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**Short Communication**

# Synthesis and Characterization of 4-(2-Methyl-4-Oxoquinazolin-3(4*H*)-Yl) Benzoic Acid Derivatives Using Some Biologically Active Alcohols and Phenols

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## ABSTRACT

*4-(2-methyl-4-oxoquinazolin-3(4H)-yl) benzoic acid was prepared by acetylation of anthranilic acid with acetic anhydride followed by ring closure which was done by direct condensation with p-aminobenzoic acid. The produced compound was then treated with thionyl chloride to produce the corresponding acid chloride which in turn was reacted with different hydroxylic compounds to produce the corresponding esters. All the synthesized compounds were identified by the spectroscopic techniques like FT- IR and $^{1}$HNMR techniques and were characterized through their physical properties.*

**Keywords:** Synthesis and characterization of new esters, use of biologically active alcohols and phenols.

## INTRODUCTION

Quinazolinones (benzopyrimidine derivative) are a large family of heterocyclic compounds with wide biological activities, including: anti-cancer, anti convulsant, anti-inflammatory, anti-tubercular and anti-bacterial activities [1-7]. A highly used method for synthesis of 4(3*H*)-quinazolinone is based on the acylation of anthranilic acid with acid chloride or anhydride followed by ring closure whichcan be done by the condensation with hydrazine hydrate or aromatic amines [8,9]. In this study *p*-amino benzoic acid have been used as an aromatic amine to produce 4-(2-methyl-4-oxoquinazolin-3(4*H*)-yl) benzoic acid which then was the starting material for synthesis of the desired esters. The synthesis of an ester can be accomplished in one of several ways. Acid chlorides or anhydrides react with alcohols or phenols to yield an ester and hydrochloric acid. Also an esterification occurs when an alcohol and a carboxylic acid are reacted in the presence of a mineral acid catalyst, such as sulfuric acid [10].

## MATERIALS AND METHODS

**General:** All chemical materials and solvents were obtained from commercial sources. Melting points were measured on a Gallan Kamp MFB-600 Melting point apparatus and were uncorrected. FTIR spectra were recorded as potassium bromide (KBr) disk on FTIR-8400S Fourer Transform Infrared Spectrophotometer "SHIMADZU". $H^{1}$ NMR spectra were recorded on Burker DMX- 500 NMR (300-600 MHz) Spectrophotometer with using DMSO as a solvent.

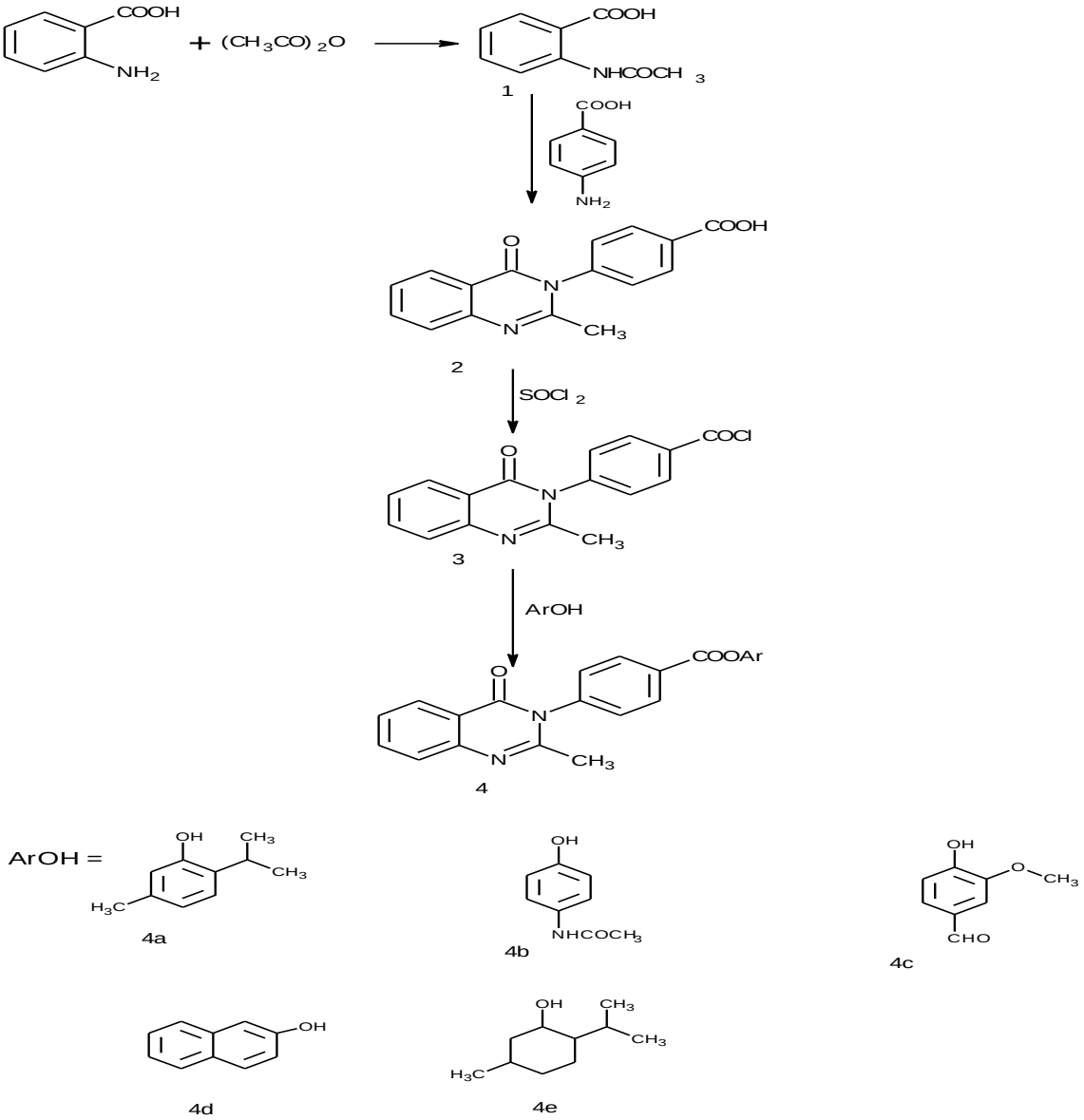
**Preparation of compound** 1 **[11]:** Anthranilic acid (0.02 mol) and acetic anhydride (0.02 mol) was mixed and heated under reflux for 15 min. The mixture was set aside to cool, then poured onto cold water (50 mL) and stirred for 15 min to produce a precipitate which was filtered off and washed with cold water (50 mL). The precipitated solid was collected as an off white solid, Yield 90%, mp =192- 194$^0$C.

