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Synthesis of Alkylated Pyrrolidine Epoxides from Amino Alcohol Derived Substrates and Study of their Antibacterial and Antifungal Activities

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Abstract

This research work is focused to design novel antibiotic compound because over time, bacterial strains became resistant to the antibiotics used to treat infections. The -NH_2 group in amino alcohol is protected with diphenylphosphonic chloride (-dpp) in the presence of $(Et)_3N$. The dpp-amino-2-propanol was treated with N-methyl morpholine-N-oxide, tetrapropylammonium perruthenate in anhydrous CH_2Cl_2 at room temperature and –dpp amino ketone was obtained. An alkylated pyrrolidine epoxide was synthesized by treating –dpp amino ketone with diphenylbromo ethyl sulfonium salt in the presence of 1,8-diazabicyclo [5.4.0] undec-7-ene at 0 ^oC. The products were purified by flash chromatography and characterized by spectroscopic techniques. The antibacterial activity of intermediates and cyclic compound was checked through well diffusion method. The *in vitro* antifungal activity of intermediates and synthesized compound was evaluated against three human pathogenic fungi.

Keywords: Amino alcohol, Diphenylphosphinic chloride, Amino ketone, Antibacterial and antifungal activities.

Introduction

In recent years, there has been a growing awareness in the general public for the development of new and safe antimicrobial agents against various microorganisms that cause contamination in different areas like the food industry, medical equipment, feed supplies, and storage spaces, i.e., *E.coli, S. aureus,* etc. [1]. Multicomponent reactions (MCRs) are those reactions in which three or more reactants are combined in a single reaction vessel to make a new product. Fewer steps to synthesize complex compounds are the major advantage of the MCR method over conventional methods. The synthesis process can be streamlined by using MCRs, which enable many reactants to react simultaneously

and produce numerous bonds in a single reaction. This efficiency can lead to higher yields, and reduce reaction time compared to traditional step-by-step synthesis methods. Furthermore, MCRs frequently yield a greater diversity of products, which makes them useful resources for drug development.

First MCR was reported by Strecker for the synthesis of α-amino nitrile in 1850 [2]. During the one and half century period, some remarkable achievements were made including the discovery of the Bayrak [3], the Mannich [4], and the Passerini reactions [5]. In 1959 Ugi published probably the most versatile MCR based on the reactivity of isocyanides [6]. Recently, MCRs have proved to be valuable tools in the synthesis of drugs like heterocyclic compounds.

Compound containing ketonic groups have a significant medicinal application including natural and synthetic steroid hormones, used as anti-inflammatory agents, and also used to develop good antibacterial and antifungal agents. Ketonic compounds are also used in chemical peeling and for acne treatments. It is reported that compounds containing pyrrolidine ring in their structure have great potential in the pharmaceutical industry [7,8]. Crooks designed a number of pyrrolidine derivatives and some showed good analgesic activity [9]. Pyrrolidine nucleus containing compounds also exhibited good antioxidant activity [10].

There are severe concerns that in the future inoperable pathogens may cause an alarming situation, this entails the design of various antimicrobial agents. The most concerning thing is that there aren't many effective substances for treating Gram-negative bacteria [11, 12].

To combat antibiotic resistance, it's crucial to develop new antibiotics and invest in alternative treatments and preventative measures. In this respect, MCRs are followed to synthesize novel alkylated pyrrolidine epoxides and characterized by using spectroscopic techniques. This work reports the synthesis of alkylated pyrrolidine epoxides via MCR in which the -NH_2 group is protected with -dpp so that other functional groups can be utilized in an annulation reaction to make the desired product. The antibacterial and antifungal activities of synthesized compounds were evaluated against different gram +ve and gram –ve bacteria and human pathogenic fungi.

Materials and Methods

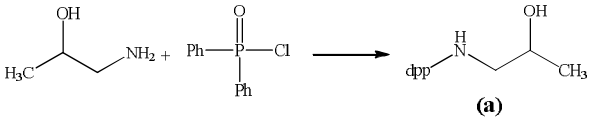
Materials

Analytical grade chemicals were used during the research work. Amino-2-propanol, diphenylphosphonic chloride, triethyl amine, N-methyl morpholine-N-oxide, tetrapropyl ammonium perruthenate, 1, 8-diazabicyclo [5.4.0] undec-7-ene, diphenylbromo ethyl sulfonium salt, and other solvents were purchased from Sigma Aldrich, UK. All chemicals were used as received. Nicolet iS50 FTIR Spectrometer with spectral range 7800 to 350 cm^{-1}, Bruker Advance-III 300 MHz with 7.05 Tesla field strength and LCMS-8045 were utilized in characterization.

