Studies on 2-substituted-6, 8-dibromo-4(H)-3,1-Benzoxazin-4-one

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Abstract

The behavior of substituted 6,8-dibromo-4(H)3,1-benzoxazin-4-one towards
nitrogen nucleophile (formamide, hydrazine hydrate, hydroxylamine, amines, o-phenylene diamine) to
Yield quinazolinone \( \text{Ta-f,4} \) and 5 respectively. When \( \text{3b} \) react with anhydride, carbon
electrophiles, aromatic ketone, benzylidine malononitrile, carbon disulphide, chloroactyl chloride
and ethylbromacetate, benzoxazinone \( \text{7} \) to yielded quinazolinone \( \text{6-15} \). The reaction of \( \text{3a} \)
with ethyl bromoacetate, methylidiodide and aromatic aldehyde were carried out to obtain the quinazolinone derivatives \( \text{1,7,19,20} \) respectively. The interaction of the
quinazolone \( \text{16} \) with \( \text{NH}_2\text{NH}_2 \) afforded the hydrazide \( \text{17} \) which was converted to
hydrazone \( \text{18} \) when reacted with aromatic aldehyds.

Keywords.

2- Substituted 6,8-dibromo-4(H)-3,1-benzoxazin-4-one, 2-substituted quinazoline and pyridizino quinazoline derivative

Introduction

4H-3,1-Benzoxazin-4-ones as a class have been known for more than a century\(^{(1,2)}\). Compounds possessing this ring system are found in nature. The phytoalexins isolated from infected carnations\(^{(3,4)}\) are dianthalexins \( \text{1} \) and
hydroxylated analogs \( \text{2} \) and \( \text{3} \). 4H-3,1-benzoxazin-4-ones have been used as linking
units in thermally stable polymers\(^{(5)}\) and have been shown to possess biological
activity. They are potent mactivators of chymotrypsin\(^{(6-8)}\) as well as inhibitors of
human leukocyte elastase\(^{(7,9,10)}\) and H5V-1 protease\(^{(11)}\).
Interaction of compound 2 with nitrogen nucleophiles mainly formamide, in an oil bath, hydrazine hydrate in boiling ethanol, hydroxyl amine hydrochloride in refluxing pyridine and aromatic amines namely (benzyl amine, aniline and \(p\)-toludine) afforded the quinazolinone derivatives 3a-f.
The structure of compounds 3 were inferred from micro analytical and spectral data.

When compound 2 was submitted to react with \(o\)-phenylenediamine in boiling butanol it yielded compound 5 which identified via elemental analysis and IR spectra.

When compound 3b was allowed to react with anhydrides namely (maleic, succinic and phthalic anhydride) by fusion in an oil bath it give 3-(imide substituted)-2-methyl-6,8-dibromo-4(3H)-quinazolinone 6a,b and 6c. Structure of the quinazolines 6 was confirmed by elemental analysis, IR spectra.

When quinazolinone 3b was allowed to react with aromatic aldehydes namely piperonal or \(p\)-chlorobenzaldehyde by fusion in an oil bath at 150°C it gives 3-(3,4-methylene dioxbenzylidene and \(p\)-chlorobenzylidene)-2- methyl-6,8-dibromo-(3H)quinazolin-4-one 7a,b.

The structure of the compound 7 was confirmed by elemental analysis, IR spectra and the electron impact fragmentation.

Interaction of compound 3b with ketones namely, cyclohexanone or cyclopentanone by fusion in an oil bath it gives Schiff bases 8a and 8b., the structure of the compound 8 was confirmed by elemental analysis, IR spectra.
When quinazolinone 3b was submitted to react with benzylidene malononitril by fusion in an oil bath at 150°C it gives 3-(2-amino-3-carbonitile-4-phenylazetiden-1-y1)2-methyl-6,8-dibromo-3(H)quinazolin-4-one 9. The structure of the compound 9 was confirmed by analytical data, IR spectra and the mass spectroscope.

