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Research Article

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

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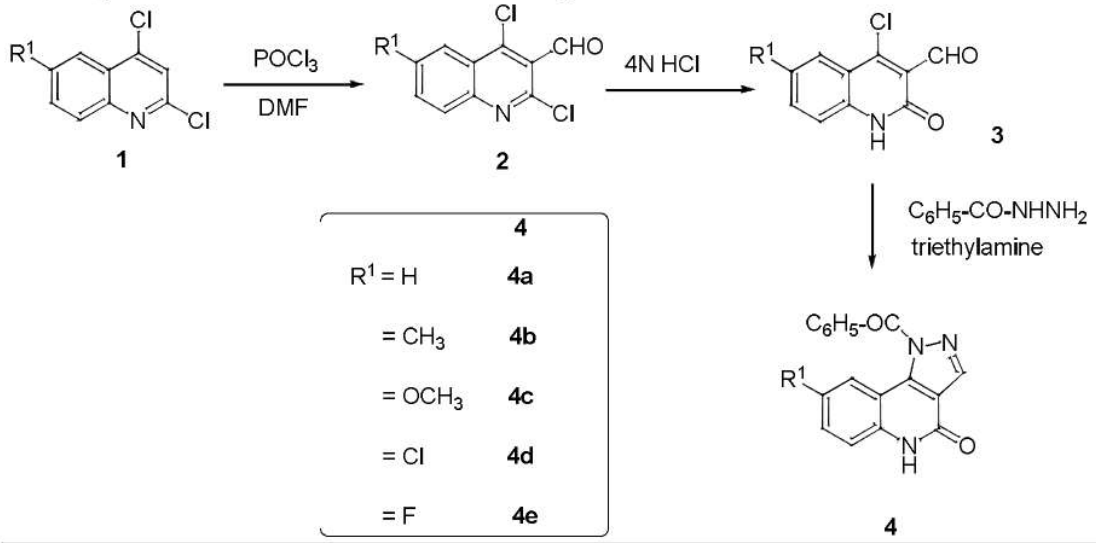
ABSTRACT
A series of 1-benzoyl-1*H*-pyrazolo [4,3-*C*]quinolin-4(5*H*)-one, carrying appropriate substituents at the Quinoline ring have been synthesized in good yields via the condensation of 4-chloro-3-formylquinolin-2[1*H*]ones with benzohydrazide using triethylamine as a base. All the synthesized 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 years[1]. 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 agents[2-5]. 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 pyrozolotriazinoquonoine system are reported in the journal[9] The authors prepared novel heterocyclic ring system containing the Quinoline skeleton with potential pharmaceutical activity[912], Pyrozoloquinoline derivative have useful biological properties as an anti tumor reagent and are active agent for the treatment of herpes virus infection,Pyrozolotriazines also have considerable biological and medicinal activities as antitumor[13],anti-inflammatory[14] and antiviral agent A literature search reveled that 1-Benzoyl-1H-Pyrazole –(4,3,-c)Quinoline-4(5H)-ones have largely ignored we envisaged that reaction of 4-chloro-3-formyl Quinoline-2(1H)one of benzolyhydrazide in the presence of absolute ethanol and catalyze the amount of triethylomine 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(**4a-e**)

MATREIAL AND METHODS
General consideration
IR spectra were recorded on a Thermo Nicolet- Model Avatar 330 in KBr pellets. ^{1}H NMR spectra were recorded on JEOL GSX 400 in $CDCl_3$ 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 [4a]
(0.001 mole) 4-Chloro-3-formylquinolin-2[1*H*]one **3a** of benzoylhyrdrazide (0.001 mole) in the presence of absolute ethanol (20 mL) and catalytic amount of triethylamine was added to reflux over the stream 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-1*H*-pyrazolo [4, 3-*C*] quinolin-4(5*H*)-one derivatives.

