https://doi.org/10.48047/AFJBS.6.8.2024.3289-3311

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Novel Synthesis of Benzimidazole-Aldehyde Derivatives & Characterization Targeting Microbial G-quadrupex Motif

Dr. Nasiruddin Ahmad Farooqui[1], Muskan Fazeel[*2] Dr. Shamim Ahamad[3]

Professor& HOD , Translam Instotute of Pharmaceutical Education and Research, Meerut U.P.

Research Scholar, Translam Instotute of Pharmaceutical Education and Research, Meerut U.P.

Professor& HOD, Translam Instotute of Pharmaceutical Education and Research, Meerut U.P. Director, Translam Instotute of Pharmaceutical Education and Research, Meerut U.P.

Abstract

Guanidine DNA quadruplex (G4-DNA) structures convey a distinctive layer of epigenetic information that is critical for regulating key biological activities and processes as transcription, replication, and repair in living cells. The information regarding their role and use as therapeutic drug targets in bacteria is still scarce. Here, we tested the biological activity of a G4-DNA ligand library, based on Benzimidazole-Aldehyde Based pharmacophore, against both Gram-positive and Gram-negative bacteria. For the best compound identified, Benzimidazole-Aldehyde Based, a different action mechanism was described for Gram-positive or negative bacteria. This asymmetric activity profile could be related to the different prevalence of putative G4-DNA structures in each group, the influence that they can exert on gene expression, and the different roles of the G4 structures in these bacteria, which seem to promote transcription in Gram-positive bacteria and repress transcription in Gram-negatives. We derived Chemical library of Benzimidazole- Aldehyde Derivatives motif .

Keywords: G quadruplex, Anti-microbial agents, Benzimidazole.

Guanine Based motif

DNA hereditary material specific twofold helical construction [1]. Essential capability of telomerase to safeguard the genomic end by the keeping up with length [2]. Replication time phonesbase pair misfortune during each and every round of substantial cell division [3]. The auxiliary framework of G-quadruplex ordered into unimolecular, bimolecular, tri-sub-atomic and tetra-atomic G-quadruplex has some commitment like, when three legs in a similar course called syn-syn-hostile to affirmation the other way around, otherwise called half breed blended G-quadruplicate center.

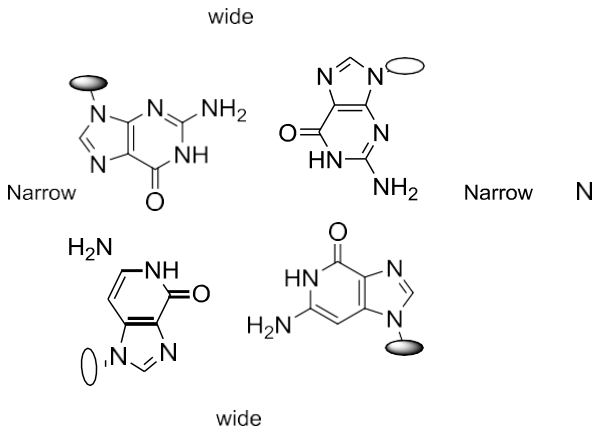


Figure 1: Representation of G-quadruplex core groove.

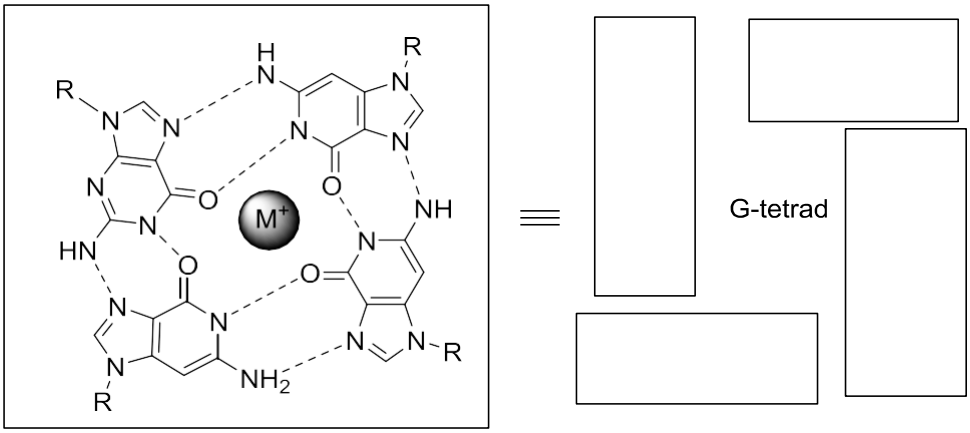


Figure :2 The coplanar representation of guanine containing tetrad.

The optional platform orders into several types of different scaffold existed in form of G DNA. it framed by DNA and RNA depend upon the grouping. Anyway it shows the G-quadruplex has some commitment like, when three legs in a similar bearing called syn-syn-hostile to affirmation the other way around, otherwise called crossover blended G-quadruplicate center [4].

1. Singular G-quadruplex

G4 can execute the different sort of the circles to be specific, the inclining circle, horizontal circle another is the outside circle. It can wrinkle into an equal quadruplicate with three G-quadruplex circles [5]. For Example, human telomeric groupings structure precious stone design through the return . It is likewise called a half and half G-quadruplex, by situate themselves in the equivalent and one is a clashing way, that further consents to hostile to against hostile to syn affirmation. It additionally encompasses one restricted and wide outer circle. The versatility of the affirmation relies upon their circumstance and cationic climate. The quadruplex has Watson-cramp duplex in a long circle that may a pivotal piece of the clever objective. The ID of that the two arrangements shaped the intramolecular G quadruplex, like the human telomeric genome. The stretch out past of telomeric DNA make out of a solitary abandoned copy of the TTAGGG unit of something like 100-200 bp long.

The in vivo structure take on the human telomere underneath physiologically critical situation is as yet ambivalent, in any case, not many reports have not mandatory cross breed construction to be the significant conformity under in vivo situation [6].

The length of the telomere is kept up with by the compound telomerase which is overexpressed in 80-85% of malignant growth cells however not in typical physical cells. There are a wealth of reports recitation their antitumor, anticancer and cell reinforcement properties. Portraying the job of plant flavonoids, as potential G-quadruplex restricting specialists. Beforehand it has been accounted for through different optical spectroscopy methods that Quercetin, a normally occurring in plant flavonoid, collaborate with monomeric and dimeric G-quadruplex construction from one finish to another stacking and groove restricting mode correspondingly [7]. [8,9]. It has additionally the capacity to regulate the quality record process. HIV-1 integrase in which the produce little sub-atomic ligand. These are affirmed through the Compact disc, NMR, and atomic docking procedures. The connection point monomer particularly two should be an enemy of against hostile to syn arrangement [10,11]. The different locked interface interlocked dimeric types of G-quadruplex are more steady, this is the explanation that goes about as the natural application, it fills in as sub-atomic objective ravine of the multimeric protein [12]. Twofold abandoned G-quadruplex [15].

Material And synthesis of proposed molecules

3-Pentoxybenzaldehyde-

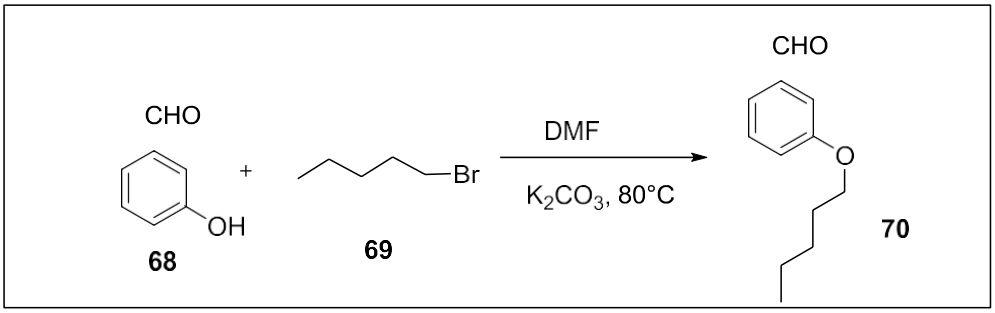


Figure:3 schematic representation of 3-pentyloxybenzaldehyde synthesis.