When quinazolnone 3b, was allowed to react with carbon disulphide in dimethylsulphoxide, sodium hydroxyed and dimethyl sulphate it give 3-(dithioxy methyl methylene amino)-2-methyl-6,8-dibromo-3(H)quinazalin-4-one 10, the reaction can be takes place via nucleophilic attack on the C=S group followed by methylation. The structure of compound 10 was confirmed by analytical data, IR spectra.

When 3-aminoquinazolinone 3b12-13 was allowed to react with chloro acetyl chloride as carbon electrophiles by reflux in dioxane it give 3-(chloroactyl amino) - 2-methyl-6.8-dibromo-3H-quinazolin-4-one 11. The structure of the compound 11 was confirmed by the elemental analysis, IR spectra and the electron impact fragmentation.

When 3-aminoquinazolinone 3b was allowed to reacts with acetyl chloride in an ice bath, it gives 3-(acetyl amino) -2- methyl-6,8-dibromo-3H-quinazolin-4-one 12. The structure of the compound 12 was confirmed by analytical data, and IR spectra.

On the other hand the compound 3b has been reacted with acetyl chloride in boiling dioxan or (with mixture of acetic acid and acetic anhydride1:1)and yielded 3-(diacet yl amino)-2-methyl-6,8-dibromoquinazolinolone 13. The structure of the compound 13 was inferred from analytical data, IR spectra and electron impact fragmentation.

When quinazolinone 3b was allowed to reacts with ethyl bromoacetate in dry actone
and anhydrous potassium carbonate it gives 3-(N,N-diethoxycarbonyl methyl)-2-methyl-6,8-dibromo-3H-quinazolin-4-one 14.

The behavior of the benzoxazinone 2 towards the amino quinazolinone 3b was investigate. Thus when quinazolinone 3b was allowed to reacts with 2-methyl-6,8-dibromo-4(3H)-3.1-benzoxazinon in an oil bath at 150°C it gives bis(2-methyl-6,8-dibromo-4-(3H)-quinazolinone 15. Formation of 15 takes place via the nucleophilic attack on the carbonyl group of benzoxazinone followed by recycilization. The structure of the compound 15 was confirmed by elemental analysis and IR spectrum.

When quinazolonone 3a was reacted with ethyl bromoacetate in dry acetone in the presence of anhydrous potassium carbonate as a catalyst it gives 3-(ethoxycarbonyl methyl)2-methyl-6,8-dibromo-4-(3H)-quinazoline 16. The structure of the compound 16 was confirmed by analytical data and IR spectrum.

The interaction of the ester 16 with hydrazine hydrate in boiling ethanol afforded the corresponding hydrazide 17.

Also in this investigation the outher sought to investigate the behavior of hydrazide 17 towards aromatic aldehyed namely benzaldehyde. Thus when compound 17 was allowed to reacts with benzaldehyde in boiling butanol it gives the hydrazone derivatives 18.

When quinazolinone 3a was allowed to react with methyl iodide in dry acetone in the presence of anhydrous potassium carbonate as a catalyst gives 3-(methyl)-2-methyl-6,8-dibromo-3H-quinazolinone 19.

The quinazolinone 3a was allowed to react with 4-N,N-dimethylaminobenzaldehyde in an oil bath at 150°C in the presence of few drops of piperidine and gave 2-(4-N,N-di methyl amino styryl)-6,8-dibromo-3H-quinazolin-4-on 20.
Interaction of the quinazolinone 20 with ethyl bromoacetat in dry acetone in the presence of anhydrous potassium carbonate as a catalyst it gave 3-(ethoxy carbonyl methyl)-2-(4-\(N,N\)-dimethyl amino styryl)-6,8-dibromo-3H -quinazolin-4-one 21.

When 3-(ethoxy carbonyl methyl)-2-methyl-6,8-dibromo-3H-quinazolin-4-one 16 was allowed to react with 4-\(N,N\)-dimethyl amino benzaldehyde in the presence of piperidine it gave 3-(ethoxy carbonyl methyl)-2(4-\(N,N\)-dimethyl amino styryl)-6,8-dibromo-3H-quinazolin-4-one 21 which was identified via mp and mmp determination.