**Preparation of compound** 2: *P*-aminobenzoic acid (0.01 mol) was added to a hot solution of compound 1(0.01 mol) in absolute ethanol and refluxed for 6 h to produce a precipitated solid which was collected by filtration and then recrystallized from ethanol, as a yellow solid, Yield 70%, mp = 155-157$^0$C.

**Preparation of compound** 3: Compound 2 (0.01 mol) was dissolved in thionyl chloride with stirring for 15 min. The yielding mixture was heated to about 40°C for 10 min. Excess thionyl chloride was removed by evaporation under air. The crude product was filtered, washed with diethyl ether and dried by air. The product was obtained as a yellow solid with yield 90%, mp = 116-118$^0$C.

**Preparation of compounds** 4a-d: Phenolic compounds (a-d) (0.01 mol) were dissolved in an aqueous solution of (0.008 mol) of KOH and stirred for overnight. Compound 3 was added by small portions with stirring to the previously prepared solutions of phenolic compounds (a-d). The produced mixtures were further stirred until a precipitated solid was obtained. The product was collected by filtration then recrystallized from DMSO. The esters were obtained as pale yellow crystals, (75% for 4a mp= 164-166$^0$C), (70% for 4b mp= 146-148$^0$C), (78% for 4c mp= 155-157$^0$C), (72% for 4d mp= 143-145$^0$C).

**Preparation of compound** 4e: Compound 2 (0.002 mol) and menthol (0.002 mol) was dissolved in acetone and few drops of sulfuric acid were added to the mixture. The mixture was then refluxed for 3 h. It was then cooled and the solid was collected by filtration and washed with cold water. The product was recrystallized from ethanol to obtain yellow precipitate (75%), mp=140-142$^0$C.




**Scheme 1:** Preparation steps of compounds

## RESULTS AND DISCUSSION

The structures of the products were confirmed on the basis of the spectral data analysis such as IR and NMR.

**Spectral data of synthesized compounds.**

**2-(acetylamino)benzoic acid 1:** IR (KBr) 3300 $cm^{-1}$ for (O-H), 3231 $cm^{-1}$ for (N-H), 3075 $cm^{-1}$ for Aromatic (C-H), 2780 $cm^{-1}$ for Aliphatic (C-H), 1712 $cm^{-1}$ for carboxylic (C=O) and 1664 $cm^{-1}$ for amide (C=O). $^1$HNMR (DMSO) 2.05 ppm(s, 3H, $COCH_3$), 7.2 ppm (d, 2H, 4,5-Ar-H), 7.8 ppm (d, H, 3-Ar-H), 8.1 ppm (d, H, 6-Ar-H), 9.8 ppm ( s, H, NH) and 11.2 ppm (s, H, OH) [12].

