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SYNTHESIS AND CHARACTERIZATION OF NEW 2-AMINOBENZOXAZOLE-5-CARBOHYDRAZIDES

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Abstract:

2-Aminobenzoxazole-5-carbohydrazide(compound C) was prepared by reacting Methyl-2-aminobenzoxazole-5-carboxylate with Hydrazine hydrate. Compound C was reacted separately with para toluene sulfonic acid and to get its respective salt 2-amino benzoxazole-5-carbohydrazidetosylate (Compound C1) and with pheynyliscyanateto yield 2-(2-Aminobenzoxazole-5-carbonyl)-N-phenylhydrainecarboxamide (Compound C2.) 2-Amino benzoxazole-5-carbohydrazide (Compound C)was also reacted with paratoluene sulfonyl chloride and Benzene sulfonyl chloride to yield respective Amide derivatives, which are, N´-(2-Amino benzoxazole-5-carbonyl)-4-methylbenzene sulfonohydrazide (Compound D1) andN´-(2-Amino benzoxazole-5-carbonyl)-benzene sulfonohydrazide (Compound D2). The chemical structure of compounds synthesized were confirmed by IR,PMR and Mass.

Key words:New2-Aminobenzoxazole-5-carbohydrazides, COX

Introduction:

Benzoxazole derivatives shows anti-inflammatory, anti-bacterial and muscle relaxant, anti-histaminic activity[1]. It is evident from the literature that the presence of the Benzoxazole nucleus found to possess various pharmacological activities[2] including anti-inflammatory activity[3][4]. It is also known that benzoxazole derivatives are good molecules for building synthetically different chemical compounds known for their biological and pharmacological applications. As Benzoxaxole compounds are classified as non steroidalanti inflammatory drugs(NSAID) [5], there is always a search to design and synthesize new derivatives of Benzoxazole which can be used for Cyclooxygenase (COX) inhibitory activity to develop new anti-inflammatory agents.

The present work involves synthesis of new benzoxazole compounds which were less toxic and chemically more stable. 2-Aminobenzoxazole-5-carbohydrazide (Compound C) was reacted withpara toluene sulfonic acid and to get its respective salt 2-amino benzoxazole-5-carbohydrazide

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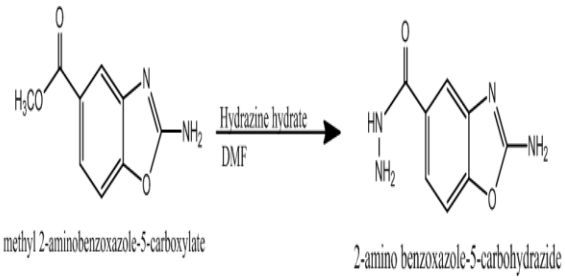
tosylate (compound C1) and with phenylisocyanate to get 2-(2-Aminobenzoxazole-5-carbonyl)-N-phenylhydrainecarboxamide (Compound C2).2-Aminobenzoxazole-5-carbohydrazide (C) was also reacted withpara toluene sulfonyl chloride and Benzene sulfonyl chloride to yield respective Amide derivatives, which are, N´-(2-Amino benzoxazole-5-carbonyl)-4-methylbenzene sulfonohydrazide (Compound D1) andN´-(2-Amino benzoxazole-5-carbonyl)-benzene sulfonohydrazide (Compound D2)in good yields. The chemical structure of compounds synthesized were confirmed by IR,PMR and Mass.

Materials and Methods:

All melting points were taken in open capillaries using a POLMON MP-96 apparatus and uncorrected IR spectra were recorded as KBr pellets on Shimadzu FTIR spectrophotometer. The 1H NMR spectra was recorded on Bruker 400 MHz spectrometer in DMSO-D6 using TMS as an internal standard and mass spectraswere recorded on Agilent mass spectrophotometer.