RESULT AND DISCUSSION

1-benzoyl-1*H*-pyrazolo [4, 3-*c*] quinolin-4(5*H*)-one 4a was synthesized by the condensation reaction of 4-chloro-3-formylquinolin-2[1*H*] 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 procedure[6]. The compound 3a was in turn prepared from dichloroquinoline 1a as per the reported procedure[7]. The ^{1}H NMR spectrum in $CDCl_3$ 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-1*H*-pyrazolo [4, 3-*c*] quinolin-4(5*H*)-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. Oflaxacin (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 ºC 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 aurous. The compound 4a and 4b were active against Escherichia coli and Bacillus subtitles whereas compound 4c registered good antibacterial against Escherichia coli and Staphylococcus aurous.

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 ^{0}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**) $CDCl_3$

Table 2: Antibacterial activity (4a-e)

Compound	Organisms		
	Diameter of inhibition zone (mm) at µg/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

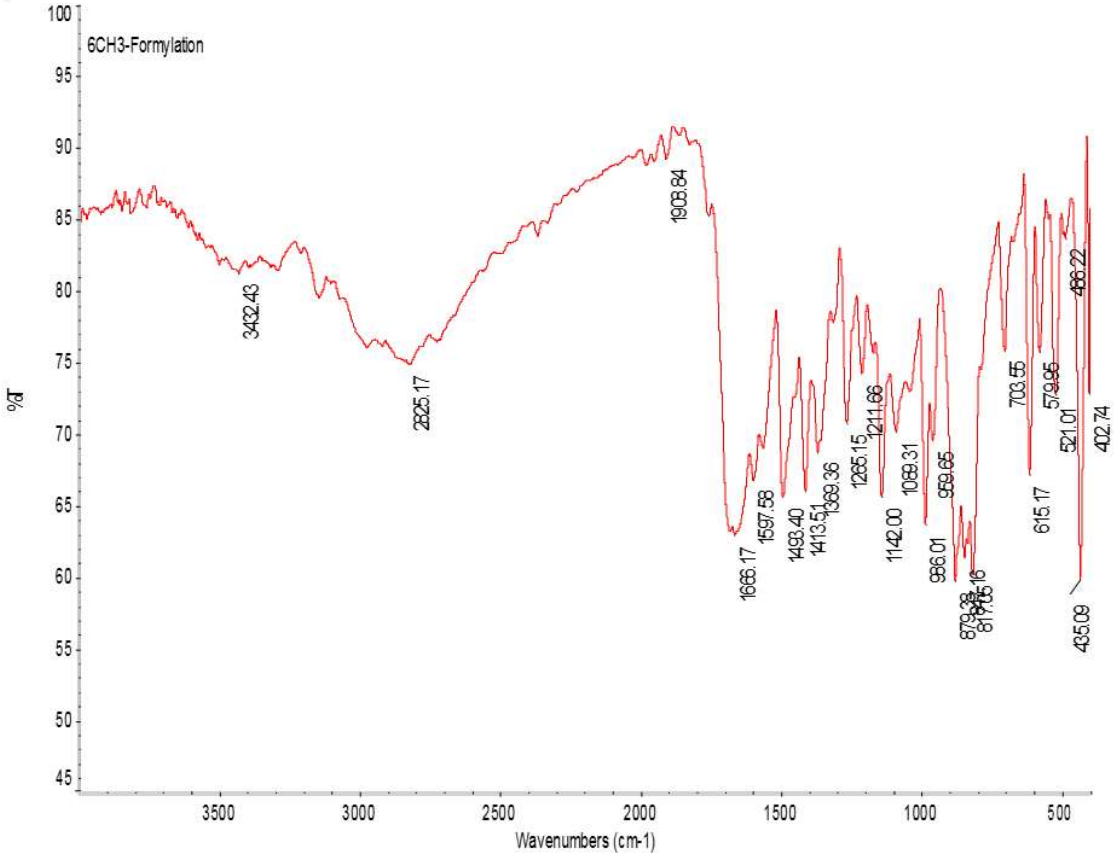

Figure 1: FTIR Spectra of Compound- 2b