Procedure-

To an answer of m-hydroxybenzaldehyde (1.0 g, 8.18 mmol) in DMF (N, N-dimethylformamide,(10 mL) trailed by expansion of 1-bromopantane (1.13 mL, 8.9 mmol)with K2CO3 was added. Refluxed it three hours 80 °C. Movement of the response was observed by the slight layer chromatography with ethyl acetic acid derivation and hexane dissolvable framework. The response was shaped it was isolated by isolating channel ethylacetate water compound concentrate in the ethyl acetic acid derivation layer, and afterward it was unadulterated by section chromatography, it gives 700 mg. Rf esteem (0.5 cm.)

Synthesis of 2-(Pentoxybenzaldehyde)

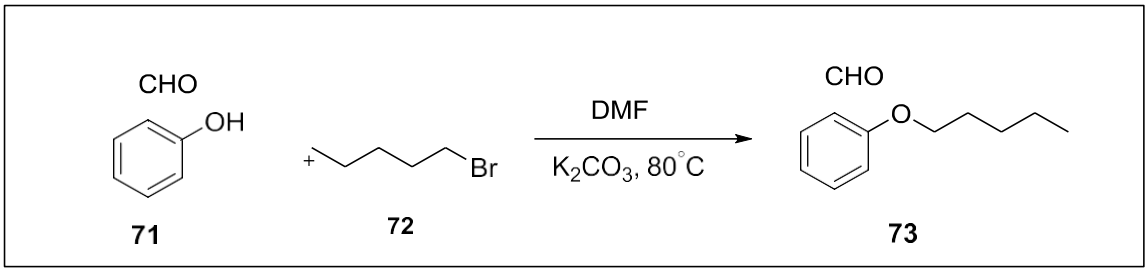


Figure: 4: 2-pentoxybenzaldehyde synthetic scheme.

Procedure-

Arrangement of salicylaldehyde (0.635 mL, 8.18 mmol)in DMF(10 mL) trailed by option of 1-bromopantane (1.13 mL, 8.9 mmol) with potassium carbonate(1.68 g,) was added. Refluxed it four hours 80∘ C. framework Rf esteem (0.7cm.). The response was finished it was isolated by isolating pipe ethyl acetic acid derivation water compound concentrate in the ethyl acetic acid derivation layer, then it was sanitized by section chromatography, to give 660 mg. The rate yield was found at 65%.

3. Synthesis of 4-(petyloxybenzaldehyde)

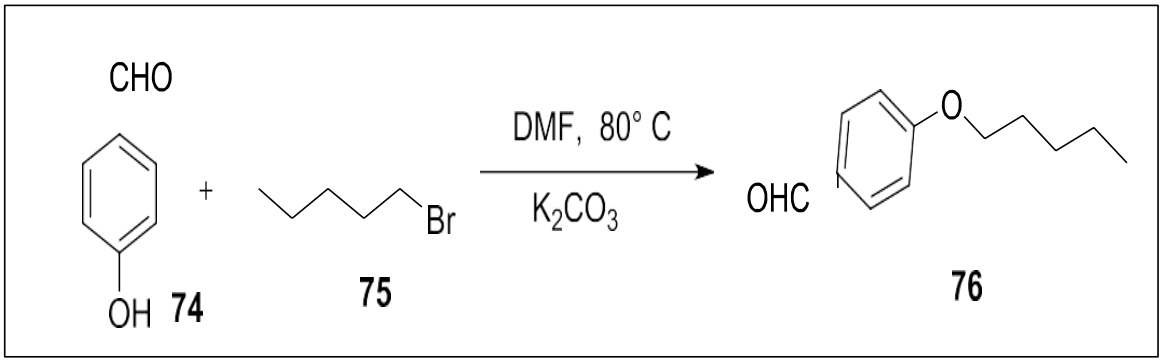


Figure :5 schematic representation of the 4-(petyloxybenzaldehyde).

Procedure:

To the response combination of p-hydroxybenzaldehyde(1.0 g, 8.18 mmol) DMF(10 mL) trailed option of 1-bromopantane (1.13 mL, 8.9 mmol). Refluxed it for two hours at 80°C. Movement of the response was observed by the Thine layer chromatography with ethyl acetic acid derivation and hexane dissolvable framework. Rf esteem(0.54 cm.). The response was shaped it was isolated by isolating pipe ethylacetate water compound concentrate in the ethyl acetic acid derivation layer, then it was cleaned by segment chromatography, to give 950 mg. The rate yield was found at 60.0%.

4: Synthesis of the 2-(propoxybenzaldehyde)

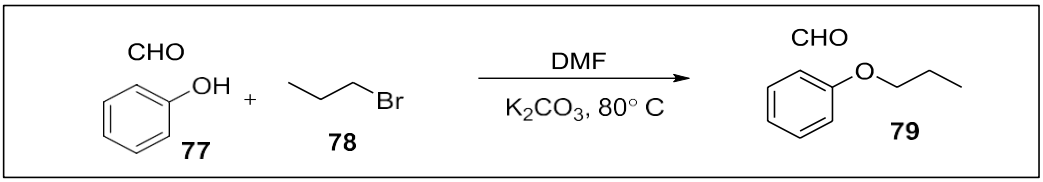


Figure: 6 schematic representation of 2-(propoxybenzaldehyde)**.**

Procedure:

To the response combination of p-hydroxybenzaldehyde(1.0 g, 8.18 mmol)in DMF(10 mL) trailed by the option of 1-bromopantane (1.13 mL, 8.9 mmol) with K2CO3 added. Refluxed it for two hours at 80°C. Movement of related to Rf esteem(0.54 cm.). The response was framed it was isolated by isolating channel ethylacetate water compound concentrate in the ethyl acetic acid derivation layer, then, at that point, it was cleaned by section chromatography, to give 950 mg. The rate yield was found at 60.0%.

5. Synthesis of the 3-(propoxybenzaldehyde)

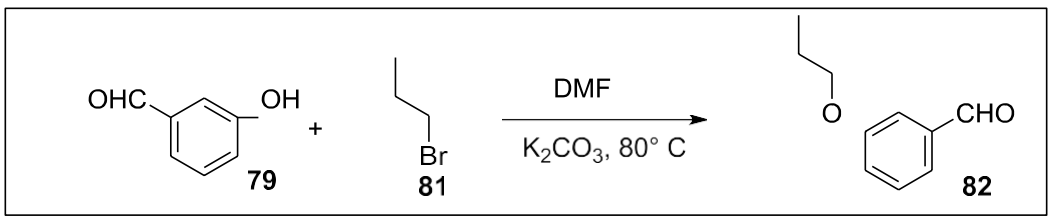
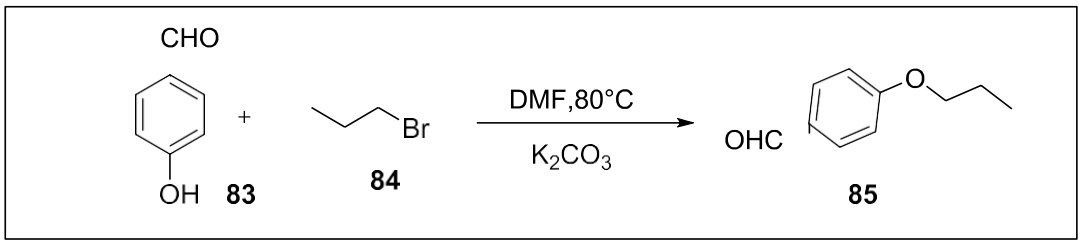


Figure : 28 schematic reprentation of 3-(propoxybenzaldehyde)**.**

Procedure-

To the arrangement of m-hydroxybenzaldehyde (1.0 g, 8.18 mmol)in DMF(10 mL) trailed by the option of n-propyl bromide (0.814 mL) with K2CO3 was mixed . Refluxed it short-term at 80°C. Movement of the response was checked by the Slight layer chromatography with ethyl acetic acid derivation and hexane dissolvable framework. Rf esteem(0.6 cm.).

