

SYNTHESIS AND EVALUATION OF ANTIMICROBIAL ACTIVITY OF 1-BENZOYL-1H-PYRAZOLO [4,3-C]QUINOLIN-4(5H)-ONES

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ABSTRACT

A series of 1-benzoyl-1*H*-pyrazolo [4,3-*C*]quinolin-4(5*H*)-one, carrying appropriate substituents at the Quinoline ring have been synthesized in good yields via the condensation of 4-chloro-3-formylquinolin-2[1*H*]ones with benzohydrazide using triethylamine as a base. All the synthesized compounds were evaluated for their antibacterial activities.

KEYWORDS: 2,4-Dichloroquinolines, 4-chloro-3-formylquinolin-2-[1*H*] ones, Pyrazolo quinolone, antimicrobial activity.

INTRODUCTION

The prominence, structural diversity and biological importance of quinolin-2(1*H*)-one have made them attractive target for synthesis over many years¹. Pyrazolo [4,3-*c*]quinolin-4(5*H*)-one form a class of fused heterocyclic compounds which reveal interesting pharmacological and biological properties. They have used as effective antitumor agents, antibacterial, anticonvulsant and antimalarial agents²⁻⁵. Due to their excellent biological activities they have been subjected to extensive experimental studies. Tetracyclic system the Quinoline moiety are expected to have wide-spectrum biological activity, methods to constructs the tetra cyclic pyrolotriazinoquonoine system are reported in the journal⁹ The authors prepared novel heterocyclic ring system containing the Quinoline skeleton with potential pharmaceutical activity^{9,12}, Pyroloquinoline derivative have useful biological properties as an anti tumor reagent and are active agent for the treatment of herpes virus infection, Pyrolotriazines also have considerable biological and medicinal activities as antitumor¹³, anti-inflammatory¹⁴ and antiviral agent A literature search revealed that 1-Benzoyl-1*H*-Pyrazole -(4,3,-*c*)Quinoline-4(5*H*)-ones have largely ignored we envisaged that reaction of 4-chloro-3-formyl Quinoline-2(1*H*)one of benzolyhydrazide in the presence of absolute ethanol and catalyze the amount of triethylamine was added to reflux over the steam both for 5-6 hour results in the formation of resulting compound To the best of our knowledge, there are no report on the synthesis of the reported compound In the present communication we report the synthesis and antimicrobial evaluation of 1-benzoyl-1*H*-pyrazolo[4,3-*c*]quinolin-4(5*H*)-ones(4*a-e*)

MATERIAL AND METHODS

General consideration

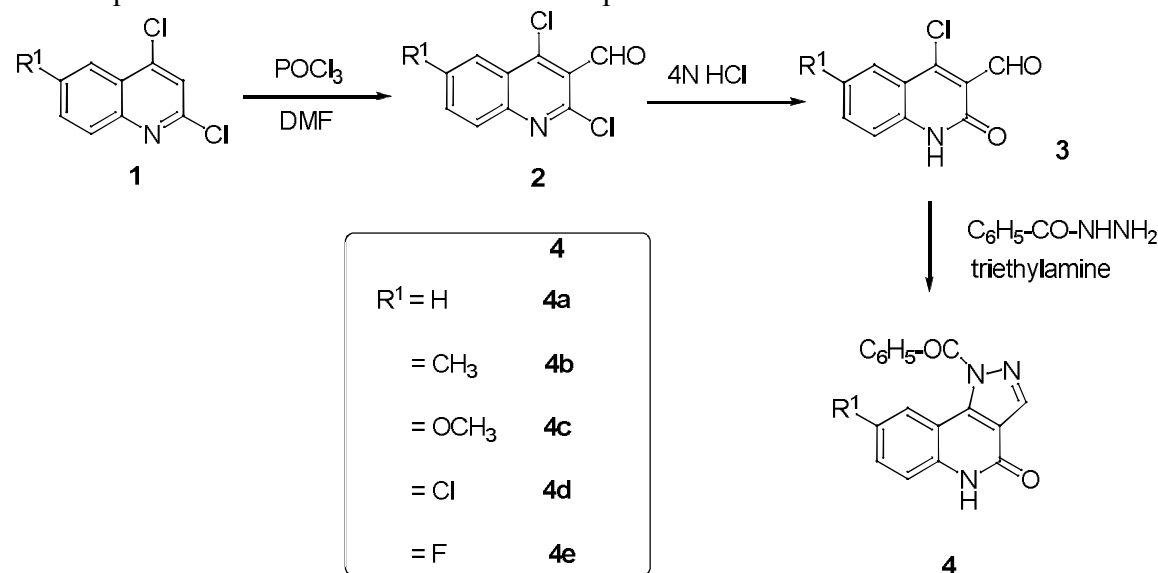
IR spectra were recorded on a Thermo Nicolet- Model Avatar 330 in KBr pellets. ¹H NMR spectra were recorded on JEOL GSX 400 in CDCl₃ as solvent.

