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# Synthesis of some N-substituted 4-(ethyl methyl amino) benzohydrazide derivatives and their chemical transformation

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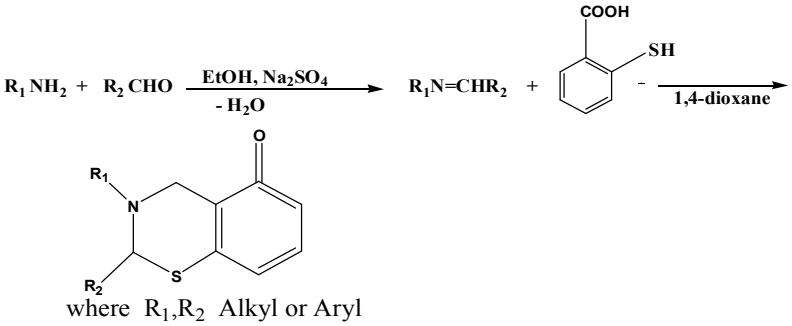
**Abstract**
In this study, a series of new N-substituted 4-(ethyl methyl amino) benzohydrazide derivatives (1-8) was synthesized using an efficient synthesis method. Reaction of these compounds with thiosalicylic acid give a new series of 1, 3-benzothiazin-4-one derivatives (9-16).The spectral (IR,$^{1}$H NMR,$^{13}$C NMR) and elemental analysis confirmed the structure of synthesized compounds.

**Keywords:** Benzhydrazide, Benzothiazin, Thiosalicylic acid, Spectral analysis.

## 1. Introduction
The reaction of hydrazides of carboxylic acids with aldehydes is known synthetic method to produce N- substituted hydrazone derivatives [1].The resulting hydrazone compounds are considered as convenient intermediates and can be used to obtain new interesting heterocyclic systems such as thiazolidin-4-one [2] or 1, 3-benzothiazin-4-one [3]. The 1, 3-benzothiazin-4-one derivatives, in recent years, have gained substantial interest in the scientific community not only due to their meaningful biological activity, but also as reactive intermediates to lots of new synthetic transformations [4, 5]. Many 1, 3-benzothiazin- 4-one derivatives exhibit a broad spectrum of biological activities, so that the purposeful of their synthesis and modification of their structure attracts great interest in pharmacology and other related fields [6, 7].
Some compounds having the 1, 3-benzothiazin-4-one structure have been reported to exhibit biological activities, like anti-proliferative [8, 9], antibacterial [10-14], antifungal [15, 16], antimalarial [17], anti-inflammatory [18] and antiviral activity, mainly against HIV virus [19] and several efficient routes to synthesis of such compounds have been published [20, 21].
Generally, methods for preparing these compounds rely on the simultaneous reaction of three components or on a two-step synthesis (Scheme 1.). During the first stage of synthesis the following starting materials are used: compound with primary amine group and an aldehyde [22-24]. Next, in the second step the resulting intermediate undergoes cyclization reaction with thiosalicylic acid. The anhydrous 1, 4-dioxane or toluene [4, 14] with the addition of anhydrous sodium sulfate [4] are used as reaction medium.
Basing on the above facts, in this paper report the synthesis and spectral analysis of a new N-substituted 4-(ethyl methyl amino) benzohydrazide derivatives and study their chemical transformation.




where $R_1$,$R_2$ Alkyl or Aryl

**Scheme1: The usual method used in the preparation of 2,3-disubstituted 1,3-benzothiazin- 4-one derivatieves.**

## 2. Materials and Methods

All chemical reagents used in this study were purchased from Aldrich (Milwaukee, WI, USA). And E.Merich Darmstadet, Germany. All solvents were purified according to standard procedures. All of the synthesized N-substituted 4-(ethyl methyl amino) benzhydrazide derivatives (1-8) and 1, 3-benzothiazin-4-one derivatives (9-16) were analyzed by IR,$^{1}$H NMR,$^{13}$C NMR spectroscopy and elemental analysis. IR spectra were recorded on Nicolet 740 Fourier Transform Infrared (FTIR) spectrometer.$^{1}$H NMR-spectra were recorded on a Varian Gemini 200 and 300 MHz instrument in $CDCl_3$ and DMSO-$d_6$ using Tetramethylsilane (TMS) as an internal standard. The $^{13}$C NMR spectra were recorded on a Bruker Avance 52 DPX 250 MHz apparatus. Melting Points measured using a Buchi-510 apparatus and were uncorrected. All instrumental analyses were performed at Bin Hayyan Laboratory (Aqaba Special Economic Zone- Jordan).

