Synthesis, Characterization and Antimicrobial Evaluation of Some new azo Compounds Derived from Thiazole Ring

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Abstract
New thiazole derivatives were synthesized from the reaction of 2- aminobenzathiazole with p-aminoacetophenone to product compound [A], and the resulting product was reacted with phosphoric acid and concentrated nitric acid with stirring and cooling to form diazonium salts by means of a coupling reaction. The prepared diazonium salt was reacted with 2-hydroxynaphthaldehyde in the presence of sodium nitrate to give azo compounds [B]. then reacted with different aromatic amines such as p- methoxyaniline, 2-amino 5-(4-bromophenyl) 1,3,4- thiadiazoles, 5-bromo 2-aminobenzathiazole. These copounds character FT-IR, -1HNMR, C13NMR and studying the biological activity of some compounds towards two types of bacteria (positive and negative).

1. Introduction

Heterocyclic compounds form a major class of organic chemistry. They play a pivotal role in the field of rational drug design. Organic compounds containing five-membered aromatic rings are widely dispersed in nature and play an essential role in various biochemical processes, 1 Benzothiazole belongs to the family of bicyclic heterocyclic compounds having benzene nucleus fused with five-membered ring comprising nitrogen and sulfur atoms,2 1,3,4-thiadiazole such as antimicrobial agents,3 benzothiazole plays an important role in the field of medicinal chemistry and renders an extensive range of biological activities including anti-cancer anti-bacterial , anti-tuberculosis,4 antimalarial, anticonvulsant,5 When the benzothiazole discovered, they helped in reducing the death percent due to many diseases that could not cure before or a kind of high cost treatment 6. Schiff base are the compound containing azomethine group (-HC=N-). They arcondensation products of ketones (or) aldehydes with primary amines and were first reported by Hugo Schiff in 1864,7 Schiff bases form an important class of the most widely used organic compounds and have a wide variety of applications in many fields including analytical, biological, and inorganic chemistry,8 Azo dyes are another interesting class of compounds owing to their color and versatile applications ,9 An Azo coupling is an organicreaction normally proceeds between a diazonium compound and other aromatic compound that produces an azo compound (-N=N-).. Azo compounds possess the importance in the synthesis of active antibiotics like sulfonamides and many other potent organic molecules used in day-to-day medications,10 They have been most widely used in dyeing textile fibers, papers and coloring agents for foods and cosmetics .11

2. Experimental

Pure starting materials from BDH and sigma were used for the preparation of synthesized compounds, all chemicals, solvents and reagents were of synthetic grade and were buy it commercially, Stuart-SMP3 electronic system has been used to measure melting points, Merck all starting chemical Spectra of FTIR were obtained in KBr pellets from (FT-IR 8300) Shimadzu spectrophotometer in the range 4000-400 (cm-1) region while Bruker (400MHz) used for recorded 1HNMR and 13C-NMR spectrums, dimethylsulfoxide (DMSO)-d6 as a solvent and TMS as a reference, thin-layer chromatography (TLC) technique was used to ensure of completion of the reaction, the spots were visualized by using UV Cabinet for TLC. Synthesis of compound (A)
Dissolves (1.9g, 14.7m.mol) of P-aminoacetophenone in (5ml) of ethyl alcohol with the addition of (5-3) drops of glacial acetic acid in flask, after which of it is added to it (2.20g, 14.7m.mol) from 2-Aminobenzothiazole while raising the mixture and rises for 7 hours at a temperature of (85co). Pour the resulting substance into a class watch leave it to evaporate the alcohol, collect the precipitate, dry it, and then wash it with water to get rid of the alcohol residue. The completion of the reaction and purity of obtained product was tested by TLC mobile phase (hexane: ethyl acetate) (6:4) percentage (V: V); Yellow, yield 80%, mp 67-70co, FTIR (Cm-1) 3394 and 3332 (NH2), 3224(C-H), aromatic, 1643(C=N), 1535 and 1442 (C=C, aromatic).

