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# SYNTHESIS OF 2-HYDRAZINO BENZOTHAIZOLES-2-AMINO-(4-SUBSTITUTED)-ACETANILIDES FOR ANTI OXIDANT ACTIVITY

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Research Article

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**ABSTRACT**

*Benzothiazoles and N-Substituted-α-chloro acetanilides have emerged as structurally novel anti oxidant activity. Therefore various 2-hydrazino benzothiazoles (substituted)-2-amino-(4-substituted) acetanilides, were synthesized by an aromatic amines treated with chloro acetyl chloride in presence of glacial acetic acid and sodium acetate which gives chloro acetanilides (part-I). The condensation of various substituted chloro acetanilides with 2-hydrazino benzothiazoles, 2-hydrazino benzothiazine and 2-acid hydrazide benzothiazole reacts in the presence of dry 1.4-dioxane and triethyl amine (part-II). The structures of the synthesized compounds ($A_{1-6}$), ($B_{1-6}$), ($C_{1-6}$) were characterized by FTIR, $^1$HNMR and elemental analysis. All the synthesized compounds were screened for antioxidant activity by 1,1-diphenyl-2-picryl hydrazil method. All the compounds showed very good anti-oxidant activity with $IC_{50}$ values in the range 6.8 to 12.93 µM.*

**KEYWORDS:** Benzothiazoles, Chloro acetanilides, Anti-oxidant, Diphenyl Picryl hydrazil.

## Introduction

Hydrazino benzothiazoles and acetanilide derivatives an important class of medicinal compounds. The search for anti-oxidant compounds with a more selective and lower toxicity continues to be an area of investigation in medicinal chemistry compounds containing a hydrazino benzothiazole, hydrazino benzothiazine and substituted chloro acetanilide components have shown a broad spectrum of chemotherapeutic properties including antimicrobial[1,2],antiviral[3,4],anthelmentic[5],analgesics[6],anti-inflammatory[7] and anticytotoxic[8,9] activities of substituted acetanilides.

The titles of the compounds prepared by the scheme to develop noval antioxidant agents to various 2-hydrazino benzothiazoles 2-amino-(4-substituted)-acetanilides. The chemical structures of the synthesized compounds were confirmed on the basis of their spectral data (FTIR, $^1$HNMR and elemental analysis) and the purity was ascertained by TLC analysis.

### Materials and Reagents:

### Chemical and Reagents:

Aromatic amines, glacial acetic acid, sodium acetate, chloroacetyl chloride, 1.4-dioxane, triethyl amine (TEA), ethanol, potassium bicarbonate.

### Experimental section:

### Part-I Synthesis of N-Substituted α- chloro acetanides[10]:

An aromatic amine (0.1 mole) was dissolved in glacial acetic acid and saturated solution of sodium acetate. Then the mixture was warmed and cooled in ice bath with stirring. To this solution was added drop wise a

solution of chloro acetyl chloride (0.12 mole), after half an hour white product separated and filtered. The product was washed with cold water and it was purified by crystallization from aqueous alcohol.

