Persian Gulf Marine Sponge/I_2: An efficient natural catalyst for quinoline synthesis

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Abstract- A natural and efficient method has been developed for the synthesis of quinoline derivatives in good-to-high yields, from various aryl aldehydes, amines and phenyl acethylene, using marine sponge/I_2 as a green catalyst.

Keywords :Marine sponge / Iodine, Aza Diels–Alder; Quinolines, Multicomponent reaction, Molecular iodine

Introduction

Quinoline and their derivatives, which usually possess diverse biological activities, play important roles as versatile building blocks for the synthesis of natural products and as therapeutic agents. [1] In particular2-arylquinolines are biologically active and occur in structures of a number of anti malarial compounds and antitumor agents. [2] Therefore, the synthesis of quinolones has attracted much attention in organic synthesis. The classic methods for the synthesis of quinolines include Skraup, Doebner–von Miller, Conrad–Limbach, Combes, and Pfitzinger quinoline syntheses. [3] A number of general synthetic methods have also been reported.[4] Among these novel strategies for the synthesis of quinolines, multicomponent reactions (MCRs) provides an easy access to the preparation of quinoline derivatives, because multicomponent reactions (MCRs) have emerged as powerful and bond forming efficient tools in organic, combinatorial, and medicinal chemistry. [5]

Recently, $FeCl_3$-catalyzed three component coupling-/hydroarylation/dehydrogenation of aldehydes, alkynes, and amines for the synthesis of 2, 4-disubstituted quinolines was developed.[6] $AuCl_3$/CuBr-catalyzed MCR strategy a sequential catalytic process for the synthesis of quinolines was reported. [7] $Cu(OTf)_2$-catalyzedtandem Grignard-type imine addition/Friedel-Crafts alkenylation of arenes with alkynes for the synthesis of the quinoline-2-carboxylates was described.[8] The synthesis of polysubstitutedquinolines via ($HClO_4$)-

modified montmorillonite catalyzed Povarov reaction was developed.[9] All these methods are through strongacid-catalyzed or metal-catalyzed sequential intermolecular addition of alkynes onto imines and subsequent intra molecular ring closure by arylation. Considering the continued importance of the quinoline core in both biological and chemical fields, new direct approaches remain highly valuable to the contemporary collection of synthetic methods. However, some of these methods suffer from several disadvantages such as harsh reaction conditions, multi steps, a large amount of promoters, and long reaction time. Therefore, the development of new synthetic approaches using mild reaction conditions remains an active research area. [9] Iodine has been used as a mild and efficient catalyst for various organic transformations.[10] Marine sponges are known as a prolific source of biologically active and structurally unique metabolites. They are known to produce a large number and diversity of secondary metabolites. [11] As there is no report of marine sponges of Iranian coast of Persian Gulf, we studied shallow sponges (Desmospongae sp.) of Khark Island. In organic chemistry, these sponges are important and optical active source for catalytic reactions such as oxidation, reduction etc.[12] We decided to use Marine sponge (Demospongiae sp.) powder as attractive and natural solid support for Quinoline synthesis.

Results and discussion

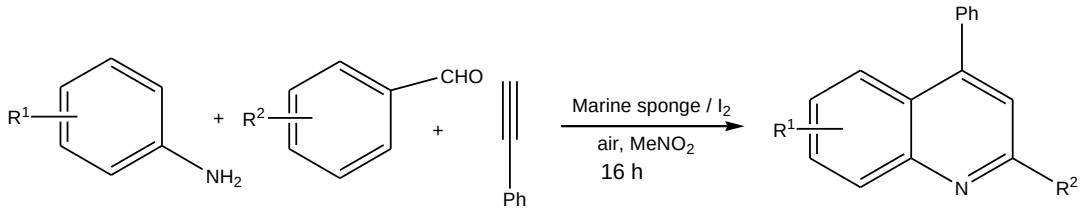
The reaction of aryl aldehydes, aryl amines and phenyl acethyleneforquinoline synthesis can be carried out using several catalysts ($FeCl_3$, $AuCl_3$/CuBr,$Cu(OTf)_2$,..)[6-8] in solvents such as CH_3NO_2.The marine sponge powder as efficient absorbent to activate the C–N and C–O bonds for imine preparation, and diels-alder reaction of desired imine and phenyl acetylene with good to high yields and can be removed easily from the product.[13]

In order to find out the most effective catalyst for quinoline synthesis, we performed the reaction of aryl aldehydes, aryl amines and phenylacethylene at reflux condition using various catalysts, as shown in Table 1.