## 3. Experimental

### 3.1 General Experimental Procedure for the Synthesis of N-substituted 4-(ethyl methyl amino) benzohydrazide derivatives (1-8)

15 mmol of appropriate aromatic aldehyde and (5-10) drops of glacial acetic acid were added to the solution of 15mmol of 4-(ethylmethylamino) benzohydrazide (2.80 g) in 15ml ethanol. The solution was heated under reflux for 6 hours. After the completion of the reaction, the solution was cooled to room temperature and left for one day. The obtained precipitate was filtered off and crystallized from ethanol, which gave the compounds N-substituted 4-(ethyl methyl amino) benzohydrazide derivatives (1-8) as a solid in 76-90% yields.

### 3.2 Spectral Data for N-substituted 4-(ethyl methyl amino) benzhydrazide derivatives (1-8): N-[(2-chlorophenyl) methylidene]-4-(ethylmethylamino) benzhydrazide (1):

Solid; Molecular formula $C_{17}H_{18}ClN_3O$, Yield :78%, m.p: 230-232 $^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3050 (CH ar.);3010,1450 (CH alph.);1705 (C=O), 1618 (C=N),1598 (NH), 1398 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =4.1(s,8H), 6.75-6.79 (dd,2H, ArH, J = 10 Hz ),7.40-7.47 (m, 2H, ArH),7.50-7.55 (m, 2H, ArH),7.82-7.86(dd,2H,ArH, J =10Hz), 7.99(s,1H,=CH),11.80 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 42(2), 110.5, 121.3, 127.4, 127.5, 128.1, 129.2, 130.6, 131.4, 132.8 (11C $_{ar.}$), 149.7 (=CH), 152.8 ($C_{ar.}$),164.5 (C=O). Elem. analysis: Calculated: C: 65.60%, H:5.68%, N: 13.92%, Found: C: 65.72%, H: 5.53%, N:13.54%.

### 3.3 N-[(4-chlorophenyl) methylidene]-4-(ethylmethylamino) benzhydrazide (2):

Solid; Molecular formula $C_{17}H_{18}ClN_3O$, Yield :82%, m.p: 221-223$^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3058 (CH ar.);3025,1447 (CH alph.);1710 (C=O), 1605 (C=N),1602 (NH), 1406 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =4.0(s,8H), 6.70-6.76 (dd,2H, ArH, J = 10 Hz ),7.35-7.43 (m, 2H, ArH),7.45-7.49 (m, 2H, ArH),7.78-7.83(dd,2H,ArH, J =10Hz), 7.97(s,1H,=CH),11.78 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.8(2), 110.2, 120.8, 127.8, 128.5, 128.9, 129.2, 131.6, 133.4, 134.8 (11C $_{ar.}$), 148.8 (=CH), 153.2 ($C_{ar.}$),163.9 (C=O). Elem. analysis: Calculated: C: 65.60%, H:5.68%, N: 13.92%, Found: C: 64.97%, H: 5.45%, N:13.65%.

### 3.4 N-[(3-bromophenyl) methylidene]-4-(ethylmethylamino) benzhydrazide (3):

Solid; Molecular formula $C_{17}H_{18}BrN_3O$, Yield:76%, m.p: 240-242$^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3052 (CH ar.);3032,1450 (CH alph.);1718 (C=O), 1598 (C=N),1608 (NH), 1401 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =4.1(s,8H), 6.71-6.74 (dd, 2H, ArH, J = 10 Hz ),7.43-7.48 (m, 2H, ArH),7.41-7.46 (m, 2H, ArH),7.72-7.78(dd,2H,ArH, J =10Hz), 7.93(s,1H,=CH),11.72 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.2(2), 111.0, 121.2, 125.6, 127.7, 128.8, 129.5, 132.2, 134.1, 135.3 (11C $_{ar.}$), 149.2 (=CH), 152.7 ($C_{ar.}$),164.0 (C=O). Elem. analysis: Calculated: C: 56.52%, H:4.68%, N: 12.64%, Found: C: 55.97%, H: 4.45%, N:12.55%.

