Reactivity of 4*H*-3,1-benzoxazin-4-ones towards nitrogen and carbon nucleophilic reagents: applications to the synthesis of new heterocycles

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(received 18 Nov 03; accepted 16 Mar 04; published on the web 19 Mar 04)

Abstract

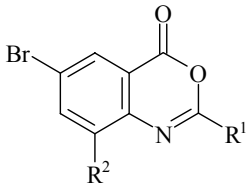
6,8-Dibromo-(4*H*)-3,1-benzoxazinone **1a** was synthesized and allowed to react with some nitrogen nucleophiles namely, hydroxylamine hydrochloride, 4-aminoacetophenone, *o*-phenylenediamine, sulfanilamide, sulfamethoxazole, semicarbazide hydrochloride and ethanolamine to afford 3-substituted-4(3*H*)-quinazolinones **2-8, 10-12** and triazolo[2,3-c]quinazoline **9**. 6-Bromo(4*H*)-3,1-benzoxazin-4-one **1b** was also synthesized and converted into 3-amino-4(3*H*) quinazolinone **13** by reaction with hydrazine hydrate. The latter product was utilized to construct new heterocyclic systems namely, triazino[2,3-c] quinazoline **14** and the thiazole derivative **16**. An interesting heterocyclic transformation occurred on treatment of benzoxazinone **1a** with malononitrile in presence of sodium ethoxide to give quinoline derivative **18** which reacted with phenyl isocyanate to yield oxazinoquinoline **19**. The reaction of benzoxazinone **1a** with Grignard' reagents afforded unexpected products **20** and **21** whereas Friedel-Crafts reaction of the same oxazinone with some aromatic hydrocarbons namely, benzene, ethylbenzene, *m*- and *p*-xylenes afforded either two benzophenone derivatives **20** and **22** or **23** and **24** in case of less bulky hydrocarbons i.e., benzene and ethylbenzene or only one product **25** and **26** in case of more bulky *m*- and *p*-xylenes. Oxazinone ring cleavage occurred when barbituric and/or thiobarbituric acid reacted with benzoxazinone **1a** in refluxing pyridine to give the corresponding 5-arylidene derivatives **27a,b**.

Keywords: Benzoxazinones, quinazolinones, cyanoquinoline

Introduction

The present work is in conjunction with our ongoing programme on the utilizing of readily obtainable starting materials for the synthesis of heterocyclic systems. [1-7] One of the most important features in (4*H*)-3,1-benzoxazinones chemistry is their use as key starting materials for

further transformations. They are indeed useful intermediates in organic synthesis affording through reaction with nitrogen nucleophiles 4(3*H*)quinazolinones. With the aim of extending information on the reactivity of 4*H*-3,1-benzoxazinones and also synthesizing from them new heterocyclic systems, potentially with biological activity [8-12] and in continuation of our work on the behaviour of stable benzoxazinones[13] towards nitrogen and carbon nucleophiles, other derivatives were obtained *via* the interaction of acetic anhydride and/or isobutyroyl chloride with anthranilic acid derivatives. The electronically unsaturated character of unstable benzoxazinones which are (4*H*)-3,1-benzoxazinones bearing saturated substituents such as CH_3, CH_2COCH_3, CH_2CN and $CH_2CH_2CO_2H$ at position 2 [14-17] renders their synthesis difficult because they are not satisfactorily stable rings. Our contribution to solve this problem includes the construction of bulky substituents involving strong conjugation power to obtain stable benzoxazinones. [13,18] Herein, we report the synthesis of 2-substituted (4*H*)-3,1-benzoxazinones **1a** and **b** *via* the reaction of freshly distilled acetic anhydride [19] and/or isobutyroyl chloride in dry pyridine [20] with 3,5-dibromo-, or 3-bromoanthranilic acids respectively.

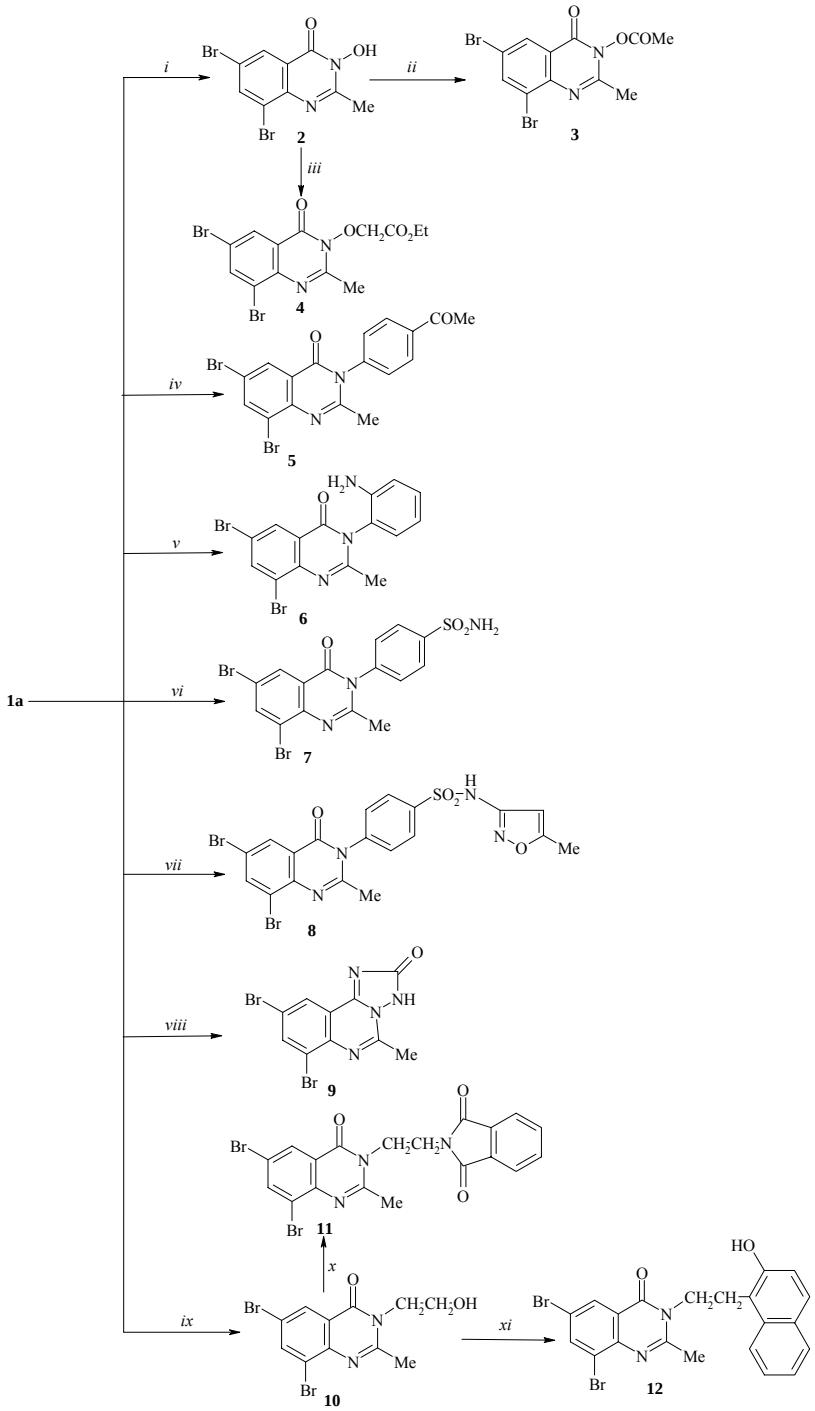


1 a, R^1 = Me, R^2 = Br; **b**, R^1 = pr^{iso}, R^2 = H

Results and Discussion

With the aim of expanding the synthetic potential of the (4*H*) 3,1-benzoxazinones formed, we have studied the reaction of **1a** with hydroxylamine hydrochloride. This is a simple and convenient route to the synthesis of 3-hydroxy-4(3*H*)-quinazolinone **2** which is a promising intermediate for diverse organic synthesis [Scheme 1]. Thus reactions of the latter compound with acetic anhydride and ethyl chloroacetate afforded 3-acetoxy- and 3-ethoxycarbonylmethoxy-4(3*H*)-quinazolin-ones **3** and **4** respectively. Aminolysis of benzoxazinone **1a** occurred when it was treated with 4-aminoacetophenone to yield 3-(4-acetophenyl)-4(3*H*)-quinazolinone **5** *via* heteroring opening followed by ring closure. [21]

A variety of 2,3-disubstituted 4(3*H*)-quinazolinones containing a heterocyclic group in position 3 have been prepared from the reaction of 2-methyl and 2-phenyl-(4*H*)-3,1-benzoxazinones with different heterocycles containing the amino functionality. [22] Various quinazolinone dyes have been synthesized from coupling diazotized aminoquinazolinone with various coupling components and their dyeing effect on viscose rayon, silk and wool fibers has been assessed. [23] The forementioned findings prompted the author to carry out the reaction of **1a** with *o*-phenylenediamine to obtain 3-(2-aminophenyl)-4(3*H*)-quinazolinone **6** which could be diazotized and coupled.

