

Synthesis and Characterization of Some New Pyrazoline Compounds Derived from Azo Chalcones

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Abstract

1-[4-(2,4-Bis-benzyloxy-phenylazo)-phenyl]-ethanone (**Az**) was prepared *via* diazotization of 4-aminoacetophenone and coupling of the product with resorcinol, then it was benzylated with benzyl bromide to give (**Bz**). The prepared benzyloxy-azo compound (**Bz**) was reacted with differently substituted benzaldehyde to obtain azo-chalcone (**Ch1-Ch6**). These chalcones were reacted with hydrazine hydrate to yield azo-pyrazoline compounds (**Py1-Py6**). The structures of prepared compounds were characterized by FT-IR and ¹H NMR spectroscopies.

1.0 Introduction

Chalcones are well-known precursors for synthesizing various heterocyclic compounds. This is due to the presence of reactive α,β -unsaturated keto group which could be reacted with diazoalkanes [1] or with hydrazine hydrate [2,3] in order to synthesize pyrazoline compounds. Pyrazoline derivatives are heterocyclic compounds which is widely used in pharmaceutical and agrochemical research.

These compounds have substantial biological activities such as antimicrobial [4], antifungal [5], antidepressant [6], immunosuppressive [7], anticonvulsant [8], anti-tumour [9], antiamebic [10], antibacterial [11] and anti-inflammatory [12]. In addition, pyrazolines have optical brighteners and whiteners properties [13]. Furthermore, these compounds show attractive fluorescent properties in the detection of some metal cations [14] and they are excellent hole transport and emissive layer materials in electroluminescence devices [15, 16]. Therefore, the focus of the present work is to synthesize some new azo-pyrazoline derivatives. Pyrazoline compounds could be synthesised by several methods such as condensation of a variety of substituted chalcones with hydrazine and its derivatives, which is the commonly used method [17, 18].

2.0. Experimental

2.1. Reagents and Solvents

All chemicals, reagents, and solvents obtained from Sigma–Aldrich and Fluka.

2.2. Instrumentation

All FT-IR spectra for the products were recorded using Shimadzu FT-IR spectrophotometer. All ¹H NMR spectra for the products measured with a Bruker Avance (400 MHz) spectrometer in deuterated dimethyl sulfoxide (CD₃SOCD₃) as a solvent. The chemical shifts were measured in parts per million (ppm).

2.3. Synthetic procedures for the Precursor

2.3.1 Synthesis of 1-(4-((2,4-dihydroxyphenyl)diazenyl)phenyl) ethan-1-one (**Az**) (19): Diazotization of 4-Aminoacetophenone

4-Aminoacetophenone (4.05 g, 0.03 mol) was dissolved in HCl solution (24 mL, 3M) in a beaker. The solution was heated gently on heating mantle in order to dissolve the starting material completely. The mixture cooled to 0 °C and to this mixture, NaNO₂ solution (30 mL, 1M) added and stirred. The reaction temperature maintain below 10 °C.

Coupling Reaction

Resorcinol (3.03 g, 0.03mol) was dissolved in NaOH solution (60 mL, 1M) in another beaker. The reaction mixture was cooled to 0 °C and then diazonium salt solution added dropwise and stirred. During the progress of the reaction, the color of the reaction mixture was changed and solidified. After addition completed, the temperature raised to room temperature and stirred for 10 minutes. The product was filtered and then purified by recrystallization from water and ethanol.

¹H NMR (400 MHz, CD₃SOCD₃, δ): 3.38 (s, 3H, COCH₃), 6.36-6.51 (dd, 2H, H-13 and H-14), 7.68 (s, 1H, H-11), 7.94-8.08 (m, 4H, H-4, H-5, H-7 and H-8), 12.40 (s, 2H, OH). FT-IR (cm⁻¹): 3296 (OH), 1656 (C=O), 1597 (C=C). All physical properties are outlined in table 1.