### 3.5 N-[(2-fluorometylidene]-4-(ethylmethylamino) Benzhydrazide (4):

Solid; Molecular formula $C_{17}H_{18}FN_3O$, Yield :84%, m.p: 212-214$^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3047 (CH ar.);3028,1445 (CH alph.);1721 (C=O), 1601 (C=N),1610 (NH), 1399 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =3.2(s,8H), 6.67-6.70 (dd,2H, ArH, J = 10 Hz ),7.54-7.56 (m, 2H, ArH),7.34-7.40 (m, 2H, ArH),7.68-7.77(dd,2H,ArH, J =10Hz), 7.95 (s,1H,=CH),11.65 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 40.9(2), 110.5, 122.2, 124.3, 126.8, 128.5, 129.1, 131.8, 134.6, 135.5 (11C $_{ar.}$), 150.1 (=CH), 151.8 ($C_{ar.}$),163.7 (C=O). Elem. analysis: Calculated: C: 67.35%, H:5.46%, N: 14.64%, Found: C: 67.27%, H:5.45%, N:14.52%.

### 3.6 N-[(4-fluorometylidene]-4-(ethylmethylamino) benzohydrazide (5):

Solid; Molecular formula $C_{17}H_{18}FN_3O$, Yield: 88%, m.p: 212-214$^{o}$C; IR (KBr), ν ($cm^{-1}$): 3045 (CH ar.); 3030, 1448 (CH alph.);1718 (C=O), 1598 (C=N),1605 (NH), 1401 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =3.3(s,8H), 6.56-6.67 (dd,2H, ArH, J = 10 Hz ),7.45-7.53 (m, 2H, ArH),7.38-7.42 (m, 2H, ArH),7.70-7.75(dd,2H,ArH, J =10Hz), 7.97 (s,1H,=CH),11.58 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 40.8(2), 111.05, 121.82, 123.7, 126.5, 128.7, 130.1, 132.5, 133.2, 135.2 (11C $_{ar.}$), 149.8 (=CH), 150.9 ($C_{ar.}$),164.1 (C=O). Elem. analysis: Calculated: C: 67.20%, H:5.32%, N: 14.14%, Found: C: 67.12%, H:5.24%, N:14.23%.

### 3.7 N-[(3-bromo-4-methoxyphenyl)methylidene]-4-(ethylmethylamino) benzhydrazide (6):

Solid; Molecular formula $C_{18}H_{20}BrN_3O_2$, Yield :78%, m.p: 220-222$^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3035 (CH ar.);3031,1450 (CH alph.);1730 (C=O), 1604 (C=N),1605 (NH), 1410 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =3.0(s,8H), 6.65-6.67 (dd,2H, ArH, J = 10 Hz ),7.50-7.55 (m, 2H, ArH),7.41-7.47 (m, 2H, ArH),7.70-7.76 (dd,2H,ArH, J =10Hz), 7.92 (s,1H,=CH),11.59 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.6 (2), 109.8, 120.3, 122.4, 125.4, 126.5, 128.3, 130.5, 132.9, 133.5 (11C $_{ar.}$), 149.6 (=CH), 150.7 ($C_{ar.}$),162.5 (C=O). Elem. analysis: Calculated: C: 56.32%, H:4.76%, N: 11.68%, Found: C: 57.12%, H:4.65%, N:11.52%.

### 3.8 N-[(5-bromo-2-hydroxyphenyl)methylidene]-4-(ethylmethylamino) benzhydrazide(7):

Solid; Molecular formula $C_{17}$ $H_{18}$ $BrN_3O_2$, Yield :85%, m.p: 245-247$^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3030 (CH ar.);3028,1452(CH alph.);1725 (C=O), 1600 (C=N),1606 (NH), 1408 (C-N). $^{1}$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.61-6.68 (dd,2H, ArH, J = 7.5 Hz ),7.54-7.59 (m, 2H, ArH),7.39-7.42 (m, 2H, ArH),7.60-7.67 (dd,2H,ArH, J =7.5Hz), 7.97 (s,1H,=CH),10.56(s,1H,OH), 11.62 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.3 (2), 110.4, 112.7, 114.4, 118.5, 121.8, 123.2, 125.6, 127.1, 129.5 (11C $_{ar.}$), 149.6 (=CH), 150.7,152.8 (2$C_{ar.}$),164.5 (C=O). Elem. analysis: Calculated: C: 54.42%, H:4.53%, N: 11.74%, Found: C: 55.20%, H:4.55%, N:11.65%.

