

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

Ch Suresh^{1*}, J Venkateshwar Rao¹, K N Jayaveera², G Jayapal Reddy¹

¹ Talla Padmavathi College of Pharmacy, Orus, Kareemabad, Warangal-506002, Andhra Pradesh, India

² Head of the Department of Chemistry-JNTU, Ananthapur- 515001, Andhra Pradesh, India

*Corresponding Author Email: ch.suresh200910@gmail.com

Research Article

RECEIVED ON 30-09-2011

ACCEPTED ON 20-10-2011

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 (A₁₋₆), (B₁₋₆), (C₁₋₆) were characterized by FTIR, ¹HNMR 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 IC₅₀ values in the range 6.8 to 12.93 μ M.

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}, anthelmintic⁵, analgesics⁶, anti-inflammatory⁷ and anticarcinogenic^{8,9} activities of substituted acetanilides.

The titles of the compounds prepared by the scheme to develop novel 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, ¹HNMR 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 acetanilides¹⁰:

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 benzothiazoles-2-amino-(4-substituted)-acetanilides¹¹

(A₁₋₆)(B₁₋₆)(C₁₋₆):0.1 mole of 2-hydrazino benzothiazole(I)/2-hydrazino

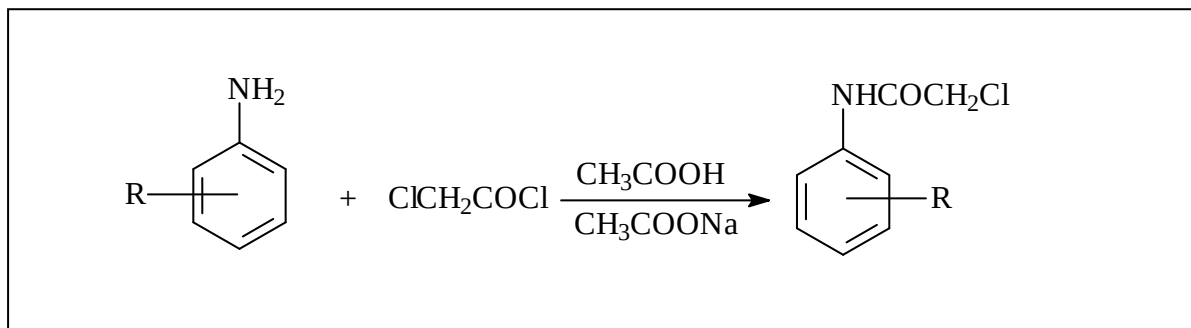
benzothiazine(II)/2-acid hydrazine benzothiazole(III) and 0.1 mole of different substituted chloroacetanilide derivatives were mixed in 25ml of dry 1,4-dioxane. To this 0.001ml or 0.101gm of triethyl amine (TEA) solution was added and the reaction mixture was refluxed for 2hrs. It was then cooled and poured on to the crushed ice. The solid product filtered washed with 1% potassium bicarbonate and water, recrystallized 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