Synthesis of compounds (B)

A mixture was prepared from dissolved (0.45g,1.78m.mol) of compound(A) by heating while stirring in(8ml- 85%)of phosphoric acid(H3PO4),

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then cool the solution in a bath of crushed ice to(OC0), add(4 ml) of concentrated nitric acid with stirring and maintain the temperature(0-5C0), Dissolve (0.13g,1.78m.mol)of sodium nitrite(NaNo2) in(2ml)of distilled water and add to the solution drop by drop, stirring for(10 minutes) and maintaining the temperature,added 0.4g,1.78m.mol 2-hydroxynaphthaldehyde with constant stirring The resulting solution was poured into 100ml of cold distilled water and left for a while, then the precipitate was filtered, washing with water several times. The completion of their action and purity of obtained product was tested by TLC mobile phase (hexane : ethyl acetate) (6:4) percentage (V:V);Red,yield 75%,mp 203–205C0, FTIR (cm-1) 3448(Ar-OH), 3217(Ar-CH), 2962 and2852(aliph-CH),1660 (-C=O), ,1612(C=N), 1537 and 1411 (Ar, C=C), (N=N)1450; the band appeared at 1219.1 and 1281.3 cm-1 were attributed to stretching vibration of (C – N) group,and the band appeared at 1138.7 cm-1 was attributed to stretchingvibration of (C – O) group.

Synthesis of compounds C (1-5)

Equal molar amounts were mixed(2.25g-5m.mol) of compound(B) With 10 mL of ethanol absolute alcohol and the addition of 7 drops of glacial acetic acid in a circular flask equipped with a magnetic stirrer and a condenser and placed in a water bath after dissolving it was added to it(5m.mol) from amine derivatives.

With the escalation of the mixture and stirring for 7 hours at a temperature of 85 c0. Pour the resulting substance into a class watchLeave it to evaporate the alcohol, collect the precipitate, dry it, and then wash it with water to get rid of the alcohol residue. The completion of the reaction and purity of the obtained product was tested TLC mobile phase(hexane: ethyl acetate) (7:3) percentage (V: V).

(C1): red, yield 71%, mp 75-77c0, FTIR (cm-1), 3471 cm-1 (Ar-OH), 3057 cm-1 (Ar-CH), (2947 and 2889) cm-1 (aliph-CH), 1643 cm-1 (C=N),1550 cm-1 (N=N), (1465 and 1404) cm-1 (Ar- C=C), (1342-1296) cm-1 (NO2) ; 1H-NMR (DMSO- d6, 400MHz)8.04-6.69 (m, 12H, Ar), 9.23 (s, 1H, OH); 13C-NMR (DMSO-d6,125MHz) 45.04 (CH3), 112.82-132.18 (Ar-rings), 138.82 (C-OH), 164-144.07 and 144.07 (1,3,4-thiadiazole, C=N),175.55(1,3-thiazol)

(C2): Dark brown, yield 65%, mp94-97c0, FTIR (cm-1) ,3456 cm-1 (Ar-OH), 3109 (Ar-C-H), and (2966 and 2913) cm-1 (aliph- CH), and band at (1643 cm-1) for C=N,1516 cm-1 (N=N), (1411 and 1489) cm-1 (Ar-C=C).

(C3): brown,Yield 77%,mp197-199c0,FT-IR (cm-1) ,3420 cm-1 (Ar-OH), 3039 cm-1 (Ar- C-H), and (2932 and 2844) cm-1 (aliph- CH), and band at 1620cm-1 ,(C=N), 1550cm1(N=N) and (1481 and 1404) cm-1 (Ar-C=C),825 cm-1(C-Br) . 1H-NMR (DMSO- d6, 400MHz)7.79-6.43 (m, 12H, Ar), 8.96 (s, 1H, OH); 13C-NMR (DMSO- d6,125MHz) 24.47 (CH3), 138.83-108.95(Ar-rings), 157.11 (C-OH), 175.55(1,3-thiazol)

(C4): Orange, yield87%, mp171-173cO, FT- IR (cm-1) ,3448 cm-1 (Ar-OH), 3062 cm-1 (Ar- C-H), and (2910 and 2884) cm-1 (aliph-CH), and band at 1627 cm-1 (C=N), 1543cm-1(N=N) and (1465and 1404) cm-1 (Ar-C=C). 1H-NMR (DMSO- d6, 400MHz)7.79-6.43 (m, 10H, Ar), 8.81 (s, 1H, OH), 13C-NMR (DMSO-d6,125MHz) 39.37 (CH3), 112.89-132.15(Ar-rings), 163.62 (C-OH), 164.38(1,3-thiazol)

(C5): light nuttly, yield60%, mp70-73co, FTIR (cm-1) 3448 (Ar-OH),3039 cm-1 (Ar-CH), (2945 and 2837) cm-1, (aliph-CH), 1651 cm-1 (C=N), 1530 cm-1 (N=N), (1473 and 1396) cm-1, (Ar, C=C). 1H-NMR (DMSO - d6, 400MHz) 8.04-6.69 (m, 11H, Ar), 8.83 (s, 1H, OH); 13C-NMR (DMSO- d6,125MHz) 48.49 (CH3), 118.70-140.31 (Ar-rings), 146.64 (C-OH), 165.94 and 159.66 (1,3,4-thiadiazole, C=N),178.23(1,3-thiazol)

(C6): Orange, yield68%, mp101-103co, FTIR (cm-1) 3441 (Ar-OH),3062(Ar-CH), 3020 and 2980(aliph-CH), 1635 cm-1 (C=N), 1550cm-1(N=N), (1473 and 1404) cm-1 (Ar, C=C).