6. Synthesis of the 4- propoxybenzaldehyde



7. Synthesis of the 4- propoxybenzaldehyde

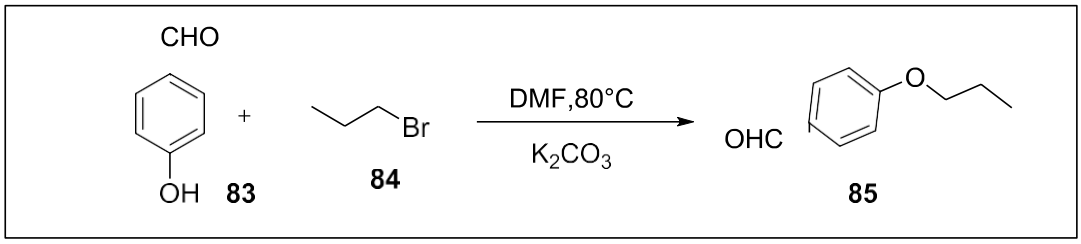


Figure : 7 synthetic scheme of the 4- propoxybenzaldehyde.

Procedure:

To the response combination of p-hydroxybenzaldehyde(1.0 g, 8.18 mmol)in DMF(10 mL) trailed by option of 1-bromopropen (0.82 mL, 8.9 mmol) with K2CO3 was added. Refluxed it to six hours at 80°C. Movement of the response was observed by the Thine layer chromatography with ethyl acetic acid derivation and hexane dissolvable framework. Rf esteem(0.54 cm.). The response was shaped it was isolated by isolating channel ethylacetate water compound concentrate in the ethyl acetic acid derivation layer, then, at that point, it was sanitized by segment chromatography, to give 690 mg. The rate yield

was found at 63%.

Synthesis of the 4-butoxybenaldehyde

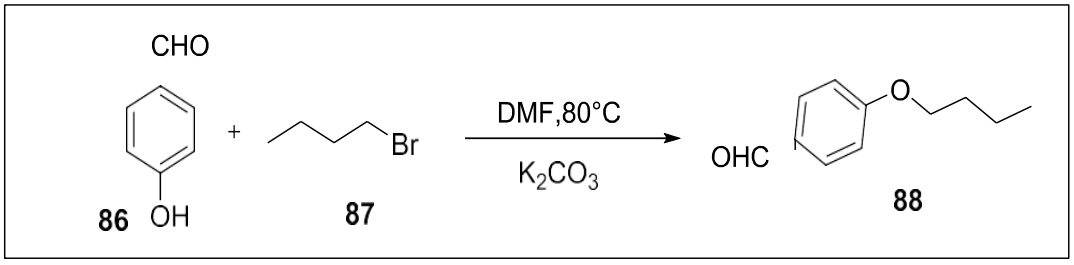


Figure 8: synthetic scheme of the 4- butoxybenzaldehyde.

Procedure:

In the response combination of p-hydroxybenzaldehyde (1.0 g, 8.18 mmol)in DMF(10 mL) trailed by option of n-butyl bromide (0.82 mL, 8.9 mmol) with K2CO3 was added. Refluxed it to six hours at 80°C. Movement of the response was observed by the Slim layer chromatography with ethyl acetic acid derivation and hexane dissolvable framework. R_f esteem(0.5 cm.). The response was shaped it was isolated by isolating pipe ethyl acetate water compound concentrate in the ethyl acetic acid derivation layer, then it was refined by section chromatography, to give 600 mg. The rate yield was found at 60.0%.

Synthesis of the 2-butoxybenaldehyde

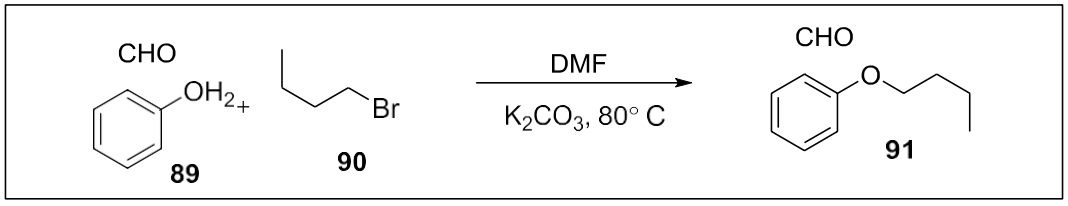


Figure: 9. synthetic scheme of the 2- butoxybenzaldehyde.

Procedure- To the response combination of O-hydroxybenzaldehyde (1.0 g, 8.18 mmol) DMF(10 mL) trailed by the option of n-butyl bromide (0.972 mL)with K2CO3 (1.68 g, 12.2 mmol)was added. Refluxed it three at 80°C. Movement Rf esteem(0.6 cm.). The response was shaped it was isolated by isolating pipe ethyl acetic acid derivation and water, compound concentrate in the ethyl acetic acid derivation layer, then, at that point, it was filtered by section chromatography, to give 650 mg. The rate yield was found at 58%.

1. Di-amino derivatives benzimidazole

Procedure:

Answer of di-amino benzoate ester (0.5 g, 3.012 mmol) N-dimethyl benzaldehyde (0.44 g, 3.012 mmol) in ethyl alcohol (20.0 mL) was added. To this combination, sodium metabisulfite (1.4 g, 7.5 mmol) was mixed, response blended at 80-degree Celsius temperature. Progress of the response was checked utilizing slender layer chromatography (tender loving care) on silica gel. After the culmination of the response, it decontaminated by segment chromatography. The ideal compound was gotten as strong (460 mg, 79 %):

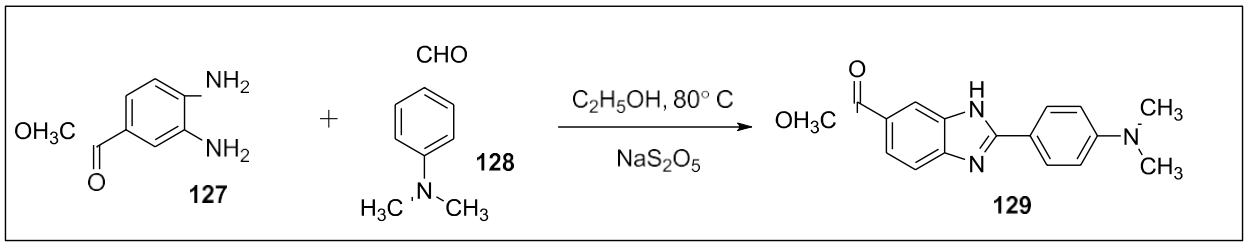


Figure: 10 synthetic scheme of benzimidazole.

2. Procedure:

Answer of Di-amino benzoate ester (0.1 g, 6.0 mmol) and 2-ethynyl benzaldehyde (0.072 g, 6.0 mmol) in ethanol (20.0 mL) was added. To this blend, sodium metabisulfite (0.2 g, 12. mmol) was added, response mixed at 80∘ C temperature. Progress of the response was checked. After the fruition of the response, it refined by section chromatography. The ideal compound was gotten as strong (80 mg, 61%).

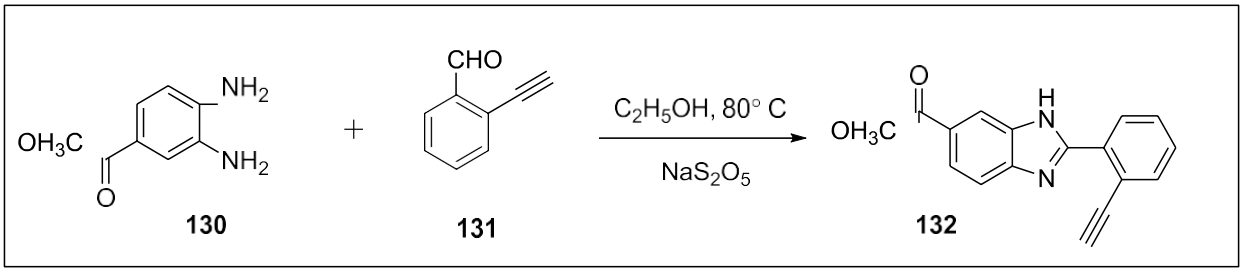
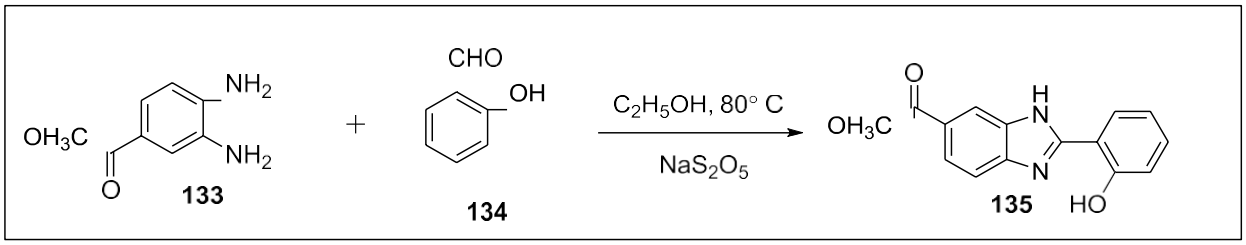


Figure: 11 Synthetic scheme of 2-ethenyl benzimidazole.