Starting compounds were synthesized according to the literature procedure

Preparation of 1-benzoyl-1*H*-pyrazolo [4, 3-*c*] quinolin-4(5*H*)-ones [4*a*]

(0.001 mole) 4-Chloro-3-formylquinolin-2[1*H*]one **3a** of benzoylhydrazide (0.001 mole) in the presence of absolute ethanol (20 mL) and catalytic amount of triethylamine was added to reflux over the steam bath for 5-6 hours. After the completion of the reaction, the excess solvent was removed. The reaction mixture poured into crushed ice and filtered, evaporated to dryness. Product was recrystallized in ethanol.

Similar procedure was followed for other compound **4b-4e**.



Scheme 1: Synthetic route for 1-benzoyl-1H-pyrazolo [4, 3-C] quinolin-4(5H)-one derivatives.

RESULT AND DISCUSSION

1-benzoyl-1H-pyrazolo [4, 3-c] quinolin-4(5H)-one **4a** was synthesized by the condensation reaction of 4-chloro-3-formylquinolin-2[1H] one **3a** with benzohydrazide in absolute ethanol and in presence of catalytic amount of triethylamine. Benzohydrazide was prepared by refluxing hydrazine hydrate and methylbenzoate in the presence of absolute ethanol as per the reported procedure⁶. The compound **3a** was in turn prepared from dichloroquinoline **1a** as per the reported procedure⁷. The ¹H NMR spectrum in CDCl₃ of **4a** showed signals at δ 7.20-7.70(m, 9H, Ar-H); 8.20(s, 1H, C3-H); 12.10(s, 1H, NH). The appearance of sharp aldehyde proton peak at δ 10.12 in compound **3a** was not seen in **4a**. Instead the aldehyde proton appeared at δ 8.20 as singlet in compound **4a**. This clearly indicates that aldehyde carbonyl got disturbed and it supports the structure of the title compound 1-benzoyl-1H-pyrazolo [4, 3-c] quinolin-4(5H)-one **4a** its physical data and spectroscopic data was shown in Table 1.

Antibacterial Activity

All the synthesized compounds were screened for their antibacterial activity by disc diffusion method⁸. Staphylococcus aureus, Escherichia coli and Bacillus subtilis were used as test organisms. The discs (6mm in diameter) impregnated with 10μl of the test compounds (500 μg/disc) at the concentration of 50mg/ml were placed on the inoculated agar. DMF was employed as the solvent to dissolve the test compound and negative control. Ofloxacin (5 μg/disc) were used as positive reference standards to determine the sensitivity of each microbial species tested. The inoculated plates were incubated at 37 °C for 24 hours. Antimicrobial activity was evaluated by measuring the diameter of zone of inhibition against test organisms. Based on the results (Table-2), it is evident that compound **4d** and **4e** have significant inhibition effect on the growth of bacteria like Escherichia coli, Bacillus subtitles and Staphylococcus aureus. The compound **4a** and **4b** were active against Escherichia coli and Bacillus subtitles whereas compound **4c** registered good antibacterial against Escherichia coli and Staphylococcus aureus.

CONCLUSION

In conclusion, 1-benzoyl-1H-pyrazolo[4,3-c]quinolin-4(5H)-one **4a-e** were synthesized and evaluated for their antimicrobial activities. All the compounds were found to possess moderated antibacterial activity when compared to the standard.