Table 1. Quinoline synthesis using the reaction of 4-Methyl benzaldehyde, 4-methoxy aniline and phenyl acetylene in CH_3NO_2 at reflux condition for 16 h, in the presence of catalysts.

Entry	Catalyst (amount)	Yield (%)
1	I_2 (0.127 g)	20
2	Marine Sponge Powder (0.1 g)	75
3	Marine Sponge Powder (0.1 g)/ I_2 (0.127 g)	82

As the results indicate, marine sponge/I_2 offered many advantages over previously used catalysts, which are as follows: mild reaction condition, room temperature, good absorbent solid supported, easy to handle, and products in good-to-high yields. The reaction of various aldehydes, anilines and phenyl acetylene was carried out in the presence of this catalyst as shown in scheme 1.



1 2 3 4

R^1= H , 4-methoxy , 4-methyl

R^2= H , 2-hydroxy , 4-methyl , 2-nitro

Scheme 1

As shown in Table 1, quinone products were obtained in good to high yields. Finally the structure of the products were characterized by their spectral (^{1}H NMR, IR, and MS) data (ref nmr, ir , ..)

Table 2. Quinine synthesis in the presence of marine sponge/I_2

entry	**R^1**	**R^2**	**product**	**Yield (%)**	**b.p (˚C)**	**b.p(ref)**
1	H	H	4a	70	-	-
2	4-methoxy	H	4b	80	117-118	119-120
3	4-methoxy	2-hydroxy	4c	77	156-158	158-159
4	4-methoxy	4-methyl	4d	82	133-135	136-137
5	4-methoxy	2-nitro	4e	65	98-101	100-101
6	4-methyl	2-hydroxy	4f	70	188-190	190-191

The plausible mechanism of this transformation involves the intermediacy of an imine, followed by the addition of phenyl acetylene as shown in figure 1.

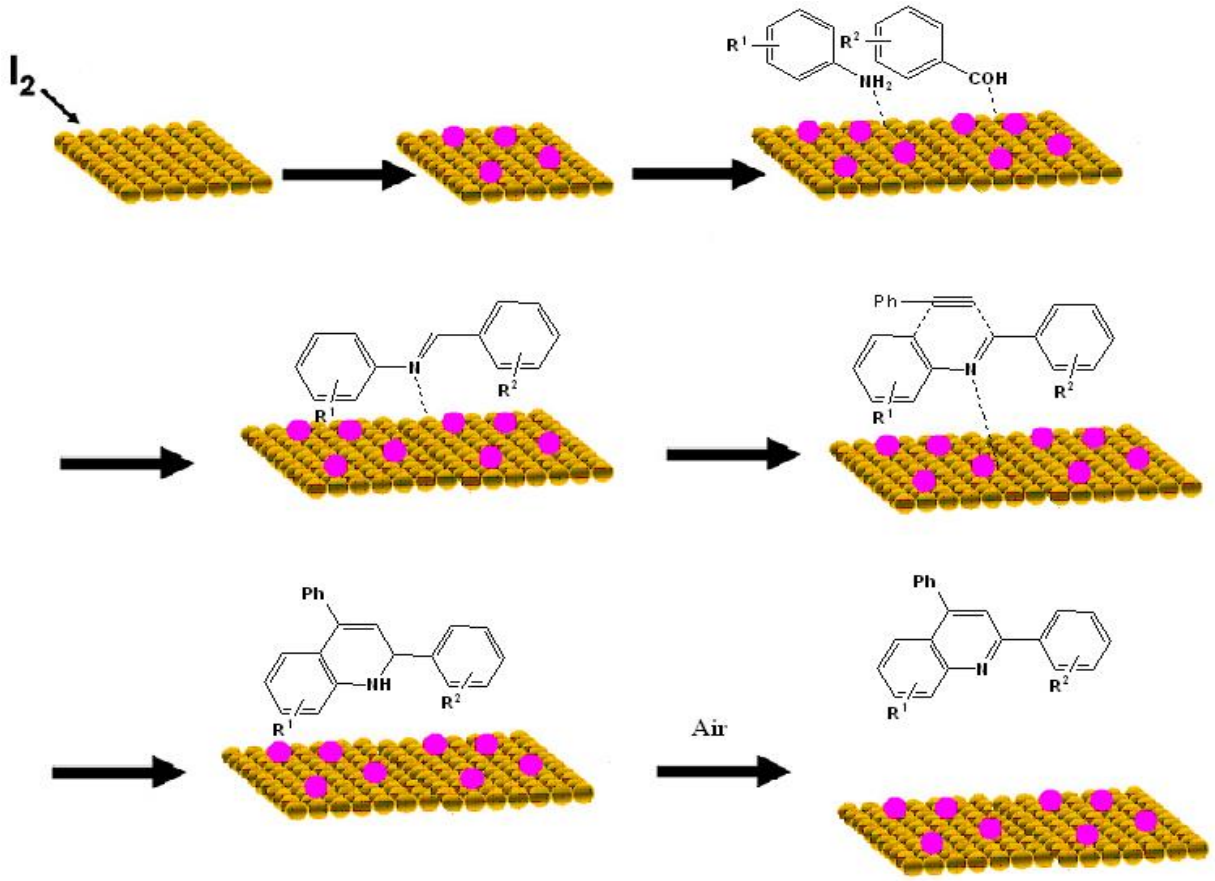
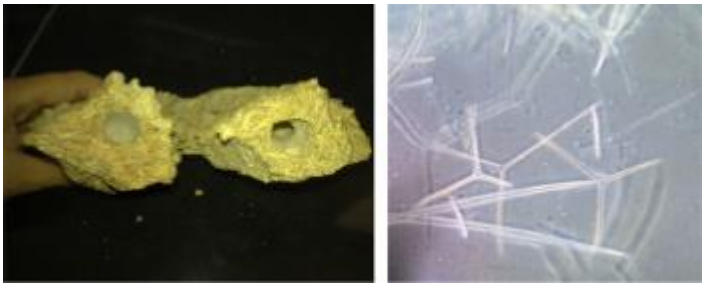