3. Procedure:

Procedure- To an answer of di-amino benzoate ester (0.1 g, 0.602) P-chloro benzaldehyde (0.036 mL, 0.602 mmol) in ethanol (15.0 mL) was added. To this blend, sodium meta bisulfite (0.2 g, 1.5 mmol) was added, response mixed at 80◦C temperature. Progress of the response was checked utilizing flimsy layer chromatography (attention) on silica gel. After the culmination of the response was gotten as strong (80 mg, 67 %):



Procedure- To an answer of di-amino benzoate ester (0.1 g) P-bromobenzaldehyde (0.113 g, 0.602 mmol) in ethanol (10.0 mL) was added. To this blend, sodium metabisulfite (0.2 g, 1.5 mmol) was added, response mixed at 80◦C. Progress of the response was checked utilizing dainty silica gel. After the fruition of the response, it sanitized by segment chromatography. The ideal compound was gotten as strong (80 mg, 56 %):

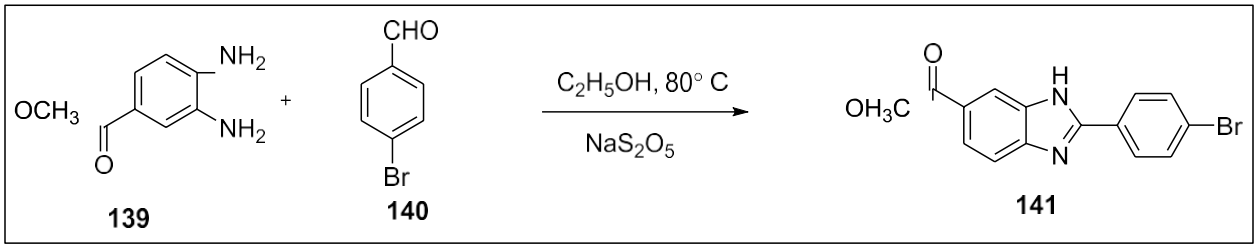


Figure: 13 Synthetic scheme of bromobenzimidazole

Spectral Characterization:

Pentoxybenzaldehyde-

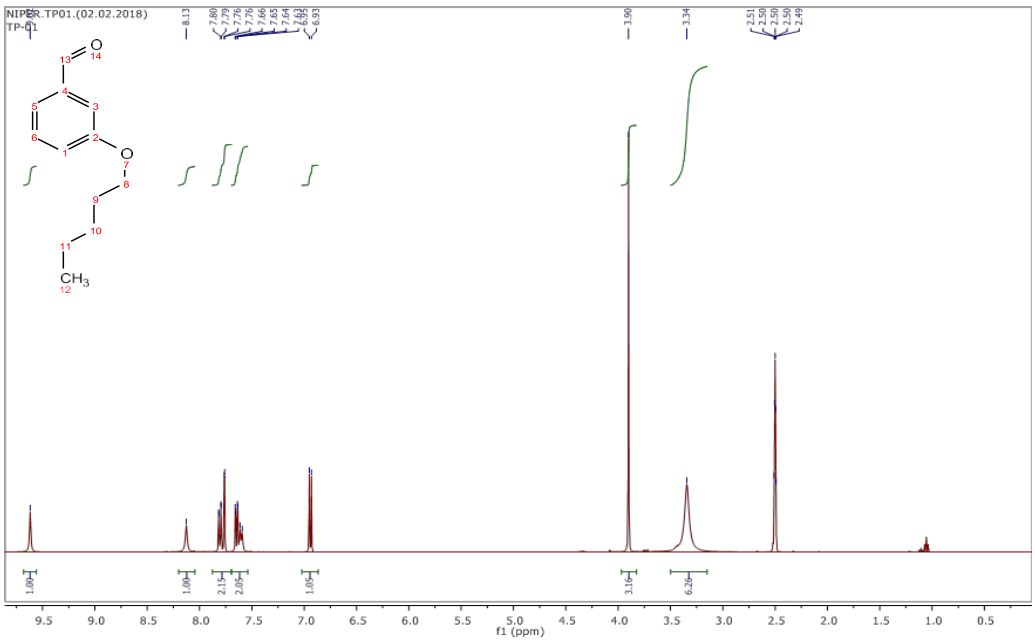


Figure:14 ^{1}H NMR of 3-(pentyloxybenzaldehyde).

Synthesis of 2-(Pentoxybenzaldehyde)

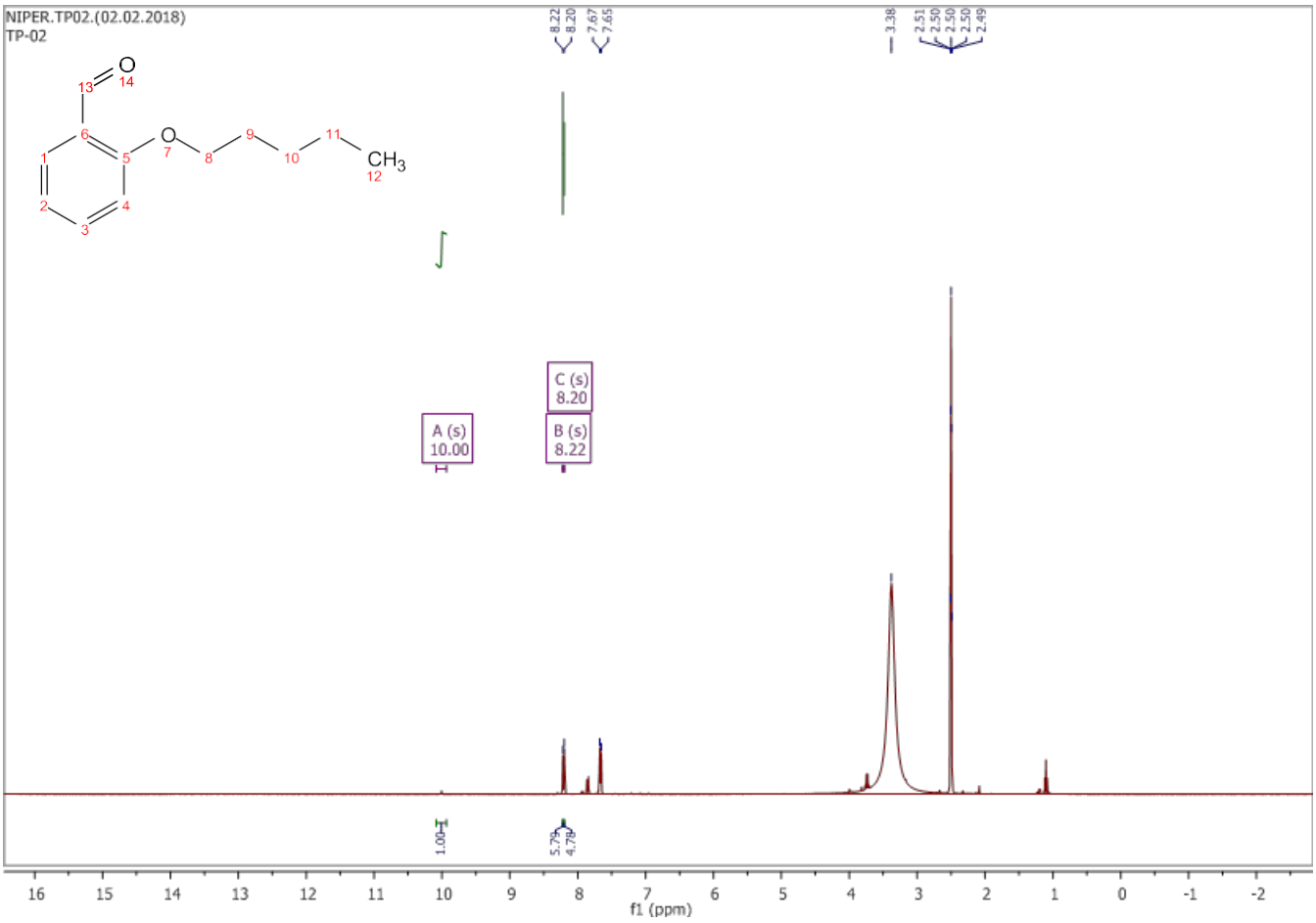


Figure:15 ^{1}H NMR of 2-(pentoxybenzaldehyde).