**Part-II: Synthesis of 2-hydrazino benzothaiozoles-2-amino-(4-substituted)-acetanilides**[11]

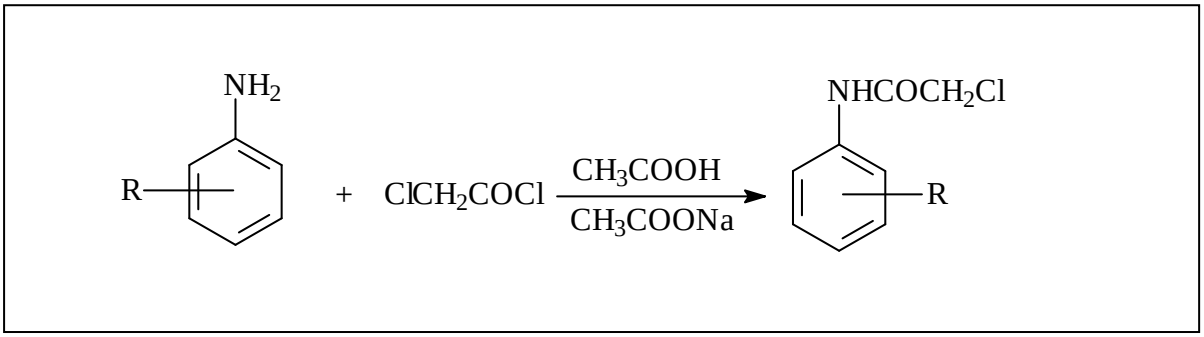
**($A_{1-6}$)($B_{1-6}$)($C_{1-6}$):**0.1 mole of 2-hydrazino benzothiozole(I)/2-hydrazino benzothaizine(II)/2-acid hydrazine benzothiozole(III) and 0.1 mole of different substituted chloroacetanilide derivatives were mixed in 25ml of dry 1,4-dioxane. To this 0.001ml or 0.101gm of triethyl amine (TEA) solution was added and the reaction mixture was refluxed for 2hrs. It was then cooled and poured on to the crushed ice. The solid product filtered washed with 1% potassium bicarbonate and water, recrystalized from ethanol to give the title of compounds as shown physical data in **Table no . 1**