Ring closure of compound 21 was allowed to reacts with hydrazine hydrate in boiling butanol gave the triazinone derivative 22.

**Experimental**

Melting points reported are uncorrected and were determined on electric melting apparatus.

Elemental analysis were performed by the micro analytical center, Faculty of Science, Cairo University.

IR spectra were recorded on spectrometer using KBr waver technique on satellite 1000, Faculty of Science, Fayoum University.

The \(^1\)HNMR were determined on avarian 300MHz Brucher Ac 300-MHz using TMS as internal standard (chemical shifts in \(\delta\)-scale).
The mass spectra were determined using HP model MS-5988 spectrometer at electron ionizing energy 70ev.

The characterization and physical data of all synthesised compounds were presented on tables.

**Synthesis of 2-methyl-6,8-dibromo-4-(3H)quinazolinone 3a:**

A solution of benzoxazine 2 (3.19gm: 0.01 mole) and formamide (15ml) was heated under reflux for (3hr), the reaction mixture was diluted with cold water, the solid which was separated out was dried and crystallized from the proper solvent to give the quinazolinone 3a.

Compound 3a Yield: 85% ; m.p.310 °C;
Anal. Calced. for(C9H6N2OBr2):C 33.96, H 1.88, N 8.80. Found: C 33.69, H 1.62, N 8.86,
IR(KBr, cm⁻¹): 1628 attributed to νC=N, 1688 attributed to νC=O and 3158 attributed to νNH.

**Synthesis of 3-amino-2-methyl-6,8-dibromoquinazolinone 3b:**

A mixture of benzoxazine 2 (3.19gm: 0.01 mole) and hydrazine hydrate (1gm: 0.02mole) in ethanol (30ml) was heated under reflux for (3hr), the reaction mixture was concentrated and the solid which was separated out was dried and crystallized from the proper solvent to give quinazolinone 3b.

Compound 3b: Yield: 90%; m.p.231 °C;
Anal. Calced. for (C9H7N3OBr2):  C 32.43, H 2.1, N 1.26. Found: C 32.42, H 2.11, N 1.21,
IR (KBr, cm⁻¹): 1620 νC=N, 1665 νC=O amide and 3202, 3305 νNH₂.
MS show m/z (332.9) (100%).

**Synthesis of 2-methyl-3(hydroxyl)-6,8-dibromoquinazolinone 3c:**

A mixture of benzoxazine 2 (3.19gm: 0.01 mole) and hydroxylamine hydro chloride
(0.69gm: 0.01mole) in pyridine (15ml) was heated under reflux for (3hr), the reaction leave to cool and poured on ice/HCl to give the quinazolinone 3c. Compound 3c: Yield: 90%; m.p.272 °C; Anal. Calced. for (C$_9$H$_6$N$_2$O$_2$Br$_2$): C 32.33, H 1.79, N 8.38. Found: C 32.31, H 1.62, N 8.29. IR (KBr, cm$^{-1}$): 1672 νC=O (amide). MS show m/z (333.9) (100%). (M$^+$,316.9) (18.07%), (301.9) (11.15%)

Synthesis of 3(Aryl)-2(methyl)-6,8-dibromoquinazolinone 3d-f:
A mixture of benzoxazine 2 (3.19gm: 0.01 mole) and aromatic amines namely benzylamine, aniline and /or p-toluidene) in ethanol (20ml) was heated under reflux for (3hr), the solid that was separated filtered off and purified by crystallization to give the quinazolinone 3d-f.

Compound 3d: Yield: 85% ; m.p.216 °C; Anal. Calced. for (C$_{16}$H$_{12}$N$_2$OBr$_2$): C 47.05, H 2.44, N 6.8. Found: C 46.82, H 2.53, N 7.13. IR (KBr, cm$^{-1}$): 1678 attributed to νC=O (amide). MS show m/z (407.9) (100%). M$^+$ (392.9) (22.48%), (300.9) (14.22%)

Synthesis of 3(2-aminophenyl)-2-methyl-6,8-dibromoquinazolinone 5:
A mixture of benzoxazine 2 (3.19gm: 0.01 mole) and o-phenelendiamine (1.08 gm: 0.01 mole) was stirred in chloroform (20ml) for (16hr) at room temp, leave aside over night to give quinazolinone 4, which was boiling in butanol to give the quinazolinone 5.

