Research Paper

Volume : 3 | Issue : 6 | June 2014 • ISSN No 2277 - 8179

Synthesis of some Novel Heterocyclic Compound and their Antimicrobial Activity

Engineering

KEYWORDS :

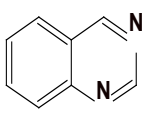
Hiral S. Tailor | Asst. Professor, Pacific School of Engineering, Surat – 394305, Gujarat, India

ABSTRACT

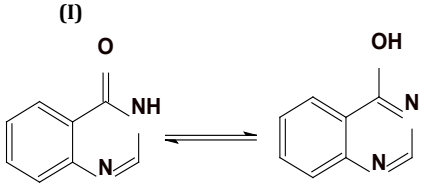
The quinazolone nucleus is embedded in a large number of alkaloids, drugs, antibiotics, agrochemicals, and antimicrobial agents. Many simple fused quinazolones are biologically active themselves or are essential component of very important naturally occurring substances (i.e. nucleic acids). The reaction of 6-Bromo -2-phenyl-4-H-3,1-benzoxazin-4-one(II) with p-amino acetophenone in presence of pyridine gives the resulting compound (III) and this compound when treated with different substituted aldehyde gives the new 6-Bromo-2-phenyl-3-[4-(3-substitutedphenyl-acryloyl)-phenyl]-3H-quinazolin-4-one. (IV). All the compounds have characterized by IR & NMR spectra and elemental analysis.

Introduction

Quinazolone [I] is Benz-1, 3-diazine containing 4-hydroxy substituent serves as nucleus to most of compounds which are associated with wide spectrum of pharmacological activities[1]. They are reported to exhibit properties of both the keto and enol forms [II].



(I)

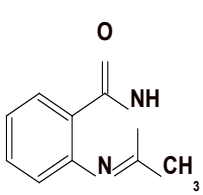


(II)

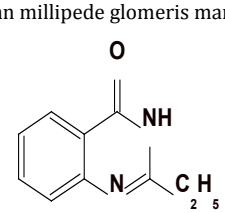
The quinazolone nucleus is embedded in a large number of alkaloids, drugs, antibiotics, agrochemicals, and antimicrobial agents. Many simple fused quinazolones are biologically active2 themselves or are essential component of very important naturally occurring substances (i.e. nucleic acids).

NATURAL QUINAZOLONES: -

The 4-ketoquinazolines have both animal and plant origin. The glomerin [III] and homoglomerin [IV] are the quinazolinone derivatives produced by european millipede glomeris marginata.



(III)



(IV)

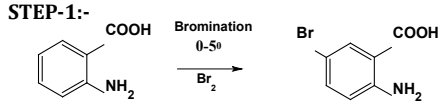
The quinazoline ring skeleton is widely found in alkaloids and many biologically active compounds.[3] Quinazolone a nitrogenous heterocycle, proved to possess a multitude of biological potency including anticancer,[4] antiproliferative agents,[5] antibacterial,[6] anti-inflammatory,[7] anticonvulsant, CNS depressant and antiHIV agents.[8] Earlier reports have shown that the presence of alkyl/aryl/heteroaryl groups at 2nd, 3rd position of quinazolone is beneficial to anti-inflammatory and anticancer activity.

The first quinazoline was synthesis by Weddinge [9] by melting the formyl or acetyl derivative of o-amidobenzamide. Bischler and Burkart[10] prepared a compound by heating the dry ammonium salt of formyl-o-amino benzoic acid and showed it to be identical with that prepared by weddige. It was later synthesized by Knape [11] who named it δ-oxyquinazoline and still later by Niemontowski [12] who first recognized the two tautomeric forms of δ- Oxyquinazoline.

OVERALL EVALUATION

REACTION OF SECTION-I

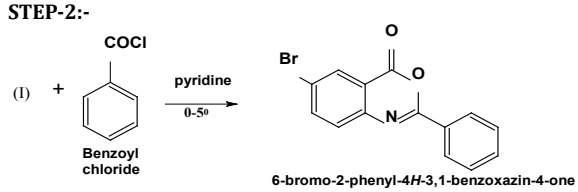
STEP-1:-



2-aminobenzoic acid — 2-amino-5-bromobenzoic acid

(I)