Synthesis of 4-Pentoxybenzaldehyde

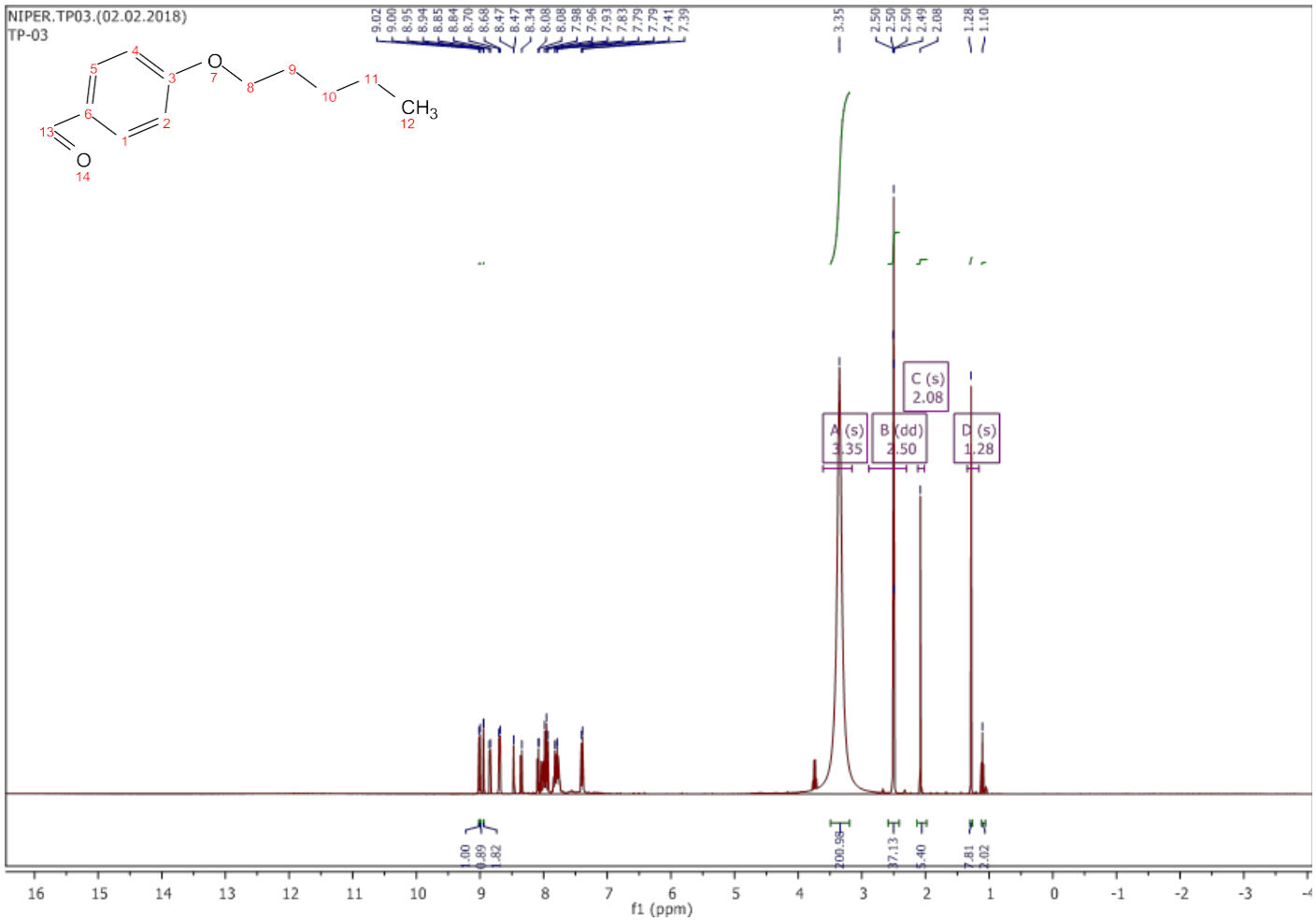


Figure:16 ^{1}H-NMR of 4-Pentoxybenzaldehyde.

1. 2-(propoxybenzaldehyde)

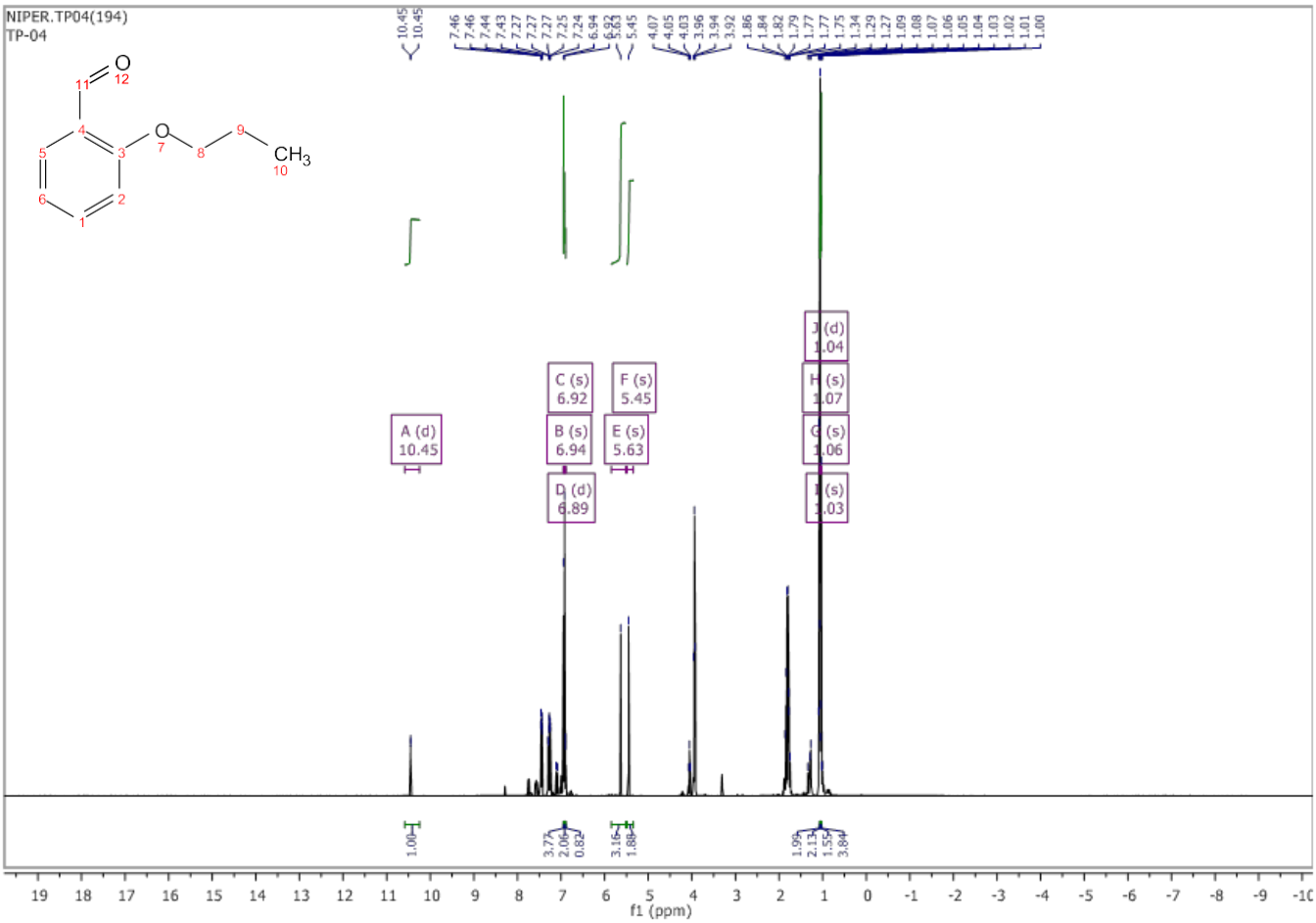


Figure: 17 ^{1}H-NMR of 2-prpoxybenzaldehyde.

