0.01 mol) and methylisothiocynate (**2**) (0.37g, 0.01 mol) were dissolved separately in methanol (10 mL) and mixed at room temperature. The reaction mixture was refluxed on a steam bath for 2 h and the solvent was distilled off at

reduced pressure. The solid residue was separated out after pouring the reaction mixture into ice-cold water and filtering. The residue was washed with ice cold water and dried. The residue was crystallized from methanol-DMF mixture (9:1) to obtain a pure bright yellow crystalline compound with a yield of 1.95 g, (84 %), m.p. 198 % IR (KBr, ν_{max}, cm^{-1}) 3214 (NH_2), 1651 (C=N), 1045 (C=S), PMR (DMSO-d_6), 3.9 (s, 3H, N-CH_3), 6.05 (s, 1H, C_4-H), 7.1-7.5 (m, 5H, Ar-H and NH_2 after D_2O exchange integrates for 3H), 9.3 (1H, C_9-H, J = 10 Hz).

3[2-Methyl-1,2-dihydropyrimido-[1,2c]-benzimidazole-1-thionyl]-6,8-dibromo-2-substituted-3*H*-quninazolin-4-one (4): An equimolar (0.01 mol) mixture of 2-substituted 1,3-bezoxazin-4-one and 3-amino-2-methyl-1,2-dihydropyrimido-[1,2-c]-benzimidazole-1-thione (**3**) was refluxed for 6 h in 10 mL of glacial acetic acid and the mixture was cooled to room temperature and poured into crushed, the solid thus obtained was recrystallized from ethanol (Table-1).

TABLE-1

Compd.	R^1	R^2	R^3	m.p. (ºC)	Yield (%)
NB1	-CH_3	H	H	241	84
NB2	-C_2H_5	H	H	266	74
NB3	-C_6H_5	H	H	258	68
NB4	-CH_3	Br	Br	278	79
NB5	-C_2H_5	Br	Br	196	66
NB6	-C_6H_5	Br	Br	135	81

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