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Table 1: Physical and spectroscopic data of compound (4a-e)^a

Compound	m.p °C Yield (%)	IR ¹ (cm ⁻¹)	¹ H NMR ² (δ)ppm
4a	>300 (76)	3200-3000(NH) 1695(NHC=O) 1590(C=N)	7.20-7.70(m,9H,Ar-H); 8.20(s,1H,C ₃ -H) 12.10(s,1H,NH)
4b	>300 (65)	3200-3000(NH) 1701(NHC=O) 1610(C=N)	2.35(s,3H,C ₆ -CH ₃);7.15-7.76(m,8H,Ar-H); 8.22(s,1H,C ₃ -H); 12.01(s,1H,NH)
4c	270-272 (60)	3250-3100(NH) 1690(C=O) 1585(C=N)	3.81(s,3H,C ₆ -OCH ₃);7.20-7.91(m,8H,Ar-H) 8.25(s,1H,C ₃ -H); 12.14(s,1H,NH)
4d	280(d) (70)	3300-2900 (NH) 1710(C=O) 1610(C=N)	7.60-8.01(m,8H,Ar-H); 8.21(s,1H,C ₃ -H); 12.10(s,1H,NH)
4e	288-290 (68)	3300-3000(NH) 1705(NHC=O) 1595(C=N)	7.30-8.25(m,8H,Ar-H); 8.44(s,1H,C ₃ -H); 11.92(s,1H,NH)

1) K.Br pellet

2) CDCl₃

Table 2: Antibacterial activity (4a-e)

Compound	Organisms		
	Diameter of inhibition zone (mm) at $\mu\text{g}/\text{disc}$		
	Escherichia coli	Bacillus subtilis	Staphylococcus aureus
4a	7	8	-
4b	6	8	-
4c	9	-	8
4d	11	9	8
4e	12	7	9
Oflaxacin (Standard)	22	21	23