Compound 5 Yield: 70% ; m.p.253 °C; Anal. Calced. for (C$_{15}$H$_{13}$N$_3$O$_2$Br$_2$): C 43.79, H 3.16, N 10.21. Found: C 43.72, H 2.68, N 10.13. IR (KBr, cm$^{-1}$): 1629 νC=N, 1678 νC=O (amide) and 3362, 3446 νNH$_2$. 


Synthesis of 3(malimido, succinimido and phthalimido)-6,8-dibromoquinazolin-6-one 6.

A mixture of quinazolinone 3b (3.33gm : 0.01 mole) and anhydride derivatives (0.01 mole) namely, (maleic, succinic and/or phthalic anhydride) was heated in an oil bath for (1hr), the reaction mixture diluted with water and filtered off, the solid that obtained was crystallized from the proper solvent to give quinazolinone derivative 6.

Compound 6: Yield: 90%; m.p.226 oC;
Anal. Calced. for (C\textsubscript{13}H\textsubscript{9}N\textsubscript{3}O\textsubscript{3}Br\textsubscript{2}): C 37.59, H 2.16, N 10.12. Found: C 37.42, H 2.03, N 10.11.
IR(KBr, cm\textsuperscript{-1}): 1613 \nu\textsubscript{C=\text{N}}, 1711 \nu\textsubscript{C=\text{O}}, 1746 \nu\textsubscript{C=\text{O}} (of two carbonyl group).
MS show m/e (463) (100%).

Synthesis of 3(\textit{N}-arylidine derivatives)2-methyl-6,8-dibromo quinazolinone 7.

A mixture of quinazolinone 3b (3.33gm: 0.01 mole) and aromatic aldehydes(0.01 mole) namely, (pipronal and/or \textit{p}-chlorobenzaldehyde), few drops of piperidine was heated in an oil bath for (1hr), the reaction mixture diluted with water, the solid that separated out, dried and crystallized from the proper solvent to give quinazolinone 7.

Compound 7: Yield: 80%; m.p.265 oC;
Anal. Calced. for (C\textsubscript{17}H\textsubscript{11}N\textsubscript{3}O\textsubscript{3}Br\textsubscript{2}): C 43.87, H 2.36, N 9.03. Found: C 43.88, H 2.27, N 9.12.
IR(KBr, cm\textsuperscript{-1}): 1678 attributed to \nu\textsubscript{C=\text{O}} (amide).
MS show m/e (318) (100%), M\textsuperscript{+}(303) (1.7%), (275) (23.3%).

Synthesis of Schiff bases 8.

A mixture of quinazolinone 3b (3.33gm: 0.01 mole) with alicyclic compound namely, cyclohexanone or cyclopentanone (0.02 mole), few drops of piperidine was heated in an oil
bath for (1hr), the reaction mixture diluted with water, the solid that separated out, dried and crystallized from the proper solvent to give Schiff bases 8.


IR (KBr, cm⁻¹): 1625 νC=N, 1672 νC=O (amide).

**Synthesis of 3-(2-aryl-3-carbonitrlyl-4-aminoazitin-1-yl) 2-methyl-6,8-dibromo-quinazolinone 9.**

A mixture of quinazolinone 3b (3.33gm: 0.01 mole), benzelydine malononitrile (1.54gm: 0.01 mole) and few drops of piperidine was heated in an oil bath for (1h)th e reaction mixture diluted with water, the solid that separated out, dried and crystalliz ed from the proper solvent to give quinazolinone 9.


IR (KBr, cm⁻¹): 1619 νC=N, 1670 νC=O (amide). 2201 νCN, 3305, 3204 νNH₂

MS show m/z (437) (17.3%).