(C7): Reddish Brown, yield72%, mp183-185co, FTIR (cm-1) 3456(Ar-OH),3024(Ar-CH), 2930 and 2824(aliph-CH), 1666cm-1 (C=N)1553cm-1(N=N), (1458and1396) cm-1 (Ar, C=C).

(C8): Yellow, yield75%, mp293-296co, FTIR (cm-1) 3410 (Ar-OH),3124cm-1 (Ar-CH) (2963and2894) cm-1(aliph-CH),1598cm-1(N=N),1681(C=N), 1596 and 1416 (Ar, C=C). 1H-NMR (DMSO- d6, 400MHz)7.79-6.43 (m, 11H, Ar), 9.17 (s, 1H, OH); 13C-NMR (DMSO- d6,125MHz) 25.35 (CH3), 124.58-98.87(Ar-rings), 155.05 (C-OH), 179.31(1,3-thiazol).

(C9): Red, yield65%, mp188-190co, FTIR (cm-1) 3402 (Ar-OH),3062(Ar-CH), (2900 and 2874) cm-1 (aliph-CH),1635cm-1(C=N),1600(N=N), (1504 and 1411) cm-1 (Ar, C=C).

(C10): Red, yield78%, mp186-188co, FTIR (cm-1) 3425 (Ar-OH),3174(Ar-CH), 2930 and 2885(aliph-CH),1620cm-1(C=N),1558(N=N), 1504 and 1450 (Ar, C=C).

3. Results and Discussion

Synthesis of Schiff bases have been achieved in high yields starting from the condensation reaction of thiazole derivatives(amine) and keton Aromatic /substituted in ethanol,12 as in the Scheme 1(A). FT-IR for compound (A) was showed the stretching of NH2 at (3394and3332) cm-1 and the stretching of C=N in (1643) cm-1.

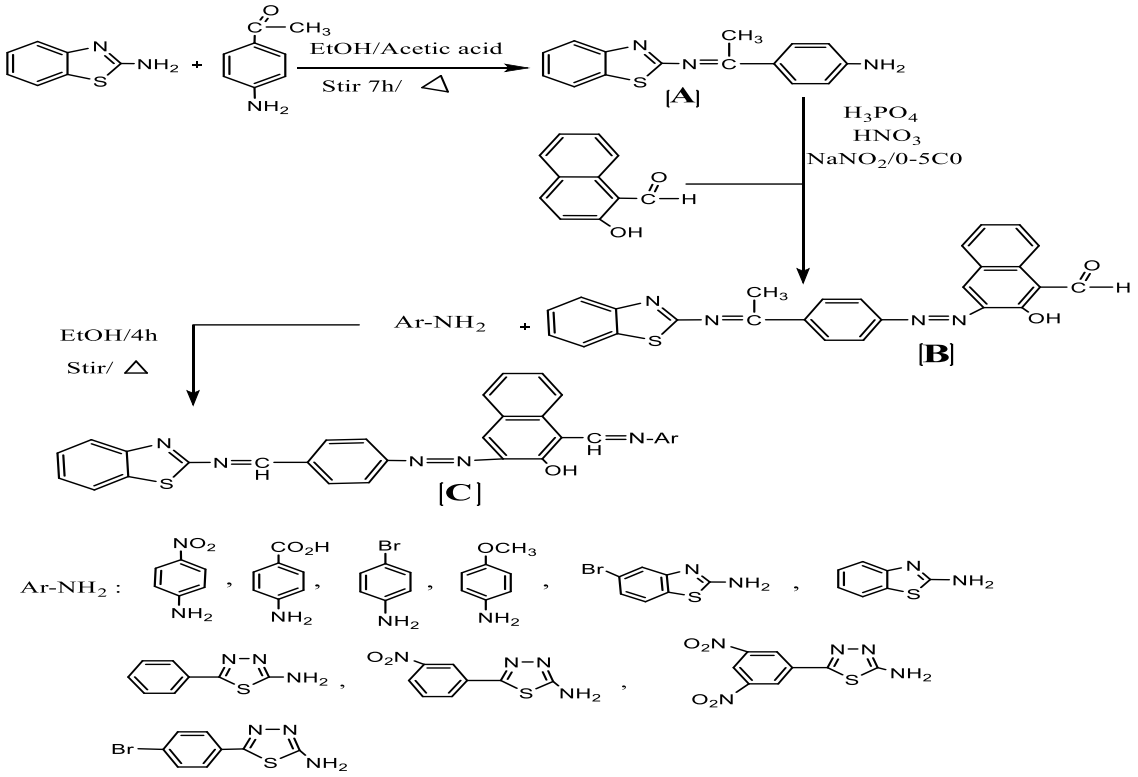
The compound Azo were synthesized according to scheme 1(B). The synthesis of an azo dye requires two organic compounds- a diazonium salt and a coupling component.

