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SYNTHESIS AND CHARACTERIZATION OF NEW CHALCONE COMPOUNDS DERIVED FROM QUINOLINE.

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ABSTRACT

Three chalcones (4'-amino-4-methoxy chalcone, 4'-amino-3,4-dimethoxy chalcone and 4'-amino-3,4,5-trimethoxy chalcone) has been synthesized by reaction of ketone (compound (3)) with appropriate aromatic aldehydes (4-hydroxy-3-methoxybenzaldehyde ,4-N,N-dimethylaminobenzaldehyde and 2-hydroxybenzaldehyde) in presence of Potassium hydroxide to obtain chalcone derivatives (4a-c). The new synthesized compounds have been characterized using Melting point, TLC, FT-IR spectroscopy and ^{1}H-NMR.

KEYWORDS: 2H-chromen-2-one, pyridine.

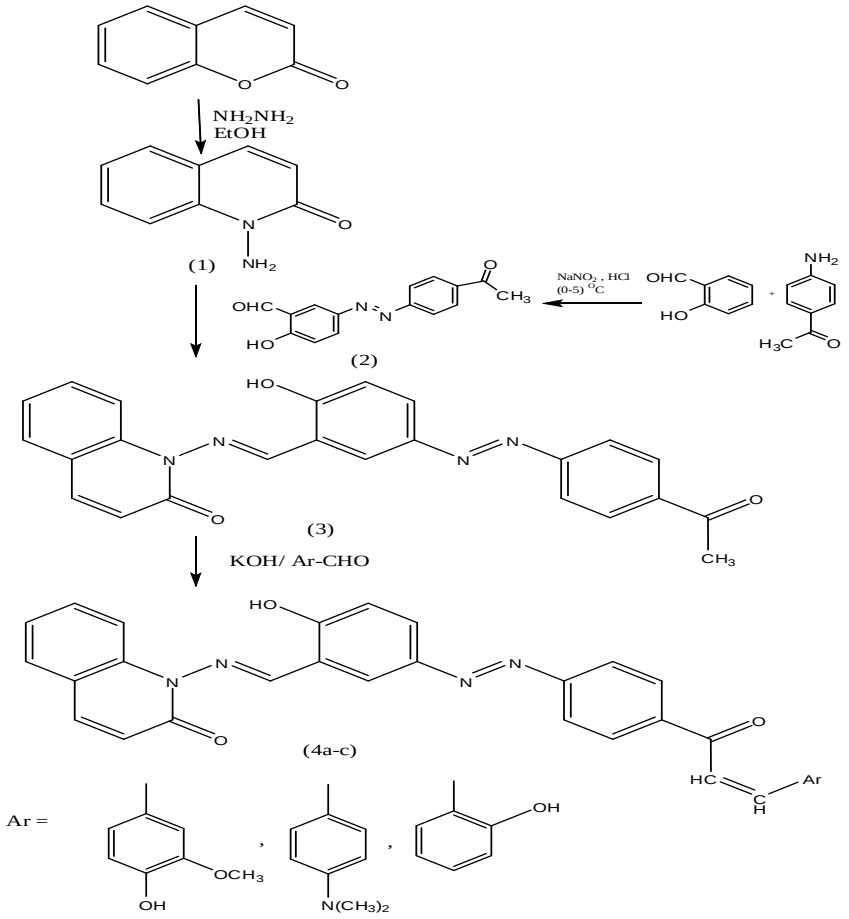
INTRODUCTION

Chalcones, or 1,3-diphenyl-2-propen-1-ones, are one of the most important classes of flavonoids across the whole plant kingdom. Chalcones are open-chain precursors for biosynthesis of flavonoids and isoflavonoids and occur mainly as polyphenolic compounds whose colour changes from yellow to orange.[1] Chalcone has conjugated double bonds with absolute delocalization and two aromatic rings that possess an p-electron system, which gives them relatively low redox potential and a greater chance of undergoing electron transfer reactions. Chalcones are naturally abundant in edible plants, including vegetables, fruits, spices, tea and natural foodstuffs. Chalcones can be designed as precursors for flavonoids and isoflavonoids.[2]

