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AN INVESTIGATION LEADING TO THE SYNTHESIS OF N-[(AMIDO/IMIDO-2-YL)ALKYL]-4-OXO-1-PHENYL-QUINAZOLIN-3(4H)-CARBOXAMIDES

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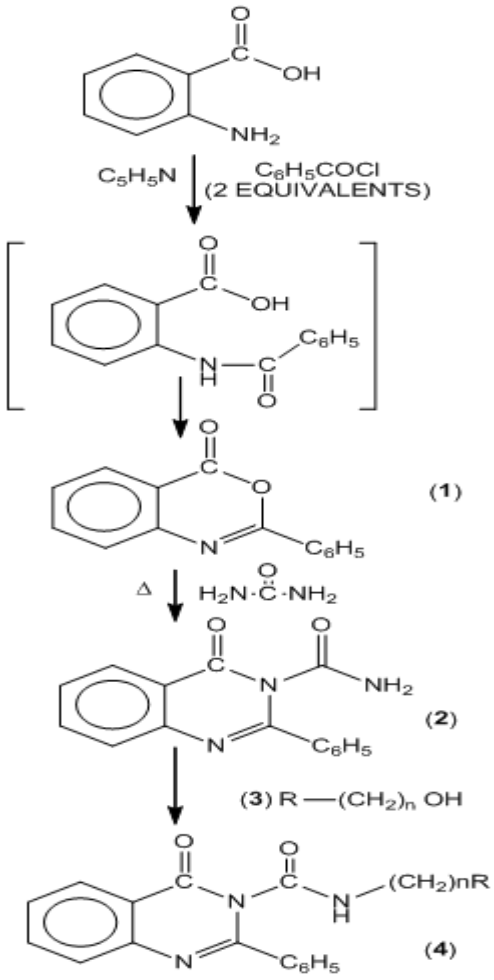
***Abstract*—2-Phenyl-4H-benzo[dJ[1,3]oxazin-4-one(I)was prepared by the reaction of anthranilic acid with benzoyl chlonide in pyridine solution. Heating of (I) with carbamide resulted in 4-oxo-2-phenyl-quinzolin-3-(4H).carboxamide(II) which on reaction with amido/imido-alcanols afforded N-[(amido/imido-2-yl)alkyl]-4-oxo-1-phenyl-quinazolin-3(4H)-carboxamides(III) as target compounds in moderate yields.**

Index Terms— amido alcohol, benzoxazine, quinazolone.

I. INTRODUCTION

Quinazolones and quinazolines as medicinal have been investigated in various health areas. The interest in quinazolone and quinazoline chemistry has increased manifolds because of their association with anticarcinogenic-activity. Some such compounds have shown excellent results against human leukemia cells and some of them showed comparatively better results than the methotrexate[1-5]. In addition, quinazolones and quinazolines have demonstrated excellent pharmacological results against highly pathogenic viruses viz; Japanese encephalitis virus(JEV) and Herpes simplex virus (HSV) type-I[6]. There are also scattered reports of quinazolones in other health areas[7-10]. These valid observations prompted the author to undertake the synthesis of some new quinazolone derivatives(Scheme I)



SCHEME-I

Experimental details

2-Phenyl-4H-benzo[d][1,3]oxazin-4-one(I)

2-Phenyl-4H-benzo[d][1,3]oxazin-$-one(I) was synthesized following the literature method.[11]

4-Oxo-2-phenyl-quinazolin-3(4H)-carboxamide(III)

A mixture consisting of 2-phenyl-4H-benzo[d][1,3]oxazin-4-one(I)and carbamide in equimolar quantity was heated at 115-120°C for one hour in such a manner that water formed during the course of the reaction escaped from the reaction mixture. Subsequently, the hot melt was allowed to cool. On attaining the room-temperature, it was treated with water in order to dissolve the unreacted carbamide. The crude quinazolone derivative was filtered off and air dried. Recrystallisation from ethanol resulted in a compound of white colour. It melted at 38°C; yield,70%.

