Synthesis and biological evaluation of some new benzoxaazinone and quinazolinone drivatives

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This work deals with the synthesis of benzoxazinone derivative in addition to studying their behavior towards some interesting nitrogen nucleophiles.The thesis consists of the following parts:Introduction:In this section brief literature review of the different methods of the synthesis and the reaction of 4H-3,1-benzoxazin-4-one .Result and discussion:This part focuses on the obtained results and discusses these results. The obtained results can be summarized as following:Synthesis of 6-iodo-2-methylbenzo[3,1]oxazin-4-one and its behavior towards some nitrogen nucleophiles:The 6-iodo-2-methyl-benzo[3,1]oxazin-4-one (2) was prepared by refluxing 5-iodoanthranilic acid (1) with acetic anhydride. The behavior of 6-iodo-2-methyl-benzo[3,1]oxazin-4-one (2) towards some nitrogen nucleophiles has been investigated. where, benzoxazinone 2 was submitted to react with formamide to produce 6-iodo-2-methyl-3H-quinazolin-4-one (3) which subjected to react with P2S5 and ethyl chloroacetate and yielded 6-iodo-2-methyl-3H-quinazoline-4-thione (4) and ethyl (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)acetate (5) respectively, where compound 5 was allowed to react hydrazine hydrate in boiling ethanol and afforded (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)acetic acid hydrazide (6).Also, -when benzoxazinone 2 was allowed to react with hydrazine hydrate and hydroxyl amine hydrochloride afforded 3-amino-6-iodo-2-methyl-3H-quinazolin-4-one (7) and 3-hydroxy-6-iodo-2-methyl-3H-quinazolin-4-one (8) respectively, while compound 8 also allowed to react with ethyl chloroacetate and furnished ethyl (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yloxy)acetate (9).Moreover, when compound 2 was subjected to react with different amines namely; ethyl amine -(aliphatic amine), benzyl amine (aralkyl amine), 4-chloroaniline, o phenylenediamine, sulphanilic acid (aromatic amines) 4-aminoantipyrine, 2-aminothiazole, 4-aminopyridine, 2-amino-6-methoxybenzothiazole and -2-amino-5,6-dimethylbenzimidazole(heteryl amine),it afforded 2-acetylamino-N ethyl-5-iodo-benzamide (10), 3-benzyl-6-iodo-2-methyl-3H-quinazolin-4-one (11), 3-(4-chlorophenyl)-6-iodo-2-methyl-3H-quinazolin-4-one (12a) , 3-(2-aminophenyl)-6-iodo-2-methyl-3H-quinazolin-4-one (12b), 4-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)benzenesulfonic acid(12c), 3-(1,5-dimet -hyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-6-iodo-2-methyl-3H quinazolin-4-one (13a), 6-iodo-2-methyl-3-thiazol-2-yl-3H-quinazolin-4-one (13b), 6-iodo-2-methyl-3-pyridin-4-yl-3H-quinazolin-4-one (13c), 6-iodo-3-(6-methoxybenzothiazol-2-yl)-2-methyl-3H-quinazolin-4-one (13d) and

3-(5,6-dimethyl-1H-benzoimidazol-2-yl)-6-iodo-2-methyl-3H-quinazolin-4-one (13e) respectively. Also reaction of 2 with ethanol amine yielded 3-(2-hydroxyethyl)-6-iodo-2-methyl-3H-quinazolin-4-one (14).Compound 2 was -subjected to react with series of amino acids namely, glycine, alanine, L-serine, DL valine and L-arginine it furnished (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)acetic acid (15a), 2-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)propionic acid (15b), 3-hydroxy-2-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)propionic acid (15c), 2-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)-3-methylbutyric acid (15d) and 5-guanidino-2-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)pentanoic acid (15e) -respectively. Also, reaction with sodium azide produced 5-iodo-2-(5-methyl tetrazol-1-yl)benzoic acid (16) and 1-acetyl-5-iodo-1,3-dihydrobenzoimidazol-2-one (17).Treatment of 2 with semicarbazide and thiosemicarbazide gave -(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)urea(18a)and(6-iodo-2-methyl-4-oxo-4H -quinazolin-3-yl)thiourea (18b) respectively.Behavior of 3-amino-6-iodo-2-methyl-3H quinazolin-4-one (7) towards carbon electrophiles:Refluxing quinazolinone (7) with -acetic acid anhydride resulted in forming N-(6-iodo-2-methyl-4-oxo-4H quinazolin-3-yl)acetamide (19). Also, compound 7 allowed to react with ethyl -chloroacetate in boiling ethanol it yielded 2-chloro-N-(6-iodo-2-methyl-4-oxo-4H quinazolin-3-yl)acetamide (20).Interaction of 7 with 4-chlorobenzalehyde in boiling -ethanol afforded 3-[(4-chlorobenzylidene)amino]-6-iodo-2-methyl-3H quinazolin-4-one (21). But, when the quinazolinone 7 was subjected to react with aldehydes namely, 2-naphthaldehyde, benzaldehyde, 4-chlorobenzaldehyde and 4-hydoxybenzaldehyde in boiling acetic acid and acetic anhydride it formed N-[6-iodo-2-(2-naphthalen-2-ylvinyl)-4-oxo-4H-quinazolin-3-yl]acetamide (22a), N-(6-iodo-4-oxo-2-styryl-4H-quinazolin-3-yl)acetamide (22b), N-{2-[2-(4-chlorophenyl)vinyl]-6-iodo-4-oxo-4H-quinazolin-3-yl}acetamide (22c) and 4-[2-(3-acetylamino-6-iodo-4-oxo-3,4-dihydro-quinazolin-2-yl)vinyl]-phenyl acetate -(22d), in similar way reaction with phthalic anhydride yielded N-[2-(1,3-dioxo indan-2-yl)-6-iodo-4-oxo-4H-quinazolin-3-yl]acetamide (23).When compound 7 was allowed to react with ethyl-3-methyl-5-(1,2,3,4-tetrahydroxybutyl)furan-2-carboxylate it afforded the quinazolinone derivative 24, condensation of compound 7 with aldohexoses namely, D-glucose and D-galactose in boiling acetic acid and acetic anhydride, it yielded -N-[6-iodo-4-oxo-2-(3,4,5,6,7-pentahydroxyhept-1-enyl)- 4H quinazolin-3-yl]acetamide(25a,b). As well as reaction of 7 with phthalimide in the -same condition gave N-[6-iodo-4-oxo-2-(3-oxo-2,3-dihydro isoindol-1-ylidenemethyl)-4H-quinazolin-3-yl]-acetamide(26).Behavior of (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)-acetic acid hydrazide (6) towards carbon electrophiles :The interaction of acetic acid hydrazide 6 with acetic anhydride -afforded 6-iodo-2-methyl-3-(5-methyl-[1,3,4]oxadiazol-2-ylmethyl)-3H quinazolin-4-one (27), also when it was allowed to react with ethyl acetoacetate in -boiling ethanol yielded 6-iodo-2-methyl-3-(2-(3-methyl-5-oxo-4,5-dihydro-1H pyrazol-1-yl)-2-oxoethyl)quinazolin-4(3H)-one (28).Also in this work, the reaction of compound 6 with acetylacetone, benzoylacetone and phenylisocyanate in boiling ethanol was performed and afforded 3-[2-(3,5-dimethyl-4,5-dihyDROPyrazol-1-yl)-2-oxo-ethyl]-6-iodo-2-methyl-3H-quinazolin-4-one (29a), 6-iodo-2-methyl-3-[2-(5-meth