Synthesis of dpp-protected amino-2-propanol

According to the procedure reported by Wuts [13], amino-2-propanol (0.52 mL, 6.65 mmol) in anhydrous CH_2Cl_2 (16.6 mL, 0.4 M) was reacted with diphenylphosphonic chloride (1.40 mL, 7.32 mmol) in the presence of $(Et)_3N$ (1.87 mL, 13.30 mmol) at 0 °C and stirred for 4 hours (Scheme 1). Reaction completion was monitored by LC-MS. The reaction mixture was then quenched with 10% aqueous citric acid solution and the product was extracted with CH_2Cl_2 (3 × 10 mL). All extracts were combined, and dried with $MgSO_4$. Dichloromethane (DCM) was

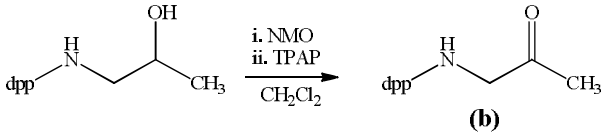
evaporated to get crude product. The crude product was purified (0.47 g, 46% yield) through flash chromatography by using 5% MeOH in DCM.



Scheme 1. **Synthesis of dpp-protected amino alcohol**

Oxidation of dpp-protected Amino Alcohol to Amino Ketone

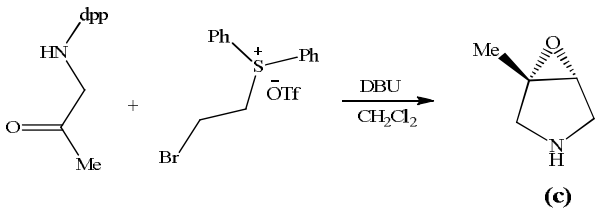
Using a procedure based on work by Tojo et al [14] dpp-amino-2-propanol (250 mg, 0.90 mL) was treated with N-methyl morpholine-N-oxide (160 mg, 1.36 mmol), tetrapropyl ammonium perruthenate (16 mg, 0.04 mmol) and molecular sieve (0.5 g) in anhydrous CH_2Cl_2 (1.8 mL, 0.09 M) at room temperature (Scheme 2). The reaction mixture was stirred for 2 hours. Completion of the reaction was determined by thin layer chromatography (TLC). The reaction mixture was then diluted with CH_2Cl_2 and filtered through celite. The filtrate was concentrated by using a rotary evaporator and crude product was obtained. The crude product (0.205 g, 84% yield) was pure enough to use in the next step.



Scheme 2. **Synthesis of dpp-protected amino ketone**

Synthesis of Annulated Epoxide Derived from dpp-amino Methyl Ketone

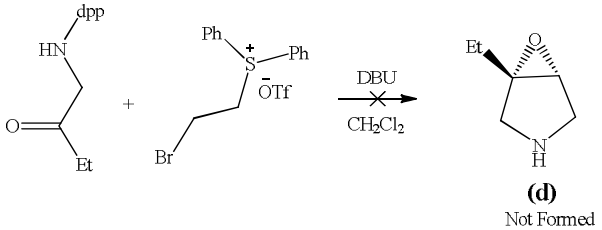
Using the procedure based on work by Unthank et al. [15] a solution of dpp-protected amino methyl ketone (50 mg, 0.18 mmol) in anhydrous CH_2Cl_2 (1.8 mL, 0.1 M) was reacted with 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU, 96.5 µL, 0.64 mmol) at 0 °C under argon with stirring. The reaction mixture was then treated with diphenylbromo ethyl sulfonium salt (97.7 mg, 0.23 mmol) for 4 hours (Scheme 3). The reaction was monitored through LC-MS. Product formation was confirmed through LC-MS. The reaction mixture was then quenched with 1 % aqueous citric acid solution (10 mL) in which –dpp group was also removed. The product was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (1 × 10 mL) and dried with $MgSO_4$. The crude product was purified (0.0122 g, 68 % yield) through flash chromatography by using 10% MeOH in DCM.