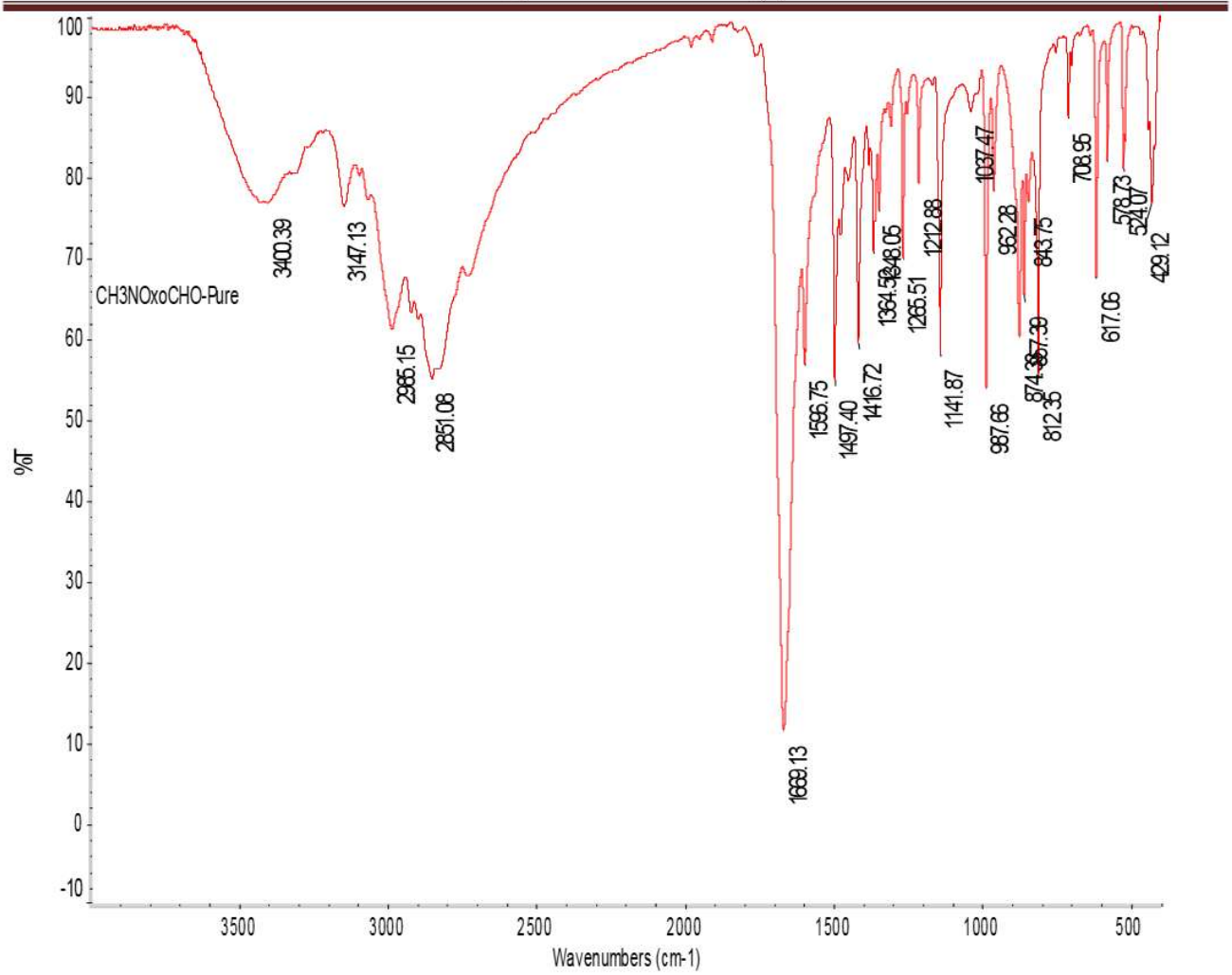

Figure 2: FTIR Spectra of Compound- 3b

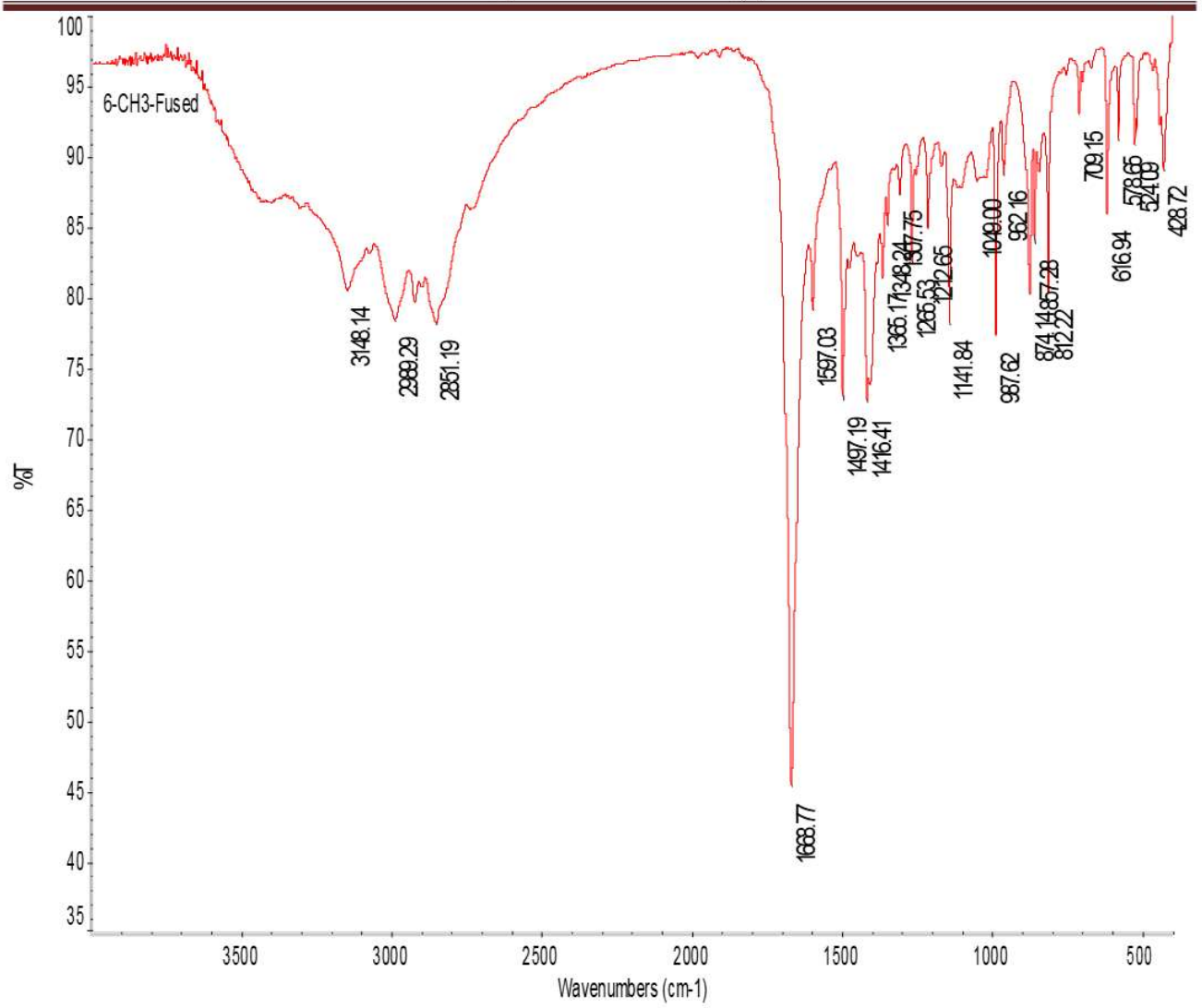

Figure 3: FTIR Spectra of Compound- 4 b

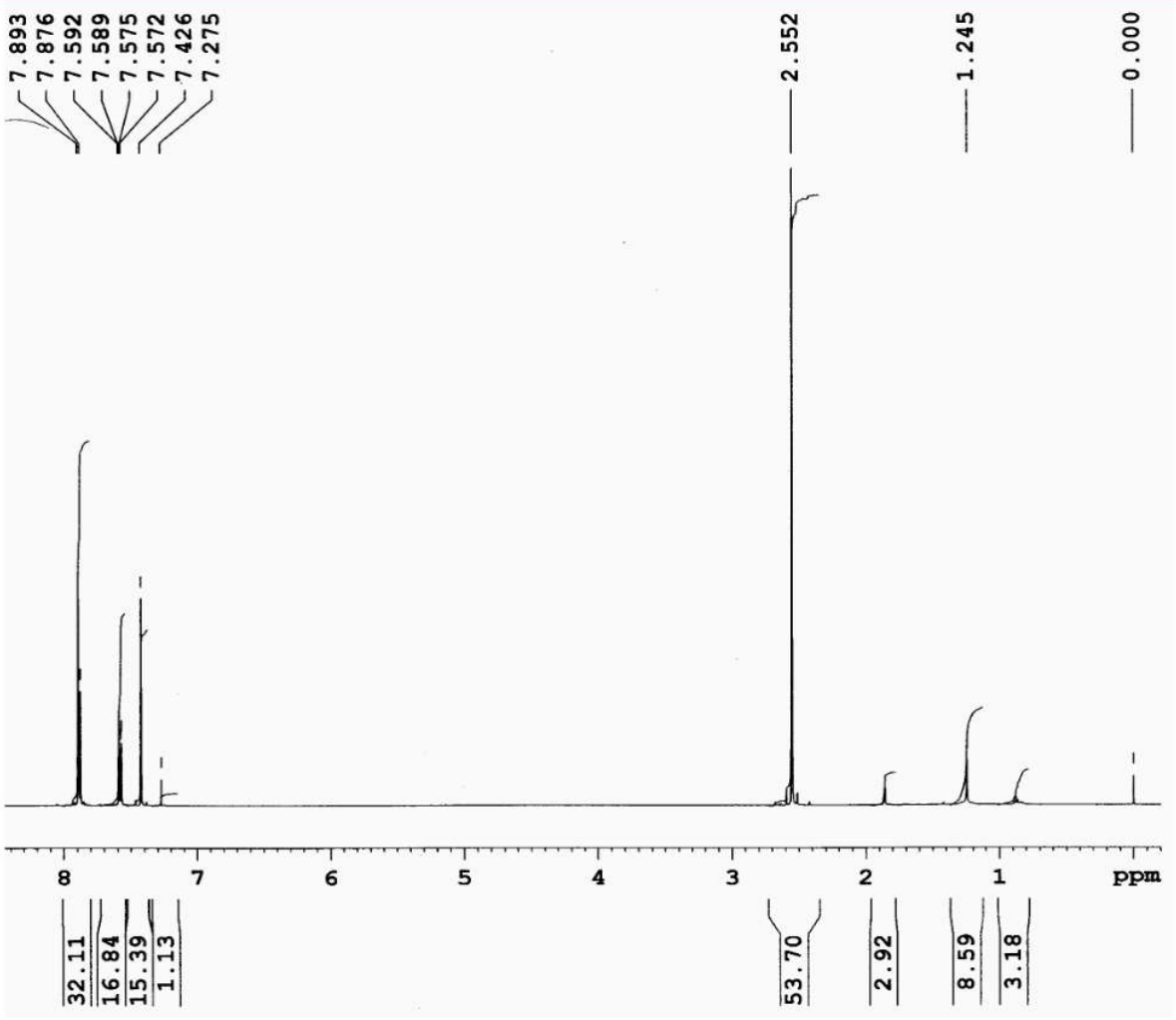

Figure 4: **^{1}H NMR & ^{13}C NMR of 6-methyl-2, 4-dichloroquinoline, 1b**

