Synthesis of oxobenzotriazino acetic, benzimidazolyl hydrazides and some their hydrazones

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Abstract -Hydrazides of oxobenzotriazine and benzimidiazole (4), (13) were synthesized from their corresponding esters (3), (12). Those two types of hydrazides were allowed to react with some substituted Benz aldehydes resulting into the formation of new hydrazone compounds (5-12), (14-18) respectively. The structure of the studied compounds were confirmed using IR,1HNMR,13CNMR, mass and well discussed .

Keywords- benzotriazino, benzimidzolyl, hydrazides, hydrazones

1 Introduction

There are numerous methods in the literature for the preparation of hydrazides, Such as carbodimide, N-Amination of amides, Nitrile hydrolysis and acylation of hydrazines [1]. The last one is the most popular methods for hydrazide synthesis. These hydrazide and their condensation products were stated to possess a wide range of biological activities [2]. Some of hydrazides and their analogous hydrazones are psychopharmacological agent, such as mono amino oxidase (MAO) inhibitor and serotrin antagonists [3] hydrazides were also used to prepare diazoles and oxadiazoles compounds [4-6] most of them are biologically active and found many applications in medical area [7] it is well known that hydrazides when allowed to react with aldehyde or lactones they will transformed into their corresponding hydrazones[8-10]. Hydrazone compounds due to their azomerhine group activity have drawn the attention of many researchers for the synthesis of numerous hydrazone compounds by the well-known hydrazinolysis method [11, 12]. These hydrazones likewise corresponding hydrazides have proofed to have a wide range. Of pharmaceutical applications [13-16]. In this work we tried to prepare two types of new hydrazide and some new derivatives of their hydrazones in an attempt to study their biological effect which will be our next work.

2 Experimental

All reagents and chemicals were from BHD and Sigma-Aldrich companies and used without further purification. Melting points were determined with Electro thermal 9300 melting point apparatus. Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR. ^{1}H, ^{13}C NMR spectra were recorded at 250 or 400 MHz on a Bruker AV-1400 model or Bruker AV-1250 model NMR instrument. Accurate masses were obtained using a Water-Micromass LCT electrospray mass spectrometer. All the measurements were performed at the Chemistry department, university of Sheffield, Sheffield, United Kingdom. Compound (1) was prepared according to the well-known procedure[17] .Compounds10,11 were prepared following the elsewhere published procedure[18]and compound(12)was also prepared following the published one[19] . Structures of these compounds were elucidated using IR, NMR and mass measurements.

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2.1 Synthesis of hydrazide compounds (4), (13) General procedure)

A mixture of the ester (3) or (12) (0.05 mol.), and hydrazine hydrate (80%), (0.10 mol.) in ethanol (20 ml) were refluxed for 2 hours. Excess ethanol was evaporated under reduced pressure and the precipitate product was crystallized from ethanol.

2.2 Synthesis of hydrazone compounds (5-9), (14-18) (General procedure)

Equimolar quantities of hydrazide (4) or (13) and substituted bezaldehyde in (25 ml) of absolute ethanol were refluxed for three hours. The reaction mixture was then cooled and the solid precipitated was recrystallized from ethanol physical and spectral data were illustrated in the following article:

3 Results and discussion

Ethyl 2-(4-oxobenzo[d][1,2,3]triazin-3(4H)-yl)acetate(3)

Oil bp100-111^{0}C, IR spectrum, υ, cm^{-1}: 3004 (Ar-CH str.), 2988 (Aliphatic-CH str.), 2110 (N=N str.), 1747 (C=O str.easter), 1685 (C=O str. amide), 1615, 1488 (C=C str.), 1436 (C-Hbend), 1275 (C-N str.). High resolution mass spectrum (EI): Found: m\z 234.08 [M]$^+$, Calculated 234.23.

2-(4-oxobenzo[d][1,2,3]triazin-3(4H)-yl)acetic hydrazide (4)

This compound (mp.243-244^{0}C)was prepared by hydrazinolysis of compound(3) as shown in scheme(1) the elucidation of its structure comes from IR,NMR and mass.IR spectrum, υ, cm^{-1}:3309 (NH str.), 3038 (Ar-CH str.), 2958 (aliphatic-CH str.), 2163 (N=N str.), 1678, 1659 (C=O str.), 1633, 1446 (C=C str.), 1375 (C-H bend), 1336 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 4.3 (2H, s, NH$_2$), 5.0 (2H, s, CH$_2$), 7.9-8.3 (4H, m, Ar-CH), 11.4 (1H, s, NH). ^{13}C NMR (DMSO-d$_6$), δ, ppm: 51.13, 119.85, 124.96, 128.54, 133.51, 136.00, 144.27, 166.12, 170.13. High resolution mass spectrum (EI): Found: m/z 220.20 [M]$^+$, Calculated 220.21