**Synthesis of 2-methyl 3-dithioxymethylmethyleneamino-6,8-dibromoquina zolin-one 10.**

To avigorously stirred solution of 3-amino-2-methyl-6,8-dibromoquinazolinone 3b (3.33gm: 0.01 mole) in dimethyl sulphoxide (30ml) at room temp., carbon disulphide (0.026 mole) and sodium hydride (1.2 ml : 2 mole) were add drop wise then stirring for about (3hr), then solid was filtrated and crystallized from ethanol to give quinazolinone 10.

Compound 10: Yield: 85%; m.p.205 °C;
Anal. Calced. for \((C_{12}H_{11}N_{3}S_{2}OBr_{2})\):  C 32.95, H 2.51, N 9.61, S 14.64. Found: C 32.17, H 2.14, N 9.87, S 14.83.
IR (KBr, cm\(^{-1}\)): 1687 \(\nu_{\text{C=O}}\) (amide).

**Synthesis of 3(4-chloroacytylamino)-2-methyl-6,8-dibromo-quinazolinone 11:**

To a solution of quinazolinone \(3b\) (3.33gm: 0.01 mole) in dioxane, in ice bath chloroacetylchloride (1.12gm: 0.01 mole) was add drop wise with stirring, and the mixture was reflux for (10hr), poured into ice, filtrated and crystallized from proper solvent to give compound 11.

Compound 11: Yield: 95%; m.p.202 \(^{\circ}\)C;
Anal. Calced. for \((C_{11}H_{8}N_{3}O_{2}Br_{2}Cl)\):  C 32.27, H 1.95, N 10.26 . Found: C 32.17, H 1.88, N 10.11.
IR (KBr, cm\(^{-1}\)): 1670, 1682 \(\nu_{\text{C=O}}\) (amide), 3219 \(\nu_{\text{NH}}\) and 3447 \(\nu_{\text{OH}}\)
MS show m/z (408) (35.31%), \(M^+\)(359) (36.7%), (331) (15.4%)

**Synthesis of 3-(acetylamino)-2-methyl-6,8-dibromoquinazolinone 12:**

To a solution of quinazolinone \(3b\) (3.33gm: 0.01 mole) in dioxane, acetylchloride (0.78gm:0.01mole) was add drop wise with stirring in ice path, poured into ice, filtrated and crystallized from proper solvent to give compound 12.

Compound 12: Yield  85%; m.p.245 \(^{\circ}\)C;
Anal. Calced. for \((C_{11}H_{9}N_{3}O_{2}Br_{2})\):  C 35.20, H 2.40, N 11.20 . Found: C 35.27, H 2.13, N 10.92.
IR (KBr, cm\(^{-1}\)):1679,1698 attributed to \(\nu_{\text{C=O}}\) (amide), 3170 attributed to \(\nu_{\text{NH}}\).
MS show m/z (408) (35.31%), \(M^+\)(359) (36.7%), (331) (15.4%)

**Synthesis of 3-(N-diacetylamino)-2-methyl-6,8-dibromoquinazolinone 13:**
**Method (A):**

To a solution of quinazolinone \(3b\) (3.33gm: 0.01 mole) in dioxane, excess acetylchloride (0.78gm: 0.01 mole) was add drop wise with stirring in ice path, the reaction mixture was refluxed for (10hr) then cooled and poured into ice, filtrated and crystallized from proper solvent to give compound 13.
**Method (B):**

A solution of quinazolinone 3b (3.33gm: 0.01 mole) in (30ml) acetic acid and (10ml) acetic anhydride was refluxed for (1hr), then cooled, filtrated and crystallized from proper solvent to give compound 13.

**Compound 13:** Yield: 90%; m.p.175 °C;
IR (KBr, cm\(^{-1}\))\(1707, 1739\) vC=O.
MS show m/z (417) (29.2%), \(\text{M}^+\) (375) (70.7%), (333) (100%).

