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Synthesis and Characterization of Benzoxazinone Derivatives

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Abstract

The present work reports synthesis and characterization of different benzoxazinone derivatives. 2-methyl-7-nitro-4*H*-3, 1-benzoxazin-4-one was prepared by refluxing 4-nitroanthranilic acid with acid anhydride. Derivatives of 2-methyl-7-nitro-4*H*-3, 1-benzoxazin-4-one were synthesized by condensation of it with different anilines. Elemental analysis and NMR spectral studies were used to confirm the formation of compounds.

Keywords: Benzoxazinone, Quinazolinone

1. Introduction

4*H*-3, 1-benzoxazin- 4-one, **1** are of great interest because of their broad range of biological properties.[1] They also exhibit excellent inhibitory activities against the human leukocyte elastase. In plant-pathogenic systems, benzoxazinones compounds play also an important role.[2] Quinazolinones **2, 3** can be considered as the building block units for various naturally occurring alkaloids which were isolated from plants, microbial sources[3] and they play a

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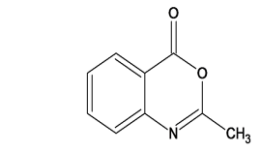
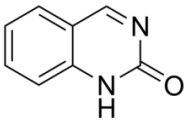
vital role in bioorganic and medicinal chemistry and have found large applications in drug discovery.[4]

Broad spectrum of biological activities[5] of substituted – quinazolin-4(3*H*)-ones were the basis to synthesize above stated benzoxazinone derivatives.



2-methyl-4*H*-3,1-benzoxazin-4-one

1



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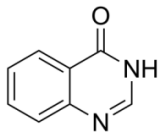

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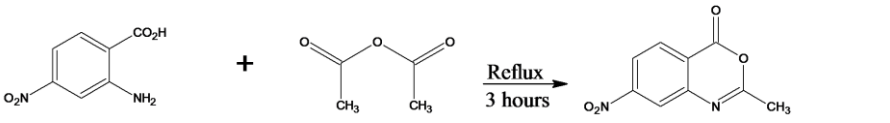
2. Experimental methods

2.4 Synthesis of 2-methyl-4*H*-3,1-benzoxazin-4-one

4-nitroanthranilic acid (0.01mol) **4** was taken in acetic anhydride (50ml) **5**. The reaction mixture was refluxed for 3 hours. It was cooled and poured to beaker containing crushed ice and stirred well. The light yellow colored crystals **6** were filtered and dried. Recrystallization was done using ethanol.[6]



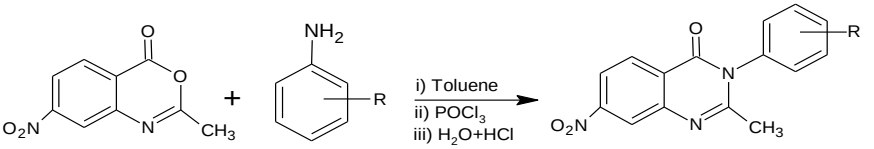
4-Nitroanthranilic acid — Acetic anhydride — 2-methyl-7-nitro-4*H*-3,1-benzoxazin-4-one

4 5 6

Synthesis of 2-Methyl-7-nitroquinazolin-4(3*H*)-one derivative:

Substituted aniline **7** (0.01mol) and **6** (0.01mol) were suspended in toluene (50ml) contained in a round bottomed flask and

phosphorous oxychloride (0.01mol) was added in half an hour gap with constant stirring. The mixture was digested with water (100ml) containing conc. HCl (10ml) for 1hour. It was neutralized by 5% $NaHCO_3$. The compound was filtered and dried. The crude sample **8 a-f** was recrystallized from ethanol and the melting point was noted. The characterization data of these compounds **8** are given in table 1.



6 7 8 a-f

where R= o-NO_2-p-NO_2(8a), o-NO_2(8b), m-NO_2(8c), p-NO_2(8d), p-Cl(8e) and p-Br(8f)

2.2 Physical measurements

Elemental analyses were performed by using a Thermoflash EA 1112 series CHNS – O – analyzer. The NMR spectra were recorded by BRUKER Spectrometer (400MHz) using internal reference TMS and solvent DMSO. Proton chemical shifts are reported in parts per million (ppm) relative to TMS.