**TABLE NO 1: ANALYTICAL DATA FOR THE SYNTHESIZED COMPOUNDS**

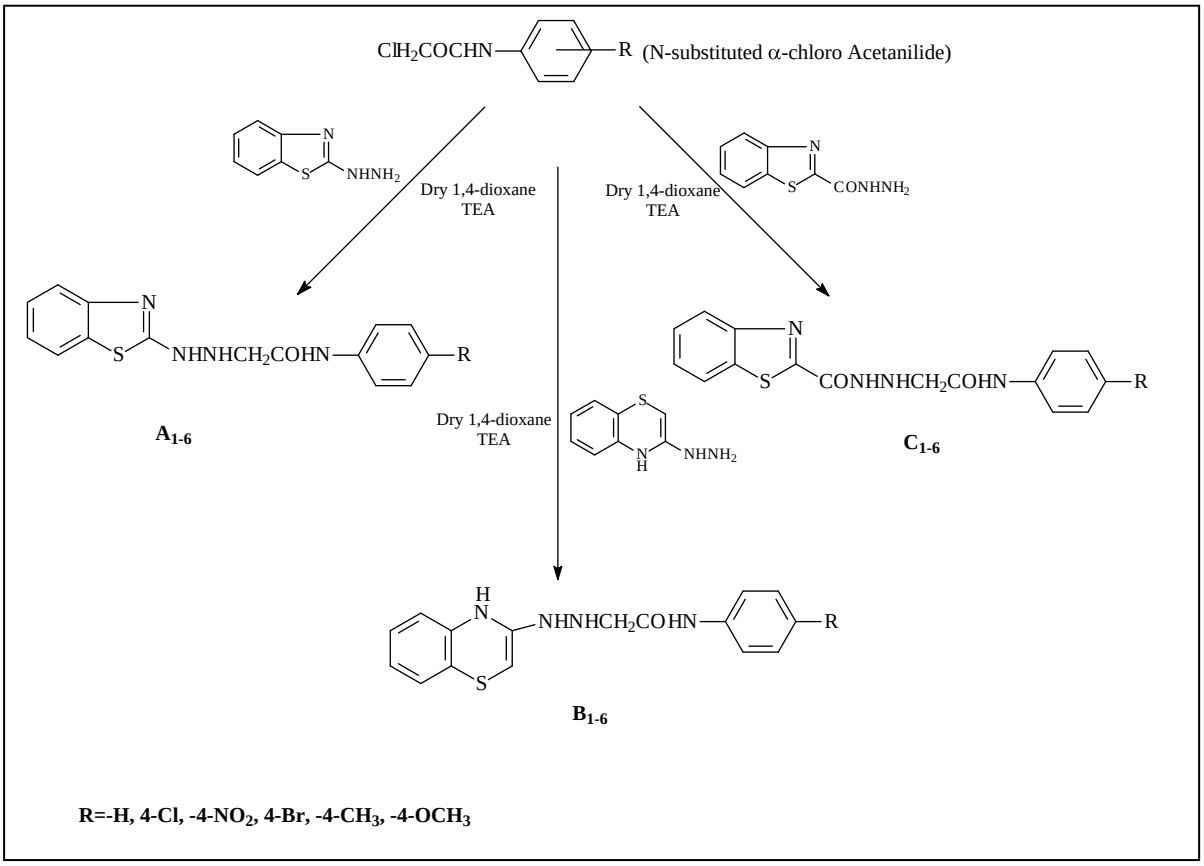
| S. No | Comp | Molecular Formula | m.p° C | % yield | Mol.wt | % Calculated | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| 01 | $A_1$ | $C_{15}H_{14}N_4OS$ | 197 | 76 | 298.36 | 60.83 | 5.09 | 19.21 |
| 02 | $A_2$ | $C_{15}H_{13}ClN_4OS$ | 194 | 85 | 332.80 | 54.73 | 4.21 | 17.19 |
| 03 | $A_3$ | $C_{15}H_{13}N_5O_3S$ | 190 | 89 | 343.34 | 53.14 | 4.28 | 20.85 |
| 04 | $A_4$ | $C_{15}H_{13}BrN_4OS$ | 197 | 68 | 368.25 | 49.82 | 3.95 | 19.72 |
| 05 | $A_5$ | $C_{16}H_{15}N_4OS$ | 196 | 72 | 311.37 | 62.19 | 5.26 | 18.22 |
| 06 | $A_6$ | $C_{16}H_{15}N_4O_2S$ | 187 | 68 | 327.37 | 59.28 | 4.92 | 17.85 |
| 07 | $B_1$ | $C_{16}H_{16}N_4OS$ | 190 | 65 | 312.38 | 62.72 | 5.69 | 18.12 |
| 08 | $B_2$ | $C_{16}H_{15}ClN_4OS$ | 170 | 70 | 346.83 | 55.83 | 4.85 | 16.85 |
| 09 | $B_3$ | $C_{16}H_{15}N_5O_3S$ | 178 | 82 | 357.38 | 54.21 | 4.92 | 16.09 |
| 10 | $B_4$ | $C_{16}H_{15}BrN_4OS$ | 158 | 66 | 382.27 | 50.78 | 4.28 | 15.12 |
| 11 | $B_5$ | $C_{17}H_{17}N_4OS$ | 162 | 69 | 325.40 | 63.48 | 5.86 | 17.86 |
| 12 | $B_6$ | $C_{17}H_{17}N_4O_2S$ | 184 | 74 | 341.40 | 60.71 | 5.29 | 16.74 |
| 13 | $C_1$ | $C_{16}H_{14}N_5O_2S$ | 179 | 81 | 326.37 | 59.23 | 4.85 | 17.68 |
| 14 | $C_2$ | $C_{16}H_{13}ClN_4O_2S$ | 171 | 79 | 360.81 | 53.82 | 4.21 | 16.05 |
| 15 | $C_3$ | $C_{16}H_{13}N_5O_4S$ | 192 | 64 | 371.36 | 52.34 | 3.97 | 19.24 |
| 16 | $C_4$ | $C_{16}H_{13}BrN_4O_2S$ | 186 | 78 | 396.26 | 59.29 | 3.82 | 14.68 |
| 17 | $C_5$ | $C_{17}H_{16}N_4O_2S$ | 194 | 81 | 340.39 | 60.45 | 5.22 | 16.84 |
| 18 | $C_6$ | $C_{17}H_{16}N_4O_3S$ | 192 | 77 | 356.58 | 57.89 | 4.92 | 16.11 |

## SCHEME

**PART-I**




**PART-II**




**R=-H, 4-Cl, -4-$NO_2$, 4-Br, -4-$CH_3$, -4-$OCH_3$**

## Spectral Data:

**2-hydrazinyl benzothiazole-N-phenyl acetamide (A)**

IR (KBr)v($cm^{-1}$); 3349.07(NH);2991.84(Ar-H);1694.74(CO); 1447.76 (N-N=C);635.35(CS);

$^1$H-NMR($CDCl_3$):δ8.5 (1H-Sec.Amide-NH); δ7.8(1H-hydrazine-NH) ;δ7.3-7.4(5H-benzine,Ar-H); δ7.1-7.2(4H-benzothiazole-Ar-H)

