

Synthesis and Studies on Heterocyclic Compounds Containing Mixed and Non-Mixed Systems

By

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(M.Sc. Degree)**

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IN
CHEMISTRY**

Under the supervision of

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Chemistry Department

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Thesis approval

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SUMMARY

Summary

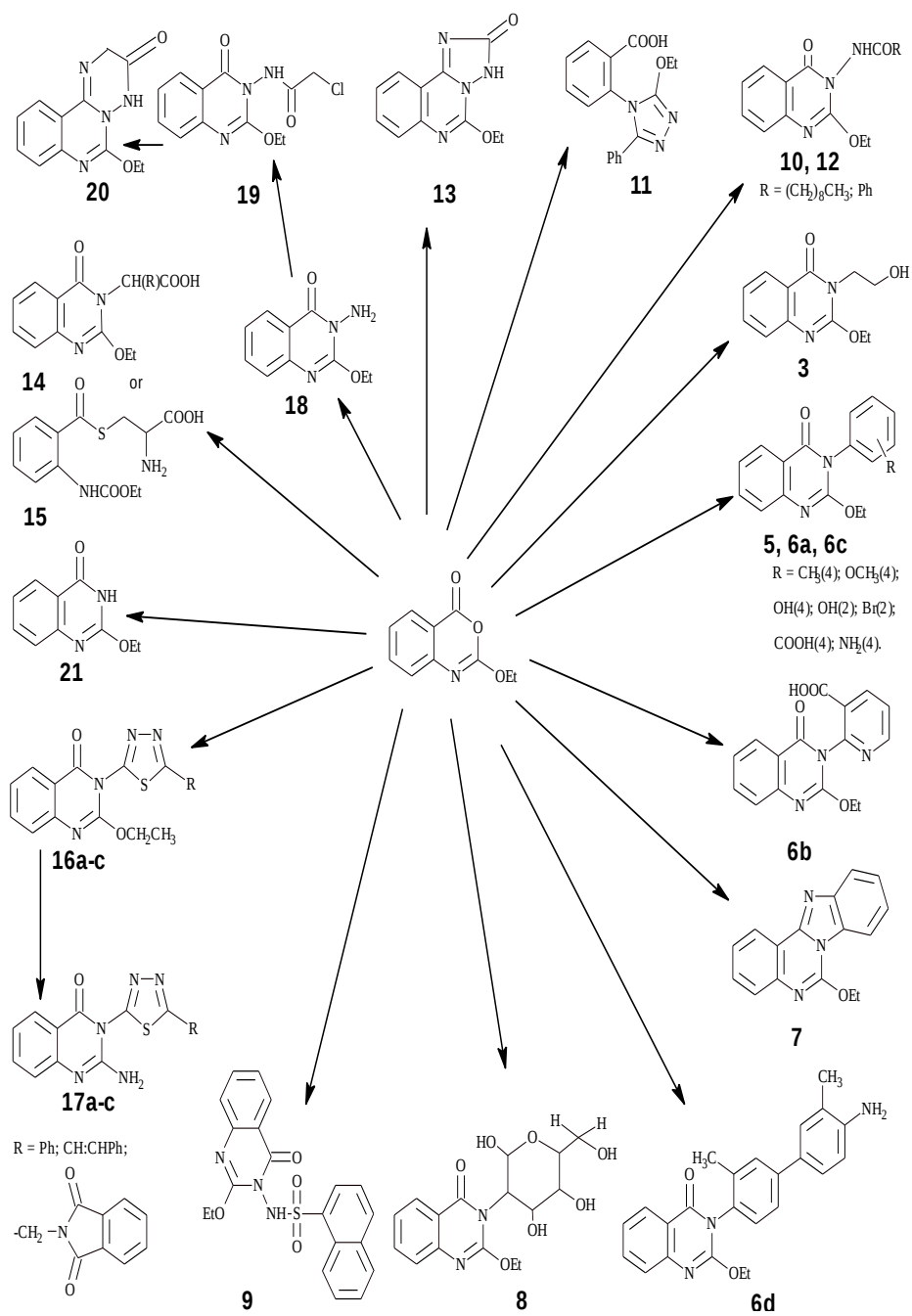
The thesis includes two parts:

Part I: The uses of 2-ethoxy (4*H*)-3,1-benzoxazin-4-one in the synthesis of quinazolinones

- Reaction of 2-ethoxy (4*H*)-3,1-benzoxazin-4-one (**1**) with 2-aminoethanol in ethanol followed by heating to give at first the open structure 2-ethoxycarbonylamino(β -hydroxyethyl)benzamide (**2**) then 2-ethoxy-3-(2-hydroxyethyl)quinazolin-4-one (**3**) respectively.
- Reaction of compound (**1**) with *p*-toluidine, *p*-anisidine, *p*-hydroxyaniline, *o*-hydroxyaniline and *o*-bromoaniline in boiling ethanol then further heating of products to give first the open structures anthranils (**4a-e**) then the novel quinazolinones (**5a-e**).
- Reactions of compound (**1**) with *p*-aminobenzoic acid, 2-aminonicotinic acid, *p*-phenylenediamine and *o*-tolidine in butanol and/or ethanol affording compounds (**6a-d**) respectively.
- Reaction of compound (**1**) with *o*-phenylenediamine in ethanol yielded compound (**7**).