2.3.2 Synthesis of 1-(4-((2,4-bis(benzyloxy)phenyl)diazanyl)phenyl) ethan-1-one (Bz) [20]:

1-(4-((2,4-dihydroxyphenyl)diazanyl)phenyl)ethan-1-one (2.57 g, 0.01 mol), benzyl bromide (3.77 g, 0.022 mol), anhydrous K₂CO₃ (8.29 g, 0.06 mol) and ethanol (50 mL, 96%) added to a flask and refluxed for 6 hr. The reaction mixture cooled to room temperature and then poured into water, solid immediately was obtained. Subsequently, the product was filtered, washed several times with cold water and dried. The product was recrystallized from a mixture of (xylene: ethanol, 2:8) to yield **Bz** as orange crystals.

¹H NMR (400 MHz, CD₃SOCD₃, δ): 3.36 (s, 3H, COCH₃), 5.21-5.37 (s, 4H, OCH₂), 6.75-8.11 (m, 24H, Ar-H). FT-IR (cm⁻¹): 3059 (C-H aromatic), 2873 (C-H aliphatic), 1674 (C=O), 1597 (C=C), 1251 (C-O). The some physical properties are outlined in table 1.

2.4 Synthesis of Chalcones (Ch1-Ch6)

(Ch1-Ch6) were prepared according to the modified procedure [21]. **Bz** (10 mmol) and substituted aldehyde (10 mmol) were dissolved in ethanol (10 mL, 96%), NaOH (0.4 g) was added, then stirred at room temperature overnight. The reaction mixture was poured into crushed ice and then acidifies with dilute HCl. The precipitate was filtered, washed with water, and then dried. The product was recrystallized from ethanol. Some physical properties are outlined in table 1.

2.4.1. (3E)-1-(4-((2,4-bis(benzyloxy)phenyl)diazanyl)phenyl)-4-phenylbut-3-en-1-one (Ch1):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 5.25 (s, 4H, OCH₂), 7.02-8.38 (m, 24 H, Ar-H and α,β-H). FT-IR (cm⁻¹): 1660 (C=O) 1597 (C=C).

2.4.2. (3E)-1-(4-((2,4-bis(benzyloxy)phenyl)diazanyl)phenyl)-4-(4-fluorophenyl)but-3-en-1-one (Ch2):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 5.24 (s, 4H, OCH₂), 6.95-7.74 (m, 23 H, Ar-H and α,β-H). FT-IR (cm⁻¹): 1664 (C=O), 1597 (C=C).

2.4.3. (3E)-1-(4-((2,4-bis(benzyloxy)phenyl)diazanyl)phenyl)-4-(4-methoxyphenyl) but-3-en-1-one (Ch3):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 3.36 (s, 3H, OCH₃), 5.12 (s, 4H, OCH₂), 7.16-8.15 (m, 23 H, Ar-H and α,β-H). FT-IR (cm⁻¹): 1658 (C=O) 1598 (C=C).

2.4.4. (3E)-1-(4-((2,4-bis(benzyloxy)phenyl)diazanyl)phenyl)-4-(p-tolyl)but-3-en-1-one (Ch4):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 5.22 (s, 4H, OCH₂), 3.36 (s, 3H, CH₃), 6.20-7.94 (m, 23 H, Ar-H and α,β-H). FT-IR (cm⁻¹): 1660 (C=O), 1600 (C=C).

2.4.5. (3E)-4-(2-(benzyloxy)phenyl)-1-(4-((2,4-bis(benzyloxy)phenyl)diazanyl)phenyl) but-3-en-1-one (Ch5):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 5.41 (s, 9H, OCH₂), 6.95-8.36 (m, 27 H, Ar-H and α,β-H). FT-IR (cm⁻¹): 1658 (C=O), 1597 (C=C).

2.4.6. (3E)-1-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-4-(2-chlorophenyl)but-3-en-1-one (Ch6):
¹H NMR (400 MHz, CD₃SOCD₃, δ): 5.26 (s, 4H, OCH₂), 7.09-8.45 (m, 23 H, Ar-H and α,β-H). FT-IR (cm⁻¹): 1672 (C=O), 1597(C=C).