Synthesis of 2-Aminobenzoxazole-5-carbohydrazide(CompoundC):

Methyl-2-amino benzoxaxole-5-carboxylate(25 gr), Toluene (125 ml), Hydrazine hydrate (50 ml) and Dimethyl formamide (85 ml) weretransferred to a round bottom flask and heated to 92-96°C under reflux and maintained for 2 hours. The reaction mass was allowed to cool to room temperature. Solvent was removed carefully, Water (375 ml) was added into the reaction mass and stirred for 30 minutes. Reaction mass was cooled, filtered and was washed with water. Material was dried at 80°c for 8 hours to get pale yellow crystal line compound. The compound was purified by chromatographic techniques and characterized by spectral data (IR, NMR and Mass). The physical data of the compounds is presented in Table-1



Synthesis of 2-Amino benzoxazole-5-carbohydrazidetosylate(C1) :A mixture of 2-Amino benzoxaxole-5-carbohydrazide (1gr), Isopropyl alcohol (4 ml), Water (0.5 ml) and Para toluene sulfonic acid (1gr) were transferred to round bottom flask and heated to 80-85°C under reflux and maintained for 15 minutes. Dimethyl sulfoxide (15 ml) was added to the reaction mass under stirring at 80-85°C and reaction mass was maintained for 30 minutes. Water(80 ml) and Methylene chloride (10 ml) were added to the reaction mass and aqueous layer was separated, dried to get Pale yellow crystalline compound. The compound was purified by chromatographic techniques and characterized by spectral data (IR, NMR and Mass). The physical data of the compounds is presented in Table-1.

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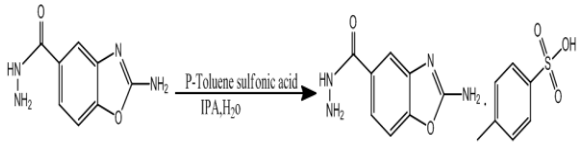
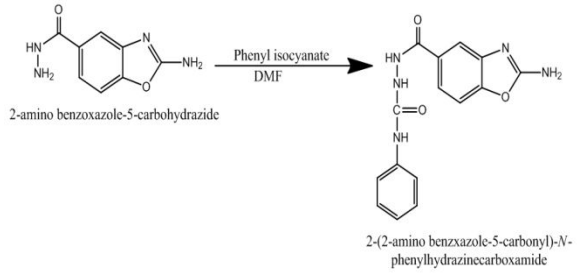


Synthesis of2-(2-Aminobenzoxazole-5-carbonyl)-N-phenylhydrainecarboxamide (C2)

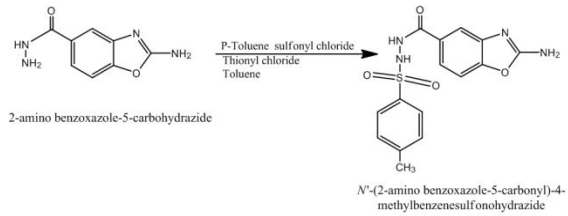
2-Amino benzoxaxole-5-carbohydrazide(1gr), Dimethyl formamide (20 ml)were transferred to round bottom flask and heated to about 80°C. Phenyl isocyanate (0.8 grams) was added to the reaction mass under stirring. The reaction mass was maintained for 5 hours at 80-85°C. The solvent was distilled off, product obtained was dried at 80°c for 8 hours to get pale yellow crystalline compound.The compound was purified by chromatographic techniques and characterized by spectral data (IR, NMR and Mass). The physical data of the compounds is presented in Table-1.



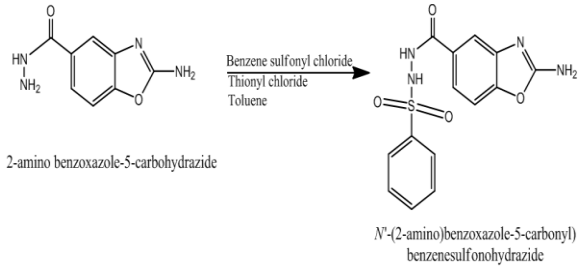
Synthesis of Amide derivatives of 2-Amino benzoxazole-5-carbohydrazide (General procedure):

