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Synthesis and Some Reactions of 2-[α-benzoylamino-β-2-furyl-vinyl]-6, 8-Dibromobenzoxazin-4(3H)-one and 3-Amino Quinazolin-4 (3H)-One Derivatives

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2-[α-Benzoylamino-β-2-furyl vinyl]-6, 8-dibromo-benzoxazin-4 (3H)-one (II) was found to undergo ring opening reactions with different nitrogen nucleophiles to give (III) and (IV). Also, (II) underwent ring opening followed by ring closure reaction, upon treatment either with formamide at 200°C to give the quinazolinone derivative (V), or with hydrazine hydrate in boiling *n*-butanol to give the 3-amino quinazolinone derivative (VI) which was converted to the Shiff's bases (VII) upon condensation with some aromatic aldehydes. (II) reacted with hydrazoic acid affording the tetrazole (IX) and the benzimidazole (X). Furthermore, the reaction of (II) with benzene and anisole under the conditions of Friedel-Crafts reaction has been studied.

INTRODUCTION

Several 4 (3H)-quinazolone as well as quinazolinone derivatives were reported to have antihypertensive[1], choleretic, antifibrilatory and anti-phlogistic[2], hypotensive, antiadrenergic and antihistaminic[3], and hypnotic, sedative and anticonvulsant activities[4]. In continuation to earlier work on on 4(3H)-quinazolinones and their medicinal applicability, it was interesting to synthesize some new benzoxazinone and quinazolinone derivatives bearing a bulky moiety at position 2, with the aim of studying the stability of benzoxazinone nucleus and its behaviour towards some nucleophiles[5].

RESULTS AND DISCUSSION

The benzoxazinone (II) was prepared from 2-[α-benzoylamino-β-2-furyl acrylamido]-3, 5-dibromobenzoic acid) (I) which was obtained in a good yields, via treatment of a solution of dibromoanthranilic acid (0.01 mol.) in pyridine, with equimolar amount of 4-furfurylidene-2-phenyl oxazole-5-one. Treatment of the acid (I) with acetic anhydride afforded the benzoxazinone (II)[6].

The benzoxazinone (II) was found to undergo ring opening reactions with phenyl hydrazine, 1° and 2° amines in refluxing ethanol to give (III) and (IV) respectively. Under some vigorous conditions, compound (II) underwent ring opening followed by ring closure, so heating of (II) with formamide at 200°C, afforded 2-[α-benzoylamino-β-2-furyl-vinyl]-6, 8-dibromo-quinazolin-4 (3H)-one (V), whose IR—spectral data (Table 1) revealed that (V) actually exists in the (Lactam ⇌ Lactim) tautomeric

TABLE 1

CHARACTERIZATION DATA OF VARIOUS COMPOUNDS PREPARED

Compound and yield %	M.p.°C and solvent	Molecular formula and M.W.	Analysis (Required/Found)				I.R. (cm^{-1})		
			C	H	N	Br	$\nu_{NH, OH}$	$\nu_{C=O}$	$\nu_{C=N}$
I	212–14	$C_{21}H_{14}N_2Br_2O_5$	47.19	2.62	5.24	29.96	3450–3340	1705–1650	—
79	Ethanol	(534)	47.30	2.80	5.33	30.17			
II	137–39	$C_{21}H_{12}N_2Br_2O_4$	48.83	2.33	5.43	31.01	3340–3150	1735–1628	1592
85	L.p. 90–100	(516)	49.21	2.52	5.61	31.20	(broad)		
IIIa	132–34	$C_{22}H_{17}N_3Br_2O_4$	48.26	3.11	7.68	29.25	3400–3220	1655–1620	—
61	L.p. 100–120	(547)	48.51	3.26	7.92	29.40	(broad)		
IIIb	159–61	$C_{28}H_{21}N_3Br_2O_4$	53.93	3.37	6.74		3400–3240	1648–1615	—
75	Benzene	(623)	54.20	3.61	6.93				
IIIc	205–7	$C_{27}H_{19}N_3Br_2O_4$	53.20	3.12	6.90	26.27	3400–3260	1658–1622	—
63	Ethanol	(609)	53.41	3.25	7.11	26.39			
IIId	238–40	$C_{27}H_{20}N_4Br_2O_4$	51.92	3.21	8.97		3400–3220	1660–1620	—
69	Ethanol	(624)	52.21	3.42	9.02				
IVa	157–59	$C_{25}H_{21}N_3Br_2O_5$	49.75	3.48	6.97	26.53	3320	1698–1655	—
76	L.p. 100–120	(603)	49.92	3.61	7.14	26.75			
IVb	115–17	$C_{26}H_{23}N_3Br_2O_4$	53.41	3.83	6.99		3310	1652–1605	—
81	L.p. 80–100	(601)	53.69	4.02	7.13				
V	>260	$C_{21}H_{13}N_3Br_2O_5$	48.93	2.52	8.16		3400–3160	1665–1605	1590
36	Acetic acid	(515)	49.20	2.71	8.34		(broad)		