- Reaction of compound (1) with glucosamine hydrochloride in pyridine afforded compound (8).
- Reaction of compound (1) with *o*-naphthalenesulfonyl hydrazide in ethanol yielded compound (9).
- Reaction of compound (1) with *n*-decanohydrazide in ethanol afforded compound (10).
- Interaction of compound (1) with benzoylhydrazine in *n*-butanol yielded compound (11) and in benzene afforded compound (12).
- Reaction of compound (1) with semicarbazide in acetic acid/fused sodium acetate gave compound (13).
- Reactions of compound (1) with amino acids namely, DL-alanine, L-asparagine, and L-arginine in pyridine yielded compounds (14a-c) and with L-cysteine in pyridine gave compound (15).
- Reactions of compound (1) with heteroaromatic amines namely, 2-phenyl-5-aminothiadiazole, 2-cinnamyl-5-aminothiadiazole and 5-phthalimido-methyl-2-aminothiadiazole in acetic acid yielded compounds (16a-c), respectively.

- Reactions of compounds (**16a-c**) with formamide afforded compounds (**17a-c**).
- Reaction of compound (**1**) with hydrazine hydrate in ethanol yielded compound (**18**).
- Reaction of compound (**18**) with chloroacetyl chloride in DMF yielded compound (**19**).
- Reaction of compound (**19**) with ammonium acetate in oil bath gave compound (**20**).
- Reaction of compound (**1**) with ammonium acetate in oil bath yielded compound (**21**).

