

Synthesis and biological evaluation of some novel quinazolinone derivatives

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Abstract : The benzodiazine ring system, which result from the function of benzene ring with diazines constitute an important class of hetrocycles. Quinazoline is 1, 3-benzodiazine, which is essentially benzopyrimidine. Amongst the hetrocycles which have received considerable attention from chemists, the quinazolines have proved to be particular interest and importance. These compounds have been known since a long time and the first compound containing the quinazoline ring system was reported by Baeyer¹.

(Keywords : Benzodiazine ring system, 1, 3-benzodiazine).

Introduction

In view of the reactivities of the methyl and amino group in positions 3 and 2 respectively in 3-amino 2-methylaminozalone-4 and other similar quinazoles. We synthesized the some new quinazolinone derivatives for their biological evaluation. The preparation of some quinazolinone has been reported by previous workers², but the method adopted by them required modification in various aspects.

Furthermore this method was not expected to proceed well with the synthesis of those substituted aminoquinazolones where the hydrazine components were insoluble. It was therefore considered desirable to examine other routes for the synthesis of N (3) substituted 4-quinazolone Josef Klosa 3 to 5 reported the preparation of 3-amino-2-methyl quinazolone-4 by a simpler method which dispensed with the need to isolate the intermediate acetyl anthranil. They heated anthranilic acid with Excess of acetic

anhydride removed almost half the volume of the anhydride by distillation and added aqueous methanoic solution of hydrazone hydrate, deposited the ppt of aminoquinazolone in nearly 60% yield.

The method of Josef and Klosa for the preparation of aminomethyl quinazolones was considered the most suitable from practical view point and it was therefore, adopted in the present work with some modifications. After the initial reaction between anthranilic acid and acetic anhydride was distilled off. Some further modifications of Klosa's procedure were also found advantageous and were adopted in the present work. The addition of methanolic solⁿ of hydrazine was carried out at ice bath temperature after which the reaction mixture was left overnight at room temp. It was again easier to control the reaction and the yield of the first crop of crystals was very satisfactory. The repeated fractionation of the mother liquors to improve overall yield was thus found unnecessary.

Experimental

1. Synthesis of 3-Amino-2-methyl-4-quinazolone

Anthranilic acid (10g) was heated under reflux with acetic anhydride (30ml) for 3 hours and then about 20ml of acetic anhydride was distilled off. The reaction mixture was chilled in ice when it solidified to a brown mass. A solution of hydrazine hydrate (10ml, 90%) in methanol (10ml) was then added to chilled mass. In the beginning each drop of the reagent reacted vigorously with considerable evolution of heat. The reaction mixture was then left overnight to complete the reaction. Next day

excess of concentrated NH_4OH solⁿ was added to the mixture from which solid separated on chilling in ice. The solid was filtered off and washed with ice cold water. After recrystallisation from water deposited the pure quinazolone as white needles (6.8 gm) m.p.-148–150°C.

Analysis:

Found = C=61.46%, H=5.53%, N=23.82%

and rest is oxygen

Theoretical = C=61.71%, H=5.14%, N=24.0% and rest is oxygen

By using substituted hydrazine as given above the value of different "R". We synthesized the new quinazolinone-4 derivatives II to X and place for their biological evaluation. Structures of all new synthesized derivative was confirmed by spectral datas.

Spectral datas of synthesised compounds and list of symbols used

a = Carbonyl Stretching
b = Quinazolone Carbonyl Stretching
c = Unsaturated Carbonyl Stretching
d = Ring (C=C) and NEC Stretching
e = Substituted benzene ring
f = Bonded –NH (hydrazide) stretching
g = C=C (Conjugated with aromatic ring) stretching
h = C–O stretching and O–H bonding
i = O–H stretching (Carboxyl)
j = Bonding and other prominent absorptions

Compound

I. b = 1682 cm^{-1}
d = 1565 cm^{-1}
e = 640, 670, 760, 1480 cm^{-1}
f = 3320, 3270, 3180 cm^{-1}
j = 1410 cm^{-1} , 1370, 1360, 1250 cm^{-1}