**2-hydrazinyl -1,4-benzothiazine-N-Phenyl acetamide (B)**

IR (KBr)v($cm^{-1}$); 3428.48(NH);2969.86(Ar-CH);1691.15(CO);1598.82(N-N=C); 1451.90(C=C);692.75(CS);

$^1$H-NMR($CDCl_3$):δ8.4(1H-Sec.Amide-NH); δ7.6(1H-hydrazine-NH) ;δ7.3-7.4(4H-benzothiazine,Ar-H); δ2.3(2H-methylene)

**2-carbo hydrazinyl N-Phenyl acetamide (C)**

IR (KBr)v($cm^{-1}$); 3449.14(NH);2991.84(Ar-CH);1694.19(CO);1589.20(N-N=C); 1448.92(C=C);632.20(CS);

$^1$H-NMR($CDCl_3$):δ8.6(1H-Hydrazide-NH); δ8.3(1H-Sec-Amide-NH) ;δ7.2-7.4(5H-benzene,Ar-H); δ6.9-7.1(4H-benzothiazole.Ar-H), δ2.5(2H-methylene)

## Antioxidant activity[12] :

The synthesized compounds by scheme were screened for antioxidant activity by blois method the model of scavenging the stable DPPH (1.1-diphenyl-2-pieryl-hydrazil) radical is widely used method to evaluate antioxidant activity in a relatively shorter time. The effect of actioxidents on DPPH radical scavenging was thought to be their hydrogen donating ability.

DPPH is a stable diamagnetic molecule[13]. The reduction capability of DPPH radical in ethanol was determined by the decrease in its absorbance at 517 nm induced by antioxidants. The decrease in absorbance of DPPH radical caused by antioxidants, because of the reaction between antioxidant molecules and radical, progresses which results in the scavenging of the radical by hydrogen donation. It is visually noticeable as a discolouration from purple to yellow. Hence DPPH is usually used as substrate to evaluate antioxidant activity, the reduction in absorbance is calculated as percentage inhibition, were tabulated in **Table No.2**

**Table No. 2 Antioxidant activity of Synthesized compounds**

| S.No | Compound | $IC_{50}$ value (µM) | S.No | Compound | $IC_{50}$ value (µM) |
|---|---|---|---|---|---|
| | **Standard** | **6.28** | | **Standard** | **6.28** |
| 1 | $A_1$ | 9.89 | 10 | $B_4$ | 9.82 |
| 2 | $A_2$ | 8.94 | 11 | $B_5$ | 8.34 |
| 3 | $A_3$ | 6.93 | 12 | $B_6$ | 13.02 |
| 4 | $A_4$ | 7.34 | 13 | $C_1$ | 9.56 |
| 5 | $A_5$ | 12.93 | 14 | $C_2$ | 11.62 |
| 6 | $A_6$ | 13.22 | 15 | $C_3$ | 12.89 |
| 7 | $B_1$ | 7.49 | 16 | $C_4$ | 9.32 |
| 8 | $B_2$ | 10.93 | 17 | $C_5$ | 10.13 |
| 9 | $B_3$ | 12.45 | 18 | $C_6$ | 13.09 |

## Results and Discussion:

All the eighteen compounds have been evaluated for their antioxidant activity by DPPH method. The results of the evaluation have been viewed by taking ascorbic acid as standard one. $IC_{50}$ values of the test compounds are compared with the $IC_{50}$ value of standard ascorbic acid. All the compounds showed very good antioxidant activity with $IC_{50}$ values in the range 6.28 to 12.93 µM.

The most significant of them was found to be series of compounds $A_5$, $B_3$, and $C_3$, showed the highest percentage of free radical scavenging activity. However, it is interesting to note that a few of this series of compounds $A_2$, $B_5$, and $C_4$ showed relatively $IC_{50}$ values (8 to 9.5µM) high percentage inhibition. Compounds $A_1$, $B_4$, and $C_5$ showed $IC_{50}$ values (9.89 to 10.5µM) moderate percentage of free radical scavenging activity.

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