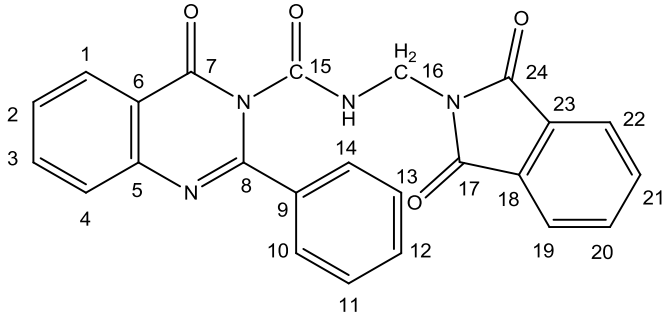
N-[(Amido/imido-2-yl)alkyl]-4-oxo-2-phenyl-quinazolin-3(4H)-carboxamides(III)

A mixture consisting of 4-oxo-2-phenyl-quinazolin-3(4H)-caboxamide(0.02 mole) and the hydroxyalkyl compound (0.02 mole) was dissolved in conc. H_2SO_4 by stirring cautiously. While dissolving the contents were frequently cooled since exothermic reaction occurred. A dark brown solutuion was obtained which was further stirred mechanically. The resultant solution was left undisturbed under refrigeration overnight and was poured into cold water slowly and carefully. Precipitation started to occur. On complete addition a thick precipitate was obtained which was allowed to settle down for one hour. It was filtered off and was washed repeatedly with water in order to remove any sulphonated products. The crude amido/imido alkylated product thus obtained, was dried in vacuo and recrytallized from diluted ethanol. The target compounds thus synthesized are reported in Table-I along with their characterization data.

Characterization data of N-[(Amido/imido-2-yl)alkyl]-4-oxo-2-phenyl-quinazolin-3(4H)-carboxamides(III)

Compound No.	R	n	m.p. (°C)	Yield	Colour	Molecular formula	Molecular Weight	Analysis Nitrogen %	
								Calcd.	Found
3a	Phthalimido	1	153	65	White	$C_{24}H_{16}N_4O_4$	424	13.20	13.25
3b	Phthalimido	2	158	60	Grey	$C_{25}H_{18}N_4O_4$	438	12.78	12.55
3c	4- Oxo- 2-phenyl-3(4H)-quinazolin	2	168	70	Grey	$C_{31}H_{23}N_5O_3$	503	11.13	10.95
3d	Benzamido	1	162	61	White	$C_{23}H_{18}N_4O_3$	398	14.07	14.32

Spectral data of N-[(phthalimido-7-yl)methyl]-4-oxo-2-phenyl-quinazolin-3(4H)-carboxamide