Aryl-N-(4-oxo benzo[d][1,2,3]triazin-3-(4H-yl) acetic hydrazones (5-9)

These series of hydrazone compounds , were prepared from the reaction of compound(4)with some substituted benzaldehydes , Scheme (1).These compounds were characterized by a combination of spectral methods IR,NMR and mass.IR indicate the presence of azomethine group(-CH=N-) absorbed around 100-1640cm^{-1},^{1}HNMR also support this finding through the signal resonated around 8.5-8.6ppm while^{13}CNMR showed signal resonating around 145.35-150.6ppm related to the azomethine carbon for the studied compounds. The details of spectral data were illustrated below:

3-nitrophenyl-N(4-oxobenzo[d][1,2,3]triazino-3(4H)-yl)hydrazone (5)

White solid,mp.278-280^{0}C,85%yield . IR spectrum, υ, cm^{-1}:3200 (NH str.), 3062 (Ar-CH str.), 2962 (aliphatic-CH str.), 1700, 1665 (C=O str.), 1605 (C=N str.), 1600, 1411 (C=C str.), 1388 (C-H bend), 1334 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 5.7 (2H, s, CH), 7.7-8.3 (8H, m, Ar-CH), 8.6 (1H, s, CH), 12.1 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm: 51.89, 119.57, 121.67, 121.79, 124.78, 125.05, 128.64, 130.88, 133.59, 136.22, 142.80, 145.64, 148.74, 155.37, 163.77, 168.47.High resolution mass spectrum (EI): Found: m/z 353.10 [M]$^+$, Calculated 353.09.

2-nitrophenyl-N(4-oxobenzo[d][1,2,3]triazin-3(4H)-yl)hydrazone (6)

Pale yellow solid,mp.142-143^{0}C,70%yield . IR spectrum, υ, cm^{-1}:3225 (NH str.), 3080 (Ar-CH str.), 3000 (aliphatic-CH str.), 1714, 1677 (C=O str.), 1600 (C=N str.), 1567, 1441 (C=C str.), 1356 (C-H bend), 1339 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 5.6 (2H, s, CH), 7.7-8.4 (8H, m, Ar-CH), 8.5 (1H, s, CH), 12.2 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm: 51.11, 119.20, 119.58, 125.06, 128.53, 128.66, 128.98, 131.20, 133.73, 134.07, 136.24, 140.67, 144.30, 148.55, 155.38, 168.44. High resolution mass spectrum (EI): Found: m/z 353.10 [M]$^+$, Calculated 353.09.

4-chlorophenyl-N(4-oxobenzo[d][1,2,3]triazino-3(4H)-yl)hydrazone (7)

Yellow solid,mp.132-133^{0}C67%yield . IR spectrum, υ, cm^{-1}:3219 (NH str.), 3064 (Ar-CH str.), 2957 (aliphatic-CH str.), 1715, 1673 (C=O str.), 1611 (C=N str.), 1597, 1448 (C=C str.), 1353 (C-H bend), 1333 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 5.6 (2H, s, CH$_2$), 7.5-8.3 (8H, m, Ar-CH), (1H, s, CH), 12.0 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm:54.99, 118.66, 119.28, 124.88, 125.66, 127.06, 129.88, 131.05, 133.21, 137.55, 143.41, 151.67, 161.25, 172.56..High resolution mass spectrum (EI): Found: m/z 342.07 [M]$^+$, Calculated 342.07.

4-hydroxyphenyl-N(4-oxobenzo[d][1,2,3]triazino-3(4H)-yl)hydrazone(8)

White solid ,mp.194-196^{0}C,72% yield.IR spectrum, υ, cm^{-1}:3220 (OH str.), 3156 (NH str.), 3050 (Ar-CH str.), 2980 (aliphatic-CH str.),1702, 1672 (C=O str.), 1654 (C=N str.),1604, 1446 (C=C str.), 1350 (C-H bend), 1332 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 5.6 (2H, s, CH$_2$), 6.8-8.3 (8H, m, Ar-CH), (1H, s, CH), 10.0 (1H, s, OH), 11.8 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm: 53.68, 121.13, 122.06, 124.88, 125.87, 128.86, 131.06, 136.00, 143.24, 145.76, 149.27, 161.87, 170.01.High resolution mass spectrum (EI): Found: m/z 324.108 [M]$^+$, Calculated 324.109.