Figure 1. The mechanism of quinine synthesis

2. Experimental section

2.1. General

All starting materials were purchased from Merck and Fluka Companies. The FT-IR spectra were recorded on a Perkin-Elmer RX 700 infrared spectrometer. NMR spectra were recorded with a Brucker Avance 300-DRX (^{1}H at 300 MHz and ^{13}C at 75 MHz) NMR spectrometer. TLC accomplished the purity of substrates and reactions were monitored on silica gel polygramSIGL/UV254 plates. Melting points reported were determined by open capillary method using a Metller melting point apparatus and are uncorrected. The marine sponge (Demospongiae sp.) Samples were collected in May 2010 in 10 Km from the kha rk Island at a depth of 10 m, Iran (Persian Gulf).Identification of sponges was carried out kindly by Dr. Sayed Mohammad Bagher Nabavi. The species investigated in this study are Demospongiae sp. (Fig. 1a) which has siliceous(SiO_2) spicules (Fig. 1b).



(a) Marine sponge (Demospongiae sp.); (b) siliceous spicules

Experimental

1.1. Preparation of marine sponge powder

Marine sponge was washed with salt water and distilled water; and then dried in an oven at 60°C. The dried marine sponge chopped; sieved with mesh 0.35 mm and the particles with an average size of were usedas catalyst.

2.2. General procedure for the synthesis of quinolines

Amine (10 mmol) and aldehyde (10 mmol) were dissolved in CH_3NO_2 (20 mL) and; the mixture of marine sponge powder(0.1 g)/ I_2 (0.127 g) and phenyl acethylene (15 mmol) were added to it, and the solution was stirred under reflux condition for 16 h. Then the reaction mixture was diluted with ethylacetate and washed with a solution of sodium thiosulfate followed by water. The organic phase was dried over anhydrous Na_2SO_4, and evaporation of the solvent followed by purification on silicagel afforded pure desired quinoline.

2.3. Characterization data

1. 2,4-Diphenylquinoline (4a). Light yellow liquid; IR (neat) ν1634 (C=Nst), 1588, 1519, 1489,