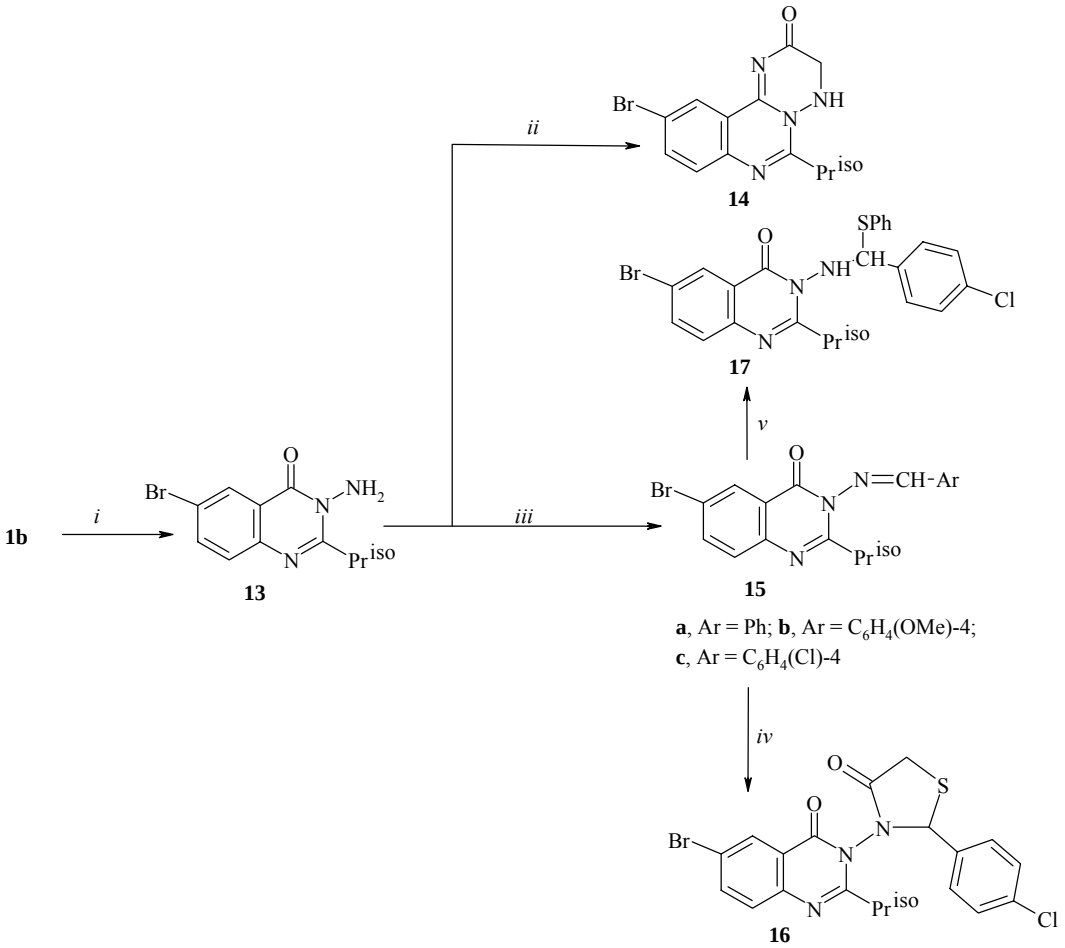


Scheme 1. Reagents and reaction conditions: (i) $NH_2OH.HCl$, pyridine, 115°C; (ii) Ac_2O, 140°C; (iii) $ClCH_2CO_2Et$, anhydrous K_2CO_3, dry acetone, 56°C; (iv) $NH_2.C_6H_4.COMe$ (1,4), EtOH, 78°C; (v) $C_6H_4(NH_2)_2$-1,2, AcOH, 116°C; (vi) sulfanilamide, dry pyridine, 115°C; (vii) sulfamethoxazole, dry pyridine, 115°C; (viii) $H_2NCONHNH_2.HCl$, dry pyridine, 115°C; (ix) $H_2NCH_2CH_2OH$, 170°C; (x) phthalimide, conc. HCl, fusion; (xi) 2-naphthol, conc. HCl, fusion.

It is of interest to compare the previous result with the cyclocondensation of 2-aryl-(4*H*)-3,1-benzoxazinones with *o*-phenylenediamine to give benzoimidazoquinazolines if the reaction is conducted in orthophosphoric acid at reflux temperature.[24] Sulfanilamide and its derivatives have great antibacterial power and are widely used in medicine against "cocci infections". Consequently, we have tried to expand the applicability of sulfanilamides, and herein we report the synthesis of novel heterocycles of anticipated biological activity containing quinazolinone moiety incorporated sulfa drug residue. Thus, treatment of 4*H*-3,1-benzoxazinone **1a** with sulfanilamide and/or sulfamethoxazole afforded 2,3-disubstituted 4(3*H*)-quinazolinones **7** and **8** respectively.[13,25] Successful attempt to construct a third heterocyclic ring condensed with quinazoline was achieved *via* reaction of **1a** with semicarboazide hydrochloride in refluxing dry pyridine to give triazolo[2,3-c]quinazoline **9**. Reaction of (4*H*)-3,1-benzoxazin-4-one **1a** with ethanolamine at refluxing temperature resulted in the hydroxyethylquinazolinone **10** which was utilized to alkylate some aromatic systems namely, phthalimide and 2-naphthol in acidic media to afford the respective quinazolinones **11** and **12**.

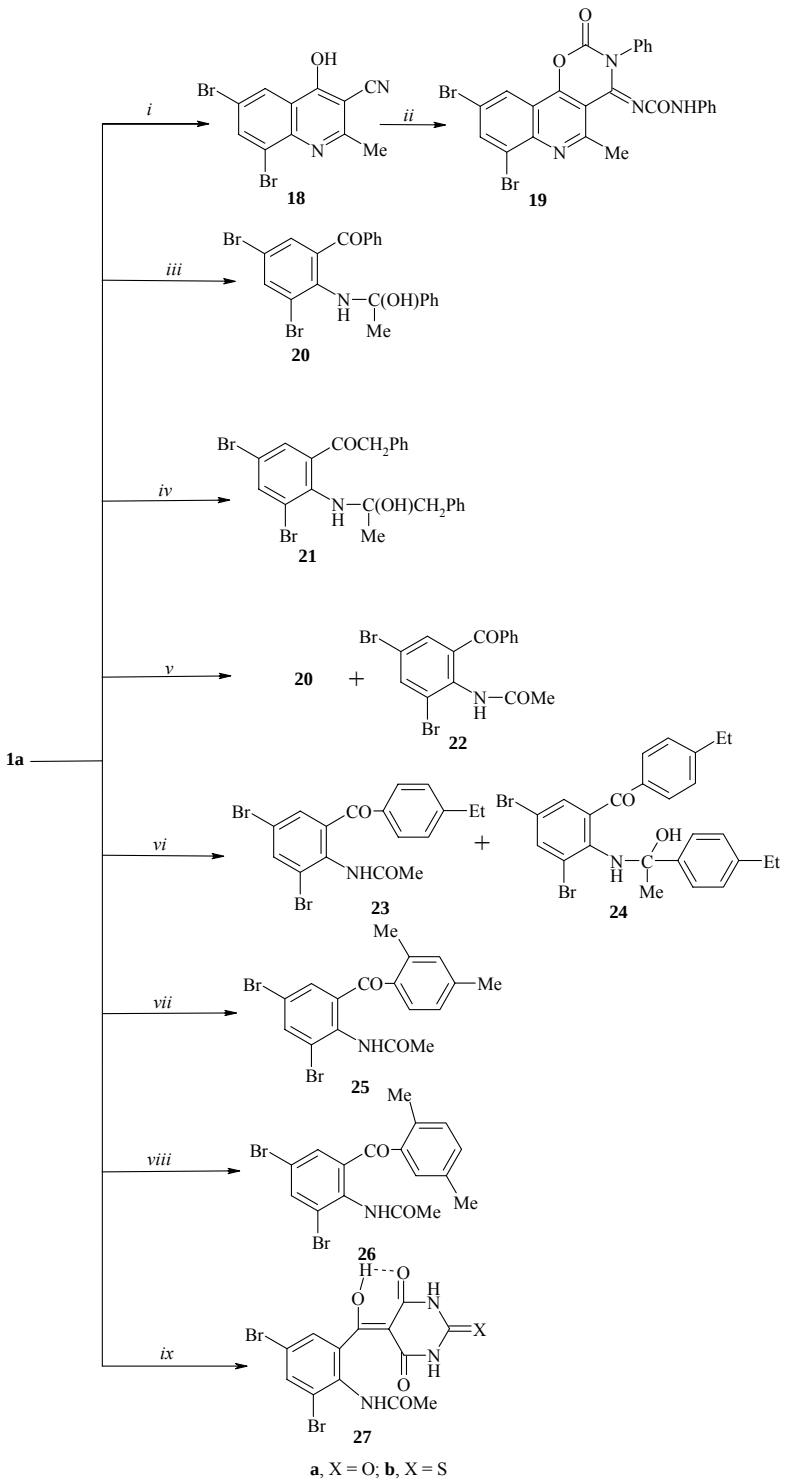
According to our previous works, the reaction of hydrazine hydrate with 2-substituted 4*H*-3,1-benzoxazinones results in the formation of 3-aminoquinazolinone derivatives when the substituent at position-2 is bulky[13] or when the reaction is carried out in presence of anhydrous zinc chloride.[6] Thus, when 4*H*-3,1-benzoxazinone **1b** was allowed to react with hydrazine hydrate in boiling ethanol, it yielded the respective 3-amino-4(3*H*)-quinazolinone **13** and this agreed well with our reported finding [cf. Scheme 2]. 3-Aminoquinazolinone **13** could be used as versatile building blocks in the synthesis of new heterocyclic systems. Thus, the amino functionality of 3-amino-4(3*H*)-quinazolinone reacts with carbon electrophiles namely, chloroacetamide and aromatic aldehydes *viz* benzaldehdye, 4-methoxy-benzaldehyde and 4-chlorobenzaldehyde to afford triazino[2,3-c]quinazoline **14** and 3-arylideneamino-4(3*H*)-quinazolinones **15a-c** respectively. The former compound was formed through 3-carbamoylmethylamino-4(3*H*)-quinazolinone intermediate followed by ring closure, whereas the latter was formed by nucleophilic attack of the amino group on the electronically deficient carbonyl carbon atom of the aldehyde followed by dehydration, a process in which the driving force of removing the bad leaving hydroxyl group is the conjugation with the aromatic nucleus in the more thermodynamically stable compound **15a-c**. It is of interest to investigate the behaviour of azomethines **15a-c** which contain an activated C=N bond towards aliphatic and aromatic mercaptans. Cyclocondensation of **15c** with 2-mercaptoacetic acid in the presence of few drops of piperidine gave the thiazolidin-4-one derivative **16**.[26]