The diazonium salt reacts as an electrophile with an electron-rich coupling component, like naphthaldehyae. The FT-IR for compound(B)showed absorption bands at stretching of OH at (3448) cm-1 and the stretching of C=N in (1612) cm-1, band at (1573,1411) cm-1 (C =C) group, the band at 1450 cm-1 (- N = N -) group.13,14

The azo aldehyde (B) reacts with the primary aromatic amines to give compound C as in (Scheme1.).

the structure of compounds (1-10) C was identified by FTIR, 1HNMR and 13C-NMR,

The FT-IR spectra of compounds (1-10)C showed the stretching of OH at between (3420-3466) cm-1 ,(Ar-CH) btween(3039-3174) cm-1 ,C–Halipha stretching absorption band near (2996 and 2830) cm-1,C=N(1681-1620)cm-1 ,N=N(1600-1516)cm-1 ,C=C(1520-1316)cm -1 ,respectively.15 shows the 1H NMR spectrum of compound singlet peak between δ (8.3-9.5) accounted to C-OH and number of peaks between δ (6.41-8.53) referred to aromatic protons .



Scheme1: Synthesis of benzothiazole derivatives (1-10) C

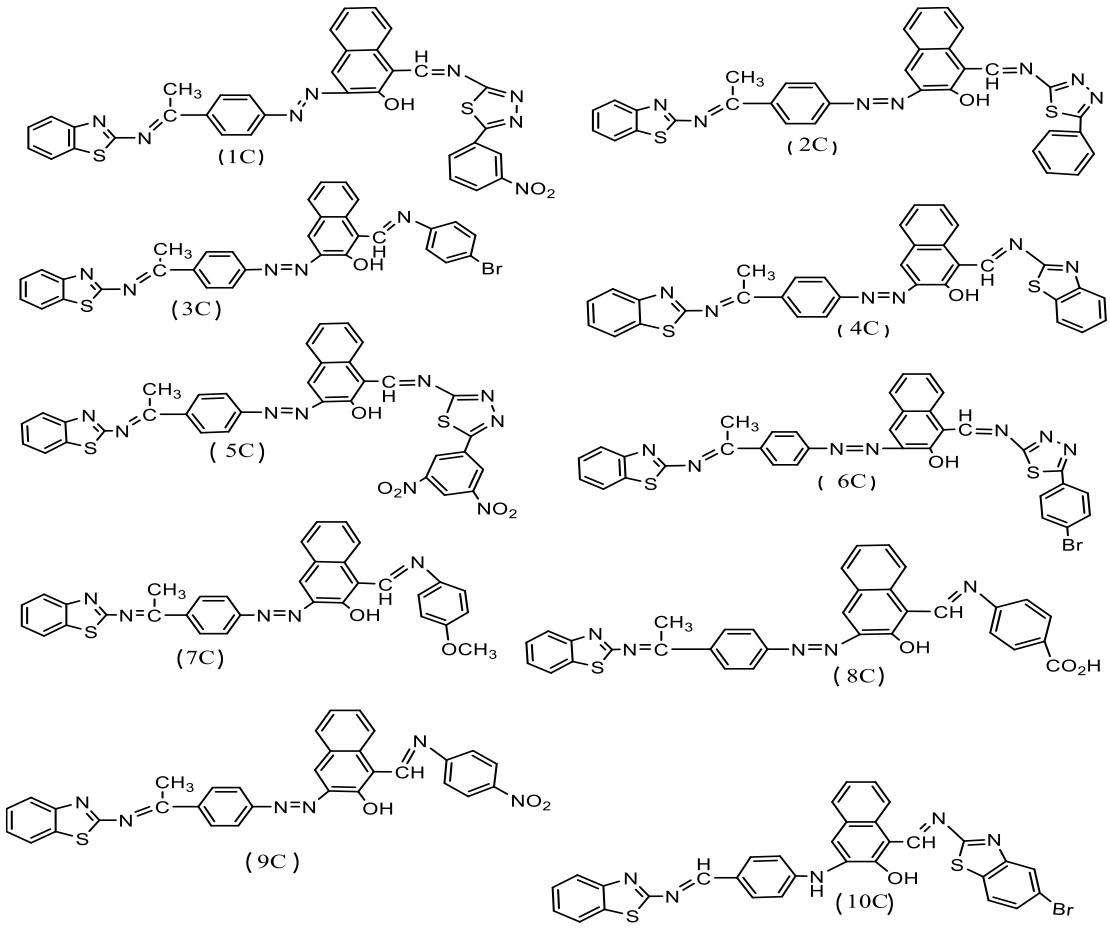


Table 1: Physical characteristics of synthesized compounds

No.	G	formula	M.Wt	Color	Mp(C^0)	Yield%	Rf
C1	$C_8H_5N_5O_4S$	$C_{34}H_{22}N_8O_3S_2$	654.72	Red	75-77	71	0.45
C2	$C_8H_7N_3S$	$C_{34}H_{23}N_7OS_2$	609.73	Dark brown	94-97	65	0.43
C3	C_6H_6BrN	$C_{32}H_{22}BrN_5OS$	604.53	Brown	197-199	77	0.46
C4	$C_7H_6N_2S$	$C_{33}H_{22}N_6OS_2$	582.70	Orange	171-173	87	0.36
C5	$C_8H_6N_4O_2S$	$C_{34}H_{21}N_9O_5S_2$	699.72	Light nuttly	70-73	60	0.51
C6	$C_8H_6BrN_3S$	$C_{34}H_{22}BrN_7OS$	688.62	Orange	101-103	68	0.53
C7	C_7H_9NO	$C_{33}H_{25}N_5O_2S$	555.66	Reddish Brown	183-185	72	0.50
C8	$C_7H_7NO_2$	$C_{33}H_{23}N_5O_3S$	569.64	Yellow	293-295	75	0.44
C9	$C_6H_6N_2O_2$	$C_{32}H_{22}N_6O_3S$	570.66	Red	188-190	65	0.38