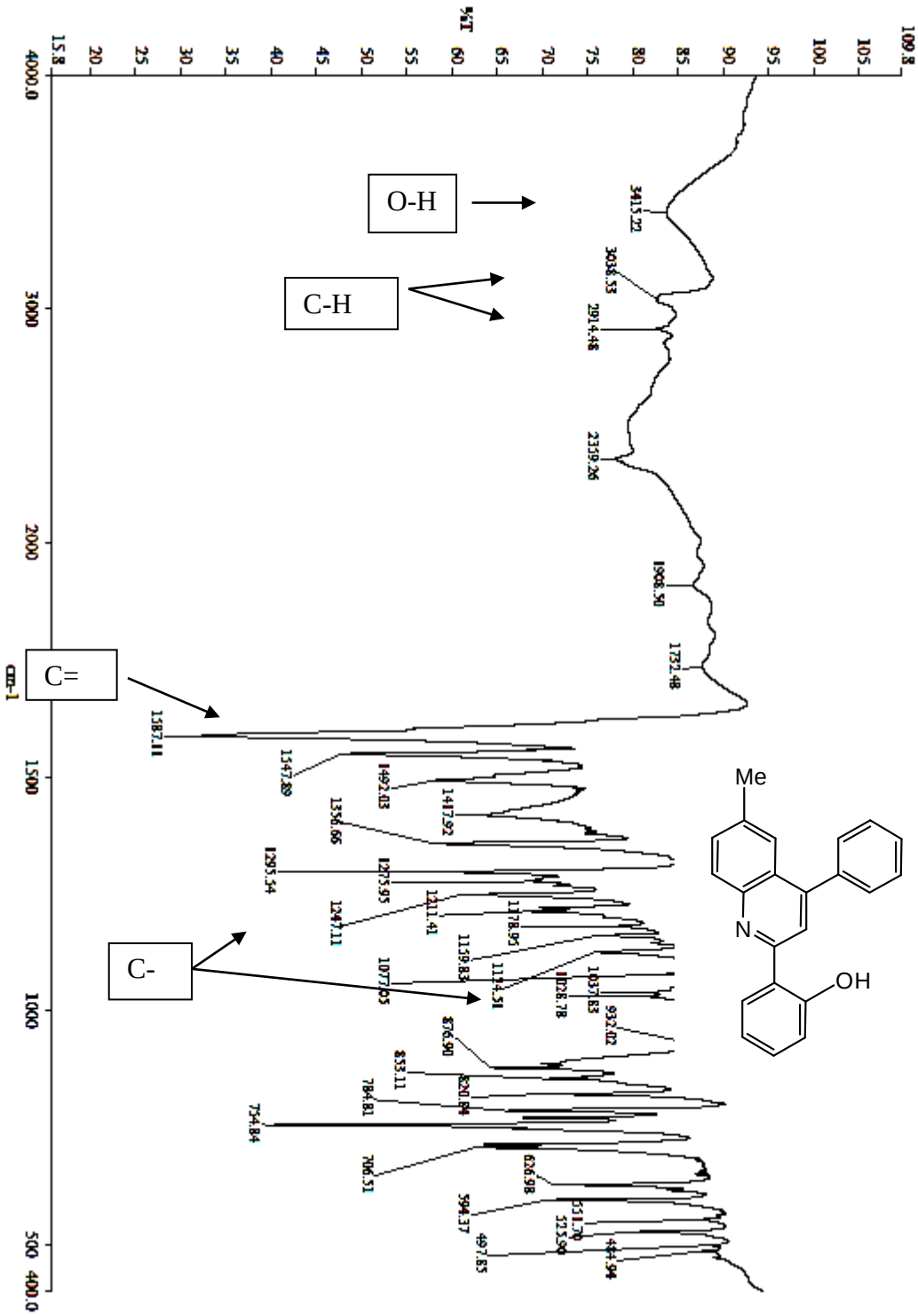
1446 (C=C), 1343(C=Nst), 768(Arcm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.24(d, 1H), 8.19 (d, 2H), 7.90 (d, 1H), 7.82 (s, 1H), 7.70-7.75 (m, 1H), 7.45-7.56(m, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.89, 149.18, 148.82, 139.66, 138.41, 130.12, 129.55, 129.50, 129.33, 128.81, 128.58, 128.39, 127.59, 126.31, 125.78, 125.63, 119.35 ppm.

2. 6-Methoxy-4-phenylquinoline (4b). Yellow liquid; IR (neat) ν 3058 (C-H Ar), 1619(C=Nst), 1584, 1493 (C=C), 1032 (meta) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.78 (d, 1H), 8.07 (d,1H), 7.46-7.55 (m, 5H), 7.38 (d, 1H), 7.27 (d, 1H), 7.19 (s, 1H), 3.77 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.80,147.41, 147.01, 144.71, 138.25, 131.15, 129.20, 128.57, 128.26, 127.61,121.65, 121.57, 103.63, 55.30 ppm.

3. 2-(6-Methoxy-4-phenylquinolin-2-yl) phenol (4c). Yellow solid, mp 158-159 ºC; IR (KBr) ν 1621(C=Nst), 1586, 1509, 1494, 1429(C=C), 1270,1122 (C-O), 1035(C=Nst), 756, 701(Ar) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 15.13 (s,1H), 7.99 (d, 1H), 7.92-7.93 (m, 2H), 7.56-758 (m, 5H),7.33-7.41 (m, 2H), 7.17 (d, 1H), 7.10 (d, 1H), 6.93 (t, 1H), 3.80(s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ157.78,154.60, 147.77, 144.87, 139.72, 138.72, 138.71, 131.57, 131.56, 129.32,128.93, 128.74, 128.65, 128.30, 127.27, 126.63, 121.76, 119.60, 103.71,55.40 ppm.