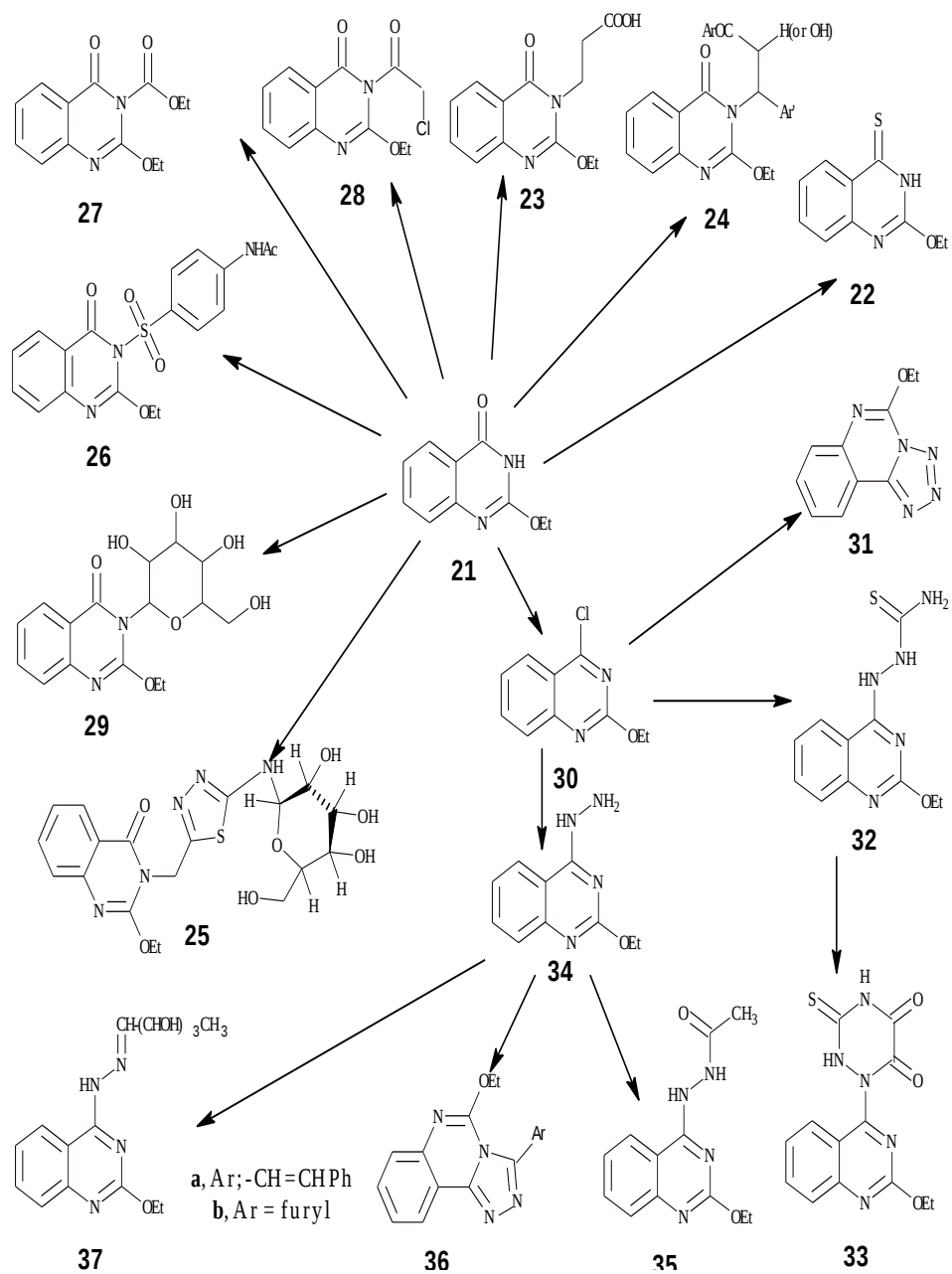


Part II: Reactivity and use of 2-ethoxy-4(3*H*) quinazolinone (21) in synthesis of quinazolines and quinazolinones

- Reaction of compound (21) with phosphorus pentasulfide / dry xylene afforded compound (22).
- Reaction of compound (21) with acrylonitrile in DMF afforded compound (23).
- Reaction of compound (21) with disubstituted oxirane in ethanol afforded compounds (24).
- Reaction of compound (21) with an *N*-glucosidated thiadiazole derivative in pyridine yielded compound (25).
- Reactions of compound (21) with *p*-acetylaminobenzenesulfonyl chloride in pyridine yielded compound (26).
- Reaction of compound (21) with ethyl chloroformate in pyridine gave compound (27).
- Reaction of compound (21) with chloroacetyl chloride in pyridine yielded compound (28).
- Reaction of compound (21) with α -bromoglucose tetraacetate in 1,4-dioxane yielded compound (29).
- Reaction of compound (21) with phosphorus pentachloride

and phosphoryl chloride on water bath giving the chloro-derivative (**30**).

- Reaction of compound (**30**) with sodium azide in acetic acid gave compound (**31**).
- Reaction of compound (**30**) with thiosemicarbazide in pyridine yielded compound (**32**).
- Reaction of compound (**32**) with diethyl oxalate in ethanol afforded compound (**33**).
- Reaction of compound (**30**) with hydrazine hydrate in butanol yielded compound (**34**).
- Reactions of compound (**34**) with acetyl chloride in pyridine yielded compound (**35**).
- Reactions of compound (**34**) with cinnamoyl chloride and furoyl chlorides in pyridine gave compounds (**36a** and **36b**).
- Reaction of compound (**34**) with D-xylose in methanol gave compound (**37**).



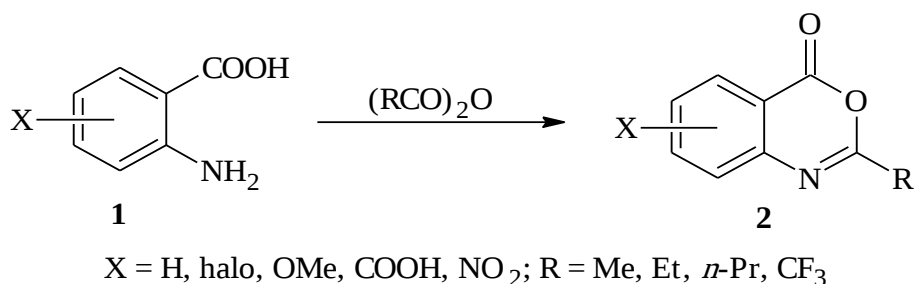
Introduction

Introduction

Synthesis of 4*H*-3,1-Benzoxazin-4-ones

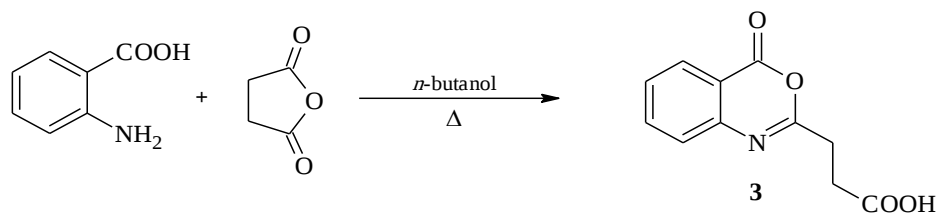
I) From anthranilic acid:

2-Substituted (4*H*)-3,1-benzoxazin-4-one derivatives **2** are prepared by reacting anthranilic acids **1** with an appropriate anhydride. Lower molecular weight anhydrides are usually employed as the solvent [21,32,52,100,101,170,247,256]. Co-solvents such as chloroform [25], dioxane [41] and toluene [300], have been successfully used.