2. 3-(propoxybenzaldehyde)

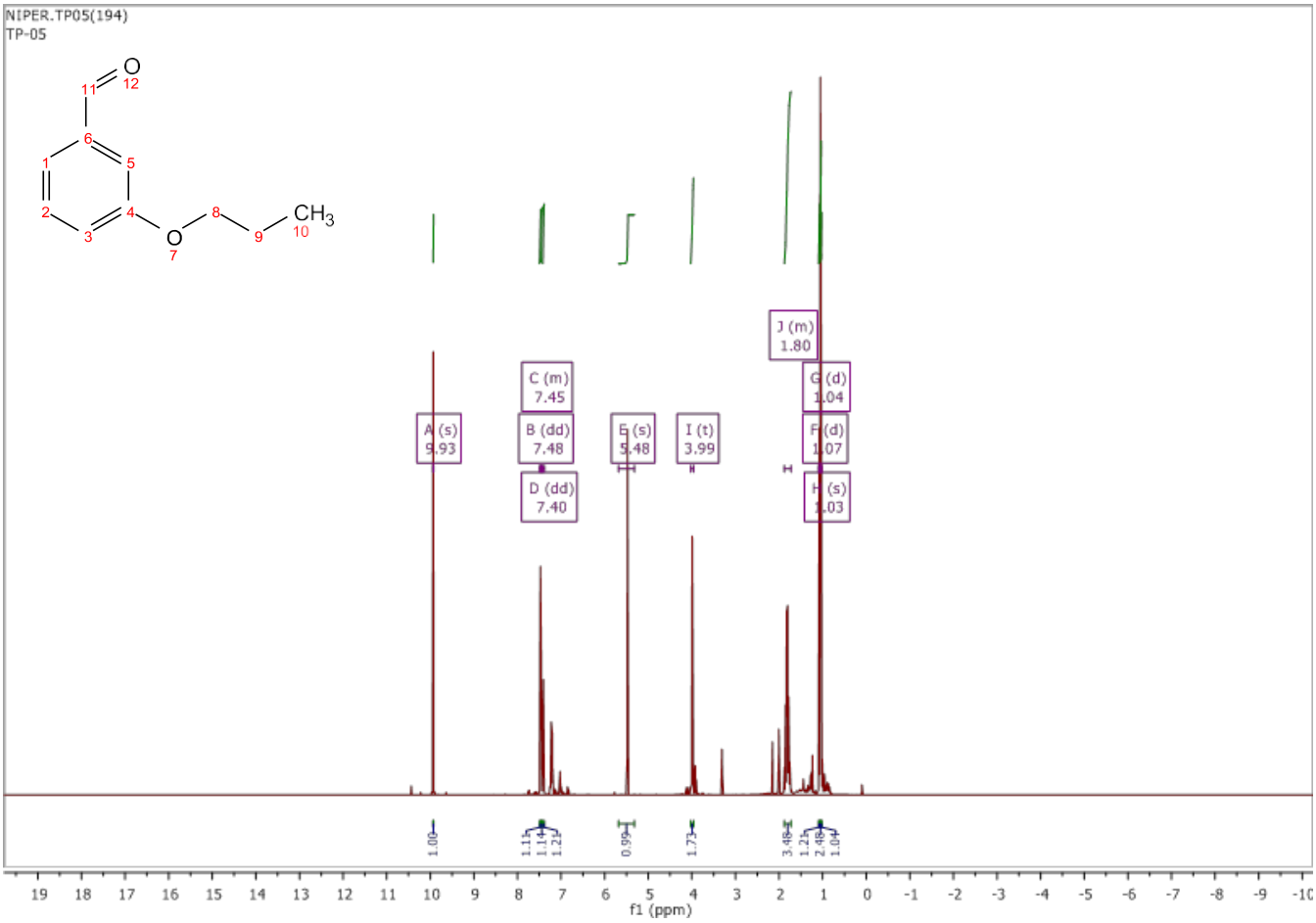


Figure:18 ^{1}H NMR of the 3- propoxybenzaldehyde.

Spectra of chalcone

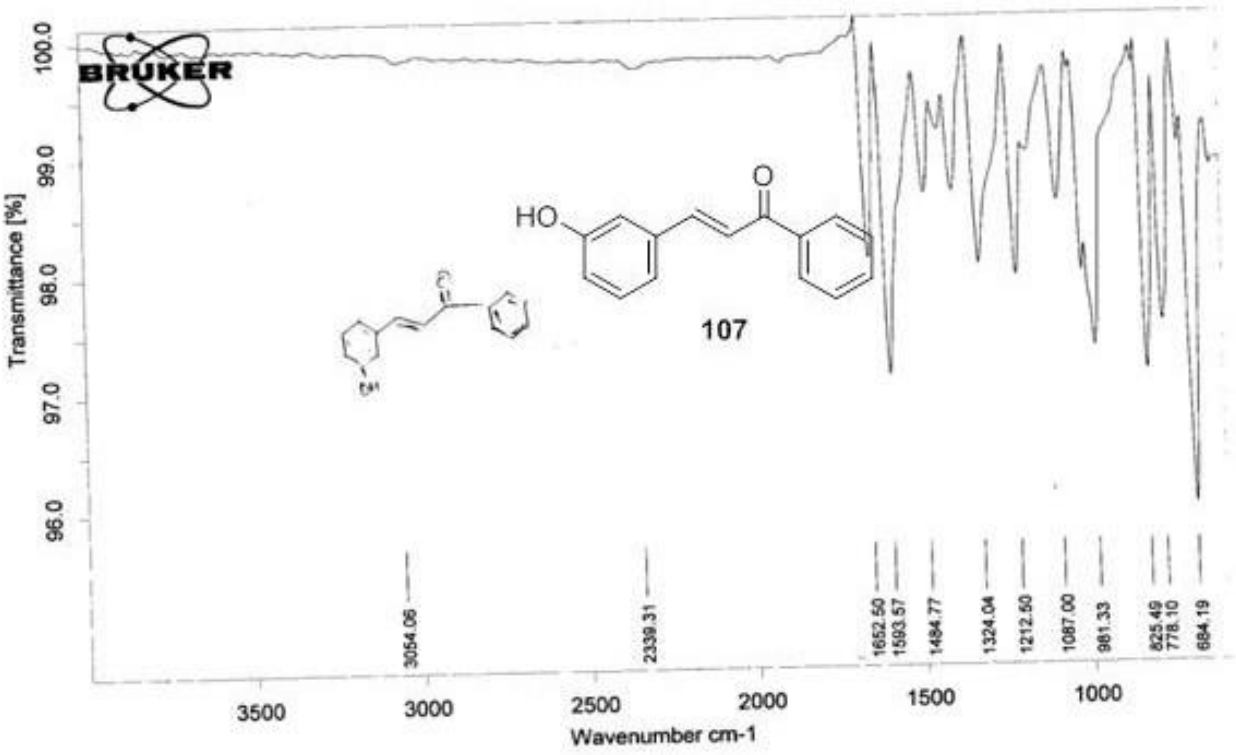


Figure 19. IR Spectrum of compound.