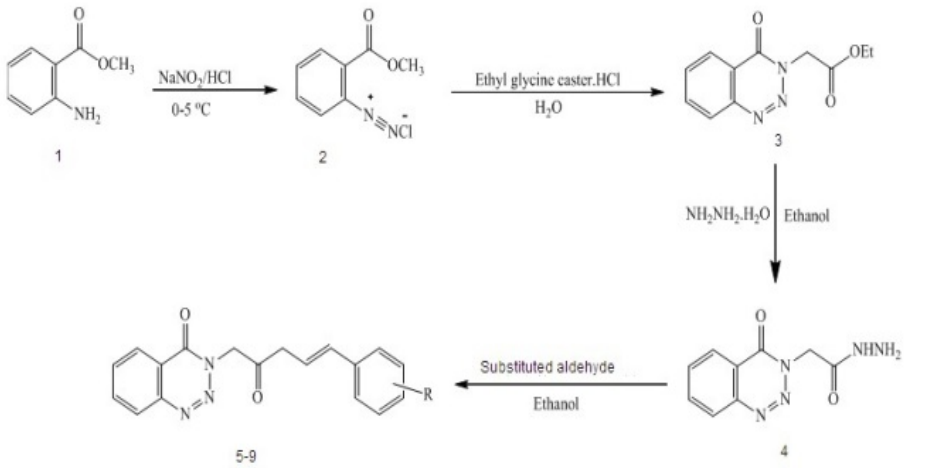
4-methylphenyl-N(4-oxobenzo[d][1,2,3]triazino-3(4H)-yl)hydrazone(9)

Pale yellow solid,mp.210211^{0}C. IR spectrum, υ, cm^{-1}:3182 (NH str.), 3063 (Ar-CH str.), 2959 (aliphatic-CH str.),1701, 1667 (C=O str.),1614 (C=N str.), 1582, 1416 (C=C str.),1392 (C-H bend),1332 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 5.6 (2H, s, CH), 7.3-8.3 (8H, m, Ar-

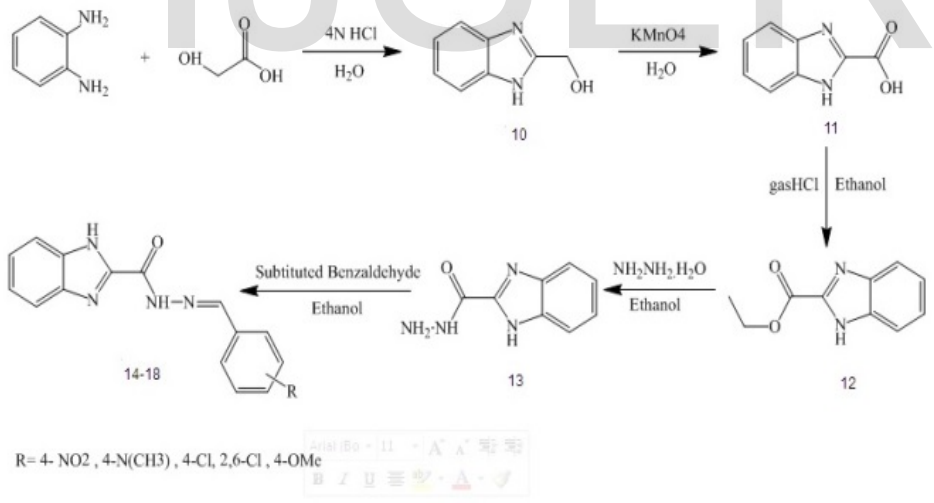
CH),(1H, s, CH), 11.9 (1H, s, NH).^{13}C NMR (DMSO-d_6), δ, ppm: 21.51, 51.85, 119.58, 125.05, 127.61, 128.62, 129.90, 131.64, 133.67, 136.18, 140.40, 144.31, 145.05, 155.36, 167.99.High resolution mass spectrum (EI): Found: m/z 322.12 $[M]^+$, Calculated 322.13.