VI	225–27	$C_{21}H_{14}N_4Br_2O_3$	47.55	2.64	10.57	30.19	3260–3190	1652–1695	1590
88	Ethanol	(530)	47.72	2.79	10.72	30.41			
VII	149–51	$C_{23}H_{16}N_4Br_2O_4$	48.25	2.80	9.79		(broad)	1722–1698	1600
66	Benzene	(572)	48.41	2.93	9.92				
VIIIa	199–201	$C_{28}H_{18}N_4Br_2O_3$	54.37	2.91	9.06	25.89	(broad)	1653	1578
56	Ethanol	(618)	54.48	3.11	9.23	26.10			
VIIIb	232–34	$C_{29}H_{20}N_4Br_2O_4$	53.70	3.09	8.64		(broad)	1660	1586
41	Ethanol	(648)	53.98	3.20	8.81				
VIIIc	120–122	$C_{28}H_{17}N_4Br_2ClO_3$	51.49	2.61	8.58	24.52		1686–1654	1580
49	L.p. 100–120	(652.5)	51.72	2.75	8.63	24.71			
VIIId	131–33	$C_{28}H_{17}N_5Br_2O_5$	50.68	2.56	10.56			1692–1650	1576
33	L.p. 80–100	(663)	50.91	2.70	10.72				
IX	191–93	$C_{21}H_{13}N_5Br_2O_4$	45.08	2.33	12.52	28.62	3290	1765–1655	
35	Ethanol	(559)	45.23	2.55	12.76	28.81			
X	243–45	$C_{21}H_{13}N_3Br_2O_4$	47.46	2.45	7.91	30.13	3328	1655–1640	—
56	Ethanol	(531)	47.62	2.49	8.11	30.20			
XIa	212–14	$C_{27}H_{18}N_2Br_2O_4$	54.55	3.03	4.71	26.94	3240	1683–1650	—
61	Ethanol	(594)	54.71	3.18	4.91	27.23			
XIb	205–7	$C_{28}H_{20}N_2Br_2O_5$	53.85	3.21	4.49		3245	1698–1660	—
56	Benzene	(624)	54.13	3.30	4.66				
XII	199–201	$C_{25}H_{15}N_2Br_2O_8$	47.54	2.38	4.44	25.56	3340–3220	1698–1650	—
43	Ethanol	(631)	47.68	2.41	4.59	25.51	(broad)		

equilibrium, also, hydrazinolysis of (II) with hydrazine hydrate in refluxing *n*-butanol gave 3-amino 2-[α-benzoylamino-β-2-furyl vinyl]-6, 8-dibromo-4 (3H) quinazolinone (VI), which upon acylation with acetic anhydride gave (VII). As expected condensation of 3-aminoquinazolinone (VI) with aromatic aldehydes, namely, benzaldehyde, *p*-anisaldehyde, *p*-chlorobenzaldehyde and/or *p*-nitrobenzaldehyde in presence of piperidine as a general catalytic base in refluxing ethanol, afforded the Shiff's bases (VIIIa–d). Reactions of (II) with hydrazoic acid[7] (sodium azide in acetic acid) gave a mixture of the tetrazole derivative (IX) and the benzimidazolone derivative (X) which are formed through nucleophilic attack at positions 2 and 4, respectively.

On the other hand, the benzoxazinone (II) was found to react with aromatic hydrocarbons such as benzene and anisole in presence of anhydrous aluminium chloride under the conditions of Friedel-Craft's reaction to give 2-[α-benzoyl amino-β-2-furyl acrylamido-]-3, 5-dibromoaroyl benzene (XIa, b). Furthermore, reaction of (II) with maleic anhydride in boiling xylene afforded the Diel's Alder adduct (XII).

The presence of bulky group in position 2 decreased the yield of the products in the above reaction as a result of steric hindrance[8].