**3.9 N-[(3-chloro-4-methoxyphenyl)methylidene]-4-(ethylmethylamino) benzhydrazide(8):**

Solid; Molecular formula $C_{18}$ $H_{20}ClN_3O_2$, Yield :90%, m.p: 225-227°C ; IR (KBr), ν ($cm^{-1}$): 3025 (CH ar.);3028,1456(CH alph.);1730(C=O), 1605 (C=N),1599 (NH), 1403 (C-N). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.59-6.63 (dd,2H, ArH, J = 7.5 Hz ),7.57-7.61 (m, 2H, ArH),7.41-7.48 (m, 2H, ArH),7.63-7.07 (dd,2H,ArH, J =7.5Hz), 7.88 (s,1H,=CH),2.96 (s,1H,$CH_3$), 11.62 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.3 (2),56.4($CH_3$) 111.2, 113.5, 114.9, 119.2, 122.5, 123.7, 124.8, 127.6, 130.2 (11C $_{ar.}$), 149.3 (=CH), 151.0,152.2 (2$C_{ar.}$),163.9 (C=O). Elem. analysis: Calculated: C:60.75%, H:4.96%, N:13.24%, Found: C: 60.44%, H:4.85%, N:13.35%.

**3.10 Synthesis of 2,3-disubstituted 1,3-benzothiazin-4-one derivatives (9-16) :**

15 mmol (1.55g) thiosalicylic acid was added in batches to the solution of (15mmol) a stirred of N-substituted derivatives of 4-(ethyl methyl amino)benzhydrazide(1-8) and (5mmol) $NH_4Cl$ in 20ml $CHCl_3$ for 15 minutes at room temperature(scheme 2).The mixture was stirred under reflux for 4 hours at 125 °C. After completed of reaction inferred by (TLC, eluent hexane/ ethyl acetate 30:70), the solvent was removed under reduced pressure and extracted with 50 ml ethyl acetate. Organic layer was washed in 25-30 ml water and dried over sodium sulfate. The perception was filtered off and purified by recrystallization from ethanol, which gave the compounds of 2,3-disubstituted 1,3-benzothiazin-4-one derivatives (9-16) in 68-82% yields.

**3.11 Spectral Data for 2,3-disubstituted 1,3-benzothiazin-4-one derivatives (9-16) :**

**N-[2-(2-chlorophenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylmethylamino)benzamide (9):**

Solid; Molecular formula $C_{24}H_{22}ClN_3O_2S$, Yield: 68%, m.p:170-172; IR (KBr), ν($cm^{-1}$) 3082 (CH ar.), 3056, 1450 (CH aliph.), 1715 (C=O), 1601 (N-H),1394 (C-N), 652 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.75-6.79 (dd,2H, ArH, J = 10 Hz ), 7.40-7.47 (m, 2H, ArH), 7.50-7.55 (m, 2H, ArH),7.82-7.86 (dd,2H,ArH, J=10 Hz), 7.99 (s,1H,=CH),11.80 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm) = 42(2), 110.5, 121.3, 127.4, 127.5, 128.1, 129.2,129.6,129.9, 130.6, 131.4,131.8, 132.8, 133.4,133.8, 145.2, 151.3,152.2 (19C $_{ar.}$), 163.7 (C=O),164.5 (C=O). Elem. anal. Calculated: C: 64.26%, H:4.86%, N: 10.32%, Found: C: 64.72%, H: 4.73%, N: 10.54%.