The reaction proceeded *via* nucleophilic addition of sulfur to C=N followed by cyclization and a thiazole nucleus attached to N3 of quinazolinone derivative **16** was obtained. On the other hand, when azomethine **15c** was allowed to react with thiophenol in the presence of piperidine as a basic catalyst, the adduct **17** was isolated.[27]



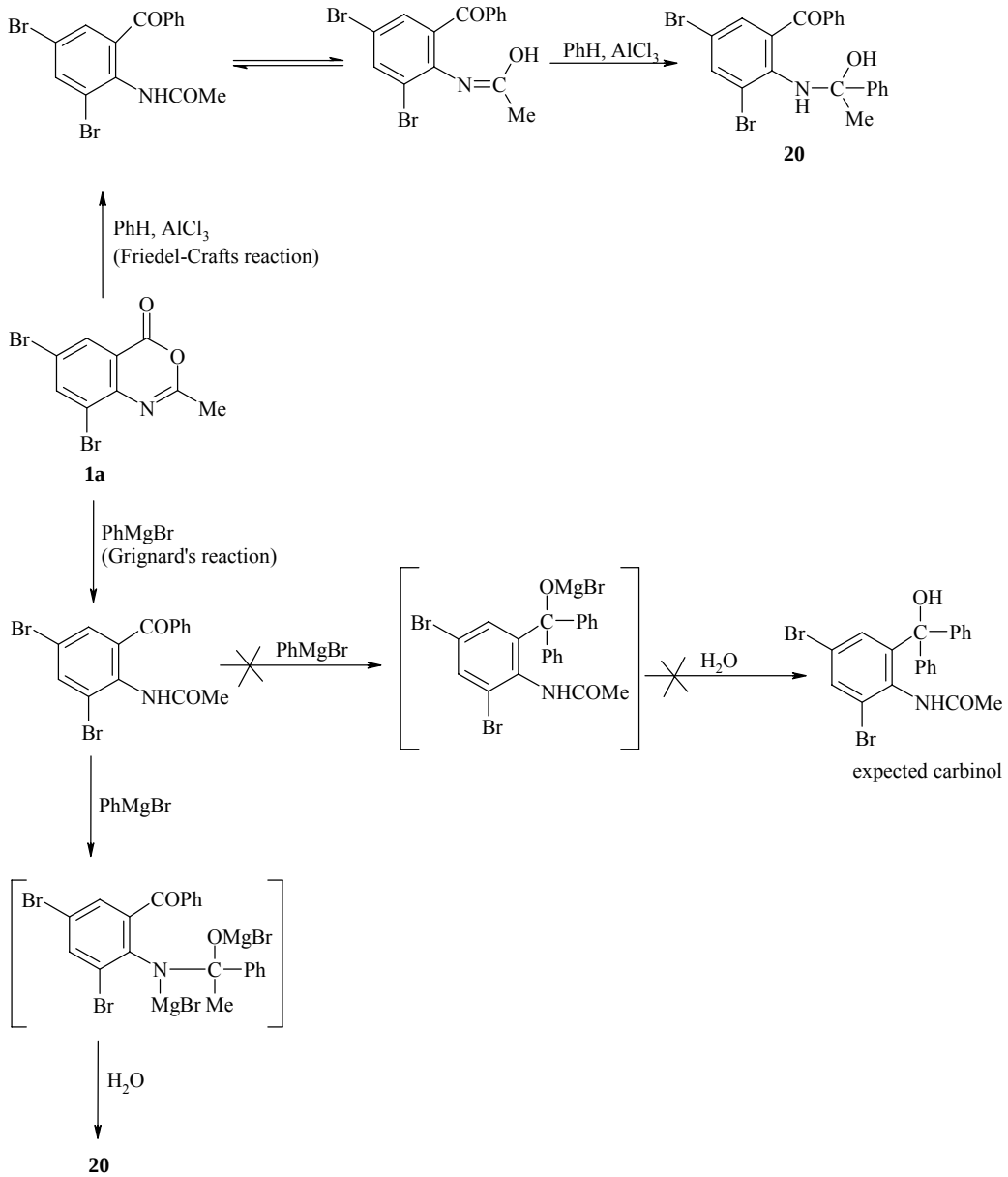
Scheme 2. Reagents and reaction conditions: (i) $N_2H_4.H_2O$, EtOH, 78°C; (ii) $ClCH_2CONH_2$, fusion; (iii) ArCHO, EtOH, 78°C; (iv) $HSCH_2CO_2H$, piperidine, steam bath; (v) PhSH, dry benzene, 80°C.

It has been reported that 2-phenyl-(4*H*)-3,1-benzoxazin-4-one underwent base-catalyzed ring opening with active methylene containing compounds e.g., ethyl acetoacetate, diethylmalonate and ethyl cyanoacetate in refluxing pyridine to afford ethyl *o*-benzamidobenzoylacetate.[28] In the present work, it has been found that hitherto unknown reaction of malononitrile with benzoxazinone **1a** in presence of ethanolic sodium ethoxide resulted in 4-hydroxy-3-cyanoquinoline derivative **18** [cf. Scheme 3]. The *o*-hydroxynitrile **18** could be versatile in the synthesis of fused heterocycles utilizing its bifunctionality. Thus, when compound **18** reacted with phenyl isocyanate in the presence of triethylamine in refluxing benzene, it gave the oxazino[5,6-c] quinoline **19**. On the other hand, it has been reported that 2-substituted (4*H*)-3,1-benzoxazin-4-ones reacted with Grignard reagents affording either tertiary carbinols through addition of two molecules of the reagent on the carbonyl carbon with the cleavage of oxazinone moiety or 4,4-disubstituted benzoxazines through dehydration of the first formed carbinol.[13, 29-33] Thus, reaction of oxazinone **1a** with ethereal solution of phenylmagnesium bromide and/or benzylmagnesium bromide yielded the unexpected carbinols **20** and **21** respectively.



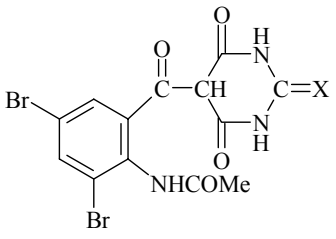
Scheme 3. Reagents and reaction conditions: (i) $CH_2(CN)_2$, EtONa, steam bath; (ii) PhNCO, Et_3N, fusion; (iii) PhMgBr, Et_2O, 25°C; (iv) $PhCH_2MgBr$, Et_2O, 25°C; (v) dry benzene, anhydrous $AlCl_3$, steam bath; (vi) C_6H_5Et, anhydrous $AlCl_3$, steam bath; (vii) dry *m*-xylene, anhydrous $AlCl_3$, steam bath; (viii) dry *p*-xylene, anhydrous $AlCl_3$, steam bath; (ix) barbituric acid and/or thiobarbituric acid, pyridine, 115°C.