2.5 Synthetic procedures for the Pyrazolines (Py1-Py6)

Chalcones (0.01 mol) in ethanol (20 mL) and NaOH (0.8 g), hydrazine hydrate (0.025 mol, 80%) were added to a flask and then refluxed for 6-7 hr. The reaction mixture was cooled and maintained at room temperature. The resulting solid was filtered and dried. The product was recrystallized from ethanol [21]. The some physical properties are outlined in table 1.

2.5.1. 3-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-5-phenyl-4,5-dihydro-1H-pyrazole (Py1):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 1.23 (s, 1H, H-8), 3.35 (s, 1H, H-7), 5.21 (s, 4H, OCH₂), 6.75-8.12 (m, 23 H, Ar-H and N-H). FT-IR (cm⁻¹): 1660 (C=N), 1597 (C=C).

2.5.2. 3-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-5-(4-fluorophenyl)-4,5-dihydro-1H-pyrazole (Py2):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 1.22 (s, 1H, H-8), 3.22 (s, 1H, H-7), 5.21 (s, 4H, OCH₂), 6.74-8.10 (m, 22 H, Ar-H and N-H). FT-IR (cm⁻¹): 1664 (C=N), 1597(C=C).

2.5.3. 3-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole (Py3):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 1.22 (s, 1H, H-8), 3.99 (s, 1H, H-7), 5.21 (s, 4H, OCH₂), 3.79 (s, 3H, OCH₃), 7.12-8.07 (m, 22 H, Ar-H and N-H). FT-IR (cm⁻¹): 1658 (C=N), 1604 (C=C).

2.5.4. 3-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole (Py4):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 1.23 (s, 1H, H-8), 3.33 (s, 1H, H-7), 5.22 (s, 4H, OCH₂), 2.32 (s, 3H, CH₃), 7.06-8.02 (m, 22 H, Ar-H and N-H). FT-IR (cm⁻¹): 1660 (C=N), 1600 (C=C).

2.5.5. 3-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-5-(2-((3-nitrobenzyl)oxy)phenyl)-4,5-dihydro-1H-pyrazole (Py5):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 1.22 (s, 2H, H-8), 3.33 (s, 1H, H-7), 5.21 (s, 6H, OCH₂), 6.50-7.87 (m, 26 H, Ar-H and N-H). FT-IR (cm⁻¹): 1658 (C=N), 1600 (C=C).

2.5.6. 3-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)-5-(2-chlorophenyl)-4,5-dihydro-1H-pyrazole (Py6):

¹H NMR (400 MHz, CD₃SOCD₃, δ): 1.22 (s, 1H, H-8), 3.32 (s, 1H, H-7), 5.20 (s, 4H, OCH₂), 6.74-8.10 (m, 23 H, Ar-H and N-H). FT-IR (cm⁻¹): 1672 (C=N), 1597 (C=C).