**3.12 N-[2-(4-chlorophenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylmethylamino)benzamide (10):**

Solid; Molecular formula $C_{24}$ $H_{22}ClN_3O_2S$, Yield :75%, m.p: 179-181°C ; IR (KBr), ν ($cm^{-1}$): 3025 (CH ar.);3028,1456(CH alph.);1710(C=O), 1599 (NH), 1403 (C-N), 650 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.59-6.63 (dd,2H, ArH, J = 7.5 Hz ),7.57-7.61 (m, 2H, ArH),7.41-7.48 (m, 2H, ArH),7.63-7.07 (dd,2H,ArH, J =7.5Hz), 7.88 (s,1H,=CH),2.96 (s,1H,$CH_3$), 11.62 (s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.3 (2),110.8, 111.2, 113.5, 114.9, 119.2, 122.5, 123.7, 124.8, 127.6, 130.2, 133.4,134.5,135.2,135.9,150.2,150.8,151.1(19C $_{ar.}$), 164.3 (C=O), 163.9 (C=O).Elem. Anal.: Calculated: C:63.15%, H:4.55%, N:10.52%, Found: C: 63.44%, H:4.35%, N:10.35%.

**3.13 N-[2-(3-bromophenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylmethylamino)benzamide (11):**

Solid; Molecular formula $C_{24}$ $H_{22}BrN_3O_2S$, Yield :78%, m.p: 184-186°C ; IR (KBr), ν ($cm^{-1}$): 3030 (CH ar.);3025,1455 (CH alph.);1714(C=O), 1600(NH), 1405 (C-N), 652 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.0(s,8H), 6.60-6.65 (dd,2H, ArH, J = 7.5 Hz ),7.58-7.63 (m, 2H, ArH),7.45-7.50 (m, 2H, ArH),7.65-7.87 (dd,2H,ArH, J =7.5Hz), 7.85 (s,1H,=CH),2.95 (s,1H,$CH_3$), 11.67(s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.3 (2),110.8, 111.2, 113.5, 114.9, 119.2, 122.5, 123.7, 124.8, 127.6, 130.2, 133.4,134.5,135.2,135.9,150.2,150.8, (18C $_{ar.}$), 164.3 (C=O), 163.9 (C=O).Elem. Anal.: Calculated: C:58.25%, H:4.75%, N:9.25%, Found: C: 68.42%, H:4.28%, N:9.33%.

**3.14 N-[2-(2-fluorophenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylimethylamino)benzamide (12):**

Solid; Molecular formula $C_{24}$ $H_{22}FN_3O_2S$, Yield :68%, m.p: 124-126°C ; IR (KBr), ν ($cm^{-1}$): 3028(CH ar.);3032,1448 (CH alph.);1710(C=O), 1598(NH), 1400(C-N), 650 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.60-6.65 (dd,2H, ArH, J = 7.5 Hz ),7.58-7.63 (m, 2H, ArH),7.45-7.50 (m, 2H, ArH),7.65-7.87 (dd,2H,ArH, J =7.5Hz), 7.85 (s,1H,=CH),2.95 (s,1H,$CH_3$), 11.67(s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.5 (2), 109.8, 112.4, 113.8, 114.6, 118.5, 120.7, 122.4, 123.9, 126.7, 131.2, 133.3, 134.5, 135.6, 136.2,150.5,151.7, (18C $_{ar.}$), 163.8 (C=O), 164.2 (C=O).Elem. Anal.: Calculated: C:65.25%, H:4.85%, N:9.62%, Found: C: 65.42%, H:4.68%, N:9.55%

**3.15 N-[2-(4-fluorophenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylmethylamino)benzamide (13):**

Solid; Molecular formula $C_{24}$ $H_{22}FN_3O_2S$, Yield :72%, m.p: 112-114°C ; IR (KBr), ν ($cm^{-1}$): 3025(CH ar.);3030,1450 (CH alph.);1711(C=O), 1599(NH), 1402(C-N), 652 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.60-6.65 (dd,2H, ArH, J = 7.5 Hz ),7.58-7.63 (m, 2H, ArH),7.45-7.50 (m, 2H, ArH),7.65-7.87 (dd,2H,ArH, J =7.5Hz), 7.85 (s,1H,=CH),2.95 (s,1H,$CH_3$), 11.67(s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.5 (2), 109.8, 112.4, 113.8, 114.6, 118.5, 120.7, 122.4, 123.9, 126.7, 131.2, 133.3, 134.5, 135.6, 136.2,155.2, (17C $_{ar.}$), 164.5 (C=O), 163.9 (C=O).Elem. Anal.: Calculated: C:65.38%, H:4.85%, N:9.65%, Found: C: 65.42%, H:4.72%, N:9.58%.