The reaction proceeded through attack of the Grignard's reagent on the carbonyl group of the oxazinone nucleus to give the *o*-acetamidobenzophenone or *o*-acetamidoacetophenone intermediate which was attacked by another molecule of the reagent to afford the corresponding carbinol. The isolation of one and the same product from two different routes; reaction of benzoxazinone **1a** with phenylmagnesium bromide and/or dry benzene in presence of anhydrous aluminium chloride led us to assume that the addition of the second Grignard's molecule occurred at the carbonyl functionality adjacent to N-Mg bond [cf. Scheme 4].

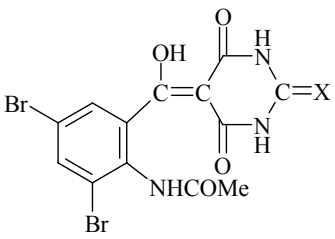


Scheme 4

The behavior of 2-methyl-(4*H*)-3,1-benzoxazin-4-one **1a** towards aromatic hydrocarbons namely, benzene, ethylbenzene, *m*- and *p*-xylenes under Friedel-Crafts reaction conditions was also studied. The present study revealed that the less bulky hydrocarbons *viz* benzene and ethylbenzene afforded two simultaneous products. The first is obtained due to attack of the acylating agent upon one molecule of the substrate hydrocarbon to give the respective benzophenone derivative **22** and **23** and the second resulted from the reaction of the acylating agent with two molecules of the hydrocarbon to afford the carbinols **20** and **24** respectively. When the reaction is carried out with more bulky hydrocarbons *viz m*- and *p*-xylenes, a sole product was isolated which was identified as the 2-acetamidobenzophenone derivatives **25** and **26**. According to our speculation, the formation of one product in case of more bulk hydrocarbons is due to the bulk of the substrate hydrocarbon. Finally, when (4*H*)-3,1-benzoxazin-4-one **1a**, was allowed to react with barbituric and/or thiobarbituric acids in refluxing pyridine, 5-arylidene-barbituric and thiobarbituric acids **27a** and **b** were obtained through fission of oxazinone nucleus. The product **27** was obtained from heteroring opening of the oxazinone nucleus followed by enolization. This seems to be reasonable owing to compound **27** is being thermodynamically stable *via* cinnamoyl resonance and hydrogen-bonding as well, while the keto form of compound **27** stabilizes by benzoyl resonance (stabilization by cinnamoyl resonance is higher than benzoyl resonance).



Keto form



Enol form

Experimental Section

General Procedures. All melting points reported are uncorrected and were determined on a Stuart electric melting point apparatus. The IR spectra were measured on a Unicam 1200 Spectrophotometer using potassium bromide Wafer technique. Mass spectra were measured on Shimadzu GC-MS-QP 1000 EX instrument operating at 70 eV. The values of m/z of the fragments are written followed by (I_r / %) percentage of relative intensity. The ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 solutions on Varian Gemini 200 MHz instrument.[34,35] TMS was used as internal standard with chemical shifts δ from downfield to upfield. TLC were performed on ready-to-use silica gel plates Merck 60. Satisfactory results were obtained for elemental analysis in Institut für Organische Chemie, Tubingen University, Tubingen, Germany: C ± 0.41%, H ± 0.29%, N ± 0.32%. Physical characteristics of the

synthesized compounds are given in Table 1. ^{13}C-NMR spectra of some synthesized compounds are listed in Table 2.

Table 1. Physical characteristics of synthesized compounds

Compound	mp/ºC	Solvent	Yield %	Colour
2	250-252	B[a]	75	White
3	190	LP_3	58	White
4	160	LP_3	85	White
5	190-192	B	72	Pale Yellow
6	230-232	E	70	Beige
7	>320	T	89	Beige
8	244-246	E	83	Beige
9	227-229	T	56	Beige
10	164	B	68	White
11	210	T	78	Pale Yellow
12	112	LP_3	70	Pale Yellow
13	120	LP_2	79	White
14	164	B	64	Yellow
15a	102	LP_2	74	Yellow
15b	154	B	65	Yellow
15c	170	B	77	White
16	124	B	80	Yellow
17	220	B	70	Yellow
18	286-288	M	60	Pale Yellow
19	240-242	E	52	Pale Yellow
20	215	LP_2-B	78	Beige
21	122-124	B	82	White
22	119-120	LP_2	60	Pale Yellow
23	134-136	LP_1	63	White
24	194-196	B	35	White
25	130-132	LP_2	88	Beige
26	158	LP_2	68	Beige
27a	300-302	M	66	Beige
27b	290-292	A	59	Beige

[a] B = benzene; LP_1 = light petroleum 40-60°C; LP_2 = light petroleum 60-80°C; LP_3 = light petroleum 80-100°C; E = ethanol; T = toluene; M = methanol; A = acetic acid.

Table 2. ^{13}C-NMR of some synthesized compounds

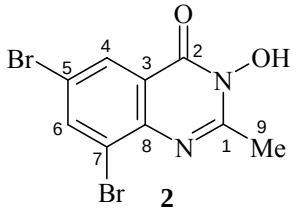
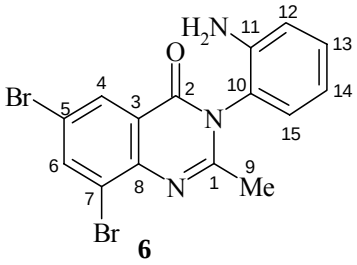
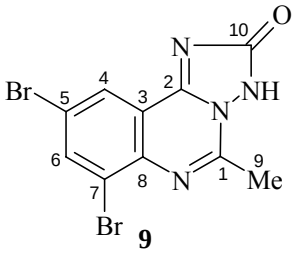
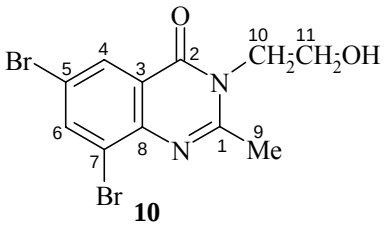
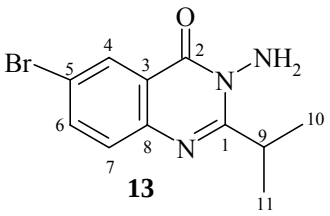
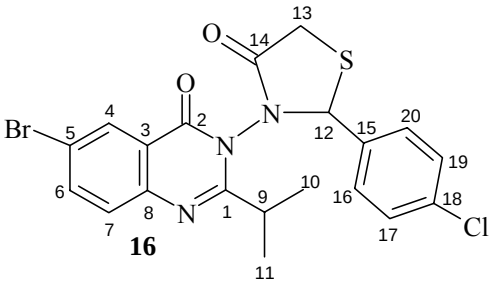
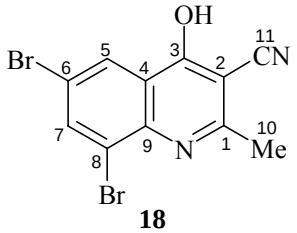
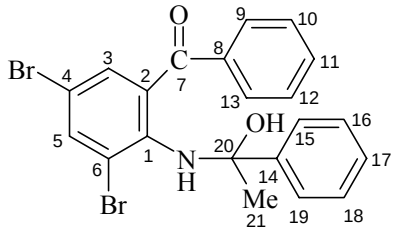
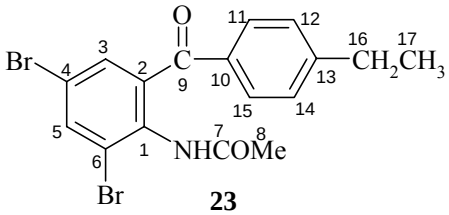
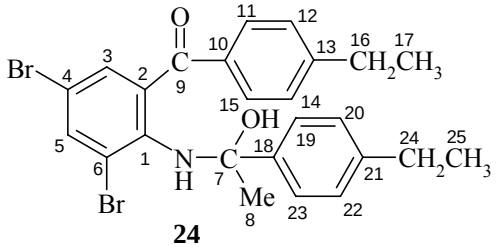
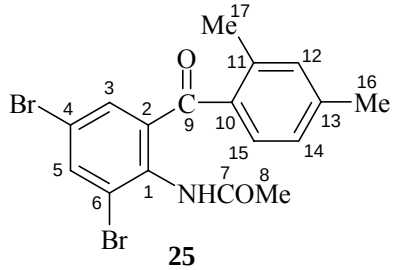
Structural Formula and Compound No.	δ (ppm) Carbon Atom No.
 **2**	163.2 (C-1), 162.3 (C-2), 131.1 (C-3), 130.7 (C-4), 123.5 (C-5), 139.4 (C-6), 118.7 (C-7), 149.8 (C-8), 11.1 (C-9)
 **6**	163.0 (C-1), 164.7 (C-3), 132.4 (C-3), 130.4 (C-4), 123.3 (C-5), 137.1 (C-6), 118.1 (C-7), 149.5 (C-8), 14.7 (C-9), 127.3 (C-10), 138.4 (C-11), 115.1 (C-12), 124.6 (C-13), 118.5 (C-14), 121.1 (C-15)
 **9**	163.6 (C-1), 158.3 (C-2), 135.0 (C-3), 132.4 (C-4), 123.8 (C-5), 138.3 (C-6), 118.5 (C-7), 151.7 (C-8), 12.6 (C-9), 161.4 (C-10).
 **10**	163.7 (C-1), 167.8 (C-2), 132.1 (C-3), 130.2 (C-4), 123.1 (C-5), 137.0 (C-6), 118.3 (C-7), 149.5 (C-8), 15.1 (C-9), 43.8 (C-10), 62.1 (C-11)
 **13**	163.5 (C-1), 167.1 (C-2), 129.2 (C-3), 131.7 (C-4), 121.5 (C-5), 136.7 (C-6), 124.3 (C-7), 146.4 (C-8), 23.0 (C-9), 13.4 (C-10), 13.6 (C-11).
 **16**	163.1 (C-1), 166.9 (C-2), 129.2 (C-3), 131.8 (C-4), 121.5 (C-5), 136.1 (C-6), 124.0 (C-7), 146.2 (C-8), 23.1 (C-9), 13.4 (C-10), 13.4 (C-11), 63.1 (C-12), 38.3 (C-13), 168.3 (C-14), 136.0 (C-15), 130.1 (C-16), 128.4 (C-17), 132.1 (C-18), 128.4 (C-19), 130.1 (C-20).