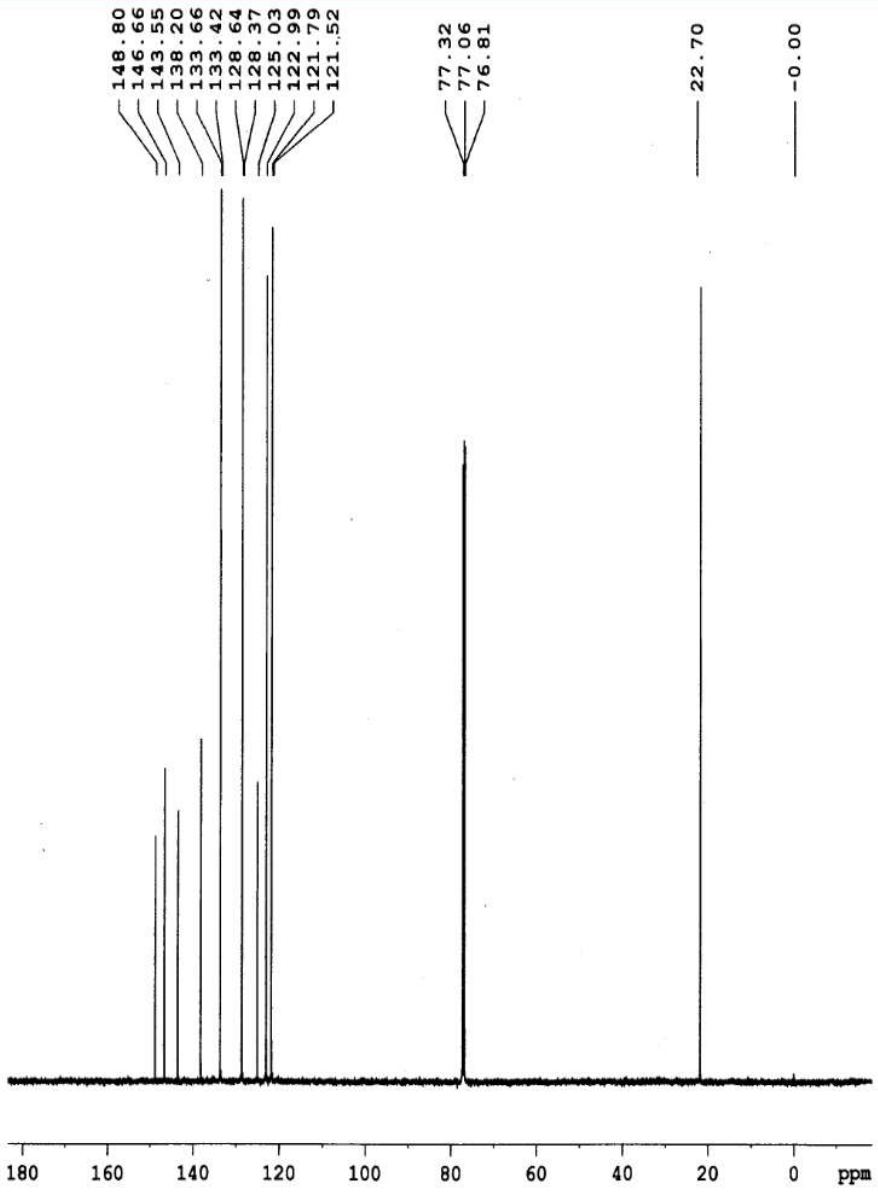

Figure 5: ^{1}H NMR & ^{13}C NMR of 6-methyl-2, 4-dichloroquinoline, 1b

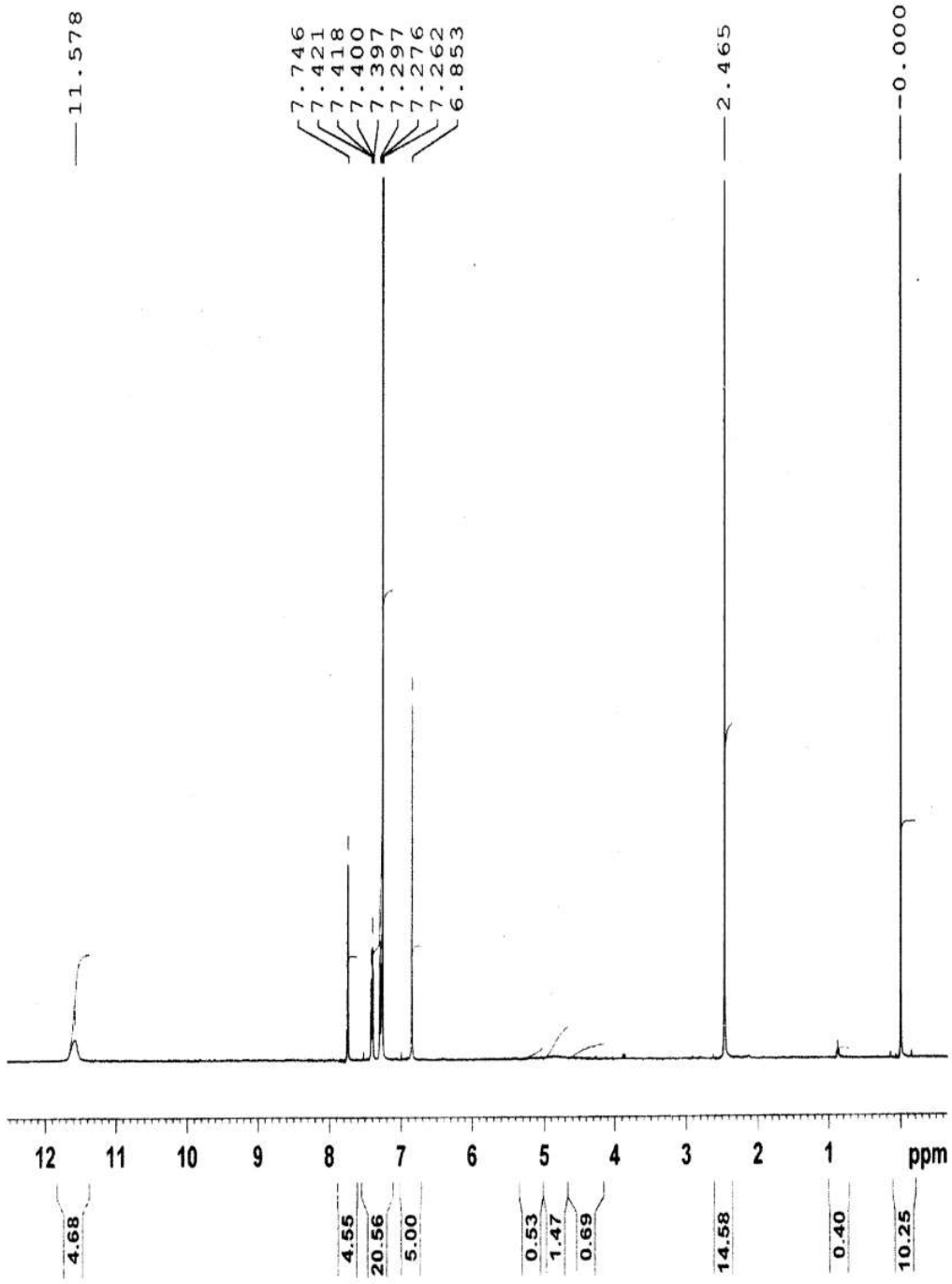

Figure 6: ^{1}H NMR of 1-benzoyl-8-methyl-*1H*-pyrazolo [4, 3-*c*]quinolin-4(*5H*)-one, 4b

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