Ethyl 1H-benzo[d]imidazole-2-carboxylate (12)

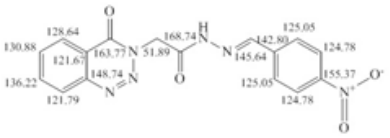
This compound was prepared by the esterification of compound (11) with ethanol, mp220-222 ^{0}C ,80%yield .The IR spectrum, υ, cm^{-1}: 3233 (NH str.), 3054 (Ar-CH str.), 2992 (aliphatic-CH str.), 1718 (C=O str.), 1622 (C=N str.), 1488 (C=C str.), 1315 (C-N str.). ^{1}H NMR (DMSO-d_6), δ, ppm: 1.3 (3H, t, CH_3), 4.4 (2H, q, CH_2), 7.4-7.7 (4H, m, Ar-CH), 13.5 (1H, s, NH). ^{13}C NMR (DMSO-d_6), δ, ppm: 21.51, 51.15, 125.05, 127.44, 127.61, 128.62, 131.64, 133.67, 140.40, 167.99. High resolution mass spectrum (EI): Found: m/z 191.082 $[M]^+$, Calculated 191.082.



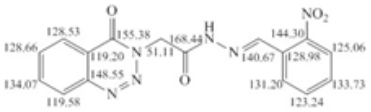
Scheme 1



Scheme 2



Comp.(5)



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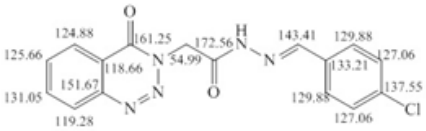

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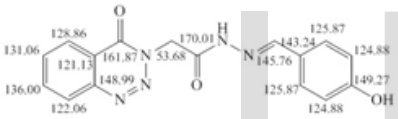

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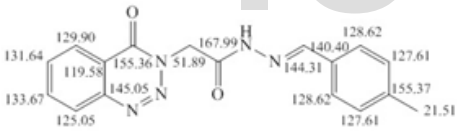
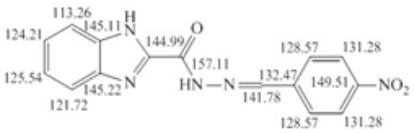
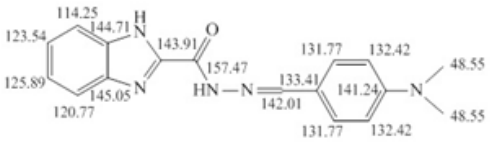


Com.(9)



Comp.(14)



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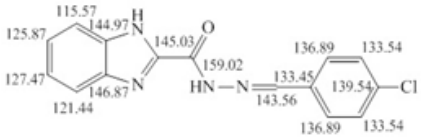
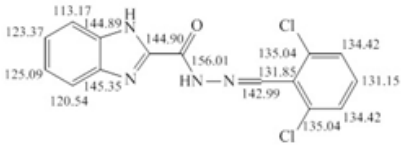
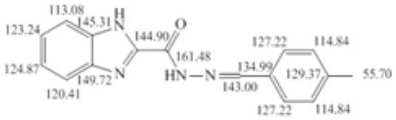


Comp.(16)



Comp.(17)



Comp.(18)

^{13}C NMR Assignment of the Synthesized componds

1H-benzo[d]imidazole-2-carbohydrazide (13)

This hydrazide was also prepared by hydrazinolysis of compound (12).Melting point of this yellow solid compound 242-243^{0}C . The following spectral data support its formation, IR spectrum, υ, cm^{-1}: 3321, 3256 (NH str.), 3064 (Ar-CH str.), 2967 (aliphatic-CH str.), 1658 (C=O str.), 1606 (C=N str.), 1596, 1474 (C=C str.), 1323 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 4.7 (1H, s, NH), 6.9 (1H, s, NH), 7.4-7.7 (4H, m, Ar-CH), 12.3 (1H, s, NH), 13.5 (1H, s, NH). ^{13}C NMR (DMSO-d$_6$), δ, ppm: 124.96, 128.54, 133.51, 136.00, 141.00, 144.28, 149.72. High resolution mass spectrum (EI): Found: m/z 177.07 [M]$^+$, Calculated 177.08.

Syntheses of Aryl - N- 1Hbenz [d] imidazole -2-yl-hydrazone (14-18)

The condensation os some substituted benzaldehydes with compound (13) resulted into the formation of the above compounds,Scheme(2) .The formation of azomethine group (-CH=N) comes from the study of IR ,NMR and mass spectra .These studies supports its formation through IR which revealed the absence of the original C=O group absorption in amide. ^{1}NMR showed –CH- of azomethine group resonating at 8.5-8.8ppm and ^{13}CNMR of the carbon of this group at 145.35-148.6ppm .Details of their spectral data where illustrated below:

4-nitrophenyl-N-1H-benzo[d]imidazole-2-yl hydrazone(14)

White solid,mp.300-302^{0}C,80% yield .IR spectrum, υ, cm^{-1}: 3233-3147 (NH str.), 3090 (Ar-CH str.), 2967 (aliphatic-CH str.), 1667 (C=O str.), 1600 (C=N str.), 1548 (asym. N-O), 1446 (C=C str.), 1344 (sym. N-O), 1323 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 7.3-8.3 (8H, m, Ar-CH), 8.8 (1H, s, CH), 12.9 (1H, s, NH) 13.6 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm: 113.26, 121.72, 124.21, 125.54, 128.57, 131.28, 132.47, 141.78, 144.99, 145.11, 145.22, 149.51, 157.11. High resolution mass spectrum (EI): Found: m/z 310.093 [M]$^+$, Calculated 310.094.