**Synthesis of 3-(\(N,N\)-diethoxy carbonyl)-2-methyl-6,8-dibromoquinazolinone 14.**

A mixture of quinazolinone 3b (3.33gm: 0.01 mole) and ethyl bromoacetate (6.68gm: 0.04 mole) and anhydrous potassium carbonate \(\text{K}_2\text{CO}_3\) (5.0gm: 0.04 mole) in dry acetone (50ml) was refluxed for (24hr), the excess acetone was evaporated and the reaction mixture was diluted with \(\text{H}_2\text{O}\), the solid that separated was crystallized from proper solvent to give compound 14.

**Compound 14:** Yield: 80%; m.p.172 °C;
IR (KBr, cm\(^{-1}\))\(1683, 1734\) vC=O.

**Synthesis of bis(2-methyl-6,8-dibromoquinazolinone) 15.**

A mixture of quinazolinone 3b (3.33gm: 0.01 mole), and benzoazinone 2 (3.719gm: 0.01 mole) was fused in an oil bath for (1hr), the solid that separated out, dried and crystallized from the proper solvent to give compound 15.

**Compound 15:** Yield: 80%; m.p.304 °C;
IR (KBr, cm\(^{-1}\))\(1701\) vC=O.
MS show m/z (634) (11.1%).
Synthesis of 3-(ethoxycarbonylmethyl)-2-methyl-6,8-dibromoquinazolinone 16.

A mixture of quinazolinone 3b (3.33gm: 0.01 mole) ethyl bromoacetate (6.68 gm: 0.04 mole) and anhydrous potassium carbonate K$_2$CO$_3$ (5.0gm: 0.04 mole) in dry acetone (50 ml) was refluxed for (24hr), the excess acetone removed by distillation and the residue poured with stirring into water, the solid that precipitated was filtered off, dried and then crystallized from proper solvent to give compound 16.

Compound 16: Yield: 75%; m.p.166 °C;
Anal. Calced. for (C$_{13}$H$_{12}$N$_2$O$_3$Br$_2$): C 38.61, H 2.97, N 6.93. Found: C 38.21, H 2.93, N 7.44.
IR (KBr, cm$^{-1}$):1679, 1736 vC=O.

Synthesis of 3-(aminocarbamyl methyl)2-methyl-6,8-dibromoquinazolinone 17.

A mixture of quinazolinone 16 (4.04gm: 0.01 mole), and hydrazine hydrate(1.0gm: 0.02mole) in ethanol (20ml) was heated under reflux for (6hr), the reaction mixture was concentrated, filtered off and the solid that separated out was crystallized to give 3-(aminocarbamyl methyl)-2-methyl-6,8-dibromoquinazolinone 17.

Compound 17: Yield: 80%; m.p.300 °C;
Anal. Calced. for (C$_{11}$H$_{10}$N$_4$O$_2$Br$_2$): C 33.84, H 2.56, N 14.35. Found: C 33.95, H 2.70, N 14.21.
IR (KBr, cm$^{-1}$):1646,1674 vC=O(amide),3209 $\nu_{NH}$ and 3246, 3337 $\nu_{NH2}$. 
**Synthesis of hydrazone 18.**

A mixture of quinazolinone 17 (3.9gm: 0.01 mole), and benzaldehyde (1.06gm: 0.01 mole) in butanol (50ml) was heated under reflux for (8hr), the reaction mixture was concentrated, filtered off and the solid that separated out was crystallized to give the corresponding hydrazone 18.

Compound 18: Yield: 80%; m.p.262 °C;
Anal. Calced. for (C_{18}H_{14}N_{4}O_{2}Br_{2}): C 45.18, H 2.92, N 11.71. Found: C 44.62, H 2.76, N 12.56.
IR (KBr, cm^{-1}): 1609 \nu_{\text{C=N}}, 1663, 1704 \nu_{\text{C=O}} and 3235 \nu_{\text{NH}}.

**Synthesis of 3-(methyl)2-methyl-6,8-dibromoquinazolinone 19.**

A mixture of quinazolinone 3a (3.17gm: 0.01 mole), and methyl iodide (1.0gm: 0.02 mole) and anhydrous potassium carbonate K_{2}CO_{3} (5.0gm: 0.04 mole) in dry acetone (50ml) was refluxed on water bath for (24hr), the excess acetone removed by distillation and the residue poured with stirring into water, the solid that precipitated was filtered off, dried and then crystallized from proper solvent to give compound 19.