Scheme 3. **Synthesis of annulated epoxide from dpp-amino methyl ketone**

Synthesis of Annulated Epoxide Derived from dpp-amino Ethyl Ketone

By following above mentioned procedure, a solution of dpp-protected amino ethyl ketone (50 mg, 0.17 mmol) in anhydrous CH_2Cl_2 (1.8 ml, 0.1 M) was treated with 1,8-diazabicyclo [5.4.0] undec-7-ene (96.5 µL, 0.64 mmol) at 0 °C under argon with stirring. The reaction mixture was then treated with diphenylbromo ethyl sulfonium salt (97.7 mg, 0.23 mmol) for 4 hours (Scheme 4). Reaction was monitored by LC-MS and results showed the presence of un-reacted reactants in the reaction mixture. Trace amount of the product was detected through LC-MS.



Scheme 4. **Synthesis of annulated epoxide from dpp-amino ethyl ketone**

Performance of Characterization Techniques

Infrared (IR) spectroscopy was performed using thin layers of a sample, known as attenuated total reflection (ATR) IR spectroscopy. In this technique, the sample was placed on a crystal with a high refractive index, and IR radiation was directed through the crystal. In this method, there is no need for extensive sample preparation.

Nuclear Magnetic Resonance (NMR) spectroscopy is a technique used to study the structure and composition of molecules. A small amount of the sample was dissolved in NMR tube. A strong and uniform magnetic field aligns the nuclear spins of certain atoms in the sample, particularly hydrogen (^{1}H) and carbon-13 (^{13}C) nuclei. After the RF pulse was applied, the nuclear spins gradually relaxed back to their equilibrium positions and the emitted radiation was detected by the RF coils in the spectrometer. The detected signals were processed by the computer system to generate an NMR spectrum, which displays the absorption of energy by the nuclei at different frequencies.

Microbiological Assay

Severe antiseptic and aseptic conditions were maintained and the procedure was carried out in laminar airflow. The agar plate diffusion technique was followed to grow test organisms. Synthesized compounds dissolved in DCM according to pre-mentioned concentration, while DCM itself was used as a control for comparison.

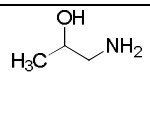
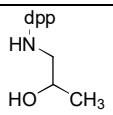
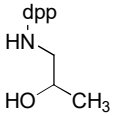
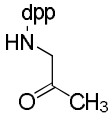
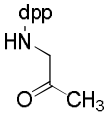
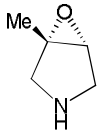
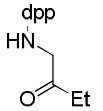
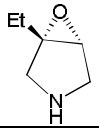
N-agar media was autoclaved, and 25-30 mL of the media was added into the 9 cm diameter Petri dish, solidified, and then one mL bacterial suspension was transferred and incubated at 27 ^{o}C for 24 hours. An autoclaved pasture pipette was used to develop wells in the plates and then synthesized compound solutions were added to them. The 100 µg/ mL concentration of the compound solution was used and the activity was calculated by measuring the inhibition zone.

Results and Discussion

Synthesis of alkylated pyrrolidine epoxides from amino alcohol-derived substrates is a fascinating area of research in medicinal chemistry, particularly in the development of antibacterial and antifungal agents. Alkylated pyrrolidine epoxides can be evaluated for their biological activities, particularly against bacterial and fungal pathogens. Since the epoxide moiety frequently confers reactivity towards cellular nucleophiles, which disrupts vital biological processes in bacteria, its presence can be critical for biological activity.

Depending on their unique structures, these chemicals can have different antibacterial and antifungal actions. A protecting group is introduced into the molecule by chemical modification of a functional group to obtain chemo-selectivity in a particular chemical reaction. It plays a vital role in multistep organic synthesis [16]. In this study $–NH_2$ group is protected by –dpp, so that -CH–OH can be oxidized into the carbonyl group. The amino ketone was then annulated with diphenylbromo ethyl sulfonium salt to form 5-membered heterocyclic epoxide. The reaction schemes for the synthesis of intermediates and the yield of final products are given below in Table 1.