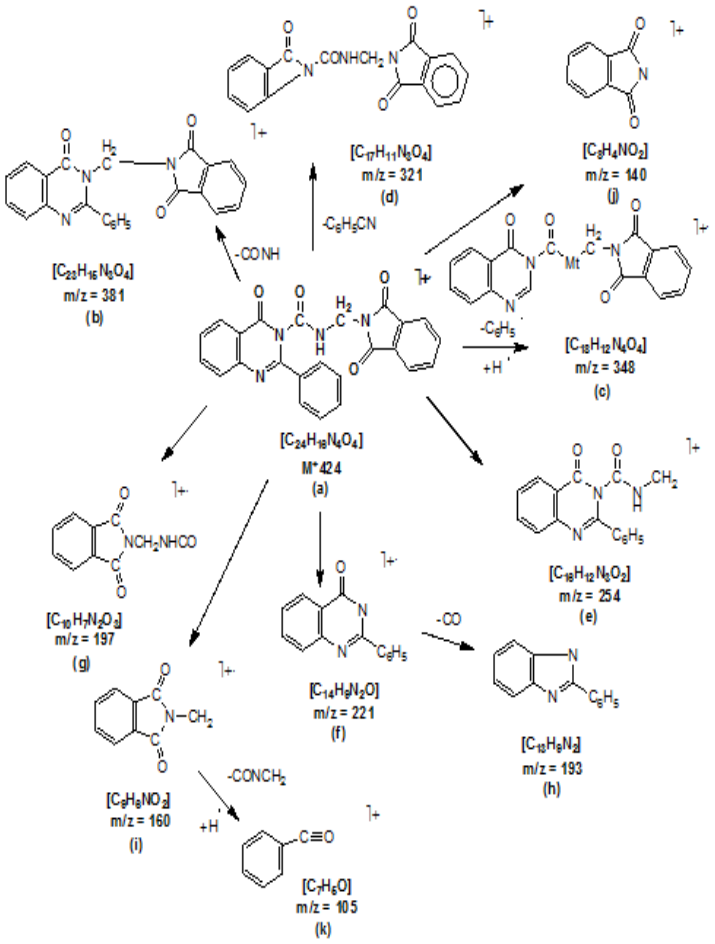


IR (KBr) (√ in cm^{-1}): 1668.2 (sec. amide C=O), 1596.0 (C=N), 1719.5 (imide C=O), 3450.3 (amide NH), 1308.6 (amide C-N)

^{1}HNMR ($CDCl_3$) (δppm): 5.46 (d, 2H, $NHCH_2$), 8.22 (t, 1H, NH), 6.27 – 7.85 (m, 13H, ArH)

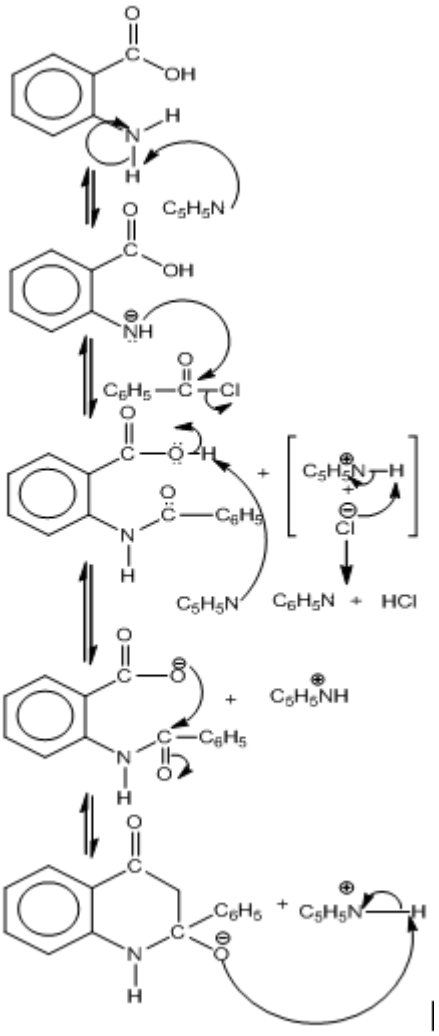
^{13}CNMR ($CDCl_3$+DMSO-d_6) (δppm): 39.98 (C-16), 115.56, 119.77, 122.20, 127.08, 127.93, 128.17, 128.36, 131.28, 131.49, 131.67, 132.32, 133.73, 134.10, 134.66, 136.32 (C-1 to C-6), (C-9 to C-14), (C-18 to C-23), 155.98 (C-8), 165.339 (C-15), 167.24 (C-17), 170.51 (C-17 to C-24)

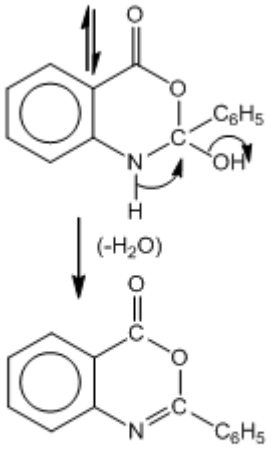
MASS SPECTRAL FRAGMENTATION PATTERN OF N- [(PHTHALIMIDO- 9- YL) METHYL] - 4- OXO-PHENYL- QUINAZOLIN- 3(4H) CARBOXAMIDE



Mechanistic details for the formation of compounds(I), (II), (III) have been provided herein.