Compound 19: Yield: 90%; m.p.140 °C;
Anal. Calced. for (C_{10}H_{8}N_{2}OBr_{2}): C 36.14, H 2.40, N 8.45. Found: C 34.92, H 1.29, N 9.32.
IR (KBr, cm^{-1}): 1671 \nu_{\text{C=O}} (amide)
MS show m/z (332) (27.2%).

**Synthesis of 2-(4-\text{N, N-dimethylaminostyryl})-6,8 -dibromoquinazolinone 20.**

A mixture of quinazolinone 3a (3.17gm: 0.01 mole), and 4(\text{N, N-dimethylaminobenzaldehyde}) (1.49gm: 0.01 mole), with a few drops of piperidine was fused in oil bath for (1hr) and
then reflux with D.M.F. for about (2hr), the reaction mixture was concentrated and the solid that precipitated was filtered off, dried and then crystallized from proper solvent to give compound 20.

Compound 20: Yield: 80%; m.p.320 °C;
IR (KBr, cm⁻¹):1625 νC=C, 1687 νC=O (amide) and 3160 νNH.

Synthesis of 3-(ethoxycarbonylmethyl)-2-(4-N,N-dimethylamino styryl)-6,8-dibromo-quinazolinone 21.

A mixture of quinazolinone 20 (4.49gm: 0.01 mole), and ethyl bromoacetate (6.68gm: 0.04 mole) and anhydrous potassium carbonate K₂CO₃ (5.0gm: 0.04 mole) in dry acetone (50 ml) was refluxed for (24hr), the excess acetone removed by distillation and the residue poured with stirring into water, the solid that precipitated was filtered off, dried and then crystallized from proper solvent to give compound 21.

Synthesis of 3-(ethoxycarbonylmethyl)-2-(4-N,N-dimethylamino styryl)-6,8-dibromo-quinazolinone 21.

A mixture of 3-(ethoxycarbonylmethyl)-2-(methyl)-6,8-dibromoquinazolinone 1 (4.04gm: 0.01 mole), and 4-(N,N-dimethylaminobenzaldehyde)(1.44gm: 0.01mole), with a few drops of piperidine was fused in oil bath for (1hr) and then reflux in dioxane for about (2hr), the reaction mixture was concentrated and the solid that precipitated was filtered off, dried and then crystallized from proper solvent to give compound 21.

Compound 21: Yield: 85%; m.p.333 °C;
IR (KBr, cm⁻¹):1602 νC=C, 1670,1736 νC=O.
MS show m/z (332) (27.2%), M⁺(375) (70.7%), (333) (100%)
The $^1$HNMR. spectrum (CDCl3) showed signals at $\delta$5 (s, 2H, NCH$_2$CO), $\delta$4.15 (q, 2H, CH$_2$-CH$_3$), $\delta$1.2 (t, 3H, CH$_3$ of ester), $\delta$3.7 (s, 6H, N(CH$_3$)$_2$) and, $\delta$6.4-8 (m, 8H, ArH).

**Synthesis of compound 22.**

A mixture of 3-(ethoxycarbonylmethyl)-2(4-4N,N-dimethyl amino styryl)-6,8-dibrom-quinazolinone 21, and hydrazine hydrate (1.49gm: 0.01mole), was reflux in boiling butanol for (5hr), the reaction mixture was concentrated and the solid that precipitated was filtered off, dried and then crystallized from proper solvent to give compound 22.

Compound 22: Yield: 75%; m.p. 310 °C;  

IR (KBr, cm$^{-1}$): 1623 $\nu$C=C, 1647 $\nu$C=O and 3223 $\nu$C=H
References:

1. P-Friedlaender and S. Wleugle, Chem. Ber., 16, 2229 (1883)
Scheme 1
Scheme 2
Scheme 3