**4-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzoic acid 2:** IR (KBr) 3385 $cm^{-1}$ for (O-H), 1708 $cm^{-1}$ for carboxylic (C=O),1697 $cm^{-1}$ for lactamic (C=O) and 1633 $cm^{-1}$ for (C=N).$^1$HNMR (DMSO) 2.25 ppm (s,

3H, $CH_3$), 7.37 ppm ( d, 2H,3,5-Ar-H(of benzoic acid moiety)), 4.09 ppm (d,2H, 2,6-Ar-H(of benzoic acid moiety)), 7.5 ppm (d, 2H, 5,6-Ar-H(oxoquinazolin moiety)), 7.7 ppm (d, H, 4-Ar-H(oxoquinazolin moiety)), 8.3 ppm (d, H, 7-Ar-H (oxoquinazolin moiety)) and 12.1ppm (s, H, COOH).

**4-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzoyl chloride 3:** IR (KBr) 1766 $cm^{-1}$ for (C=O) of acid chloride, 1696 $cm^{-1}$ for lactamic (C=O), 1631 $cm^{-1}$ for (C=N) and 924 $cm^{-1}$ for (C-Cl). $^1$HNMR (DMSO) 2.25 ppm (s, 3H, $CH_3$), 7.37 ppm ( d, 2H,3,5-Ar-H(of benzoic acid moiety)), 4.09 ppm (d,2H, 2,6-Ar-H(of benzoic acid moiety)), 7.5 ppm (d, 2H,5,6-Ar-H(oxoquinazolin moiety)), 7.7 ppm (d, H, 4-Ar-H (oxoquinazolin moiety)) and 8.3 ppm (d, H, 7-Ar-H(oxoquinazolin moiety)).

**2-Isopropyl-5-methylphenyl 4-(2-methyl-4-oxoquinazolin-3(4H)-yl) benzoate 4a:** IR (KBr) 2835, 2775 and 2745 $cm^{-1}$ for aliphatic (C-H), 1735 $cm^{-1}$ for esteric (C=O), 1694 $cm^{-1}$ for lactamic (C=O) and 1635 $cm^{-1}$ for (C=N). $^1$HNMR (DMSO) 1.2 ppm (d, 6H, $2CH_3$), 2.25 ppm (s, 3H, $CH_3$), 2.3ppm (s, 3H, $CH_3$), 3.0 ppm (m, H, $CH(CH_3)_2$) and 7.1-8.1 ppm (d, 11 H, Ar-H).

**4-(acetylamino)phenyl4-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)benzo- ate 4b:** IR (KBr) 3231 $cm^{-1}$ for (N-H), 2875 and 2745 $cm^{-1}$ for aliphatic (C-H)**,** 1729 $cm^{-1}$ for esteric (C=O), 1692 $cm^{-1}$ for lactamic (C=O) and 1665 $cm^{-1}$ for amide (C=O). $^1$HNMR (DMSO) 2.0 ppm (s, 3H, $COCH_3$), 2.25 ppm (s, 3H, $CH_3$), 7.2-8.1 ppm (d, 12H, Ar-H) and 9.8 ppm (s, H, NH).

**4-formyl-2-methoxyphenyl4-(2-methyl-4-oxoquinazolin-3(4*H*)-yl) benzoate 4c:** IR (KBr) 2909 $cm^{-1}$ for aldehyde (C-H), 2872 and 2755 $cm^{-1}$ for aliphatic (C-H)**,** 1739 $cm^{-1}$ for esteric (C=O) and 1691 $cm^{-1}$ for lactamic (C=O). $^1$HNMR (DMSO) 2.25 ppm (s, 3H, $CH_3$), 3.7 ppm (s, 3H, $OCH_3$), 7.3-8.0 ppm (d, 11H, Ar-H) and 9.8 ppm (s, H, CHO).

**Naphthalen-1-yl 4-(2-methyl-4-oxoquinazolin-3(4H)-yl)benzoate 4d:** IR (KBr) 1737 $cm^{-1}$ for esteric (C=O) and 1691 $cm^{-1}$ for lactamic (C=O). $^1$HNMR (DMSO) 2.25 ppm (s, 3H, $CH_3$) and 7.1-8.1 ppm (d, 13H, Ar-H).

**2-isopropyl-5-methylcyclohexyl 4-(2-methyl-4-oxoquinazolin-3(4H) -yl)benzoate 4e:** IR (KBr) 2839, 2772 and 2741 $cm^{-1}$ for aliphatic (C-H), 1733 $cm^{-1}$ for esteric (C=O) and 1696 $cm^{-1}$ for lactamic (C=O). $^1$HNMR (DMSO) 0.83 ppm (d, 9H, $3CH_3$), 1.4 ppm (m, H, $CH(CH_3)_2$), 1.5 ppm (m, H, 5-C-H (of cyclohexyl moiety)), 1.6 ppm (m, 4H, 3,4-$CH_2$(of cyclohexyl moiety)), 1.8 ppm (m, H, 2-C-H(of cyclohexyl moiety)), 1.9 ppm (t, 2H, 6-C-H(of cyclohexyl moiety)), 4.5 ppm (q, H, 1-C-H (of cyclohexyl moiety)), 2.25 ppm (s, 3H, $CH_3$) and 7.2-8.1 ppm (d, 8H, Ar-H).

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