4. 6-Methoxy-4-phenyl-2-p-tolylquinoline (4d). Yellow solid, mp 136-137 ºC; IR (KBr) ν 1617(C=Nst), 1590, 1546, 1488(C=C), 1222, 1027(C-O), 834 (para) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.05-8.25(m, 3H), 7.74 (s, 1H), 7.46-7.59 (m, 5H), 7.28-7.37 (m,3H), 7.17 (s, 1H), 3.76 (s, 3H), 2.40 (s, 3H) ppm; ^{13}C NMR (100 MHz,$CDCl_3$) δ 157.59, 154.52, 147.59, 144.83, 138.88, 138.74, 138.86,136.45, 131.45, 129.44, 129.29, 128.59, 128.22, 127.09, 121.60, 119.38, 103.68, 55.32, 21.23 ppm.

6. 2-(6-Methyl-4-phenylquinolin-2-yl) phenol (4f). Yellow solid, mp 190-191 ºC; IR (neat) ν1587(C=Nst), 1546, 1492,1418(C=C), 1295(C-HAr), 1246(C-O),754 (orto) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 15.26 (s, 1H),7.95 (d, 1H), 7.89-7.91 (m, 2H), 7.60 (s, 1H), 7.50-7.57 (m,6H), 7.30-7.34 (m, 1H), 7.06-7.09 (m, 1H), 6.90 (t, 1H), 2.44(s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ160.98, 156.49, 149.41,143.68, 138.10, 136.69, 132.38, 131.71, 129.38, 128.63, 128.57, 127.63,126.76, 125.24, 124.59, 119.03, 118.58, 118.51, 117.51, 21.72 ppm.



FT-IRof 2-(6-Methyl-4-phenylquinolin-2-yl)phenolfigure 1.