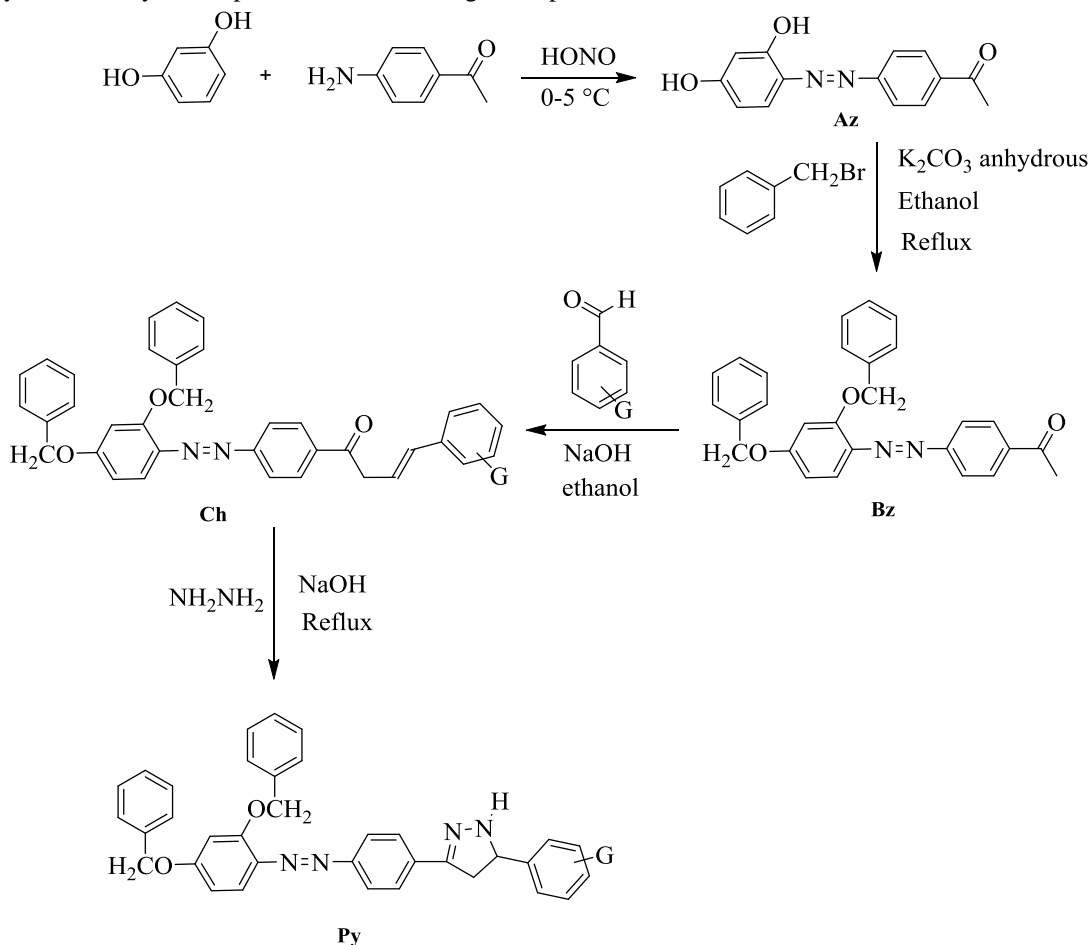
Table 1: Physical properties for the synthesized compounds

No.	Comp.	(G) group	Chem. formula	Molecular weight	Yield (%)
1	Az	-	C ₁₄ H ₁₂ N ₂ O ₃	256.257	79
2	Bz	-	C ₂₈ H ₂₄ N ₂ O ₃	436.502	62.8
3	C1	H	C ₃₆ H ₃₀ N ₂ O ₃	524.608	78.2
4	C2	4-F	C ₃₆ H ₂₉ FN ₂ O ₃	542.599	93.7
5	C3	4-OCH ₃	C ₃₇ H ₃₂ N ₂ O ₄	554.634	82.5
6	C4	4-CH ₃	C ₃₇ H ₃₂ N ₂ O ₃	538.635	96.2
7	C5	2-(3-NO ₂ -benzoxy)	C ₄₃ H ₃₆ N ₂ O ₄	675.728	68.1
8	C6	2-Cl	C ₃₆ H ₂₉ ClN ₂ O ₃	559.053	63.7
9	Py1	H	C ₃₆ H ₃₂ N ₄ O ₂	538.638	97.5
10	Py2	4-F	C ₃₅ H ₂₉ FN ₄ O ₂	556.64	82.7
11	Py3	4-OCH ₃	C ₃₆ H ₃₂ N ₄ O ₃	568.67	72.3
12	Py4	4-CH ₃	C ₃₆ H ₃₂ N ₄ O ₂	552.67	91.5
13	Py5	2-(3-NO ₂ -benzoxy)	C ₄₂ H ₃₅ N ₅ O ₅	689.758	92
14	Py6	2-Cl	C ₃₅ H ₂₉ ClN ₄ O ₂	573.09	64.3

Where benzyloxy: OCH₂C₆H₄

3.0 Results and Discussion

The present study was designed to synthesize and characterization of some new pyrazoline derivatives with azo-linkage and benzyloxy moiety. All target compounds have been synthesized in moderate to high yields. The synthetic process of the new target compound is outlined in scheme 1.