Table 2. Continued

Structural Formula and Compound No.	δ (ppm) Carbon Atom No.
 **18**	164.8 (C-1), 95.2 (C-2), 167.1 (C-3), 111.2 (C-4), 121.9 (C-5), 120.7 (C-6), 138.9 (C-7), 124.1 (C-8), 152.0 (C-9), 17.6 (C-10), 117.5 (C-11)
 **20**	146.5 (C-1), 121.9 (C-2), 132.3 (C-3), 113.5 (C-4), 139.2 (C-5), 108.9 (C-6), 186.7 (C-7), 133.0 (C-8), 129.2 (C-9), 128.5 (C-10), 132.1 (C-11), 128.5 (C-12), 129.2 (C-13), 136.9 (C-14), 127.8 (C-15), 128.1 (C-16), 126.3 (C-17), 128.1 (C-18), 127.8 (C-19).
 **23**	143.7 (C-1), 129.3 (C-2), 131.7 (C-3), 120.3 (C-4), 138.9 (C-5), 117.1 (C-6), 167.9 (C-7), 17.5 (C-8), 186.8 (C-9), 130.1 (C-10), 129.2 (C-11), 128.1 (C-12), 143.9 (C-13), 128.1 (C-14), 129.2 (C-15), 28.2 (C-16), 15.9 (C-17).
 **24**	146.4 (C-1), 121.1 (C-2), 132.3 (C-3), 113.5 (C-4), 139.7 (C-5), 108.9 (C-6), 85.7 (C-7), 31.2 (C-8), 186.5 (C-9), 129.8 (C-10), 129.0 (C-11), 127.4 (C-12), 143.5 (C-13), 127.4 (C-14), 129.0 (C-15), 28.6 (C-16), 16.1 (C-17), 134.3 (C-18), 128.7 (C-19), 127.2 (C-20), 138.2 (C-21), 127.2 (C-22), 128.7 (C-23), 28.4 (C-24), 15.7 (C-25).
 **25**	144.2 (C-1), 129.2 (C-2), 131.8 (C-3), 120.9 (C-4), 138.7 (C-5), 116.9 (C-6), 168.0 (C-7), 17.5 (C-8), 186.6 (C-9), 130.7 (C-10), 138.5 (C-11), 129.8 (C-12), 141.3 (C-13), 126.1 (C-14), 129.0 (C-15), 21.0 (C-16), 18.3 (C-17)

6,8-Dibromo-3-hydroxy-2-methyl-4(3*H*)-quinazolinone (2). An equimolar mixture of benzoxazinone **1a** (3.19 g; 10 mmol) and hydroxylamine hydrochloride (0.69 g; 10 mmol) in 30 mL of dry pyridine was heated under reflux for 6 h, left to cool and then poured into cold water with constant stirring. The solid product that separated out was filtered off; thoroughly washed with water, dried and then recrystallized from the appropriate solvent to give

quinazolinone **2**. Elemental analysis for $C_9H_6Br_2N_2O_2$ (M. wt. 334); Found: C, 31.98; H, 1.63; N, 8.25; Calcd: C, 32.34; H, 1.80; N, 8.38. IR spectrum, $\tilde{\nu}$ / cm^{-1}: 1671 (CO), 3073 (C-H arom), 2980 (C-H aliph), 3358 (OH, hydrogen bonded and 3465 (OH, free). ^{1}H NMR ($CDCl_3$), δ: 8.39 (d, 1H, J = 2.16 Hz, C_5-H), 8.16 (d, 1H, J = 2.05 Hz, C_7-H), 6.61 (s, 1H, OH) and 2.48 (s, 3H, -N=C-CH_3).

3-Acetoxy-6,8-dibromo-2-methyl-4(3*H*)quinazolinone (3). 10 mmol of compound **2** (3.34 g) was heated under reflux in 20 mL of freshly distilled acetic anhydride for 2 h. The reaction solution was left to cool and the solid that deposited was filtered off, washed several times with light petroleum, dried and recrystallized from proper solvent to afford the desired product **3**. Elemental analysis for $C_{11}H_8Br_2N_2O_3$ (M. wt. 376); Found: C, 35.30; H, 2.24; N, 7.77; Calcd: C, 35.11; H, 2.13; N, 7.45. IR spectrum, $\tilde{\nu}$ / cm^{-1}; 1674 (CO quinazolinone), 1756 (CO ester), 2927 (C-H aliph) and 3071 (CH arom) with the lack of $\tilde{\nu}_{OH}$. ^{1}H NMR ($CDCl_3$), δ: 8.43 (d, 1H, J = 2.25 Hz, C_5-H), 8.21 (d, 1H, J = 2.25 Hz, C_7-H) and 2.51 (s, 6H, $2CH_3$).

6,8-Dibromo-3-ethoxycarbonylmethoxy-2-methyl-4(3*H*)-quinazolinone (4). To a solution of 3-hydroxyquinonazolinone **2** (3.34 g; 10 mmol) in 50 mL of dry acetone were added ethyl chloroacetate (4.92 g; 40 mmol) and anhydrous potassium carbonate (5.52 g; 40 mmol). The reaction mixture was heated under reflux for 24 h. The excess acetone was removed by distillation and the residue was poured into cold water with stirring. The solid that separated out was filtered by suction, washed with cold water, dried and purified by recrsytallization from suitable solvent to afford product **4**. Elemental analysis for $C_{13}H_{12}Br_2N_2O_4$ (M. wt. 420); Found: C, 36.90; H, 2.59; N, 6.43; Calcd: C, 37.14; H, 2.86; N, 6.67. IR spectrum, $\tilde{\nu}$ / cm^{-1}: 1672 (CO quinazolinone), 1734 (CO ester), 2987 (CH aliph) and 3066 (CH arom) and disappearance of $\tilde{\nu}_{OH}$. ^{1}H NMR spectrum ($CDCl_3$), δ: 8.28 (d, 1H, J = 2.20 Hz, C_5-H), 8.09 (d, 1H, J = 2.20 Hz, C_7-H), 4.83 (s, 2H, OCH_2CO), 4.23 (q, 2H, J = 7.26 Hz, $C\underline{H}_2CH_3$), 2.57 (s, 3H, N=C-CH_3) and 1.29 (t, 3H, J = 7.04, $CH_2C\underline{H}_3$).

3-(4-Acetophenyl)-6,8-dibromo-2-methyl-4(3*H*)-quinazolinone (5). To a solution of benzoxazinone **1a** (3.19 g; 10 mmol) in ethyl alcohol (30 mL) 4-aminoacetophenone (1.35 g; 10 mmol) was added and the reaction mixture was heated under reflux for 6 h and left to cool after distilling off the excess solvent. The solid product which deposited was filtered off, dried and recrystallized from suitable solvent to yield compound **5**. Elemental analysis for $C_{17}H_{12}Br_2N_2O_2$ (M. wt. 436); Found: C, 46.57; H, 2.46; N, 6.23; Calcd: C, 46.79; H, 2.75; N, 6.42. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1667 (CO quinazolinone), 1702 (CO acetyl), 2945 (CH aliph), and 3072 (CH arom). ^{1}H NMR (DMSO-d_6), δ: 8.92-8.11 (m, 6H, ArH), 2.48 (s, 3H, N=C-CH_3) and 2.22 (s, 3H, $COCH_3$)

3-(2-Aminophenyl)-6,8-dibromo-2-methyl-4(3*H*)-quinazolinone (6). An equimolar mixture of benzoxazinone **1a** (3.19 g; 10 mmol) and o-phenylenediamine (1.08 g; 10 mmol) in 30 mL of ethyl alcohol was heated under reflux for 8 h. The excess alcohol was distilled off and the reaction solution was left to cool. The solid so obtained was filtered off, dried and recrystallized from proper solvent to afford **6**. Elemental analysis for $C_{15}H_{11}Br_2N_3O$ (M. wt. 409); Found: C, 43.62; H, 2.45; N, 9.98; Calcd: C, 44.01; H, 2.69; N, 10.27. IR spectrum, $\tilde{\nu}$ / cm^{-1}: 1677 (CO

quinazolinone), 3359 and 3468 (NH_2). ^{1}H NMR (DMSO-d_6), δ: 8.85-7.67 (m, 6H, ArH), 3.17 (s, 2H, NH_2) and 2.39 (s, 3H, CH_3).