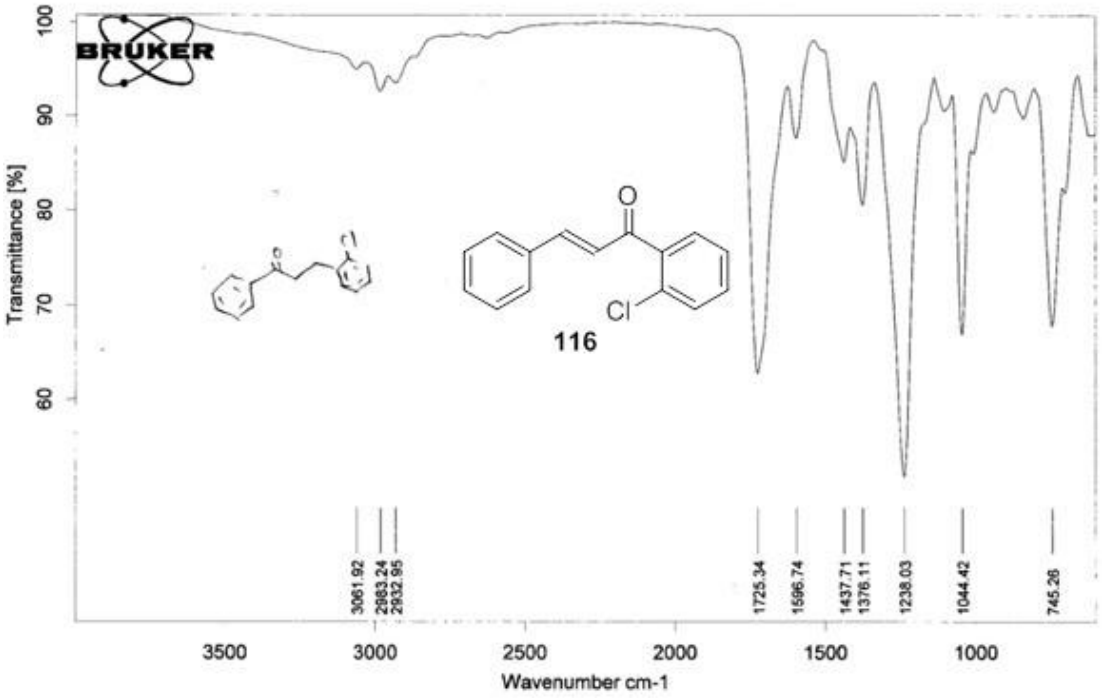
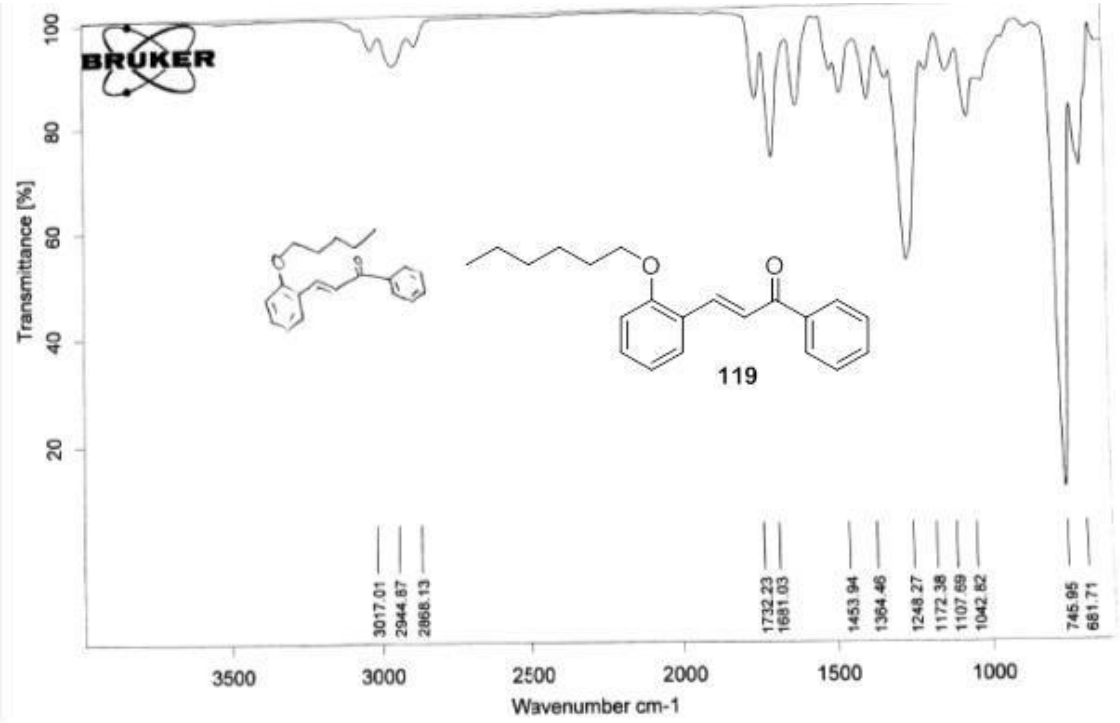


Figure: 55 IR spectrumof compound 116.

5.



Figiure:21 IR spectrum of compound 119.

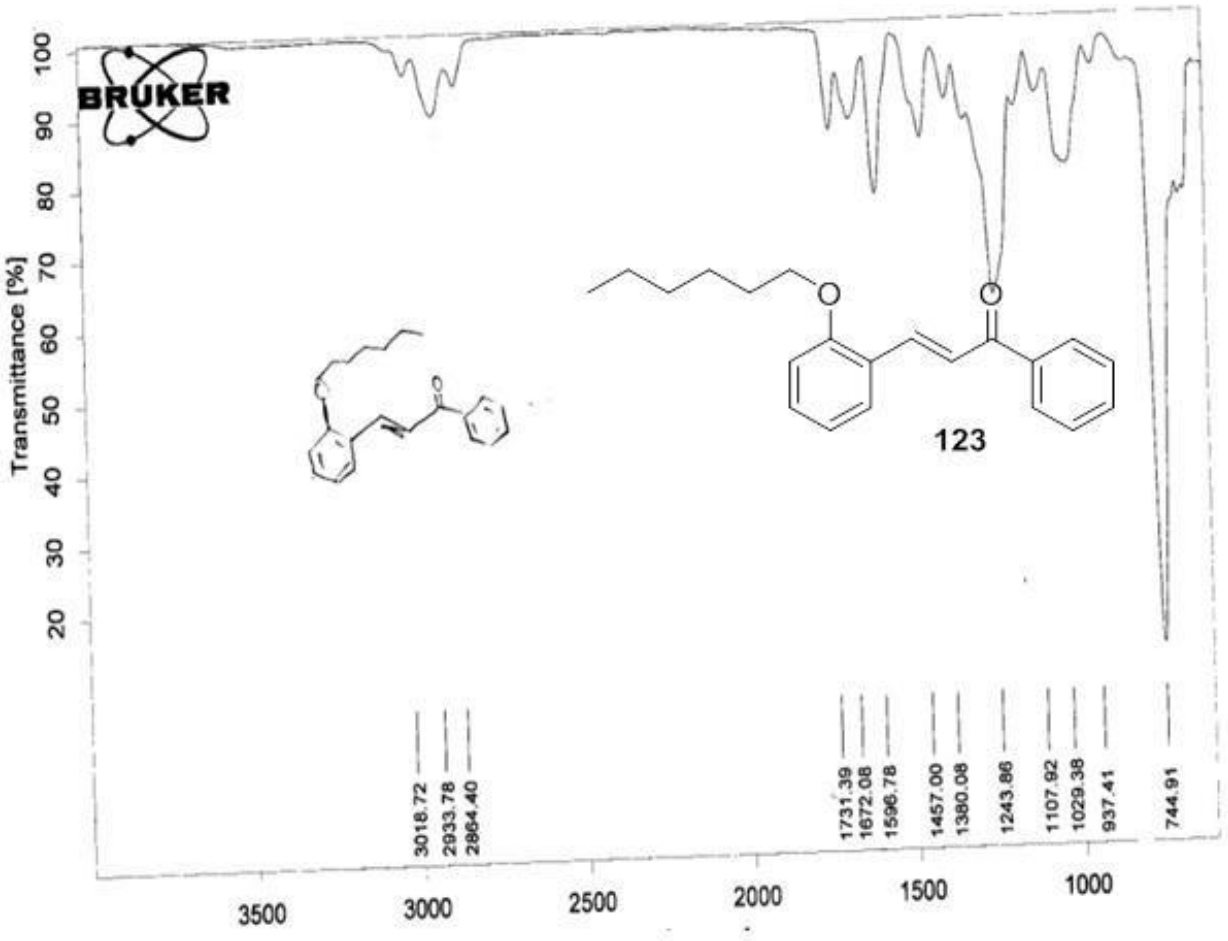


Figure:22 IR spectrum of compound .

7.