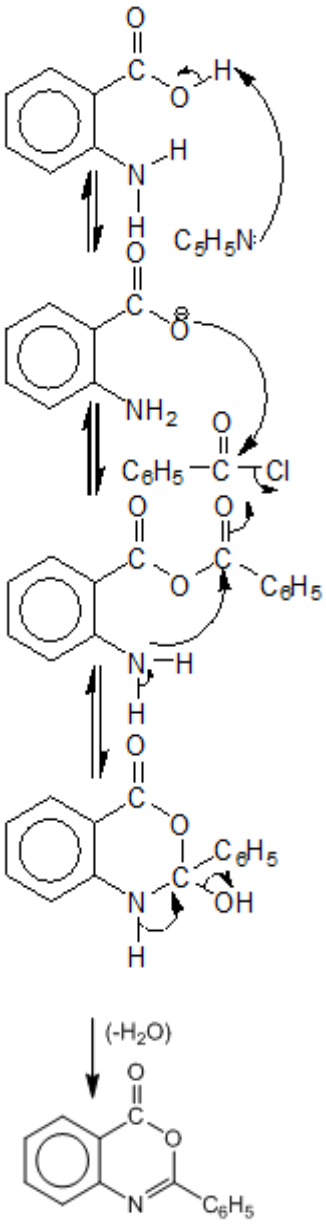
Formation of I





(I)

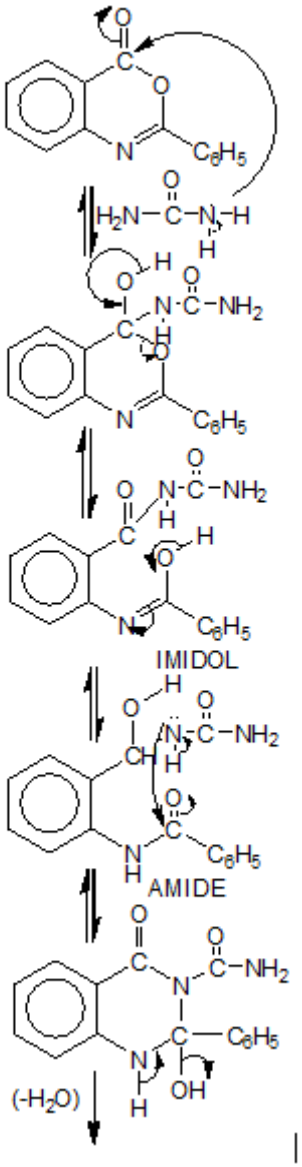
Since an excess of benzoyl-chloride is taken, it is suggested here that an alternative mechanism may also operate as suggested here:

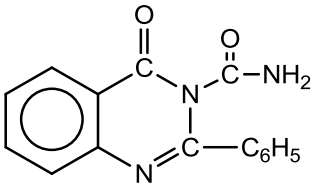


(I)

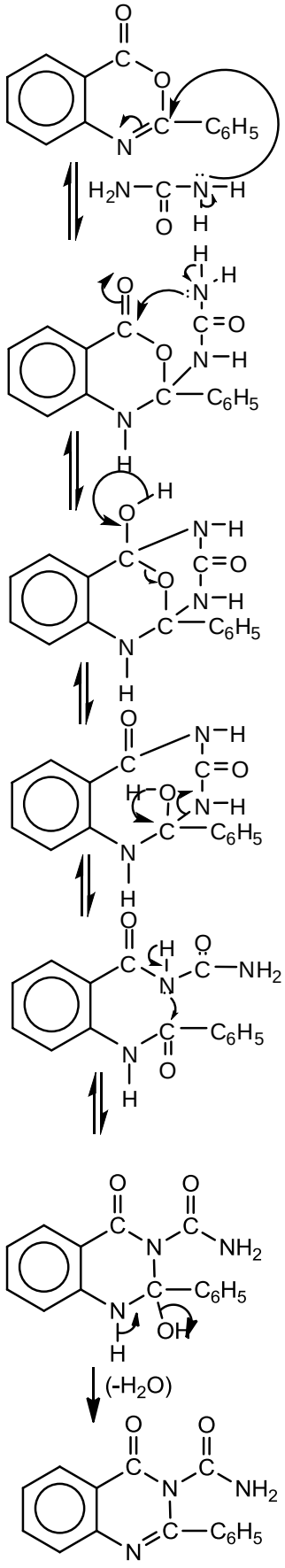
FORMATION OF COMPOUND (II)