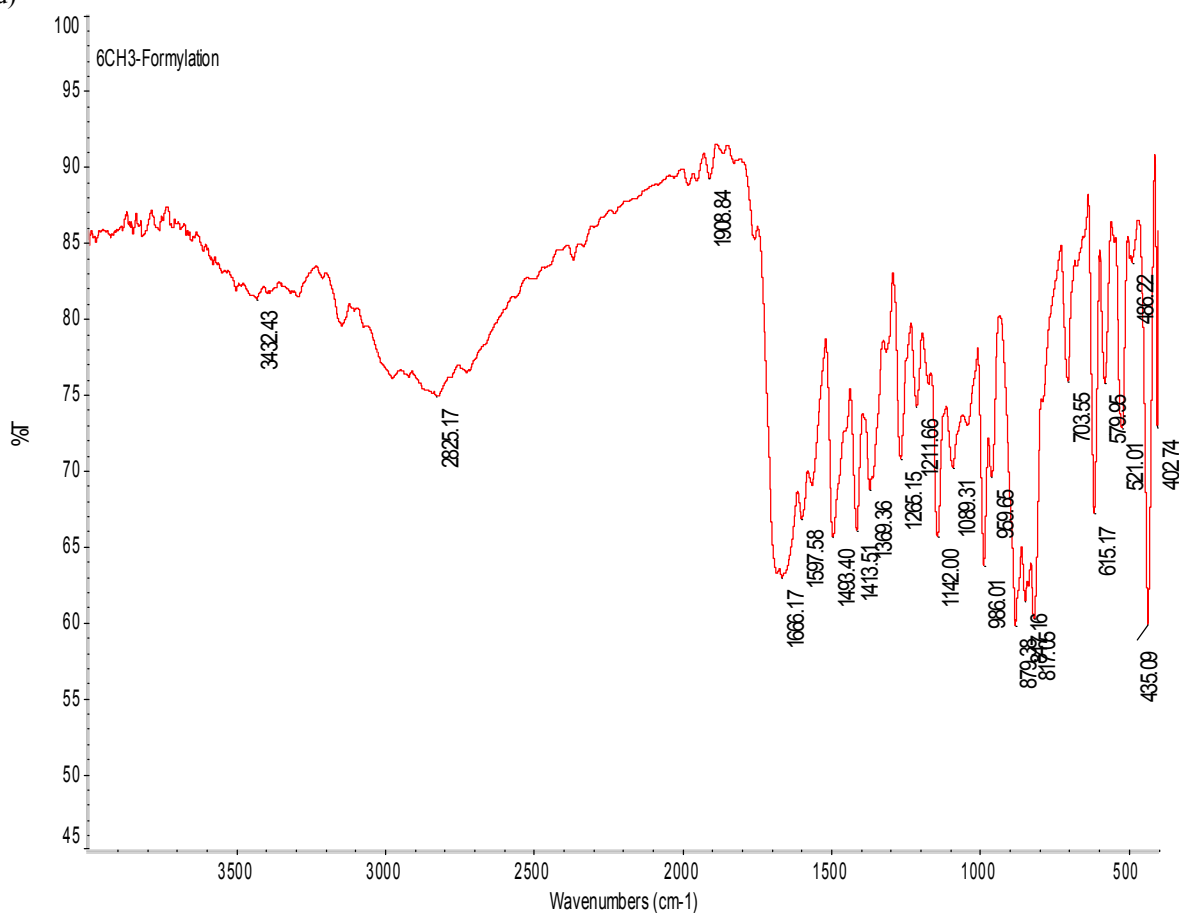


Figure 1: FTIR Spectra of Compound- 2b

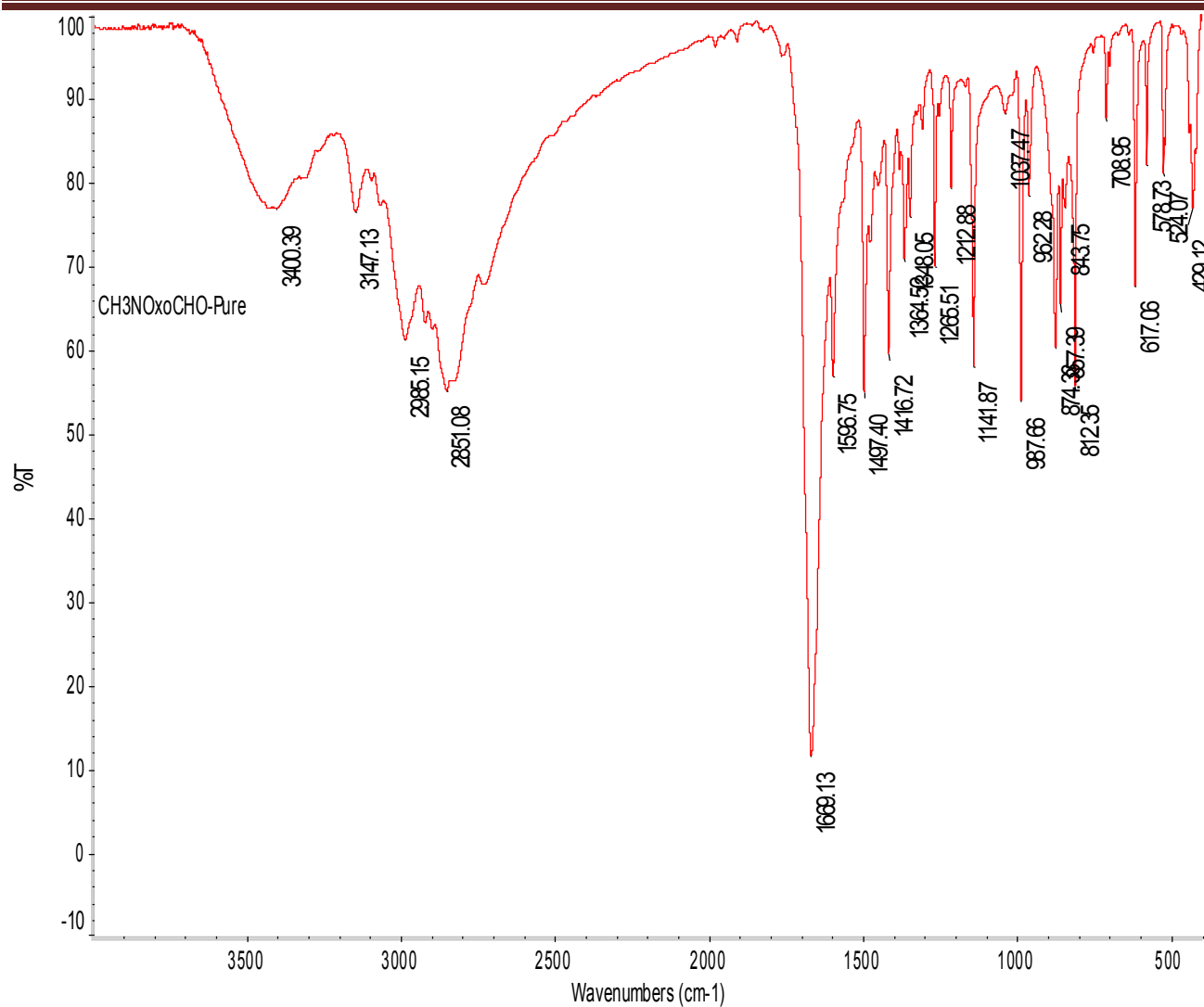