C10	$C_7H_5BrN_2S$	$C_{33}H_{21}BrN_6OS_2$	661.60	Red	186-188	78	0.43

Antibacterial Activity

The chemical compounds were tested for their biological activity by Agar diffusion well assay,12 in vitro against ten microorganisms (Table2); For bacterial isolates (two of them were gram negative: Escherichia coli; Klebsiella pneumoniae; two of them gram positive cocci: Staphylococcus aureus; Streptococcus epidermidis; A sterile cotton swab is dipped into the suspension prepared and then swabbed evenly across the surface of a Muller-Hinton agar plate; 7 holes with 7 mm diameter cut in the agar gel, 20 mm apart from one another After that 100 µL from each prepared diluted concentration (25, 50, 100, mg) were added to each of the wells. DMSO and ethanol 20% were used as a solvent. One of these holes were filled with DMSO or ethanol to see the effect of solvent. The plates without converting were incubated for 24 h at 37°C, under aerobic conditions ;In this study ten novel heterocyclic compound synthesized and tested against four multidrug resistant gram positive and gram-negative bacteria (Table2)

Table 2: Antibacterial activity of synthesized compounds

Comp.NO	Concentration mg/ml	Zone of inhibition (in mm)			
		Gram-positive		Gram-negative	
		S.aureus	S.epidermidis	K.pneumonia	E.coli
2_5		13	12	12	13
C_1	50	15	15	15	15
	100	17	17	17	17
C_5	25	-	11	-	-
	50	12	14	-	12
	100	14	18	-	16
C_6	25	13	14	11	12
	50	14	16	13	13
	100	17	18	14	15
C_8	25	12	12	13	12
	50	14	15	14	13
	100	16	17	15	16
C_{10}	25	14	14	-	12
	50	14	16	17	16
	100	18	18	13	20
Erythromycin	15	18	-	-	17
Ceftriaxone	30	-	-	17	-
Clarithromycin	15	21	-	-	-

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Acknowledgements may be included as a separate section.

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