**3.16 N-[2-(3-bromo-4-methoxyphenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylmethylamino)benzamide (14):**

Solid; Molecular formula $C_{24}$ $H_{24}BrN_3O_2S$, Yield :82%, m.p: 185-187°C ; IR (KBr), ν ($cm^{-1}$): 3025(CH ar.);3030,1450 (CH alph.);1711(C=O), 1599(NH), 1402(C-N), 652 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s,8H), 6.60-6.65 (dd, 2H, ArH, J = 7.5 Hz ),7.58-7.63 (m, 2H, ArH),7.45-7.50 (m, 2H, ArH),7.65-7.87 (dd,2H,ArH, J =7.5Hz), 7.85 (s,1H,=CH),2.95 (s,1H,$CH_3$), 11.67(s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.3 (2), 109.8, 112.4, 113.8, 114.6, 118.5, 120.7, 122.4, 123.9, 126.7, 131.2, 133.3, 134.5, 135.6, 136.2,155.2,158.4 (18C $_{ar.}$), 162.8 (C=O), 163.5 (C=O).Elem. Anal.: Calculated: C:56.40%, H:4.32%, N:8.77%, Found: C: 56.24%, H:4.70%, N:8.67%.

**3.17 N-[2-(5-bromo-2-hydroxyphenyl)-4-oxo-2H-1,3-benzothiazin-3(4H)-yl]-4-(ethylmethylamino) benzamide (15):**

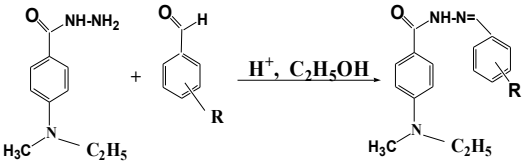
Solid; Molecular formula $C_{24}$ $H_{24}BrN_3O_2S$, Yield :70%, m.p: 118-120$^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3032(CH ar.);3028,1451 (CH alph.);1715(C=O), 1602(NH), 1402(C-N), 654 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.0(s,8H), 6.60-6.65 (dd,2H, ArH, J = 7.5 Hz ),7.58-7.63 (m, 2H, ArH),7.45-7.50 (m, 2H, ArH),7.65-7.87 (dd,2H,ArH, J =7.5Hz), 7.85 (s,1H,=CH),2.95 (s,1H,$CH_3$), 11.67(s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.3 (2), 110.2, 111.8, 114.6, 117.5, 119.3, 122.8, 124.7, 128.1, 129.7, 132.5, 134.2, 136.8, 137.5, 139.2,151.6,152.5 (18C $_{ar.}$), 162.5 (C=O), 164.2 (C=O).Elem. Anal.: Calculated: C:57.32%, H:4.80%, N:8.92%, Found: C: 57.14%, H:4.68%, N:8.88%.

**3.18 N-[2-(3-chloro-4-methoxyphenyl)-4-oxo-2H-1,3-benzothiazine-3(4H)-yl]-4-(ethylmethylamino)benzamide (16):**

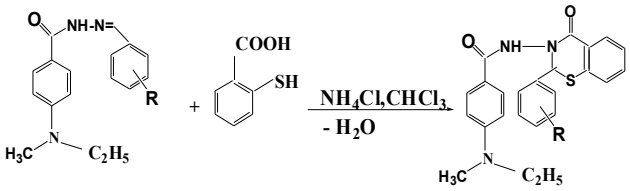
Solid; Molecular formula $C_{25}H_{24}ClN_3O_2S$, Yield :78%, m.p: 110-112 $^{o}$C ; IR (KBr), ν ($cm^{-1}$): 3025(CH ar.);3030,1450 (CH alph.);1711(C=O), 1599(NH), 1402(C-N), 652 (C-S). $^1$H NMR (DMSO-$d_6$) δ (ppm) =3.1(s, 8H), 6.60-6.65 (dd,2H, ArH, J = 7.5 Hz ),7.58-7.63 (m, 2H, ArH),7.45-7.50 (m, 2H, ArH),7.65-7.87 (dd,2H,ArH, J =7.5Hz), 7.85 (s,1H,=CH),2.95 (s,1H,$CH_3$), 11.67(s,1H,NH). $^{13}$C NMR (DMSO) δ (ppm)= 41.5 (2), 111.5, 112.4, 114.2, 116.7, 118.6, 120.8, 122.1, 124.2, 126.8, 130.8, 133.5, 136.7, 138.8, 139.5,150.9,151.6 (18C $_{ar.}$), 163.4 (C=O), 163.9 (C=O).Elem. Anal.: Calculated: C:62.18%, H:4.37%, N:8.76%, Found: C: 62.11%, H:4.25%, N:8.64%