Scheme 1: Synthetic Steps of the Pyrazoline Derivatives

The precursor 1-(4-((2,4-bis(benzyloxy)phenyl)diazenyl)phenyl)ethan-1-one (**Bz**) has prepared successfully *via* diazotization of 4-aminoacetophenone and reacted with resorcinol as a coupling agent to afford 1-(4-((2,4-dihydroxyphenyl)diazenyl)phenyl)ethan-1-one (**Az**). The next step was benzylation of **Az** with benzyl bromide to form **Bz** was carried out in the presence of anhydrous K_2CO_3 and ethanol as a solvent. The structure was confirmed by FT-IR and ^1H NMR spectroscopies. In the FT-IR spectrum of **Bz**, a broad band at 3296 cm^{-1} and a singlet peak at 12.40 ppm in the ^1H NMR spectrum disappear which is good evidence that the benzylation reaction was successful.

The Chalcones were synthesized as intermediate compounds *via* Claisen-Schmidt condensation of **Bz** with several substituted benzaldehyde in alcoholic NaOH solution. The processes were succeeded to yield chalcones. The most important evidence for the formation of chalcones is the shifting of carbonyl group bands to approximately 1660 cm^{-1} and exhibited the characteristic of deshielding for α - and β - protons at approximately $(6.95-8.45\text{ ppm})$ in ^1H NMR spectrum.

The target compounds synthesized were chalcone derivatives subjected to hydrazine hydrate and refluxed. In the FT-IR spectra for (**Py1-Py6**) compounds the disappearance of ($\text{C}=\text{O}$) group band for enone system is robust evidence for the formation of imine in five membered cyclic system [22]. The ^1H NMR spectra displayed signals assigned to N-H at approximately $7.87-8.10\text{ ppm}$.

4.0 Conclusion

In this study, the results show that new azo-pyrzaoline derivatives synthesized successfully by multiple-steps in good yields. It can be concluded that achieve many organic compounds and used in different fields, for example, medicine and Industry of dyes. All the synthesized compounds were characterized by FT-IR and ¹H NMR spectroscopies.

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6. References

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Appendix

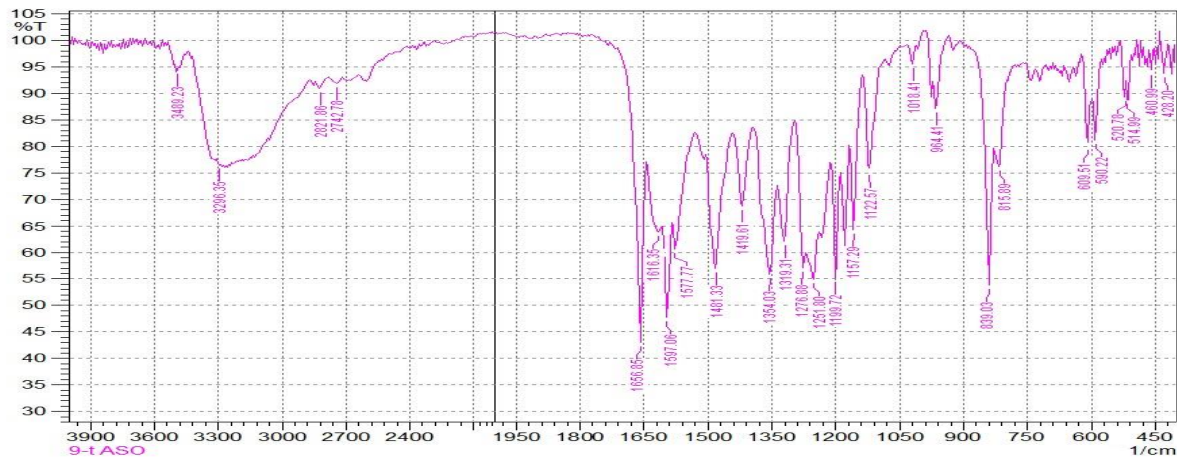


Figure 1: FT-IR spectrum of compound Az.