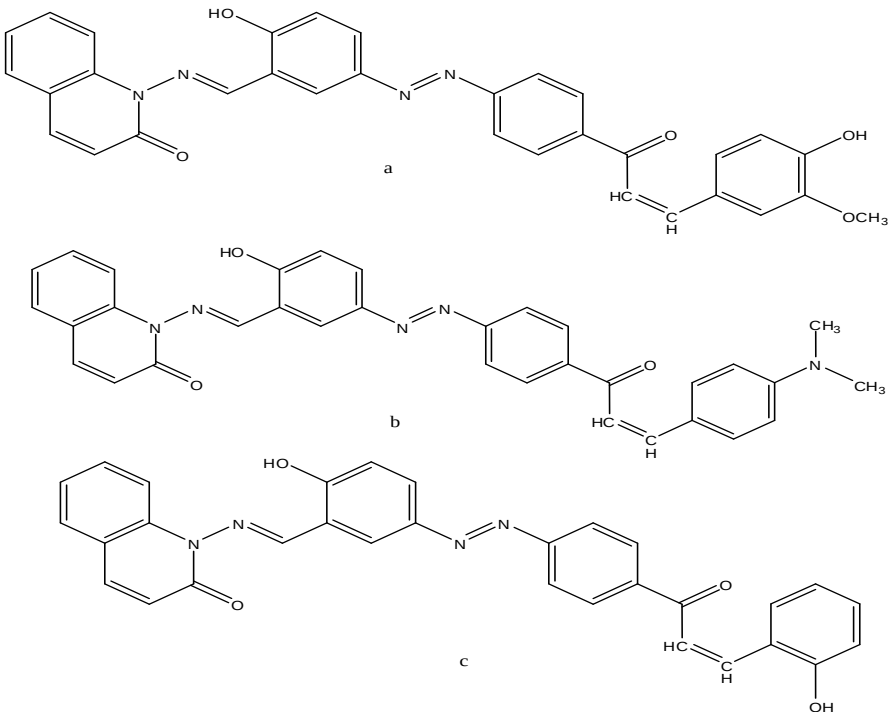
The chemistry of chalcones remains a fascination among researchers in the 21st century due to the large number of replaceable hydrogens that allows a large number of derivatives and a variety of promising biological activities to be generated, e.g., anti-inflammatory,[3] anti-gout,[4] anti-histaminic,[5] anti-oxidant.[6]

It has been widely reported that flavonoids have potential as positive and negative regulators as that potential as anticancer. One class of flavonoids that have the potential as an anticancer is chalcone and its derivatives.[7]

Chalcone activity generally depends on the number and position of the hydroxyl group, methoxy and other groups on the rings A and B, so that the research will be synthesized 3 chalcone derivatives that have variations of methoxy group,hydroxyl group and amino group in ring B of chalcone. Reaction sequences of the synthesized compounds are appeared in Scheme.[1]



Scheme 1: Steps for Preparing chalcone Derivatives.



2. EXPERIMENTAL

2.1 Synthesis of 1-aminoquinolin-2(1H)-one (1)

A mixture of 2H-chromen-2-one (0.02 mole) in ethanol (25ml), hydrazine hydrate (80%) (1g.,0.02 mole) is added drop wise with stirring.[8] The mixture was refluxed for 24 hrs. After cooling the solid formed, is filtered off, and recrystallized from ethanol:water (1:1) to give of compound (1), white precipitate ,yield 88%, M.P

(136-138°C). The FTIR spectral data showed absorption at (1639cm^{-1}, for υC=O, quinoline), (1597,1452cm^{-1}, for υC=C, Ar.), (3045cm^{-1}, for υC-H, Ar.), (1242 cm^{-1}, for υC-N) and (3292, 3199 cm^{-1}, for υNH$_2$). ^{1}H-NMR spectra data showed signal at 4.2 (s,2H,NH$_2$-), 6.8-7.5(m,6H,Ar-H).

2.2 Synthesis of Azo Derivative (2)

4-aminoacetophenone (0.01 mole) was added to a mixture of water (4 ml) and concentrated hydrochloric acid (4.5 ml). The resulting solution was stirred for 10 min. before being cold to (0-5) ^{0}C. A solution of sodium nitrite (0.69g.,0.01 mole) in water (2.5 ml) is added dropwise [9]. After being stirred for 10 min., the resulting solution of diazonium salt was added dropwise to a mixture of salicylaldehyde (1.22g., 0.01 mole) in ethanol and 10% NaOH (10ml.) at (0-5)^{0}C at pH=5.5 and the disappearance of reactants was figured according to TLC technique. After the addition was completed, the mixture was stirred for further 20 min. then was left for 1 hr. The resulting solid was filtered off, dried and recrystallized from ethanol to get the compound (2), orange precipitate ,yield 84%, M.P (104-106°C). The FTIR spectral data showed absorption at (1662cm^{-1}, for υC=O), (1570,1472cm^{-1}, for υC=C, Ar.), (2990,2920cm^{-1}, for υCH, aliphatic), (1738cm^{-1}, for υC=O, ketone), (3040cm^{-1}, for υC-H, Ar.), (1280 cm^{-1}, for υC-O), (3200 cm^{-1}, for υOH) and (1595 cm^{-1}, for υN=N).