A mixture of 2-Amino benzoxaxole-5-carbohydrazide (1 gr), Toluene (5 ml), Thionyl chloride (5 ml) and 5 grams of appropriate aliphatic or aromatic acid chloride (for example, Para toluene sulfonyl chloride, Benzene sulfonyl chloride, Methane sulfonyl chloride and Benzoyl chloride) were transferred to a round bottom flask and heated to 105-110°C under reflux and maintained for 7 hours. The solvent was distilled off. The reaction mass was allowed to cool to room temperature, Water (5 ml) was added into the reaction mass under stirring and water layer was discarded. Ethyl acetate (3 ml) was added to the reaction mass under stirring and continued the stirring for 15 minutes, filtered and washed with Ethyl acetate. Material was dried at 80°c for 8 hours to get off white crystalline compound. Adopting this procedure the following compounds were prepared

a) N´-(2-Aminobenzoxazole-5-carbonyl)-4-methylbenzene sulfonohydrazide(Compound D1).



b) N´-(2-Amino benzoxazole-5-carbonyl)-benzene sulfonohydrazide (Compound D2).



The compounds was purified by chromatographic techniques and characterized by spectral data (IR, NMR and Mass). The physical data of the compounds is presented in Table-2.

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Table-1:

Compound Name	Yield %	Melting point °C
2-Amino benzoxazole-5-carbohydrazide (Compound C)	85	270
2-Amino benzoxazole-5-carbohydrazide tosylate (Compound C1)	70	229
2-(2-Aminobenzoxazole-5-carbonyl)-N-phenylhydraine carboxamide (Compound C2)	70	219

Table-2:

Compound Name	Yield %	Melting point °C
N′-(2-Amino benzoxazole-5-carbonyl)-4-methylbenzene sulfonohydrazide (Compound D1)	80	241
N′-(2-Amino benzoxazole-5-carbonyl)-benzene sulfonohydrazide (Compound D2):	90	229

Results :

Compound C:

IR(KBr, cm-1): 3116(NH), 1692 (C=0), 1551 (C=C), 1183 (C-N).

1H-NMR (DMSO-D6)δ : 7.3- 7.8 (m, 3H, Ar-H, 2H, Ar-N H2), 9.7 (s,1H,NH), 4.4 (s,2H, NH2).

MS (m/z) : M+ calculated 192. Found 193.

Compound C1:

IR(KBr, cm-1): 3121 (NH), 1710 (C=0), 1604 (C=C), 1261 (S=O), 1167 (C-N).

1H-NMR (DMSO-D6) δ :9.7 (s, 1H-OH), 7-7.7 (m, 7H-Ar-H), 4.8(s, 2H-NH2), 2.5 (s,3H- CH3).

Compound C2:

IR(KBr, cm-1): 3210 (NH), 1660 (C=0), 1560 (C=C), 1189 (C-N)

1H-NMR (DMSO-D6) δ :10.2 (s,1H, NH), 8.9 (s, 1H, NH), 6.9- 8.1 (m, 8H-Ar-H, 2H-NH2 , 1H-NH,).

MS (m/z) : M+ calculated 311. Found 311.9.

Compound D1:

IR(KBr, cm-1): 3256(NH), 1718 (C=0), 1552 (C=C), 1272(S=O), 1171 (C-N)

1H-NMR (DMSO-D6) δ :2.2 (s,2H, Ar-NH2), 11.3 (s,1H,NH), 6-9 (m, 11H, Ar-H).

MS (m/z) : M+ calculated346. Found 347.

Compound D2:

IR(KBr, cm-1): 3174(NH), 1722 (C=0), 1607(C=C), 1267(S=O), 1165 (C-N)

1H-NMR (DMSO-D6) δ : 10.3(s,1H,NH), 10(s,1H,NH), 6-9 (m,8H- Ar-H, 2H-NH2).

MS (m/z) : M+ calculated332. Found 331.7

Discussion and conclusion:

The new derivative of Benzoxazole, 2-amino benzoxazole-5-carbohydrazide synthesized from Methyl-2-amino benzoxazole-5-carboxylate, new salt of 2-amino benzoxazole-5-carbohydrazide was synthesized with para toluene sulfonic acid, new Phenyl ureido derivative of 2-methyl benzoxazole-5-carbohydrazide was synthesized with Phenyl isocyanate andnew sulfonohydrazide derivatives of 2-amino benzoxazole-5-carbohydraizde were synthesized with different aromatic acid chlorides (C, C1, C2, D1 and D2). The structures of the synthesized compounds are characterized by IR, 1H NMR and Mass spectral analysis.

Acknowledgement:

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