## 4. Results and Discussion

Condensation reaction between 4-(ethyl methyl amino) benzohydrazide with appropriate aromatic aldehydes in (EtOH) gives N-substituted 4-(ethyl methyl amino) benzohydrazide derivatives (1-8). 2,3-disubstituted-1,3-benzothiazin-4-one derivatives (9-16) were obtained by the cyclization reaction of N- substituted derivatives of 4-(ethyl methyl amino)benzhydrazide with thiosalicylic acid in the presence of $NH_4Cl$ / $CHCl_3$ as a solvent (Scheme 2). Synthesized compounds were confirmed by TLC, IR,$^1$H NMR, $^{13}$ C NMR and elemental analysis. Melting Points (m.p) and yields have been identified for each of these compounds. All the spectra data (IR,$^1$H NMR,$^{13}$ C NMR) confirmed the formation of 2,3-disubstituted-1,3-benzothiazin-4-one derivatives (9-16).All compounds are stable solids, dissolved in DMSO at room temperature. The titled compounds were confirmed by IR spectral data showing characteristic at 1398-3200 $cm^{-1}$, included the presence of (CH ar., CH alph.,C=O,C-N,N-H,C=N) and 650 $cm^{-1}$ (C-S). In the $^1$H NMR spectra of the synthesized compounds (1-8) one typical proton singlet signal for =CH group was observed in the range of δ(7.30-845 ppm) and for NH group at δ (10.45- 11.80ppm). The $^{13}$C NMR of compounds (1-8) shows two signals for =CH and C=O at δ(144.5-144.9 ppm) and δ(163.9-164.3 ppm) respectively, which confirmed the formation of synthesized products. Other aromatic and aliphatic signals were found at usual regions. In the $^1$H NMR spectra of 1,3-benzothiazin-4-one derivatives (9-16) respectively appeared two signals in the range of δ(6.25-9.35 ppm) and δ(9.55-9.84 ppm). This confirms the existence of each of the CH and NH groups. In the $^{13}$C NMR spectra for these compounds, the typical signal of CH group appeared about δ (55 ppm) and two C=O groups appears about δ (163 ppm).




compounds (1-8)




compounds (9-16)

**Sheme 2 :Route preparation compounds in this study.**

**R = 2-Cl(1,9); 4-Cl(2,10); 3-Br(3,11); 2-F(4,12); 4-F(5,13); 3-Br-4-$OCH_3$(6,14); 5-Br-2-OH(7,15); 3-Cl-4-$OCH_3$(8,16).**

## 5. Conclusion

The 1,3-benzothiazin-4-one derivatives, in recent years, have gained substantial interest in the scientific community not only due to their meaningful biological activity, but also as reactive intermediates to lots of new synthetic transformations [4, 5]. 1,3-benzothiazin-4-one derivatives can be synthesized by the reaction of N-substituted derivatives of 4-(alkyl amino) benzhydrazide with thiosalicylic acid [1, 2].

The obtained yields of final products when 1,4-dioxane was used as solvent, are rather low. in this study we synthesized some 2,3-disubstituted-1,3-benzothiazin-4-one derivatives using simple and inexpensive method using ammonium salts as catalysts. The yields of synthesized compounds were in the range of 68-82%.The purity of the synthesized compounds were assessed by TLC and melting points. Hence, it can be concluded that the 1,3-benzothiazin-4-one derivatives can potentially be developed into useful, interesting heterocyclic system, with enhanced activity.

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