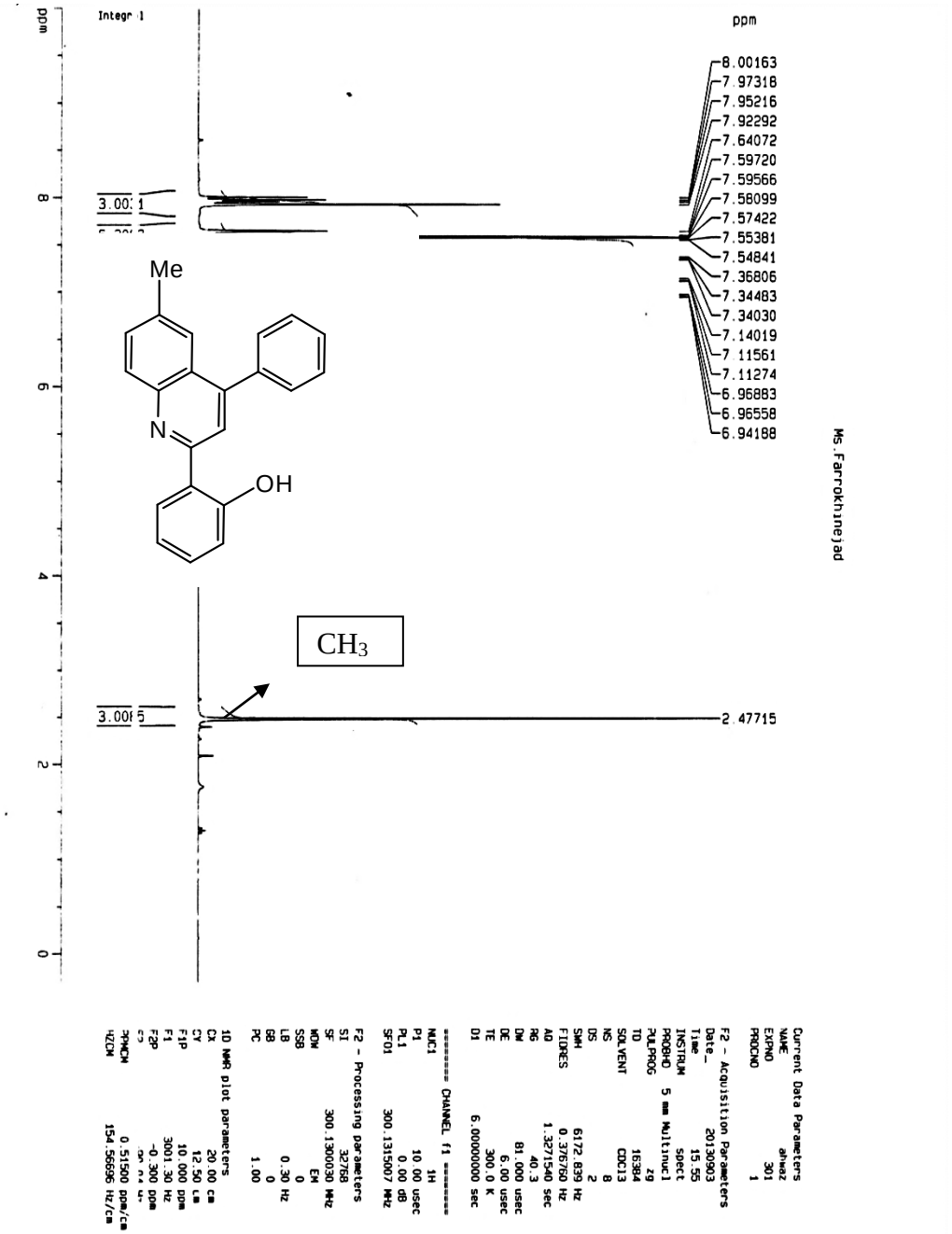


figure 2.[1]HNMRfor2-(6-Methyl-4-phenylquinolin-2-yl)phenol