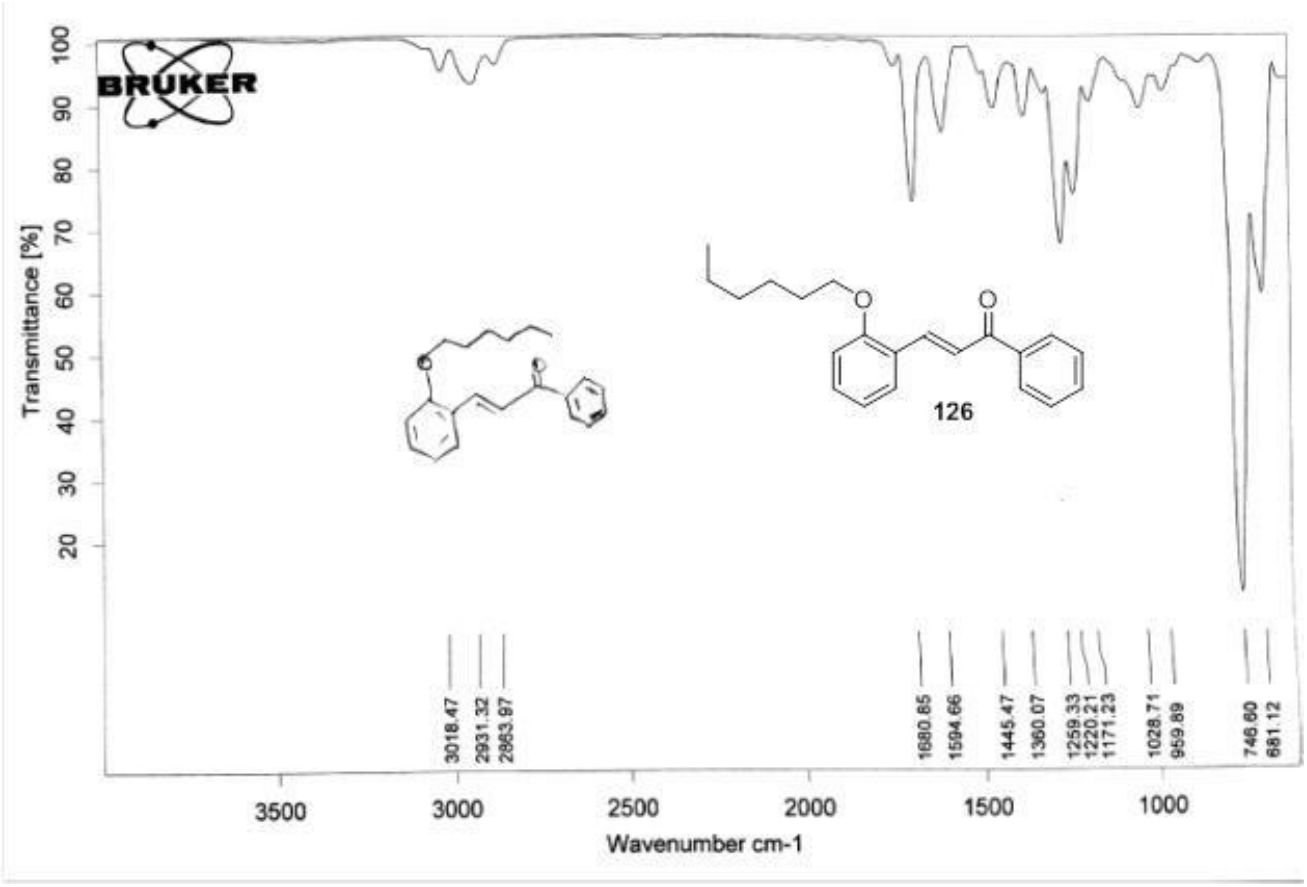


Figure: 23 IR sectrum of compound 126.

1. Spectra of benzimidazoles

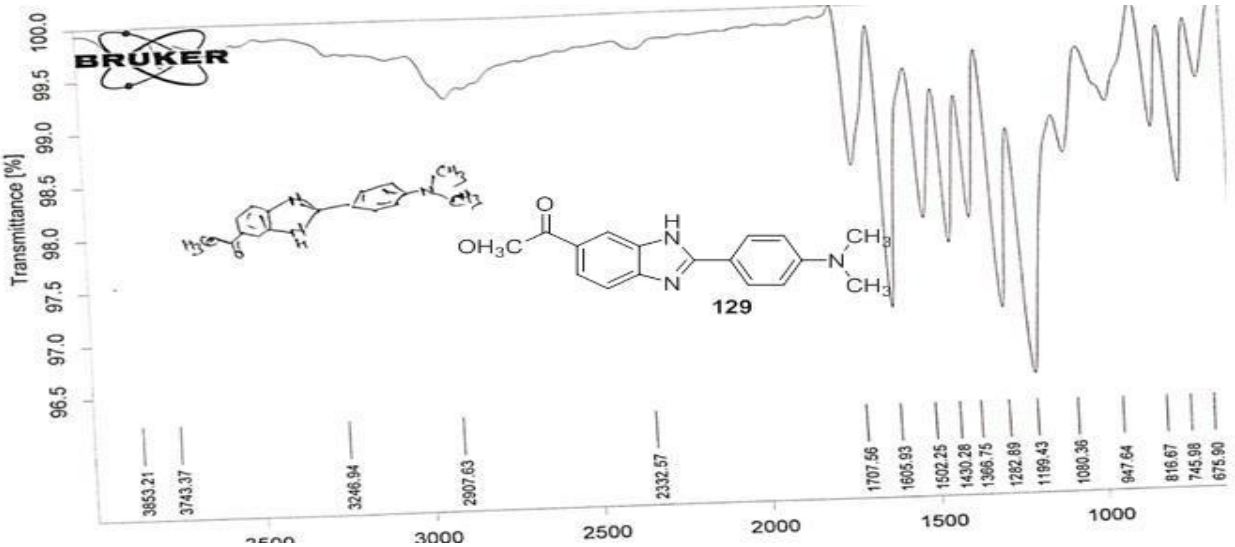


Figure:24 IR spectrum of compound .

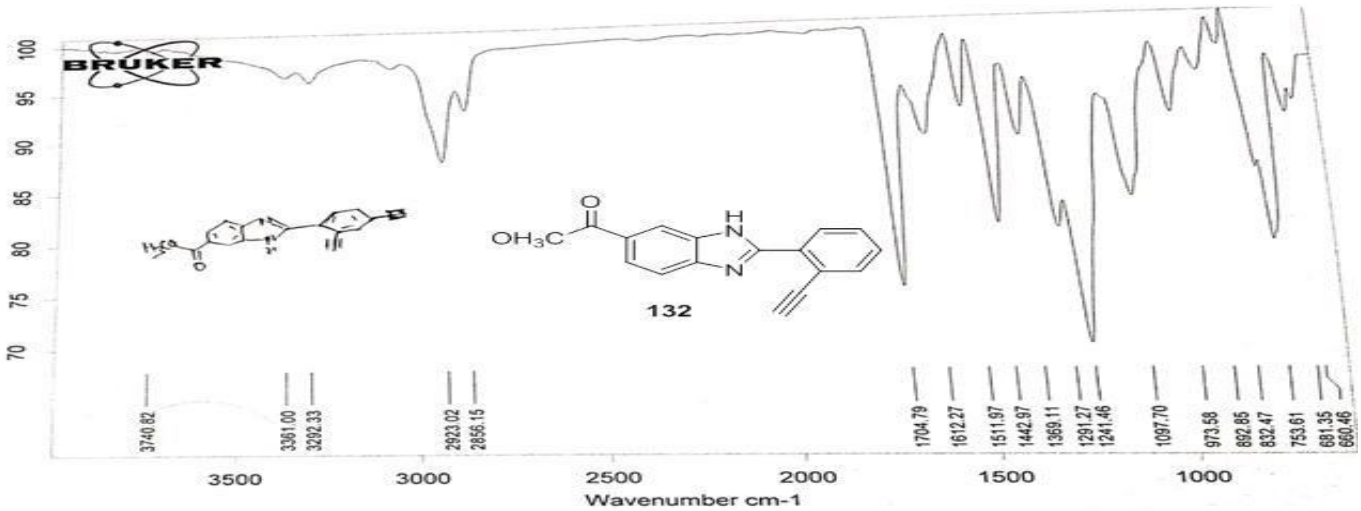


Figure:25 IR spectrum of compound .

Conclusion and future Indications

The new benzimidazole-Aldehyde hybrids molecules, stepwise synthesis done and all possible characterization done. Firstly we synthesize the different alkyl chain derivatives aldehyde. The reaction of different substituted aldehyde that gives good yield and it get purified by column chromatography. The solvent used in purification of the alkyl substituted aldehyds were ethyl acetate and hexane which is first steps. In the second step we synthesized Aldehyde benzimidazole substituted product which is characterized by the spectroscopic methedology NMR express the confirmation of carbon as well as proton in the ring system.

These hybrids is very promising targets for microbial DNA such as bafcteria and fungus strain and help in reducing infection and other fungal attack.

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