yl-3-phenyl-4,5-dihyDROPyrazol-1-yl)-2-oxo-ethyl]-3H-quinazolin-4-one (29b) and -6-iodo-2-methyl-3-(5-phenyl-amino[1,3,4]- oxadiazol-2-ylmethyl)-3H quinazolin-4-one (30) respectively.Fusion of 6 with tatrabromophthalic anhydride -gave 2-(6-iodo-2-methyl-4-oxo-4H quinazolin-3-yl)-N-(4,5,6,7-tetrabromo-1,3-dioxo-1,3-dihydroisoindol-2-yl)acetamide (31). Also, compound 6 was allowed to react with ethyl-3-methyl-5-(1,2,3,4-tetrahydroxybutyl)furan-2-carboxylate in boiling ethanol to afford 2-methyl-5-(1,2,3,4-tetrahydroxybutyl)furan-3-carboxylic acid N'-[2-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)acetyl]-hydrazide (32).When the hydrazide 6 was submitted to react with carbon disulphide in absolute alcohol and -potassium hydroxide and produced potassium N(6-iodo-3,4-dihydro-2-methyl-4-oxoquinazolin-3-yl)acetyldithiocarbazinate (33) which also, allowed to react with hydrazine hydrate to yield 3-(4-amino-5-mercapto-4H-[1,2,4]triazol-3-ylmethyl)-6-iodo-2-methyl-3H-quinazolin-4-one (34). Also, reaction of 6 with mono saccharide such as D-glucose and D-galactose in boiling ethanol afforded the corresponding sugar hydrazone derivatives 35a-b.Finally, the condensation of acetic acid hydrazide 6 with aromatic aldehydes namely, benzaldehyde, 4-chlorobenzaldehyde, 4-hydroxy-benzaldehyde, 2,4-dihydroxybenzaldehyde, cinnamaldehyde and furfural, afforded the -corresponding condensation products (6-iodo-2-methyl-4-oxo-4H -quinazolin-3-yl)acetic acid benzylidenehydrazide (36a), (6-iodo-2-methyl-4-oxo-4H quinazolin-3-yl)acetic acid (4-chlorobenzylidene)hydrazide (36b), (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)acetic acid -(4-hydroxybenzylidene)hydrazide (36c), (6-iodo-2-methyl-4-oxo-4H quinazolin-3-yl)acetic acid (2,4-dihydroxy-benzylidene)hydrazide (36d), (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)-acetic acid (3-phenylallylidene)hydrazide (36e) and (6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)acetic acid furan-2-ylmethylenehydrazide (36f) respectively. A further proof for the structure 36a came from their reaction with acetic anhydride to give 3-(4-acetyl-5-phenyl-4,5-dihydro-[1,3,4]oxadiazol-2-ylmethyl)-6-iodo-2-methyl-3H-quinazolin-4-one (37). Also compound 36e was chemically proofed by their reaction with thioglycolic acid -afforded 2-(6-iodo-2-methyl-4-oxo-4H-quinazolin-3-yl)-N-(4-oxo-2-styryl thiazolidin-3-yl)acetamide (38).Experimental:In this part, the practical procedures used for the synthesis of the new compounds, in addition to their physical, spectral and microanalytical data are cited.Some of the synthesized compounds were screened for their antimicrobial activities against some selected bacteria and fungi, and it was found that, most of these compounds have remarkable biological activity.