6,8-Dibromo-2-methyl-3-(4-sulfonamidophenyl)/[4-*N*-(5-methyl-3-isoxazolyl)-sulfonamidophenyl]-4(3*H*)-quinazolinones 7 and 8. A mixture of benzoxazinone **1a** (3.19 g, 10 mmol) and 10 mmol of sulfanilamide (1.72 g) and/or sulfamethoxazole (2.53 g) was heated under reflux in 50 mL of dry pyridine for 8h. The excess solvent was removed by distillation and the reaction solution was left to cool, then poured into crushed ice with stirring to obtain the crude products which were filtered off, thoroughly washed with cold water, dried and recrystallized from the proper solvent to afford products **7** and **8** respectively.

Compound 7. Elemental analysis for $C_{15}H_{11}Br_2N_3O_3S$ (M. wt. 473); Found: C, 38.35; H, 2.52; N, 9.09; Calcd: C, 38.05; H, 2.33; N, 8.88. IR spectrum, $\tilde{\nu}$ / cm^{-1}: 1687 (CO), 2922 (CH aliph), 3067 and 3107 (CH arom), 3222 and 3316 (NH_2). ^{1}H NMR (DMSO-d_6), δ: 8.42 (d, 1H, J = 1.36 Hz, C_5-H), 8.18 (d, 1H, J = 1.36 Hz, C_7-H), 8.05-7.70 (m, 4H, ArH), 7.58 (s, 2H, NH_2) and 2.18 (s, 3H, CH_3).

Compound 8. Elemental analysis for $C_{19}H_{14}Br_2N_4O_4S$ (M. wt. 554); Found: C, 41.44; H, 2.79; N, 10.34; Calcd: C, 41.16; H, 2.53; N, 10.11. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1661 (CO), 2923 (CH aliph), 3071 (CH arom), 3386 (NH). ^{1}H NMR (DMSO-d_6), δ: 8.42 (d, 1H, J = 2.20 Hz, C_5-H), 8.16 (d, 1H, J = 2.18 Hz, C_7-H), 8.10-7.75 (m, 4H, ArH), 7.38 (s, 1H, proton of isoxazole nucleus), 6.24 (s, 1H, exchangable, NH), 2.35 (s, 3H, CH_3 of isoxazole nucleus) and 2.14 (s, 3H, CH_3 of quinazolinone nucleus).

7,9-Dibromo-5-methyl-2-oxo-1,2,4-triazolo[2,3-c]quinazoline (9). To a solution of benzoxazinone **1a** (3.19 g; 10 mmol) in 30 mL of pyridine semicarbazide hydrochloride (3.36 g; 10 mmol) was added and the reaction mixture was heated under reflux for 6 h, left to cool, poured into cold water with stirring. The solid crude product that separated out was filtered off by suction, washed with cold water, dried and recrystallized from the appropriate solvent to give compound **9**. Elemental analysis for $C_{10}H_6Br_2N_4O$ (M. wt. 358); Found: C, 33.88; H, 1.78; N, 15.95; Calcd: C, 33.52; H, 1.68; N, 15.64. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1677 (CO), 2933 (CH aliph), 3071 (CH arom), 3206 and 3314 (NH hydrogen-bonded and free). ^{1}H NMR (DMSO-d_6), δ: 8.16 (d, 1H, J = 2.18 Hz, C_{10}-H), 8.07 (d, 1H, J = 2.18 Hz, C_8-H), 5.78 (s, 1H, NH) and 2.28 (s, 3H, CH_3).

6,8-Dibromo-3-(2-hydroxyethyl)-2-methyl-4(3*H*)-quinazolinone (10). A solution of benzoxazinone **1a** (3.19 g; 10 mmol) in ethanolamine (20 mL) was refluxed for 3 h. Most of the solvent was removed, the solid that formed was collected, washed with light petroleum, dried and recrsytallized from appropriate solvent to afford compound **10**. Elemental analysis for $C_{11}H_{10}Br_2N_2O_2$ (M. wt. 362); Found: C, 36.87; H, 2.97; N, 7.90; Calcd: C, 36.46; H, 2.76; N, 7.73. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1677 (CO), 2931 (CH aliph), 3070 (CH arom) and 3452 (OH). ^{1}H NMR ($CDCl_3$), δ: 8.20 (d, 1H, J = 2.00 Hz, C_5-H), 8.07 (d, 1H, J = 1.86 Hz, C_7-H), 4.79 (s, 1H, OH exchangable), 4.29 (t, 2H, J = 5.02 Hz, -C$\underline{H_2}$OH), 4.03 (t, 2H, J = 4.96 Hz, -C$\underline{H_2}$-N) and 2.72 (s, 3H, CH_3).

6,8-Dibromo-3-(*N*-phthalimidoethyl)/[(2-hydroxy-1-naphthyl)ethyl]-2-methyl-4(3*H*)-quinazolinones 11 and 12. A mixture of compound **10** (3.58 g; 10 mmol) and 10 mmol of phthalimide (1.47 g) and/or 2-naphthol (1.44 g) was heated without solvent and 110-120°C in presence of few drops of concentrated hydrochloric acid for 3 h. The solid was triturated with warm light petroleum. The solid separated was filtered, dried and crystallized to afford **11** and **12** respectively.

Compound 11. Elemental analysis for $C_{19}H_{13}Br_2N_3O_3$ (M. wt. 491); Found: C, 46.21; H, 2.51; N, 8.30; Calcd: C, 46.44; H, 2.65; N, 8.55. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1720 and 1680 (CO of phthalimide and quinazolinone), 2927 and 2977 (CH aliph) and 3072 (CH arom) with the disappearance of $\tilde{\nu}_{OH}$. ^{1}H NMR ($CDCl_3$), δ: 8.83-7.72 (m, 6H, ArH), 4.23 (t, 2H, J = 5.16 Hz, $CH_2N(CO)_2$), 3.97 (t, 2H, J = 5.16 Hz, CH_2-NCO) and 2.49 (s, 3H, CH_3).

Compound 12. Elemental analysis for $C_{21}H_{16}Br_2N_2O_2$ (M. wt. 488); Found: C, 51.43; H, 3.03; N, 5.57; Calcd: C, 51.64; H, 3.28; N, 5.74. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1674 (CO), 2972 (CH aliph), 3100 (CH arom) and 3294 (OH). ^{1}H NMR ($CDCl_3$), δ: 8.77 (d, 2H, J = 6.70 Hz, ArH of phenolic nucleus), 8.31 (d, 1H, J = 2.11 Hz, C_7-H), 8.13 (d, 1H, J = 2.09 Hz, C_5-H), 7.01 (s, 1H, OH), 6.92-6.14 (m, 4H, ArH of benzene nucleus), 4.35 (t, 2H, J = 5.24 Hz, CH_2-NCO), 4.14 (t, 2H, J = 5.24 Hz, CH_2-C=) and 2.55 (s, 3H, CH_3).

6-Bromo-2-isopropyl-3-amino-4(3*H*)-quinazolinone (13). To a solution of benzoxazinone **1b** (2.48 g; 10 mmol) in 50 mL of ethyl alcohol, hydrazine monohydrate 98% (0.75 g, 15 mmol) was added and the solution was heated under reflux for 3 h. The solid that deposited on cooling after distilling off most of the solvent was filtered off and recrystallized from appropriate solvent to yield **13**. Elemental analysis for $C_{11}H_{12}BrN_3O$ (M. wt. 282); Found: C, 46.50; H, 4.19; N, 14.71; Calcd: C, 46.81; H, 4.26; N, 14.89. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1645 (C=N), 1684 (C=O), 3350 and 3447 (NH_2). ^{1}H NMR (DMSO-d_6), δ: 4.38 (s, 2H, NH_2), 8.42-7.51 (m, 3H, ArH), 3.66 (septet, 1H, methine proton of isopropyl group) and 1.32 (d, 6H, J = 6.25 Hz, 2 Me of isopropyl group). MS, m/z (I_r/%): 282 ([$M^{+\cdot}$], 100), 283 (M+1, 82), 266 (8.8), 253 (41.5), 239 (7.5), 224 (6.1), 184 (5.4), 159 (4.8), 144 (3.4), 116 (2.7) and 76 (4.8).