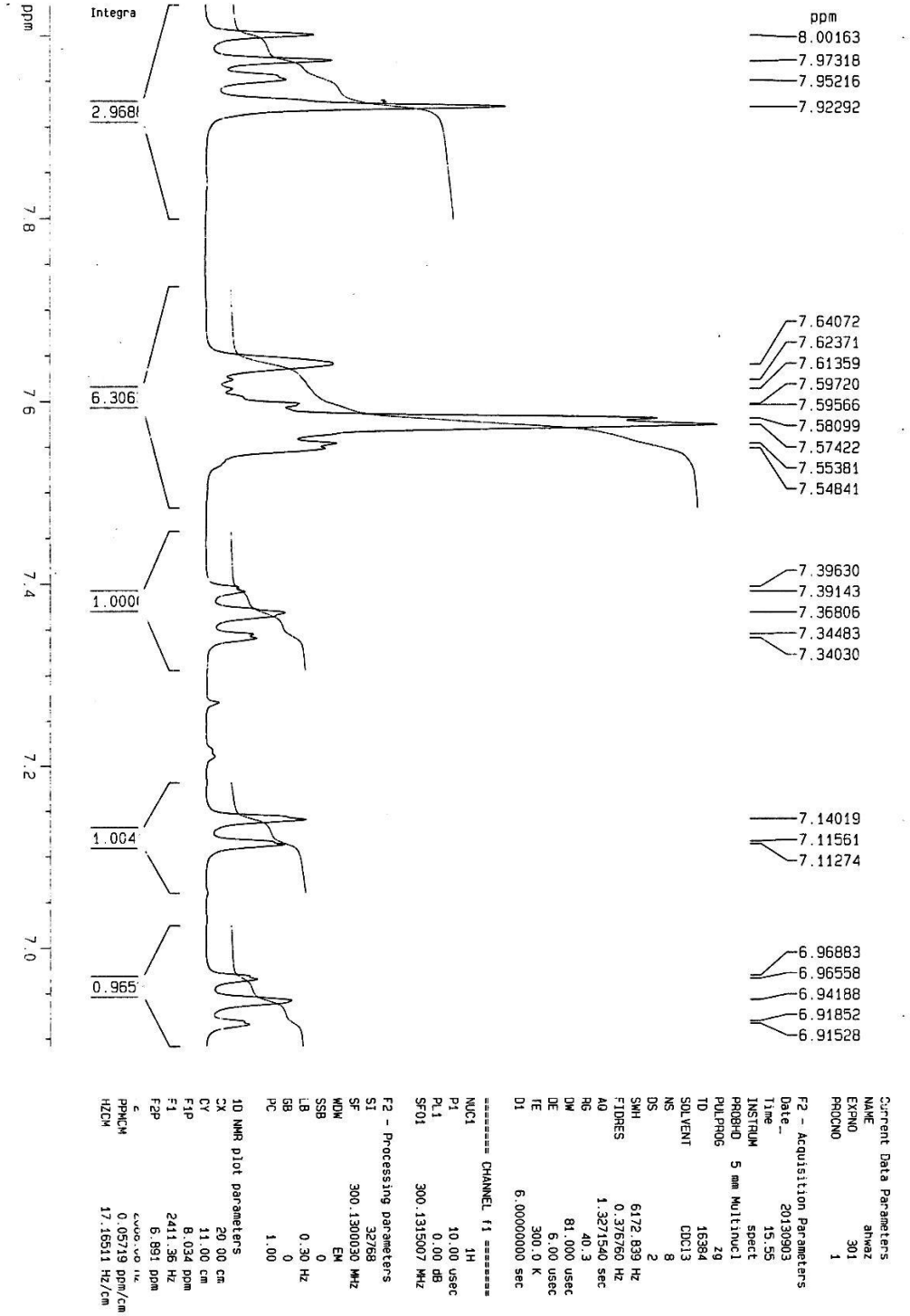
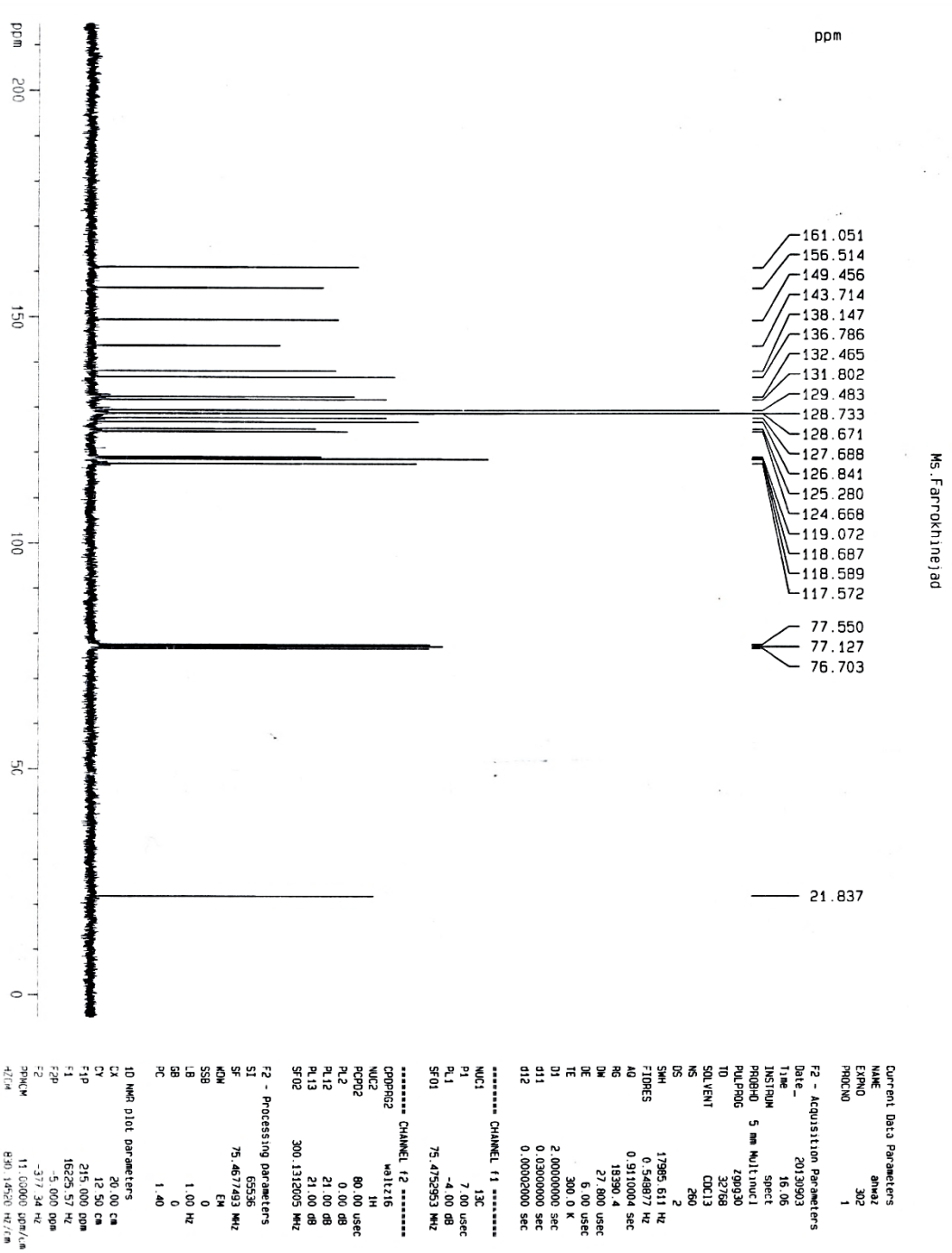