Figure 2: FTIR Spectra of Compound- 3b

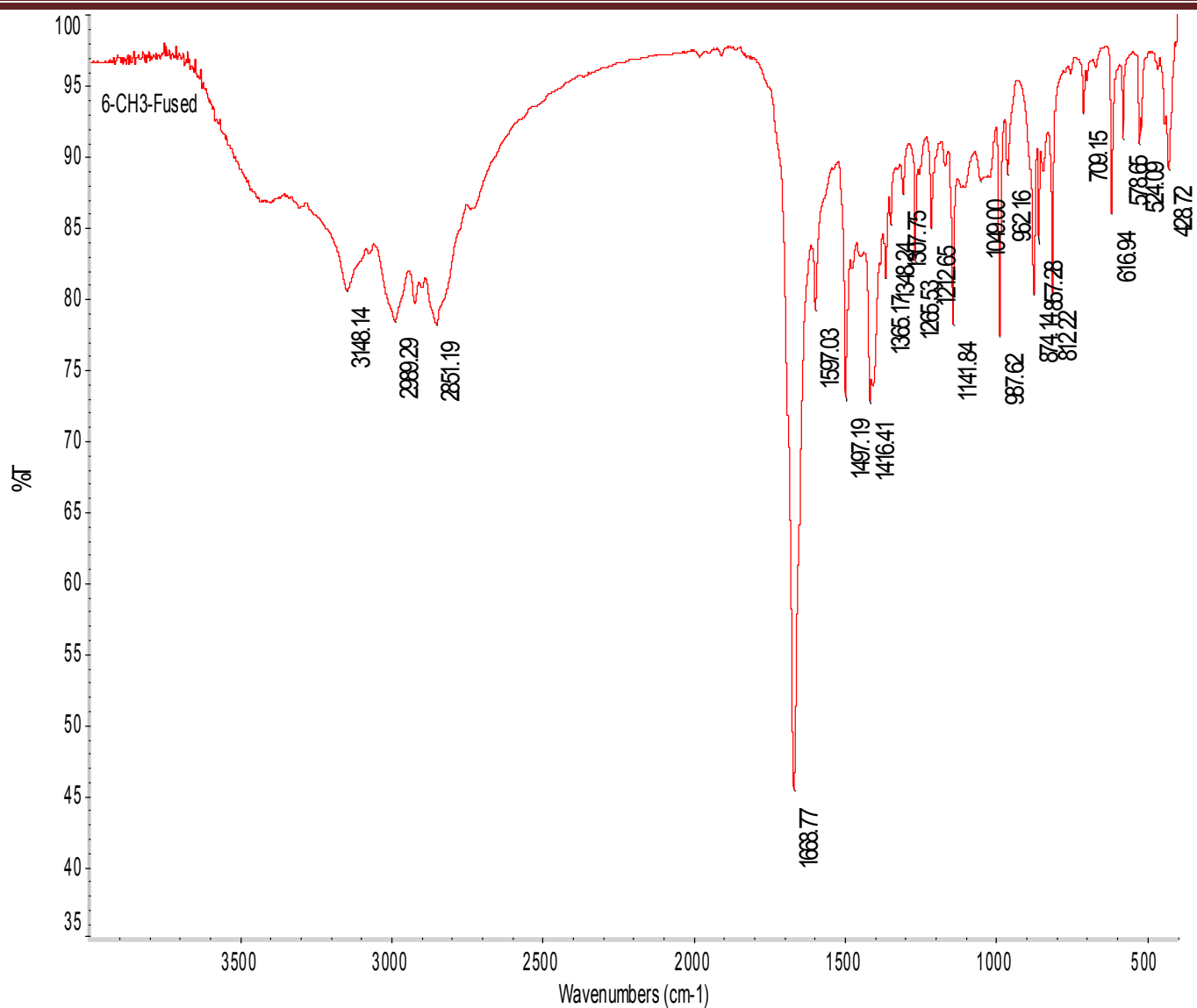


Figure 3: FTIR Spectra of Compound- 4 b