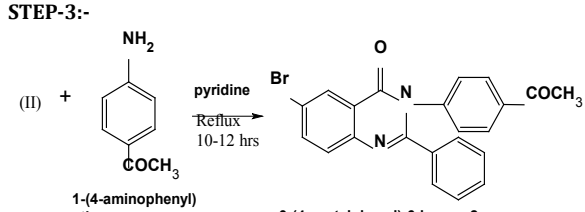
STEP-2:-



Benzoyl chloride — 6-bromo-2-phenyl-4*H*-3,1-benzoxazin-4-one

(II)

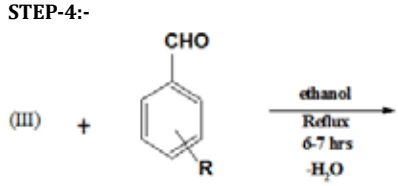
STEP-3:-

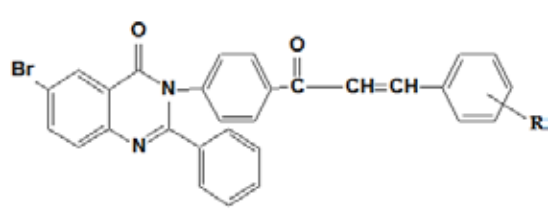


1-(4-aminophenyl) ethanone — 3-(4-acetylphenyl)-6-bromo-2-phenylquinazolin-4(3*H*)-one

(III)

STEP-4:-





(IV)

6-Bromo-2-phenyl-3-[4-(3-substitutedphenyl-acryloyl)-phenyl]-3H-quinazolin-4-one.

[NP 1 to NP 10]

EXPERIMENTAL

→ Preparation of 2-amino-5-bromo benzoic acid. In a 250 ml beaker Anthranilic acid (1.37 g, 0.01 moles) was dissolve in glacial acetic acid (10 ml, 0.01 moles) and cooled below 16^0C. After bromine (0.52 ml, 0.01 moles) at 0-5 ^{0}C was added drop wise to the reaction mixture. Reaction mixture consisting of the hycrobromide of the mono- and di-bromo anthranilic acids was stirred for further 2-3 hours and then boiled up with water (50 ml) containing concentrated hydrochloric acid (10 ml) and filter when hot with suction. The insoluble residue was extracted twice more with boiling water. The filtrate upon cooling yielded abundant precipitate of the 5-bromo anthranilic acid and insoluble residue consisted of the 3, 5-dibromo anthranilic acid.

M.P-219-20^{0}C YIELD - 80 %

→ Preparation of 6-bromo-2-phenyl-4H-3, 1-benzoxazin-4-one.5-bromo anthranilic acid (0.01mole) was dissolve in pyridine (30ml). The solution was cooled and benzoyl chloride (0.02 moles) was added drop wise with constent stirring. After the addition was complete, the mixture was further stirred for 30 min. at room temperature. It was then treated with sodium bicarbonate solution (5%) to remove any unreacted acid. When the effervescences ceased, it was filtered and washed repeatedly with water in order to remove excess of pyridine. It was crystallized from dilute ethanol.

M.P-205-207^{0}C YIELD - 77 %

→ Preparation of 3-(4-acetylphenyl)-6-bromo-2-phenylquinazolin- 4(3H)-one. A mixture of 6-bromo-2-phenyl-4H-3, 1-benzoxazin-4-one (0.01 moles) and p-amino acetophenone (0.01 moles) in dry pyridine (25ml) was refluxed for 10-12 hours under anhydrous condition, and excess of pyridine was removed under reduced pressure. The concentrated mass was cooled and poured into ice cold hydrochloric acid to give a solid product which was filtered and washed with water till neutral.

M.P-190-91^{0}C YIELD - 60 %

→ Preparation of 6-Bromo-2-phenyl-3-[4-(3-substituted-phenyl-acryloyl)-phenyl]-3H-quinazolin-4-one. In a 250 ml R.B.F., 3- (4-acetylphenyl) - 6 - bromo - 2 - phenylquinazolin-4(3H)-one (0.01 mole) in methanol (20 mL) and diff. type of substituted aldehyde (0.01 mole) were taken and to it (5-6 mL) of 5% NaOH solution was added. The reaction mixture refluxed for 5-8 hours and then poured into ice water. The solid product was filtered and washed with water, dried and recrystallised from methanol.