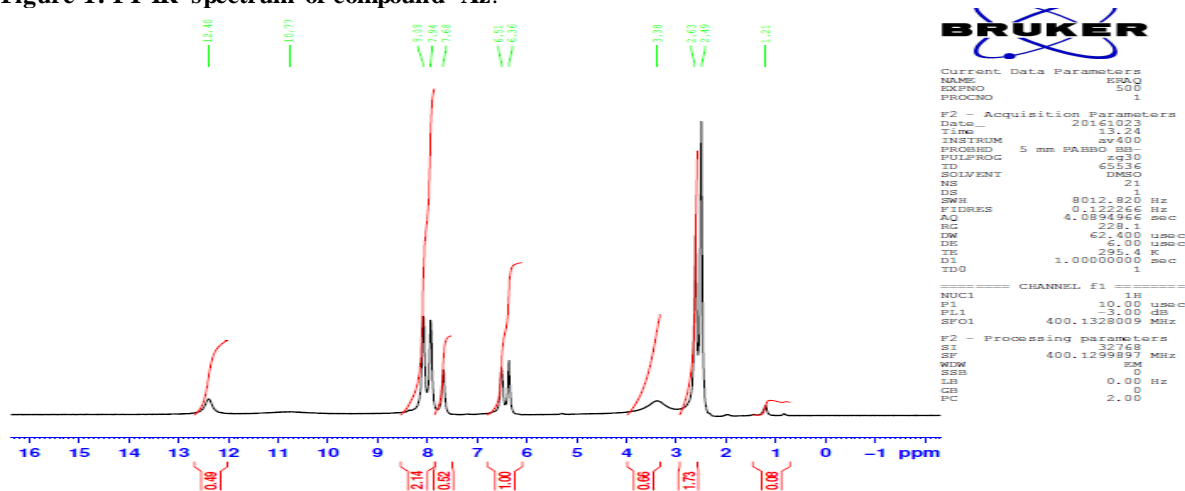


Figure 2: ¹H NMR spectrum of compound Az.

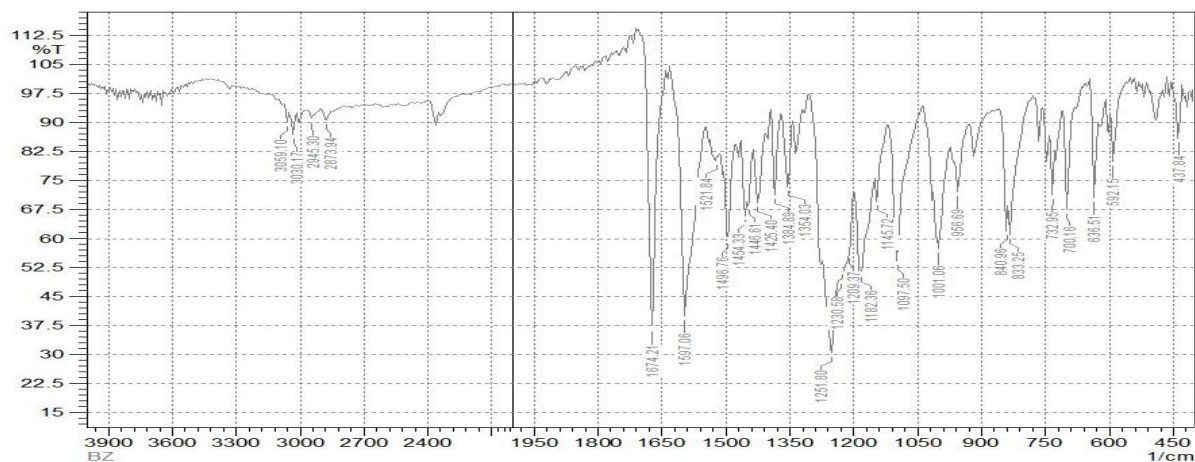


Figure 3: FT-IR spectrum of compound bz.