2.3 Synthesis of Schiff base compound (3)

A mixture of (0.01mole) of compound (1) in (10ml) of absolute ethanol, and compound (2) (0.01mole) was refluxed for 12 hours in the presence of (3-4) drops of glacial acetic acid. The reaction was monitored through TLC (hexane: ethylacetate, 7:3, Rf = 0.61). After cooling the product, a solid formed, was filtered, dried and purified by recrystallized from ethanol,[10,11] dark orange precipitate ,yield 54%, M.P (218-220°C). The FTIR spectral data showed absorption at (1672cm^{-1}, for υC=O, quinoline), (1612cm^{-1}, for υC=N), (1433,1487cm^{-1}, for υC=C, Ar.), (2995,2918cm^{-1}, for υCH, aliphatic), (1738cm^{-1}, for υC=O, ketone), (3039cm^{-1}, for υC-H, Ar.) and (1595 cm^{-1}, for υN=N) .

2.4 General procedure for synthesis of chalcone (4a-c)

A mixture of compound (3) (0.003 mole) in 30 ml ethanol was added substituted benzaldehyde(0.003 mole) and 4ml of 10% KOH solution and stirred for 24 hrs. at room temperature. The precipitate products are formed upon pouring onto ice-water containing few drops of hydrochloric acid. The reaction mixture is collected by filtration and recrystallized from ethanol.

2.4.1 Synthesis of 1-((E)-2-hydroxy-5-((E)-(4-((Z)-3-(4-hydroxy-3-methoxyphenyl) acryloyl) phenyl) diazenyl) benzylideneamino) quinolin-2(1H)-one (4a)

Melting point: 347-349 ^{0}C, orange precipitate, Yields: 85%. TLC (hexane:ethylacetate, 7:3, Rf = 0.54). The FTIR spectral data showed absorption at (3041 cm^{-1}, for □C-H Ar.), (2918cm^{-1}, for □C-H aliph.), (1680cm^{-1}, for □C=O quinoline), (1668cm^{-1}, for □C=O), (1614cm^{-1}, for □C=N), (1485cm^{-1}, for □C=C, Ar.), (1575 cm^{-1}, for □N=N). ^{1}H-NMR spectra data showed signal at 1.2(s,3H,CH$_3$), 6.8-8.9(m,19H,(Ar-H,HC=CH for quinoline ring and N=CH), 9 (s,H,OH) and 11.1 (s,H,OH) .

2.4.2 Synthesis of 1-((E)-5-((E)-(4-((Z)-3-(4 (dimethylamino)phenyl)acryloyl)phenyl)diazenyl)-2 hydroxybenzylideneamino) quinolin-2(1H)-one (4b

Melting point: 225-227 ^{0}C, orange precipitate, Yields: 80%. TLC (hexane:ethylacetate, 7:3, Rf = 0.52).The FTIR spectral data showed absorption at (3064cm^{-1}, for □C-H Ar.), (2970,2873cm^{-1}, for □C-H aliph.), (1678cm^{-1}, for □C=O quinoline), (1660cm^{-1}, for □C=O), (1622cm^{-1}, for □C=N), (1525,1483cm^{-1}, for □C=C, Ar.), (1575 cm^{-1}, for □N=N). ^{1}H-NMR spectra data showed signal at 3(s,6H,2CH$_3$), 6.7-9(m,20H,(Ar-H,HC=CH for quinoline ring and N=CH) and 11.3 (s,H,OH) .