M.P-175-78^{0}C YIELD - 66 %

No.	R	Molecular formula(M. wt.)	Yield %	M.P. ^{0}C.
NP-1	3-OCH_3,4-OH	$C_{30}H_{21}BrN_2O_4$ (553.40)	71	207
NP-2	4-CH_3	$C_{30}H_{21}BrN_2O_2$ (521.4)	68	196
NP-3	2-Cl	$C_{29}H_{18}N_2O_2BrCl$ (541.8)	65	176
NP-4	4-Cl	$C_{29}H_{18}N_2O_2BrCl$ (541.8)	69	183
NP-5	2,4-$(Cl)_2$	$C_{29}H_{17}N_2O_2BrCl_2$(576.26)	68	203
NP-6	2-OCH_3	$C_{30}H_{21}N_2O_3Br$ (537.40)	66	181
NP-7	4-OCH_3	$C_{30}H_{21}N_2O_3Br$ (537.40)	72	208
NP-8	4-H	$C_{29}H_{19}N_2O_2Br$ (507.3)	73	214
NP-9	4-$N(CH_3)_2$	()	71	228
NP-10	2-OH	$C_{29}H_{19}N_2O_3Br$ (523.37)	70	198

ANTIMICROBIAL ACTIVITY

A short review of results of antimicrobial screening of the compounds of this section is mentioned here.

ANTIBACTERIAL ACTIVITY

[I] Against S. aureus and B. Subtilis as gram positive bacteria

Maximum activity was found in compound NP-7 (Zone of inhibition 21.0 mm) against S.aureus and NP-9 (Zone of inhibition 21.0 mm) against B.subtilis respectively. Minimum activity was found in compound NP-6 (Zone of inhibition 6.0 mm) and NP-10 (Zone of inhibition 5.0 mm) respectively.

[II] Against E. coli and P.aeruginosa as gram negative

Maximum activity was found in compound NP-5 (Zone of inhibition 21.0 mm) against E.coli and NP-1 (Zone of inhibition 21.0 mm) against P.aeruginosa respectively. Minimum activity was found in compound NP-6 (Zone of inhibition 6.0 mm) and NP-10 (Zone of inhibition 6.0 mm) respectively.

Spectral Data:-

Infra-Red Spectra-

IR Spectral Data of Compound [NP-5] R=2, 4-$(Cl)_2$

Vibration Mode	Frequency in cm^{-1}
Quinazoline (C=O) Str	1718
(C=N) Str	1642
(N-C-N) str	1332
-C6H4 aeromatic (C=C)	1576
(C-Br) str	680
R- Halide (C-Cl) str	819

IR Spectral Data of Compound [NP-3] R=2 Cl

Vibration Mode	Frequency in cm^{-1}
Quinazoline (C=O) Str	1720
(C=N) Str	1655
(N-C-N) str	1360
-C6H4 aeromatic (C=C)	1561
(C-Br) str	578
R- Halide (C-Cl) str	739

NMR Spectra:-

NMR Spectral Data of compound[NP-2]

Inference	Signal Position
α-proton of chalcone	6.79
β-proton of chalcone	7.09
R=4-CH3	2.03
Ar-H(15 H)	6.83-7.57
Ar-H(1H)	8.21

REFERENCE

1. H M F Madkour, ARKIVOC, (i), 2004, 36. | 2. M Srivastava, B Mishra, & Nizamuddin, Ind. J. Chem., 40B, 342, 2001. | 3. F R Alenx&re, A Berecibar & T Besson, Tetrahedron, 59, 1413-1419, 2003. | 4. Yixia, Z Y Yang & K H Lee, Bioorg Med Chem Lett, 11, 2001, 1193. | 5. A J Barker, K H Gibson, W Grundy, A A Godfrey, J J Barlow & M P Healy, Bioorg Med Chem Lett 11, 2001, 1911 | 6. K R Desai & K M Mistry, E-Journal of Chem, 2(2), 2005, 47. | 7. J Sarvanan & K S Manjunatha, Indian J Heterocycl Chem, 8(1), 55, 1998. | 8. A Rosowsky, R A Forsch & S F Queener, J Med Chem, 42, 1007,1999. | 9. Weddige, A., J Prakt Chomic Neuo Folge 31, 124 (1885). | 10. Aug. Bischler and Ed. Burkart, Ber 26, 1349 (1893). | 11. Emil Knape, J. Prakt. Chemie 43, 214 (1891). | 12. Niemontowski, St Von,. J Prakt. Chemie 51, 564 (1895). |