figure 3-[1] HNMR (expand spectrum)of2-(6-Methyl-4-phenylquinolin-2-yl)phenol

^{13}CNMR of 2-(6-Methyl-4-phenylquinolin-2-yl)phenolfigure 4-



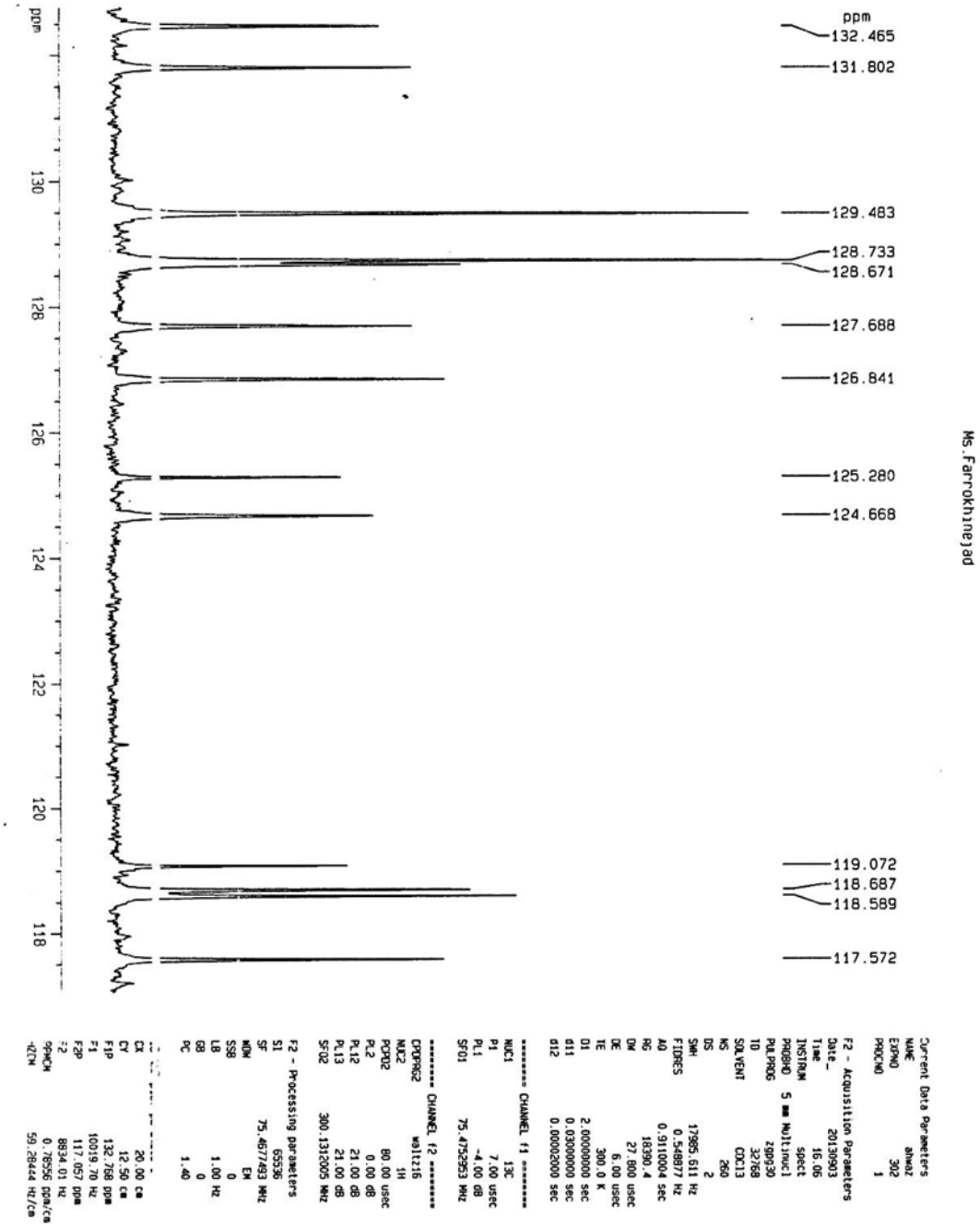


figure 5-^{13}CNMR (expand spectrum) offor2-(6-Methyl-4-phenylquinolin-2-yl)phenol

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