10-Bromo-6-isopropyl-2-oxo-3*H*,4*H*-1,2,4-triazino[2,3-c] quinazoline (14). A mixture of quinazolinone **13** (2.82 g; 10 mmol) and chloroacetamide (0.94 g; 10 mmol) was heated without solvent on an oil bath at 130-140°C for 6 h. The reaction solid mixture was left to cool, triturated with water and the solid which separated out, was filtered off, washed with water, dried and recrystallized from proper solvent to afford **14**. Elemental analysis for $C_{13}H_{13}BrN_4O$ (M. wt. 321); Found: C, 48.92; H, 4.30; N, 17.58; Calcd: C, 48.60; H, 4.05; N, 17.45. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1632 (C=N), 1675 (C=O) and 3320 (NH). ^{1}H NMR ($CDCl_3$), δ: 8.86-8.21 (m, 3H, ArH), 5.62 (s, 1H, NH), 5.25 (s, 2H, -COC$\underline{H}_2$-N), 3.70 (septet, 1H, methine proton of isopropyl) and 1.36 (d, 6H, J = 6.18 Hz, 2 Me of isopropyl).

3-Arylidenamino-6-bromo-2-isopropyl-4(3*H*)-quinazolinones 15a-c. A mixture of 3-amino-4(3H)-quinazolinone **13** (2.82 g; 10 mmol) and the appropriate aldehyde (10 mmol) in ethyl alcohol (50 mL) was heated under reflux for 4 h in presence of catalytic amount of piperidine.

The excess alcohol was distilled off and the reaction solution was left to cool to obtain the crude product which was recrystallized from suitable solvents to give **15a-c**.

Compound 15a. Elemental analysis for $C_{18}H_{16}BrN_3O$ (M. wt. 370); Found: C, 58.55; H, 4.51; N, 11.62; Calcd: C, 58.38; H, 4.32; N, 11.35. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1625-1620 (C=N), 1678-1685 (CO), 2875-2985 (CH aliph), and 3080-3098 (CH arom).

Compound 15b. Elemental analysis for $C_{19}H_{18}BrN_3O_2$ (M. wt. 400); Found: C, 56.81; H, 4.38; N, 10.36; Calcd: C, 57.00; H, 4.50; N, 10.50. ^{1}H NMR (DMSO-d_6) for **15b**, δ: 8.92 (s, 1H, N=CH), 8.76-8.11 (m, 7H, ArH), 3.684 (septet, 1H, methine proton of isopropyl), 3.67 (s, 3H, OMe) and 1.41 (d, 6H, J = 6.22 Hz, 2 Me of isopropyl).

Compound 15c. Elemental analysis for $C_{18}H_{15}BrClN_3O$ (M. wt. 404.5); Found: C, 53.03; H, 3.48; N, 10.08; Calcd: C, 53.40; H, 3.71; N, 10.38.

6-Bromo-3-[2-(4-chlorophenyl)-4-oxo-1,3-thiazol-3-yl]-2-isopropyl-4(3*H*)-quinazolinone (16). A mixture of **15c** (4.00 g; 10 mmol) of **15c** and 2-mercaptoacetic acid (0.92 g; 10 mmol) was stirred in dry benzene (50 mL) and then refluxed for 3 h. The yellow solution was distilled to get rid of the excess solvent and the residue was recrystallized from suitable solvent to afford **16**. Elemental analysis for $C_{20}H_{17}BrClN_3O_2S$ (M. wt. 478.5); Found: C, 50.39; H, 3.81; N, 9.06; Calcd: C, 50.16; H, 3.55; N, 8.78. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 692 (C-S), 1670 and 1697 (two C=O groups) with the lacking of any N-H bond. ^{1}H NMR ($CDCl_3$), δ: 8.87-8.18 (m, 7H, ArH), 5.62 (s, 1H, benzylic proton), 4.81 (s, 2H, COC$\underline{H}_2$S), 3.71 (septet, 1H, methine proton) and 1.38 (d, 6H, J = 6.20 Hz, 2Me of isopropyl).

6-Bromo-3-[(4-chlorophenylthio-phenyl)]methylamino-2-isopropyl-4(3*H*) quinazolinone (17). To a mixture of **15c** (4.00 g; 10 mmol) and thiophenol (1.10 g, 10 mmol) in dry benzene (40 mL) was added few drops of piperidine and the reaction mixture is then heated under reflux for 2 h. Distilling off the excess solvent and cooling gave a crude solid which was filtered off, washed with light petroleum (2 x 10 mL) and recrystallized to afford product **17**. Elemental analysis for $C_{24}H_{21}BrClN_3OS$ (M. wt. 514.5); Found: C, 56.15; H, 4.17; N, 8.35; Calcd: C, 55.98; H, 4.08; N, 8.16. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 684 (C-S), 1677 (C=O) and 3400 (NH). ^{1}H NMR ($CDCl_3$), δ: 8.80 (s, 1H, NH), 8.10-6.90 (m, 12H, ArH), 4.00 (s, 1H, CH-S), 3.68 (septet, 1H, methine proton of isopropyl group) and 1.40 (d, 6H, J = 6.78 Hz, 2 Me of isopropyl group).

3-Cyano-6,8-dibromo-4-hydroxy-2-methylquinoline (18). To 40 mL of absolute ethanol containing 0.23 g (10 mmol) of sodium metal was added 0.66 g of malonitrile (10 mmol). After few minutes 3.19 g of benzoxazinone **1a** (10 mmol) was added. The reaction mixture was heated under reflux with stirring for 20 h. Most of the solvent was distilled off and the reaction solution was acidified with hydrochloric acid to give a crude product which was filtered off, washed several times with cold water, dried, and recrystallized to yield quinoline-3-carbonitirle **18**. Elemental analysis for $C_{11}H_6Br_2N_2O$ (M. wt. 342); Found: C, 38.86; H, 1.83; N, 8.37; Calcd: C, 38.60; H, 1.75; N, 8.19. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1645 (C=N), 2220 (C≡N), 2926 and 2996 (CH aliph), 3082 (CH arom) and 3320 and 3384 (OH H-bonded and free respectively). ^{1}H NMR (DMSO-d_6), δ: 10.34 (s, 1H, phenolic OH), 8.82 (d, 1H, J = 2.18 Hz, C_7-H), 8.60 (d, 1H, J = 2.18

Hz, C_5-H) and 2.38 (s, 3H, Me). MS, m/z (I_r / %): 345 (51), 344 (17.8), 343 (100), 342 (7.6), 341 (38), 278 (16), 277 (11), 276 (13), 155 (13), 128 (10), 63 (11) 62 (17), and 61 (13).

7,9-Dibromo-2-oxo-3-phenyl-4-[phenylaminocarbonyl]imino-1,3-oxazino [5,6-c]quinoline (19). A mixture of **18** (3.4 g; 10 mmol) and phenyl isocyanate (2.38 g; 20 mmol) in 50 mL of benzene was heated under reflux in presence of catalytic amount of triethylamine for 12 h. Removal of excess benzene afforded a crude solid after cooling. The crude solid was filtered off, dried and recrystallized to yield compound **19**. Elemental analysis for $C_{25}H_{16}Br_2N_4O_3$ (M. wt. 580); Found: C, 52.09; H, 2.96; N, 9.81; Calcd: C, 51.72; H, 2.76; N, 9.66. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1667 (CO amide), 1704 (CO oxazinone), 2922 (CH aliph), 3072 (CH arom) and 3263 (NH). ^{1}H NMR ($CDCl_3$), δ: 8.80-7.69 (m, 12 H, ArH), 5.79 (s, 1H, NH), 2.15 (s, 3H, Me).

3,5-Dibromo-2-(1-hydroxy-1-phenyl)ethylaminobenzophenone 20 and benzyl 3,5-dibromo-2-(1-hydroxy-1-benzyl)ethyl-aminophenyl ketone (21). To a solution of benzoxazinone **1a** (3.19 g; 10 mmol) in dry ether (20 mL) was added portionwise an ethereal solution of Grignard's reagent namely, phenylmagnesium bromide and/or benzylmagnesium bromide (30 mmol). The reaction mixture was heated under reflux on a steam bath for 4 h, left at room temperature overnight, decomposed with saturated ammonium chloride solution and finally extracted by ether. The ether extract was dried over anhydrous magnesium sulfate and the ether was removed to yield a crude solid which was recrystallized from suitable solvent to afford **20** and **21** respectively.

Compound 20. Elemental analysis for $C_{21}H_{17}Br_2NO_2$ (M. wt. 475); Found: C, 52.87; H, 3.33; N, 2.83; Calcd: C, 53.05; H, 3.58; N, 2.95. IR spectrum $\tilde{\nu}$ / cm^{-1}: 1675 (CO), 2990 (CH aliph), 3083 (CH arom), 3251 (NH) and 3380 (OH). ^{1}H NMR ($CDCl_3$), δ: 7.78 (d, 1H, J = 2.22 Hz, C_4-H), 7.74 (d, 1H, J = 2.27 Hz, C_6-H), 7.36-6.82 (m, 10H, ArH), 4.08 (s, 1H, NH exchangable), 1.62 (s, 1H, OH exchangeable) and 1.54 (s, 3H, Me).