Table 1. **List of starting materials and products with their yields.**

Entry Number	Starting Material	Product	Yield
1			46%
2			84%
3			68%
4			Not formed

Characterization dpp-protected Amino-2-propanol (a)

Fig. 1 presents FTIR spectrum of dpp-protected amino-2-propanol (a). **IR (film): ν (cm^{-1})** 3620 (O-H stretch), 3320 (N-H Stretch), 2968 (-CH Stretch), 1280 (C-N Stretch), 1110 (C-O stretch), 1027 (N-P stretch).

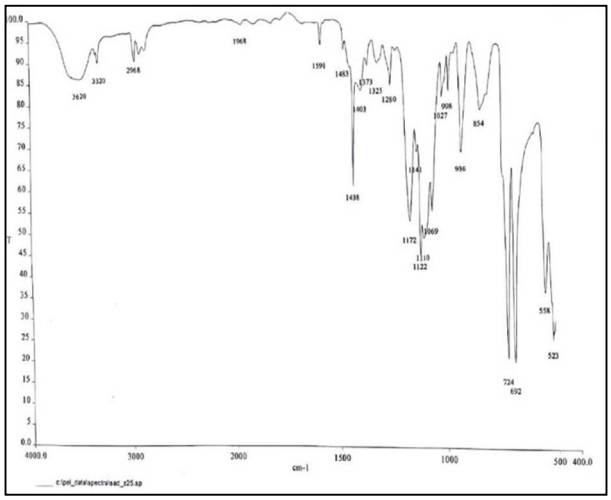


Figure 1. **FTIR Spectrum of dpp-protected amino-2-propanol (a)**

In Fig. 2, the structure of dpp-protected amino-2-propanol is confirmed through ^{1}H NMR.**δ_H (300 MHz; $CDCl_3$)** 7.84-7.89 (4 H, dd, *J 12.1, 7.7*, -Ar*H*), 7.38-7.49 (6 H, m, -Ar*H*), 3.86-3.93 (1 H, m,-C*H*(OH)CH_3), 3.62 (1 H, br s,-OH), 2.99-3.07 (1 H, td, *J 13.4, 7.1*, -CH*H*NH-), 2.79-2.88 (1 H, td, *J 13.4, 6.7*, -C*H*HNH-), 2.77 (1 H, s, -N*H*PO-), 1.11-1.12 (3 H, d, *J 6.4*, -CH_3).

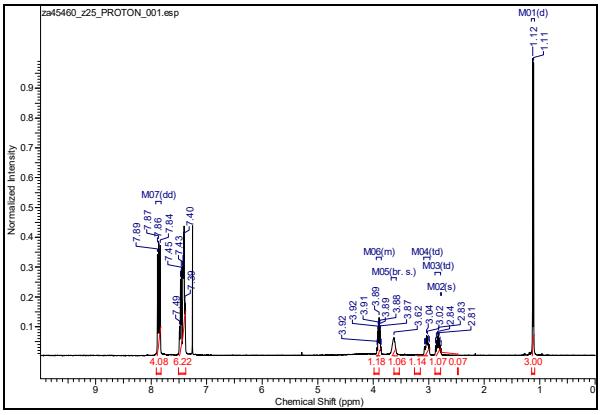


Figure 2 **.^{1}H NMR of dpp-protected amino alcohol (a)**

Different peaks in ^{13}C spectrum represent the non-identical carbon atoms in synthesized compound which are represented as FS-1,**δ_C (75 MHz; $CDCl_3$)** 132.37 (ArCH), 132.08 (ArCH), 128.64 (ArCH), 128.51 (ArCH), 67.81 (CH), 49.25 (CH_2), 20.35 (CH_3).

DEPT (75 MHz; $CDCl_3$): Chemical shift values for methyl and methine group are shown in its spectrum as FS-2 i.e. 20.34 (-CH_3), 67.76 (-CH), 128.51 (-ArCH), 128.64 (-ArCH), 132.02 (-ArCH), 132.17 (-ArCH), chemical shift values for methylene group 49.24 (-CH_2).