Formation of the compound (II) is suggested on the basis of the nucleophilic attack on the carbonyl carbon atom of (I) as proposed here mechanistically.



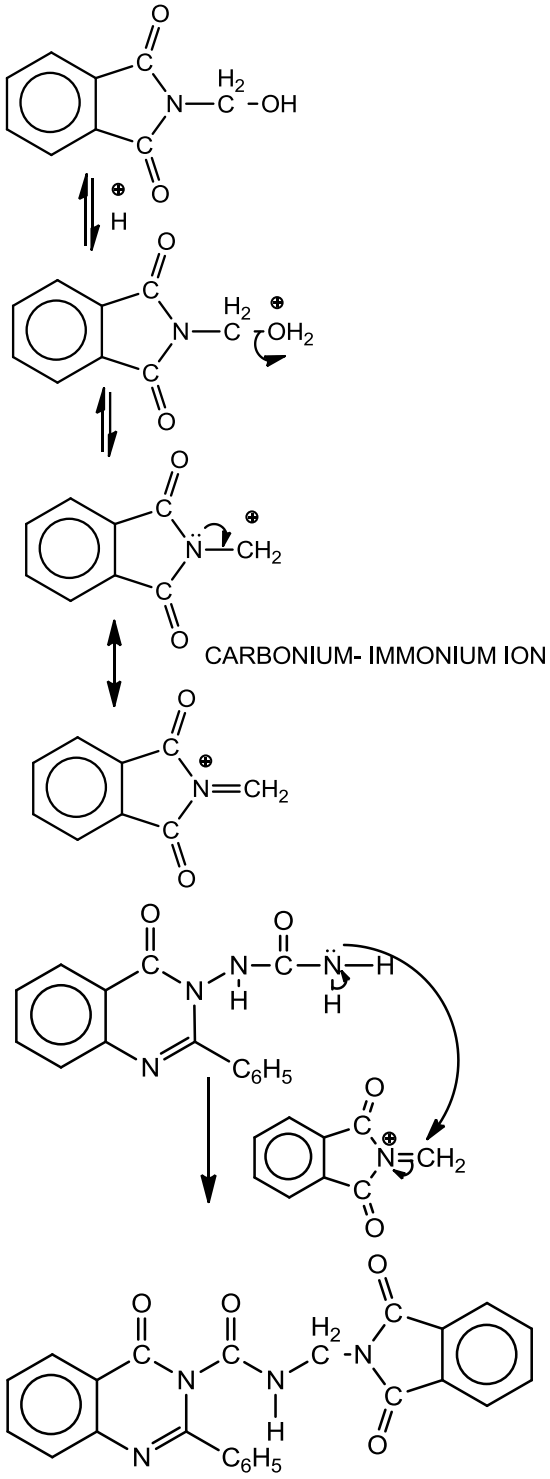


Second possibility is the attack by the nitrogen on the imino carbon atom as suggested here by the following proposed mechanism.