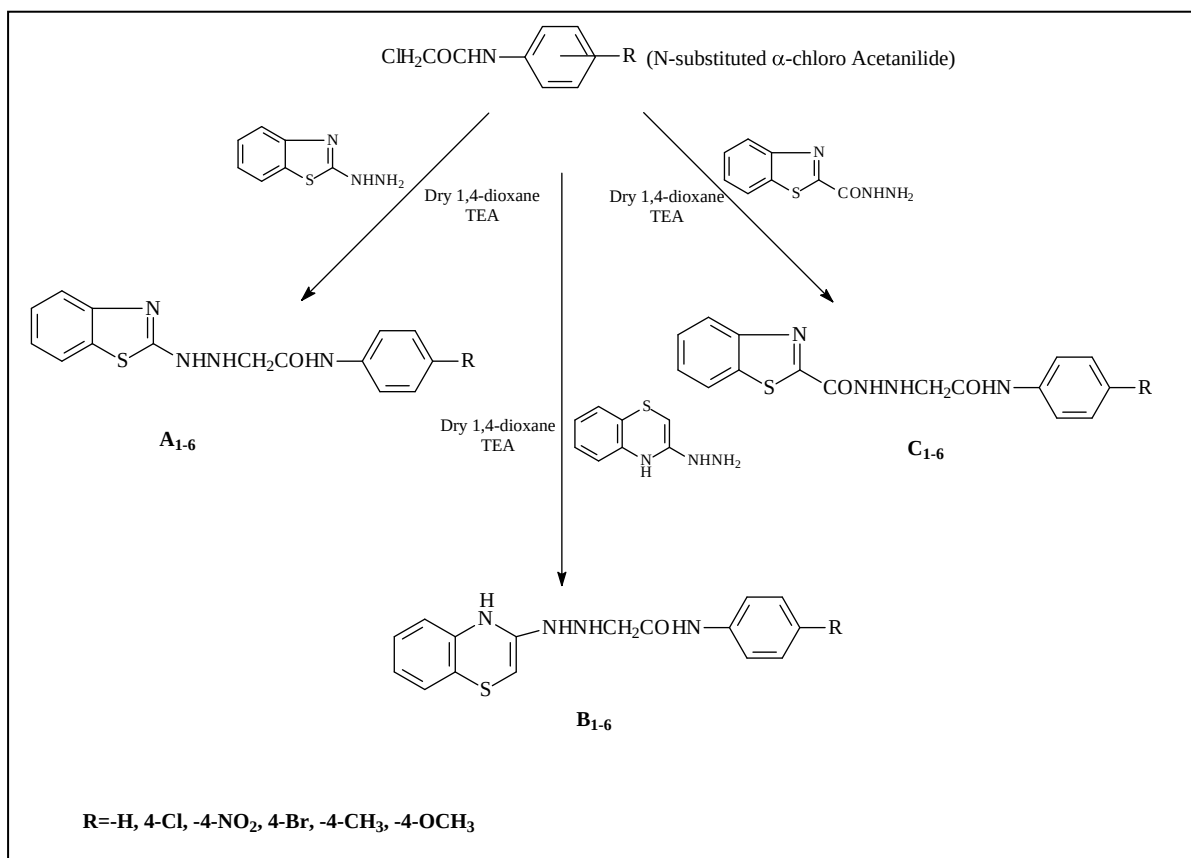
S. No	Comp	Molecular Formula	m.p ^o C	% yield	Mol.wt	% Calculated		
						C	H	N
01	A ₁	C ₁₅ H ₁₄ N ₄ OS	197	76	298.36	60.83	5.09	19.21
02	A ₂	C ₁₅ H ₁₃ ClN ₄ OS	194	85	332.80	54.73	4.21	17.19
03	A ₃	C ₁₅ H ₁₃ N ₅ O ₃ S	190	89	343.34	53.14	4.28	20.85
04	A ₄	C ₁₅ H ₁₃ BrN ₄ OS	197	68	368.25	49.82	3.95	19.72
05	A ₅	C ₁₆ H ₁₅ N ₄ OS	196	72	311.37	62.19	5.26	18.22
06	A ₆	C ₁₆ H ₁₅ N ₄ O ₂ S	187	68	327.37	59.28	4.92	17.85
07	B ₁	C ₁₆ H ₁₆ N ₄ OS	190	65	312.38	62.72	5.69	18.12
08	B ₂	C ₁₆ H ₁₅ ClN ₄ OS	170	70	346.83	55.83	4.85	16.85
09	B ₃	C ₁₆ H ₁₅ N ₅ O ₃ S	178	82	357.38	54.21	4.92	16.09
10	B ₄	C ₁₆ H ₁₅ BrN ₄ OS	158	66	382.27	50.78	4.28	15.12
11	B ₅	C ₁₇ H ₁₇ N ₄ OS	162	69	325.40	63.48	5.86	17.86
12	B ₆	C ₁₇ H ₁₇ N ₄ O ₂ S	184	74	341.40	60.71	5.29	16.74
13	C ₁	C ₁₆ H ₁₄ N ₅ O ₂ S	179	81	326.37	59.23	4.85	17.68
14	C ₂	C ₁₆ H ₁₃ ClN ₄ O ₂ S	171	79	360.81	53.82	4.21	16.05
15	C ₃	C ₁₆ H ₁₃ N ₅ O ₄ S	192	64	371.36	52.34	3.97	19.24
16	C ₄	C ₁₆ H ₁₃ BrN ₄ O ₂ S	186	78	396.26	59.29	3.82	14.68
17	C ₅	C ₁₇ H ₁₆ N ₄ O ₂ S	194	81	340.39	60.45	5.22	16.84
18	C ₆	C ₁₇ H ₁₆ N ₄ O ₃ S	192	77	356.58	57.89	4.92	16.11

SCHEME

PART-I



PART-II



Spectral Data:

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

IR (KBr) ν (cm⁻¹); 3349.07(NH);2991.84(Ar-H);1694.74(CO); 1447.76 (N-N=C);635.35(CS);

¹H-NMR(CDCl₃); δ 8.5 (1H-Sec.Amide-NH); δ 7.8(1H-hydrazine-NH) ; δ 7.3-7.4(5H-benzene,Ar-H); δ 7.1-7.2(4H-benzothiazole-Ar-H)

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

IR (KBr) ν (cm⁻¹); 3428.48(NH);2969.86(Ar-CH);1691.15(CO);1598.82(N-N=C); 1451.90(C=C);692.75(CS);

¹H-NMR(CDCl₃); δ 8.4(1H-Sec.Amide-NH); δ 7.6(1H-hydrazine-NH) ; δ 7.3-7.4(4H-benzothiazine,Ar-H); δ 2.3(2H-methylene)