4-dimethylaminophenyl-N-1H-benzo[d]imidazole-2-yl hydrazone(15)

Yellow solid,mp283-285^{0}C75% yield.IR spectrum, υ, cm^{-1}: 3193 (NH str.), 3022 (Ar-CH str.), 2886 (aliphatic-CH str.), 1654 (C=O str.), 1611 (C=N str.), 1442 (C=C str.), 1309 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 3.0 (6H, s, $(CH_3)_2$), 6.8-7.7 (8H, m, Ar-CH), 8.5 (1H, s, CH) , 12.2 (1H, s, NH) , 13.5 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm: 48.55, 114.25, 120.77, 123.54, 125.89, 131.77, 132.42, 133.41, 141.24, 142.01, 143.91, 144.71, 145.05, 157.47. High resolution mass spectrum (EI): Found: m/z 308.15 [M]$^+$, Calculated 308.14.

4-chlorophenyl-N-1H-benzo[d]imidazole-2-yl hydrazone(16)

Red solid,mp.270-272^{0}C,70% yield.IR spectrum, υ, cm^{-1}: 3230-3140 (NH str.), 3090 (Ar-CH str.), 2967 (aliphatic-CH str.), 1667 (C=O str.), 1600 (C=N str.), 1548 (asym. N-O), 1446 (C=C str.), 1344 (sym. N-O), 1323 (C-N str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 7.3-8.3 (8H, m, Ar-CH), 8.8 (1H, s, CH), 12.9 (1H, s, NH), 13.6 (1H, s, NH).^{13}C NMR (DMSO-d$_6$), δ, ppm: 115.57, 121.44, 125.87, 127.47, 133.45, 133.54, 136.89, 143.56, 144.97, 145.03, 146.87 159.02. High resolution mass spectrum (EI): Found: m/z 310.09 [M]$^+$, Calculated 310.09.

2,6-dichlorophenyl-N-1H-benzo[d]imidazole-2-yl hydrazone(17)

White solid,mp.265-266^{0}C,85%yield. IR spectrum, υ, cm^{-1}: 3225-3303 (NH str.), 3057 (Ar-CH str.), 2920 (aliphatic-CH str.), 1684 (C=O str.), 1619 (C=N str.), 1442 (C=C str.), 1314 (C-N str.), 852-785 (C-Cl str.). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 7.4-7.8 (7H, m, Ar-CH), 8.8 (1H, s, CH), 12.9 (1H, s, NH), 13.6 (1H, s, NH). ^{13}C NMR (DMSO-d$_6$), δ, ppm: 113.17, 120.54, 123.37, 125.09, 129.54, 131.15, 131.85, 134.42, 135.04, 142.99, 144.89, 145.35, 156.01. High resolution mass spectrum (EI): Found: m/z 333.030 [M]$^+$, Calculated 333.031.

4-methoxyphenyl-N-1H-benzo[d]imidazole-2-yl hydrazone(18)

White solid,mp.280-281^{0}C65% yioeld.IR spectrum, υ, cm^{-1}: 3200 (NH str.), 3097 (Ar-CH str.), 2980 (aliphatic-CH str.), 1664 (C=O str.), 1601 (C=N str.), 1446 (C=C str.), 1323 (C-N str.), 1248 (asym. O-CH_3), 1026 (sym. O-CH_3). ^{1}H NMR (DMSO-d$_6$), δ, ppm: 3.8 (3H, s, CH_3), 7.0-7.8 (8H, m, Ar-CH), 8.6 (1H, s, CH), 12.4 (1H, s, NH), 13.5 (1H, s, NH). ^{13}C NMR (DMSO-d$_6$), δ, ppm: 55.7, 113.08, 114.84, 120.41, 123.24, 124.87, 127.22, 129.37, 134.99, 143.00, 145.31, 149.72, 155.60, 161.48. High resolution mass spectrum (EI): Found: m/z 295.119[M]$^+$, Calculated 295.119.

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