Compound 21. Elemental analysis for $C_{23}H_{21}Br_2NO_2$ (M. wt. 503); Found: C, 55.08; H, 4.28; N, 3.02; Calcd: C, 54.87; H, 4.17; N, 2.78. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1664 (CO), 2930 and 2989 (CH aliph), 3065 (CH arom), 3257 (NH) and 3416 and 3618 (OH H-bonded and free). ^{1}H NMR ($CDCl_3$), δ: 7.69 (d, 1H, J = 2.20 Hz, C_4-H), 7.37 (d, 1H, J = 2.28 Hz, C_6-H), 7.27-7.06 (m, 10H, ArH), 3.25 and 3.14 (dd, 4H, J = 13.96 Hz and 13.72 Hz, two C$\underline{H}_2$Ph), 2.72 (s, 1H, NH exchangable), 2.05 (s, 3H, Me), and 1.78 (s, 1H, OH exchangeable).

20, 2-Acetylamino-3,5-dibromobenzophenone 22, 2-acetylamino-3,5-dibromo-4`-ethylbenzophenone 23, 3,5-dirbomo-2-[1-(4-ethylphenyl)-1-hydroxy]ethylamino-4-ethylbenzopheone 24 and 2-acetylamino-3,5-dibromo-2`,4`/5`-dimethylbenzophenone (25 and 26). To a vigorously stirred suspension of benzoxazinone **1a** (3.19 g; 10 mmol) in dry aromatic hydrocarbon namely, benzene, ethylbenzene, *m*- and/or *p*-xylene (100 mL) was added anhydrous aluminium chloride (4.0 g; 30 mmol) portionwise then the reaction mixture was heated on steam bath for 6 h, allowed to stand at room temperature overnight, then it was added with continuous stirring to ice-hydrochloric acid (50 mL). The organic layer was separated, washed with cold water (3 x 30 mL) and the excess hydrocarbon was removed by steam distillation. The organic material was extracted with ether, dried over anhydrous magnesium

sulfate, then ether was distilled off to obtain the crude product which was recrystallized or fractionally crystallized to afford the product(s).

Compound 22. Elemental analysis for $C_{15}H_{11}Br_2NO_2$ (M. wt. 397); Found: C, 45.65; H, 2.82; N, 3.68; Calcd: C, 45.34; H, 2.77; N, 3.53. IR spectrum, $\tilde{\nu}$ /cm^{-1} 1692 (CO ketone), 1646 (CO of NHCOMe), 2925 and 2974 (CH aliph), 3061 (CH arom) and 3270 (NH). ^{1}H NMR ($CDCl_3$), δ: 8.78 (d, 1H, J = 2.18 Hz, C4-H), 8.49 (d, 1H, J = 2.1 Hz, C6-H), 7.43-6.96 (m, 5H, ArH), 4.73 (s, 1H, NH) and 2.46 (s, 3H, Me).

Compound 23. Elemental analysis for $C_{17}H_{15}Br_2NO_2$ (M. wt. 425); Found: C, 48.19; H, 3.80; N, 3.40; Calcd: C, 48.00; H, 3.53; N, 3.29. IR spectrum, $\tilde{\nu}$ / cm^{-1} : 1698 (CO of diaryl ketone), 1646 (CO of NHCOMe), 2927 and 2960 (CH aliph), 3065 (CH arom) and 3247 (NH). ^{1}H NMR (DMSO-d_6), δ: 9.90 (s, 1H, NH exchangable), 8.21 (d, 1H, J = 2.14 Hz, C_4-H), 7.94 (d, 1H, J = 2.24 Hz, C_6-H), 7.69-7.25 (m, 4H, ArH), 2.75 (q, 2H, J = 7.38 Hz, C$\underline{H}_2$CH$_3$), 1.76 (s, 3H, COCH$_3$), and 1.26 (t, 3H, J = 7.50 Hz, CH$_2$C$\underline{H}_3$).

Compound 24. Elemental analysis for $C_{25}H_{25}Br_2NO_2$ (M. wt. 531); Found: C, 56.65; H, 4.89; N, 2.87; Calcd: C, 56.50; H, 4.71; N, 2.64. IR spectrum, $\tilde{\nu}$ / cm^{-1}: 1676 (CO), 2930 and 2972 (CH aliph), 3064 (CH arom), 3315 (NH) and 3460 (OH). ^{1}H NMR (DMSO-d_6), δ: 9.92 (s, 1H, NH exchangable), 8.62 (d, 1H, J = 2.18 Hz, C_4-H), 8.27 (d, 1H, J = 2.18 Hz, C_6-H), 8.12-7.74 (m, 8H, ArH), 5.36 (s, 1H, OH exchangable), 2.69 (q, 4H, J = 7.44 Hz, two C$\underline{H}_2$CH$_3$), 1.52 (s, 3H, NHC-Me), 1.22 (t, 6H, 7.44 Hz, two CH$_2$C$\underline{H}_3$).

Compound 25. Elemental analysis for $C_{17}H_{15}Br_2NO_2$ (M. wt. 425); Found: C, 48.33; H, 3.75; N, 3.45; Calcd: C, 48.00; H, 3.53; N, 3.29. IR spectrum $\tilde{\nu}$ / cm^{-1}: 1645 (CO of COMe), 1670 (CO of Ar_2CO), 2980 (CH aliph), 3063 (CH arom) and 3227 (NH). ^{1}H NMR ($CDCl_3$), δ: 8.28 (s, 1H, NH), 7.69 (d, 1H, J = 2.11 Hz, C4-H), 7.31 (d, 1H, J = 2.08 Hz, C_6-H), 7.40 (d, 1H, J_{ortho} = 7.78 Hz, ArH), 7.02 (s, 1H, ArH), 7.02 (d, 1H, J_{ortho} = 7.74 Hz, 1H, ArH), 2.49 (s, 3H, Ar-Me), 2.26 (s, 3H, Ar-Me) and 2.11 (s, 3H, COMe).

Compound 26. Elemental analysis for $C_{17}H_{15}Br_2NO_2$ (M. wt. 425); Found: C, 48.27; H, 3.68; N, 3.60; Calcd: C, 48.00; H, 3.53; N, 3.29. IR spectrum: $\tilde{\nu}$ /cm^{-1}: 1640 (CO of COMe), 1673 (CO of Ar_2CO), 2922 and 2957 (CH aliph), 3100 (CH arom) and 3221 (NH). ^{1}H NMR ($CDCl_3$), δ : 8.33 (s, 1H, NH), 7.75 (d, 1H, J = 2.14 Hz, C_4-H), 7.36 (d, 1H, J = 2.09 Hz, C_6-H), 7.45 (d, 1H, J_{ortho} = 7.88 Hz, Ar-H), 7.02 (s, 1H, Ar-H), 7.03 (d, 1H, J_{ortho} = 2.94 Hz, Ar-H), 2.53 (s, 3H, ArMe), 2.37 (s, 3H, ArMe) and 2.07 (s, 3H, COMe).

1-Hydroxy-1-(2-acetylamino-3,5-dibromophenyl)methylidene barbituric and thiobarbituric acids (27a,b). An equimolar mixture of benzoxazine **1a** (3.19 g; 10 mmol) and barbituric acid (1.28 g; 10 mmol) or 2-thiobarbituric acid (1.44 g, 10 mmol) was heated under reflux in pyridine (30 mL) for 7 h. The reaction solution was left to cool, poured into ice/hydrochloric acid with stirring. The solid that separated out was filtered off, washed with cold water, dried and crystallized from suitable solvent to afford **27a** and **b.**

Compound 27a. Elemental analysis for $C_{13}H_9Br_2N_3O_5$ (M. wt. 447); Found: C, 35.14; H, 2.12; N, 9.53; Calcd: C, 34.90; H, 2.01; N, 9.40. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1730 (CO of CONH), 1690 (CO of COMe), 2920 (CH aliph), 3034 (CH arom), 3261 (NH) and 3500 (OH). ^{1}H NMR

(DMSO-d_6), δ: 13.62 (s, 1H, NH of acetyl, exchangable), 10.97 (s, 1H, NH, exchangable), 10.66 (s, 1H, NH, exchangable), 9.98 (s, 1H, OH, exchangeable), 8.35 (d, 1H, J = 2.20 Hz, C_4-H), 8.08 (d, 1H, J = 2.20 Hz, C_6-H/ and 2.30 (s, 3H, COMe).

Compound 27b. Elemental analysis for $C_{13}H_9Br_2N_3O_4S$ (M. wt. 463); Found: C, 33.81; H, 2.07; N, 9.29; Calcd: C, 33.69; H, 1.94; N, 9.07. IR spectrum, $\tilde{\nu}$ /cm^{-1}: 1742 (CO of CONH), 1675 (CO of NHCOMe), 2876 (CH aliph), 3064 (CH arom), 3317 (NH) and 3450 (OH).

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