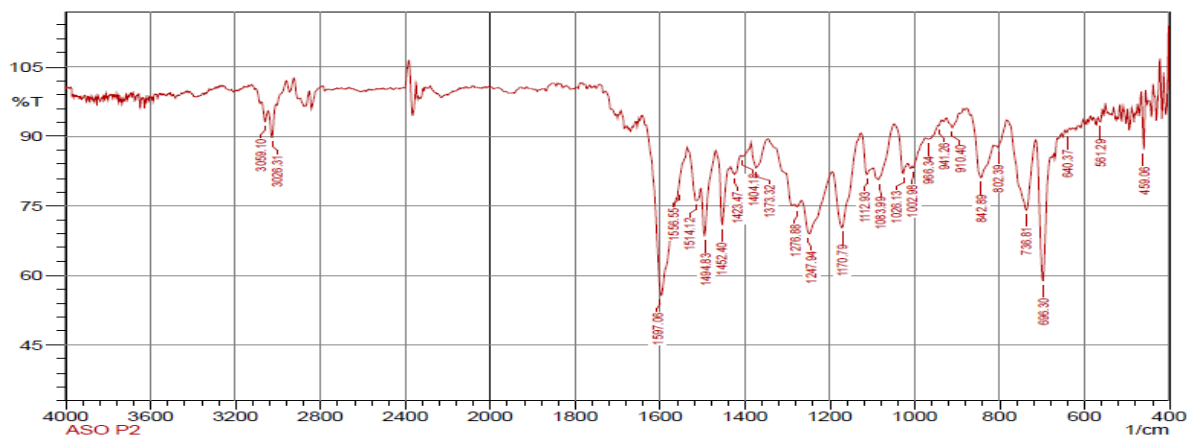


Figure 7: FT-IR spectrum of compound Py1

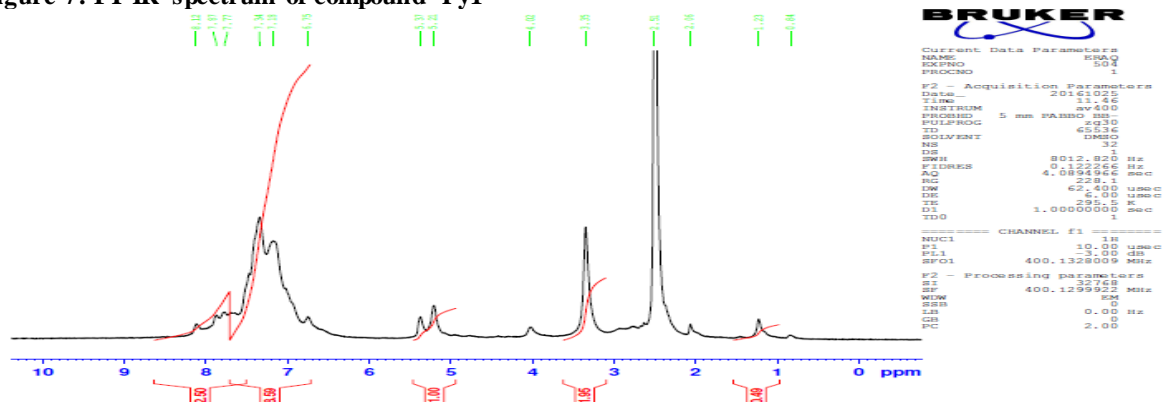


Figure 8: ¹H NMR spectrum of compound Py1