EXPERIMENTAL

IR-spectra were recorded in KBr on a Beckmann infrared spectrophotometer (ν_{max} in cm^{-1}). All melting points are uncorrected. Characterization data of all the compounds prepared are given in Table (1).

Formation of 2-[α-benzylamino-β-2-furylacrylamido]-3,5-dibromobenzoic acid (1)

A solution of dibromo anthranilic acid (0.01 mole) in pyridine (30 ml) was added to 4-furfurylidene 2-phenyl oxazole-5-one (0, 01 mole). The reaction mixture was shaken for 1 hr. and stirred in cold water. The solid obtained was crystallized from the suitable solvent to give (I).

Formation of 2-[α-benzoylamino-β-2-furyl vinyl]-6, 8-dibromobenzoxazin-4[3H]-one (II)

A mixture of (I) (0.01 mole) and acetic anhydride (20 ml) was refluxed for 1 hr. The solution was then left to evaporate slowly in a porcelain dish. The solid product was treated with the proper solvent to give (II). Acidic hydrolysis of II afforded anthranilic acid (I)

Formation of (IIIa-d) & IVa, b

A solution of compound (II) (0.01 mole) and amines namely methylamine, benzylamine and aniline, also phenylhydrazine, piperidine or

morpholine (0.01 mole) in 30 ml of ethyl alcohol was refluxed for 3 hrs. The product that separated on cooling was crystallized from the suitable solvent, to give IIIa-d and IVa, b, respectively.

Formation of (V)

A mixture of (II) (0.01 mole) and formamide (0.015 mole) was heated at 200°C for 3 hrs. The product obtained was washed with water and then crystallized from the suitable solvent to give (V).

Formation of 3-amino-2-[α-benzoylamine β-2-furyl vinyl]-6,8-dibromo-4(3H)-quinazolin-4-one (VI)

A solution of (II) (0.01 mole) and hydrazine hydrate (0.01 mole) in 50 ml of *n*-butyl alcohol was heated under reflux for 3 hrs. The solid that separated on cooling was crystallized from the proper solvent to give (VI).

Formation of 3-acetylamino-2-[α-benzoylamino-β-2-furyl-vinyl]-6,8-dibromo-4-(3H)-quinazolin-4-one (VII)

Compound (VI) (0.01 mole) was refluxed with an excess of acetic anhydride for 6 hrs. The reaction mixture was then left to evaporate slowly. The solid product was crystallized from suitable solvent to give (VII).

Formation of the Schiff's bases (VIIIa-d)

A solution of (VI) (0.01 mole) and the aromatic aldehydes namely, benzaldehyde, *p*-anisaldehyde, *p*-chlorobenzaldehyde, and *p*-nitrobenzaldehyde in 50 ml ethyl alcohol containing few drops of piperidine was heated under reflux for 4 hrs. The solid that separated on cooling was crystallized from the suitable solvent to give the Schiff's bases (VIIIa-d).

Formation of (IX) and (X)

A mixture of (II) (0.01 mole) in glacial acetic acid (5 ml) was treated with a solution of sodium azide (0.015 mole) in the minimum amount of water. The mixture was heated on a steam bath for 4 hrs. The solid separated was filtered and crystallized from ethanol to give (X). The filtrate was diluted with water to give (IX) which was crystallized from the same solvent.

Formation of 2-[α-benzoylamino β-2-furyl acrylamido]-3,5-dibromo aryl ketone (IXa and b)

A mixture of (II) (0.01 mole) in the dry hydrocarbon (benzene or anisole) (100 ml) was added gradually to a cold suspension of anhydrous aluminium chloride (0.04 mole) in a large excess of the same hydrocarbon. The temperature of the mixture was not allowed to rise above 60°C. The suspension was stirred for 10 hrs at 60°C and than poured into ice-cold

hydrochloric acid mixture. The solid obtained was crystallized from the suitable solvent to give (XIa, b).

Formation of adduct (XII)

A solution of (II) (0.01 mole) and maleic anhydride (0.1 mole) in 50 ml of dry xylene was refluxed for 20 hrs., after concentration and cooling, the reaction product that separated was crystallized from the proper solvent to give (XII).

Reaction of (II) with maleic anhydride : Formation of adduct (XII)

A solution of (II) (0.01 mole) and maleic anhydride (0.1 mole) in 50 ml of dry xylene was refluxed for 20 hrs., after concentration and cooling, the reaction product separated and crystallised from the proper solvent to give (XII).

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