3. Results and Discussion

3.1 Elemental Analyses

The benzoxazinone derivative is soluble in dimethyl formamide. The elemental analyses data including colour, m.p. and yield are given in Table 1.

Compd	Mol. formula	Mol. Wt.	M.P. (°C)	Yield (%)	Color	Elemental Analysis Found (Calculated)		
						%C	%H	%N
8a	$C_{15}H_9N_5O_7$	371	161-163	66	Yellow orange solid	47.8 (48.5)	24.21 (24.25)	18.81 (18.86)
8b	$C_{15}H_{10}O_5N_4$	326	209-211	75	Dark orange crystalline solid.	55.2 (55.21)	30.62 (30.67)	17.15 (17.17)
8c	$C_{15}H_{10}N_4O_5$	326	195-197	86	Yellow orange solid	54.95 (55.21)	30.34 (30.67)	17.12 (17.17)
8d	$C_{15}H_{10}N_4O_5$	326	129-131	25	Yellow orange solid	55.3 (55.21)	30.66 (30.67)	17.18 (17.17)
8e	$C_{15}H_{10}N_3O_3Cl$	315.5	233-235	14	Pale yellow solid	56.98 (57.05)	31.16 (31.69)	13.21 (13.31)
8f	$C_{15}H_{10}O_3N_3Br$	360	159-161	24	Orange crystalline solid	49.95 (50.0)	27.67 (27.77)	11.59 (11.66)

Table 1 Physical properties of the substituted quinazolinone

3.2 NMR Spectra

The structures of the synthesized compounds were confirmed by NMR (1H and 13C NMR).

Compound 6; Yellow solid, Melting Point: 185°C, Yield (98.2%), 1H NMR (400 MHz, DMSO) δH (ppm): 2.2 (s, 3H), 7.95 (d, J=7.6 Hz, 1H), 8.18 ppm (d, J=8.8 Hz, 1H), 9.28 (s, 1H). 13C NMR (400 MHz, DMSO) δ(ppm): 25.38 (CH3), 169.67 (C=O), 168, 150.5, 141.5, 133, 122.7, 119, 118.

Compound 8a; Yellow orange solid, Melting Point: 161-163°C, Yield(66%), 1H NMR (400 MHz, DMSO) δH (ppm): 2.2 (s, 3H), 8.8 (s, 1H), 8.17 (d, J= 8.8 Hz, 1H), 7.12 (d, J=9.2Hz, 1H), 8.4 (s, 1H), 7.9 (d, J = 7.6 Hz, 1H), 7.2 (d, J = 6.4Hz, 1H). 13C NMR (400 MHz, DMSO) δ(ppm): 13.5(CH3), 168.78 (C=O), 152.2 (C=N), 152, 151.19, 150.2, 138, 135, 135.5, 134.59, 133.5, 129.79, 129.16, 123.88, 120.25.

Compound 8c; Yellow orange solid, Melting Point: 195-197°C, Yield(86%), 1H NMR (400 MHz, DMSO) δH (ppm): 2.3 (s, 3H), 8.25

(s, 1H), 8.12 (d, J= 8.8 Hz, 1H), 7.4 (t, J=7.8Hz, 1H), 7.9, (d, 8.8Hz, 1H), 8.4 (s, 1H), 7.9 (d, J = 7.6 Hz, 1H), 7.2 (d, J = 6.4Hz, 1H). 13C NMR (400 MHz, DMSO) δ(ppm): 13 (CH3), 169.5 (C=O), 152 (C=N), 151.9, 151.17, 150.1, 138, 135.4, 134.9, 134.57, 133.5, 129.78, 129, 123.8, 122.

4. Conclusion

The starting material, 2-methyl-7-nitro-4*H*-3,1-benzoxazin-4-one was prepared on refluxing 4- nitroanthranilic acid with acid anhydride. Differently substituted 2-Methyl-7-nitroquinazolin-4(3*H*)-one were derived from the condensation of 2-methyl-7-nitro-4*H*-3,1-benzoxazin-4-one with different anilines. Anilines selected were, 2,4-dinitroaniline, 2-nitroaniline, 3-nitroaniline, 4-nitroaniline, 4-chloroaniline and 4-bromoaniline. The prepared compounds were characterized by Elemental analysis and NMR spectral studies.

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