II. b = 1660 cm^{-1}
d = 1580, 1570 cm^{-1}
e = 1480, 1490, 690, 760, 780, 890 cm^{-1}
f = 3280 cm^{-1}

j = 1380, 1320, 1260, 935 cm^{-1}

III. b = 1680 cm^{-1}
d = 1560 cm^{-1}
e = 645, 710, 770, 790, 850 cm^{-1}
f = 3310 cm^{-1}
j = 1120, 1190, 1250, 1350 cm^{-1}

IV. b = 1680 cm^{-1}
d = 1580, 1510, 1480, 840, 770, 690 cm^{-1}
e = 1620, 1510, 1480, 840, 770, 690 cm^{-1}
f = 3250, 3080 cm^{-1}
j = 1420, 1340, 1150, 1150, 1010, 910 cm^{-1}

V. b = 1670 cm^{-1}
d = 1670, 1580 cm^{-1}
e = 1480, 770, 765, 690 cm^{-1}
j = 1370, 1320, 1300, 1280, 1170, 950 cm^{-1}

VI. b = 1650 cm^{-1}
d = 1620, 1580 cm^{-1}
e = 1550, 750, 760, 680 cm^{-1}
g = 1610 cm^{-1}
j = 1480, 1370, 1270, 1180, 910 cm^{-1}

VII. b = 1670 cm^{-1}
d = 1570 cm^{-1}
e = 1460, 1510, 980, 860, 790, 710, 680 cm^{-1}
f = 3280 cm^{-1}
j = 3010, 3020, 1420, 1390, 1310, 1220 cm^{-1}

VIII. b = 1680 cm^{-1}
d = 1620, 1580 cm^{-1}
e = 1550, 770, 760, 690 cm^{-1}
g = 1605 cm^{-1}
j = 1480, 1370, 1250, 1180, 910 cm^{-1}

IX. b = 1650 cm^{-1}
d = 1620, 1560 cm^{-1}
e = 1480, 760, 680 cm^{-1}
f = 3220 cm^{-1}
j = 1420, 1310, 1020 cm^{-1}

X. b = 1670 cm^{-1}
d = 1620, 1590 cm^{-1}
e = 1480, 790, 770, 690 cm^{-1}
j = 1390, 1320, 1310, 1280, 1170, 950 cm^{-1}

Biological evaluations

All newly synthesised compounds were found to inhibit the growth of the fungus *Ustilago tritici* rostr, which is destructive pathogen of wheat causing loose smut disease in the plant. The test was performed by poisons food technique in Dox Agar medium at three concentrations. The remarkable feature in these quinazolinone is found highly effective in comparison to other heterocyclic compounds.

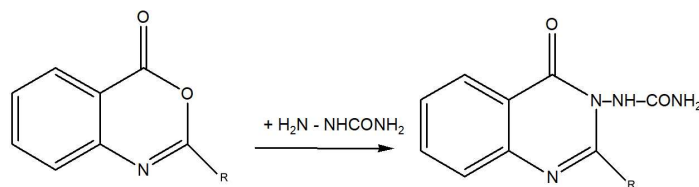
Results and Discussion

The preparation of 3-amino-2-methylquinazolinone was therefore carried out according to Klossa's modified method⁶⁻⁷. For the preparation of new quinazolinone, anthranilic acid was heated under reflux with acetic anhydride after which most of the anhydride was distilled off. The resulting acetantranilic which solidified on cooling was washed free from anhydrous acetic anhydride and then reacted with phenyl hydrazine, p-nitrophenyl

hydrazine 2,4-dinitrophenyl hydrazine in glacial acetic solution at reflux temperature to give respectively. The quinazolinone were obtained in high yields over 80%.

The acetantranilic was treated with hydrazine followed by different aromatic aldehydes then new quinazolinone derivatives were synthesised (1 to 10).

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|-------|-----|--|
| i) | R = | -CH ₃ |
| ii) | R = | Phenyl (Ph) -C ₆ H ₅ |
| iii) | R = | -C ₆ H ₄ -NO ₂ (p) |
| iv) | R = | -C ₆ H ₄ -NO ₂ (m) |
| v) | R = | -C ₆ H ₄ -OH (p) |
| vi) | R = | C ₆ H ₄ -OH (m) |
| vii) | R = | C ₆ H ₄ -OH (o) |
| viii) | R = | C ₆ H ₄ -OCH ₃ (p) |
| ix) | R = | C ₆ H ₄ -Cl (p) |
| x) | R = | C ₆ H ₃ (-p and m-OCH ₃) |



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