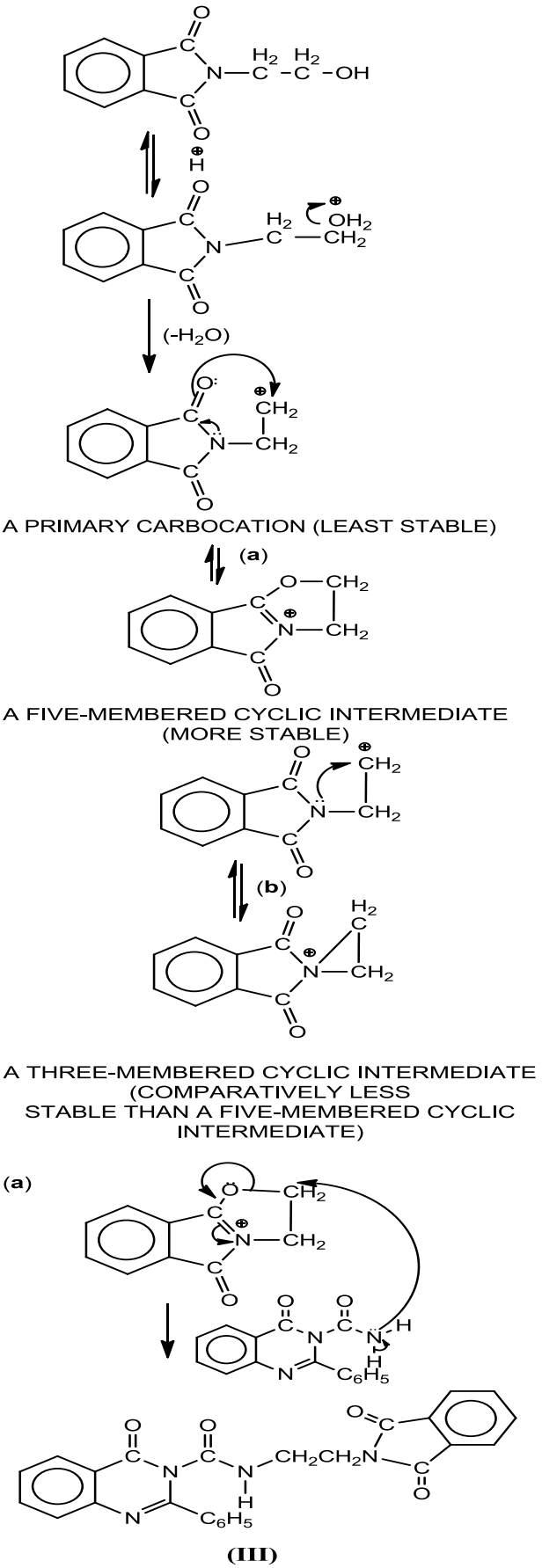
FORMATION OF COMPOUND (III)

Transformation of (**II**) into (**III**) is an example of amido/ imido alkylation reaction followed by Tscherniac procedure[12]. This transformation has been explained here taking the example of N-methylol phthalimide.



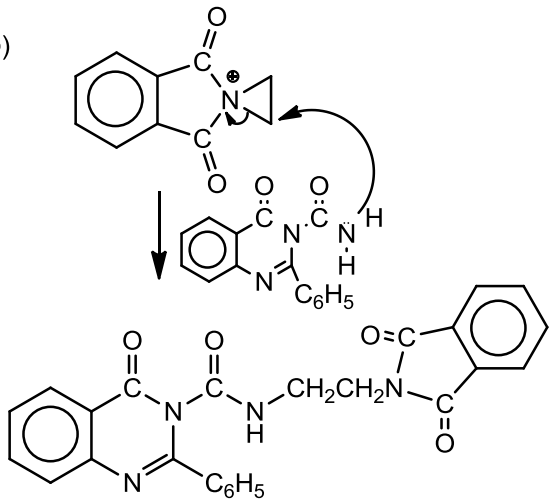
(III)

However, with N-ethylol phthalimide a different mechanism may operate which either involves a five-membered cyclic intermediate or a three-membered cyclic intermediate but a five-membered cyclic intermediate is more preferred.



(III)

(**b**)



(III)

II. AKNOWLEDGEMENT

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