2-carbo hydrazinyl N-Phenyl acetamide (C)

IR (KBr) ν (cm⁻¹); 3449.14(NH);2991.84(Ar-CH);1694.19(CO);1589.20(N-N=C); 1448.92(C=C);632.20(CS);

¹H-NMR(CDCl₃); δ 8.6(1H-Hydrazide-NH); δ 8.3(1H-Sec.Amide-NH) ; δ 7.2-7.4(5H-benzene,Ar-H); δ 6.9-7.1(4H-benzothiazole-Ar-H), δ 2.5(2H-methylene)

Antioxidant activity¹² :

The synthesized compounds by scheme were screened for antioxidant activity by blois method the model of scavenging the stable DPPH (1.1-diphenyl-2-picryl-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 molecule¹³. 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 (μ M)	S.No	Compound	IC ₅₀ value (μ M)
	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 μ M.

The most significant of them was found to be series of compounds A₅, B₃, and C₃, showed the highest percentage of free radical scavenging activity. However, it is interesting to note that a few of this series of compounds A₂, B₅, and C₄ showed relatively IC_{50} values (8 to 9.5 μ M) high percentage inhibition. Compounds A₁, B₄, and C₅ showed IC_{50} values (9.89 to 10.5 μ M) moderate percentage of free radical scavenging activity.

Acknowledgment:

The authors are thankful to Shri. Talla Mallesham Secretary and Correspondent L.S Educational Society, Warangal for providing necessary facilities through the principal Dr.J. Venkateshwar Rao, Talla Padmavathi College of Pharmacy, Warangal to carry out this work.

References:

1. Nagori BP, Gupta G and Balaram S. Synthesis and antimicrobial activity of some 5-[2-(1,3-Benzothiazole-2-yl-amino(ethyl)-4-(arylideneamino)-3-mercapto-(4H)-1,2,4-triazoles. *Ind Drugs*,46 (12), 936 (2009).
2. Mittal S, Somottra MK, Kaur & Gita Seth. Synthesis, Spectral, and antifungal evaluation of Phosphorylated and thiophosphorylated Benzothiazole derivatives, Phosphorous, sulfur and Silicon and related elements 9:2015-2113, (2007)
3. Pandeya SN, Sriram D, Nath G and De clerq E synthesis antibacterial antifungal and anti HIV evaluation of Schiff and Mannich bases of isatin with N-[6-chlorobenzothiazole-2-yl] thio semicarbazide, *Indian Journal of Pharmaceutical Sciences*, 61(6): 358, (1999)
4. Selvam P, Muruges N, Chandra Mohan M. Keyerts E. *Indian Journal of Pharmaceutical Sciences* 70(1):91-94, (2008)
5. Munirajasekar D, Himaja M and Mali Sunil, synthesis and anthemintic activity of 2-amino-6-substituted benzothiazoles. *International Research Journal of Pharmacy*, 2(1); 114-117, (2011)
6. Pramila T, Bheemachari, Rajesh V and Udupi RH, Condensed bridge head nitrogen heterocyclic systems synthesis and biological evaluation of substituted-s-triazole-thiazolethiones and s-triazolo-thiadiazinones, *Indian J Het Chem*,17,229, (2008)
7. Mathews ME, Garden SJ, and Fermades PD, Isatin inhibit cyclooxygenase-2 and inducible nitric oxide synthase in a mouse macrophase celliness; *European Journal of Pharmacology* 206,356, (2007)
8. Sirisoma N, Azra Pervin, John Drewe and Ben Tseng, *Bio organic and medical chemistry letters*; 19; 2710-2713, (2009)
9. Srivastava N, Attet Gupta A and Anil K, synthesis and CNS activity of some 1-substituted amino methyl-3-[P-(N,N-diethyl carbamoyl)phenylimino]-substituted indolin-2-ones. *Indian Journal of Chemistry*, 21(B); 787, (1982)
10. Pattan SR, Babu S.N, Angadi J.S. Synthesis and Biological activity of 7-chloro-(6-Fluoro benzothiazole)-2-amino (substituted) acetanilides. *Indian drugs*. 39(10) ,515-517, (2002)
11. I Speciale, PC Hann, *J American Chem. Society* (18),2556, (1956)
12. Blois MS, Antioxidant determinations by the use of a suitable free radical nature, 181, 1199,(1958)
13. Fei Deng, Fu Jun Zhang, Ming Zhao synthesis and anti oxidant activity of noval 2-indolinones, *Chinese chemical letter*, 17(9), 11771,(2006)



*Address for the Correspondence:

CH Suresh

Associate Professor,

**Talla Padmavathi College of Pharmacy,
Warangal-506002, Andhra Pradesh,
India**

E-Mail: ch.suresh200910@gmail.com