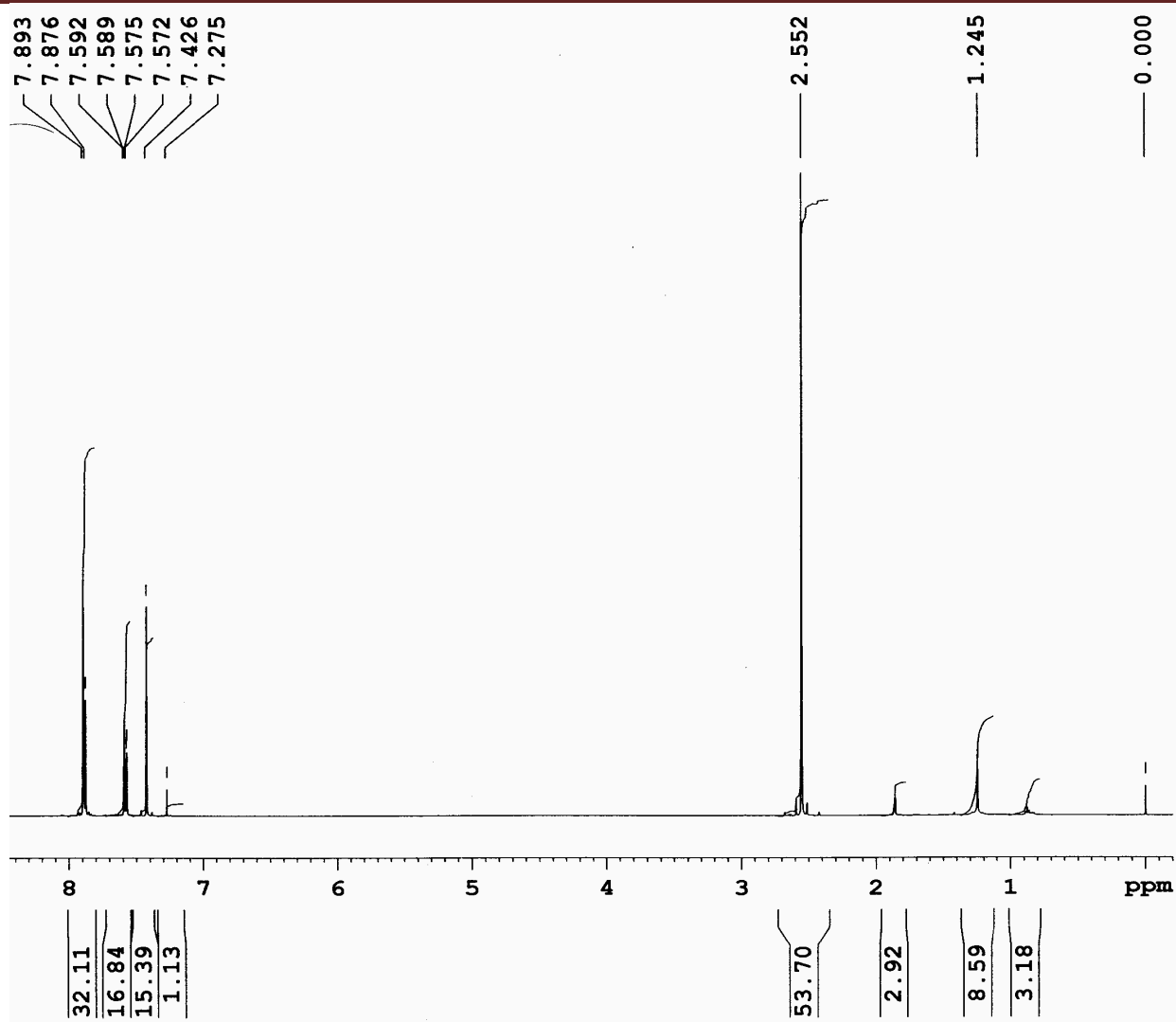


Figure 4: ^1H NMR & ^{13}C NMR of 6-methyl-2, 4-dichloroquinoline, 1b

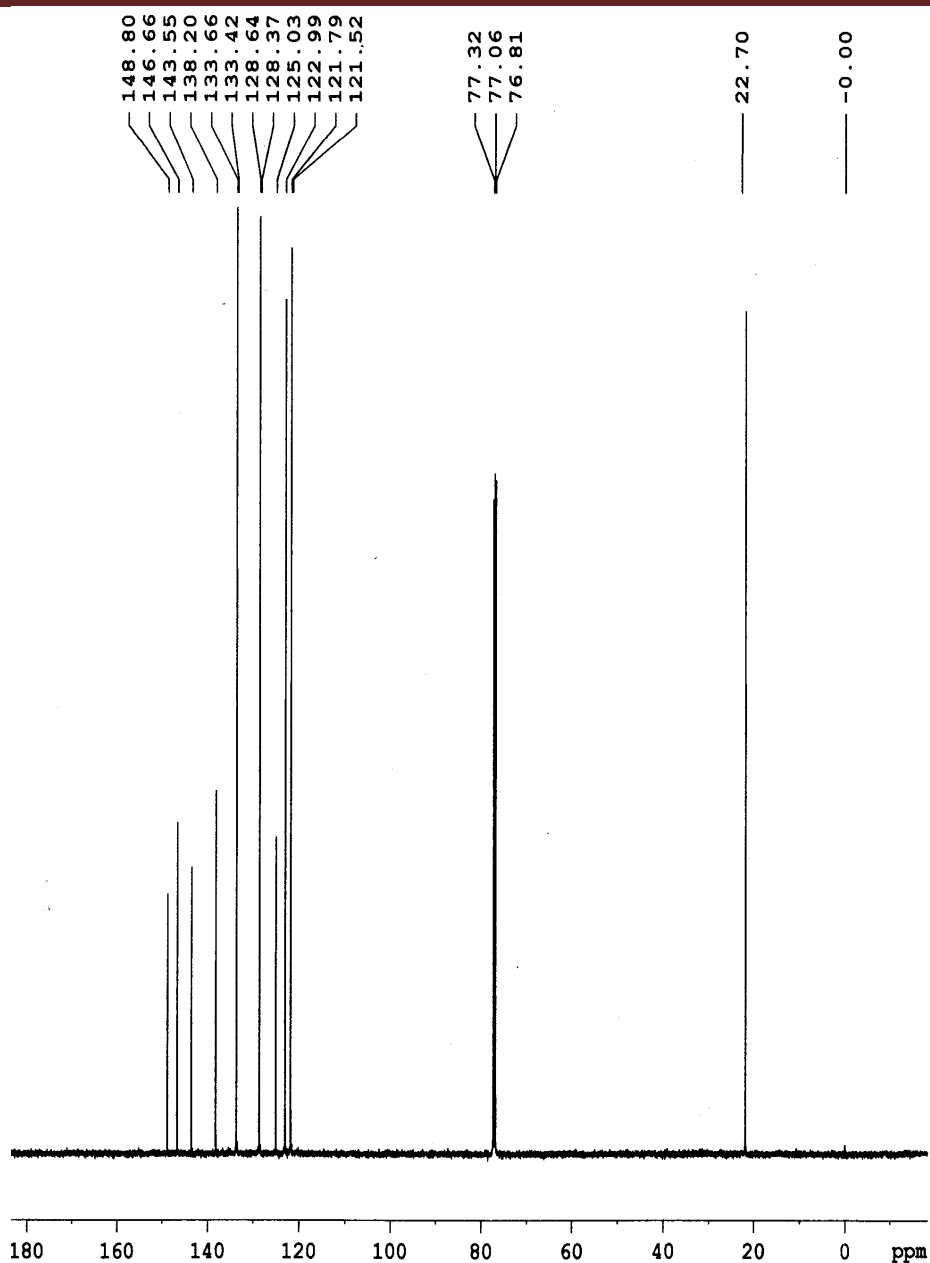