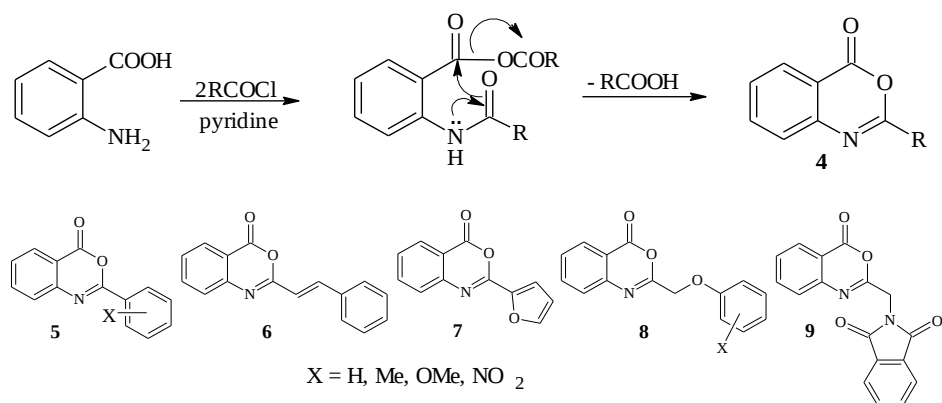


Similarly, 2-(β -carboxyethyl) (4*H*)-3,1-benzoxazin-4-one **3** has been obtained by heating anthranilic acid with succinic anhydride in butanol [105].

Introduction

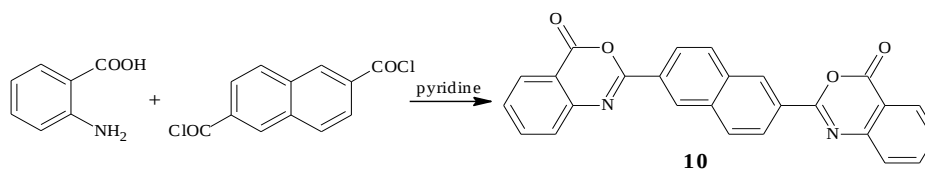


Anthranilic acid reacts with two equivalents of an acid chloride in pyridine solution to give 2-alkyl-3,1-benzoxazin-4-one **4**. 2-Phenyl analog **5** containing a variety of substituents (X = H, Cl, Br, Me, OMe, CF₃, NO₂, COOH) at the ortho-, meta- or para-positions have been prepared [33,83,123,162,151,248]. Also, both α - and β -naphthyl analogs [212], as well as the styryl derivative **6** [33,290,291] and furyl derivatives **8** and phthalimide derivatives **9** have been reported [178,280].

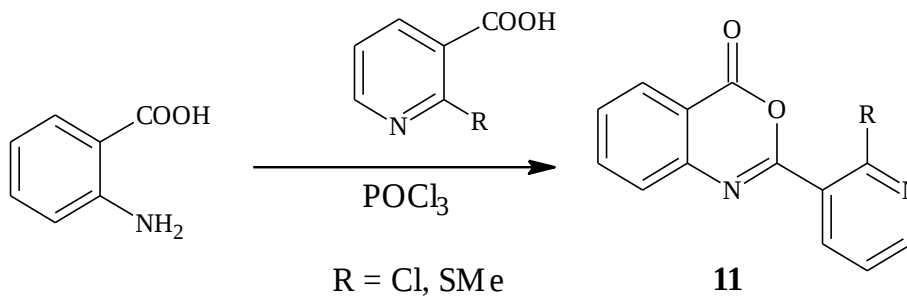


Introduction

Sunscreen containing a cyclic imino esters **10** as a UV absorbent, has been obtained *via* interaction of 2,6-naphthalene dicarboxylic acid chloride with anthranilic acid in pyridine [313].



The reaction of equimolar quantities of anthranilic acid and nicotinic acid in phosphorus oxychloride solvent produced interesting pyridyl analogs **11** [269].



The aminobenzoxazinone derivative **13** is prepared from the reaction of equimolar quantities of 3-trifluoromethylantranilic acid **12** and a Boc-protected amino acid with two equivalents of isobutyl chloroformate in the presence of *N*-methylmorpholine [62,64].