2.4.3 Synthesis of 1-((E)-2-hydroxy-5-((E)-(4-((Z)-3-(2-hydroxyphenyl)acryloyl) phenyl)diazenyl) benzylideneamino) quinolin-2(1H)-one (4c)

Melting point: 272-274 ^{0}C, brown precipitate, Yields: 77%. TLC (hexane:ethylacetate, 7:3, Rf = 0.62).The FTIR spectral data showed absorption at (3190cm^{-1}, for □C-H Ar.), (2931,2852cm^{-1}, for □C-H aliph.), (1670cm^{-1}, for □C=O quinoline), (1653cm^{-1}, for □C=O), (1620cm^{-1}, for □C=N), (1521,1487cm^{-1}, for □C=C, Ar.), (1572 cm^{-1}, for □N=N). ^{1}H-NMR spectra data showed signal at 6.6-9(m,20H,(Ar-H,HC=CH for quinoline ring and N=CH), 11.2 (s,H,OH) and 11.8 (s,H,OH)

3. RESULTS AND DISCUSSION

Chalcone been synthesized through Claisen-Schmidt condensation reaction of compound (3) and substituted benzaldehyde in the presence of KOH. Three chalcone derivative was synthesized through Claisen-Schmidt condensation reaction between compound (3) and benzaldehyde derivatives (Figure 1).

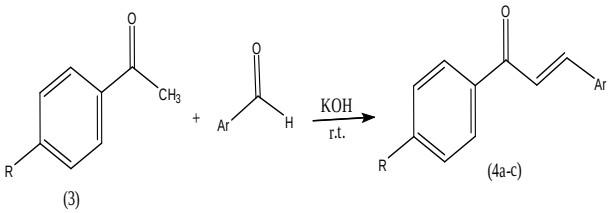


Figure 1: Synthesis of chalcone derivatives (4a-c).

The mechanism of chalcone formation including Deprotonation 1, Addition, and Proton Equilibration steps has been eliminated to be rate-limiting step of the reaction. This leaves us with the dehydration as the rate-limiting step in chalcone mechanism. There are two steps in dehydration process shown in Figure 2 including Deprotonation 2, the removal of proton and forming an enolate, and Elimination, the leaving of hydroxide group and forming a double bond.[12]

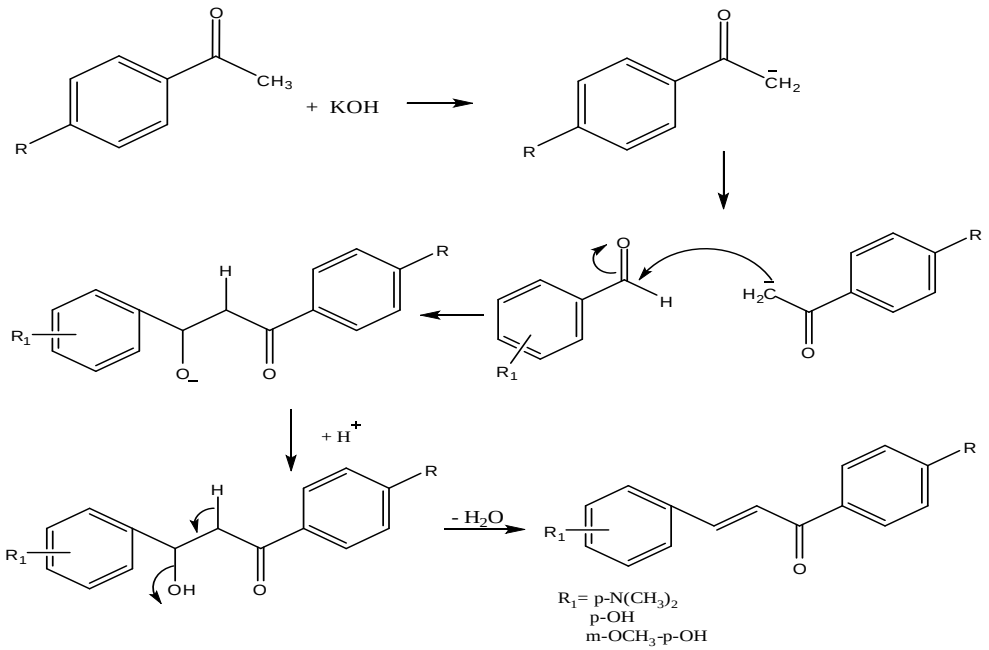


Figure 3: Mechanisms of the reaction.

The compounds synthesized in the form of giving a yellow orange color with Mg/HCl, showed positive flavonoids. The yield of the compounds 77 to 85%. Structures of the synthesized compounds were confirmed by FT-IR spectroscopy and ^{1}H-NMR.

CONCLUSIONS

In summary, a series of novel chalcones have been synthesized by Claisen-Schmidt condensation reaction compound (3) with appropriate aromatic aldehydes (4-hydroxy-3-methoxybenzaldehyde, 4-N,N-dimethylaminobenzaldehyde and 4-hydroxybenzaldehyde) in presence of , isolation, and characterization of a new compounds.

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