Figure 5: ^1H NMR & ^{13}C NMR of 6-methyl-2, 4-dichloroquinoline, 1b

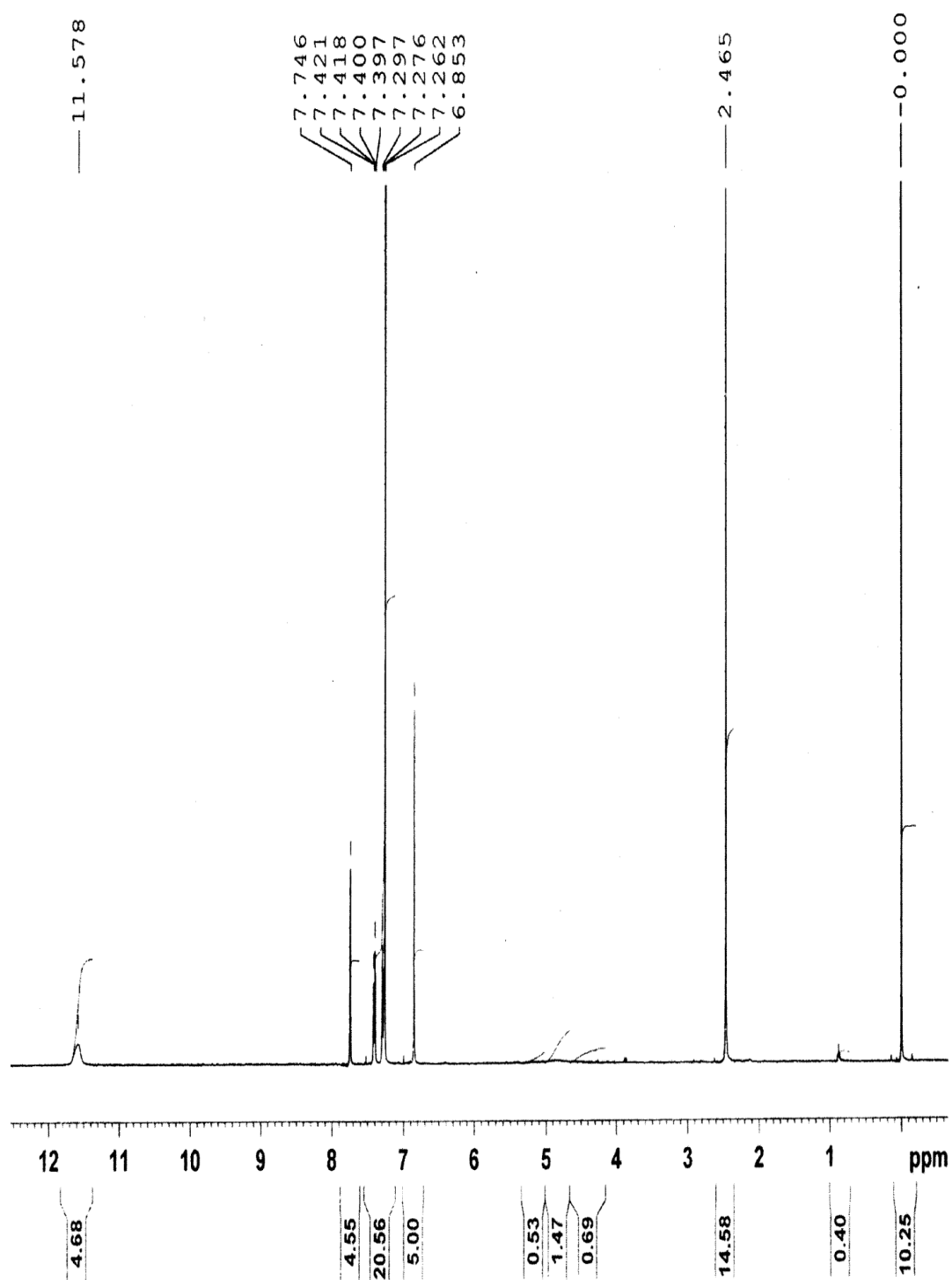


Figure 6: ^1H NMR of 1-benzoyl-8-methyl-1*H*-pyrazolo [4, 3-*c*]quinolin-4(5*H*)-one, 4b

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