R_f**:** 0.40 (MeOH-DCM, 5:95);

Characterization of dpp-protected Amino ketone (b)

The FTIR spectra of dpp-protected amino ketone (b) is presented in Fig. 3. **IR (film): ν (cm^{-1})** 3335 (N-H Stretch), 2970 (-CH Stretch), 1720 (C=O stretch), 1296 (C-N Stretch), 1110 (C-O stretch), 1012 (N-P stretch).

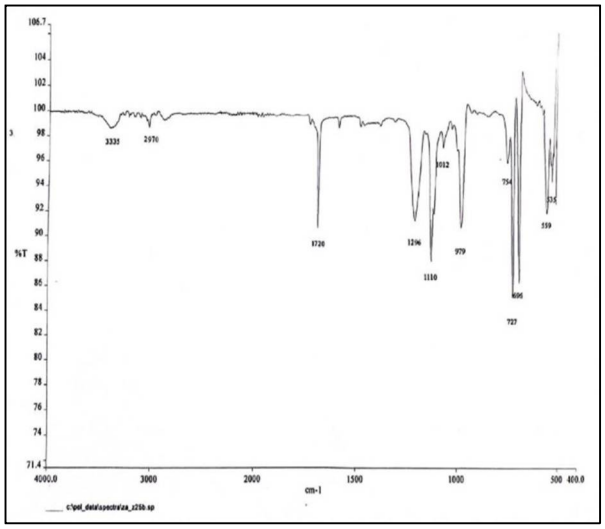


Figure 3. **FTIR Spectrum of dpp-protected amino ketone (b)**

Formation of dpp-protected amino ketone was confirmed through ^{1}H NMR shown in Fig. 4. **δ_H (300 MHz; $CDCl_3$)** 7.86-7.91 (4H, d, *J 12*.1 -Ar*H*), 7.47-7.52 (6H, m, -Ar*H*), 3.97 (1 H, s, -N*H*), 3.88-3.91 (2 H, d, *J 5*.7, -CH_2), 2.18 (3 H, s, -CH_3).

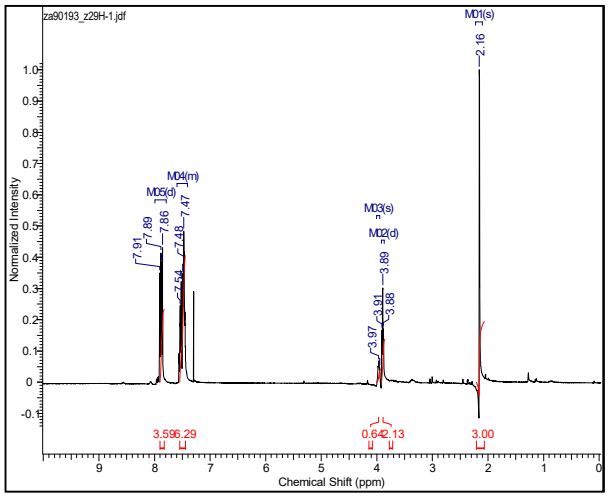


Figure 4 . **^{1}H NMR of dpp-protected amino ketone (b)**

Non identical ^{13}C atoms in the synthesized compounds show different chemical shift values which are shown as FS-3, **δ_C (75 MHz; $CDCl_3$)** 203.34 (C=O), 132.70 (-Ar*C*H), 132.15 (-Ar*C*H), 132.05 (-Ar*C*H), 128.90 (-Ar*C*H), 50.23 (-*C*H_2), 27.21 (-*C*H_3).

DEPT (75 MHz; $CDCl_3$): Chemical shift values for methyl and methine groups in the synthesized compound are represented as FS-4 i.e 27.20 (CH_3), 128.76 (ArCH), 128.88 (ArCH), 132.03 (ArCH), 132.12 (ArCH), Chemical shift values for methylene group 50.21 (CH_2).

***R*$_f$:** 0.67 (MeOH-DCM, 5:95)

Characterization of Annulated Epoxide Derived from dpp-amino methyl ketone (c)

Fig. 5 shows the FTIR spectrum of annulated epoxide derived from dpp-amino methyl ketone (c). **IR (film): ν (cm^{-1})** 3350 (N-H Stretch), 2850 (-CH Stretch), 1250 (C-O epoxide stretch), 1000 (N-P stretch), 817 (C-N Stretch).

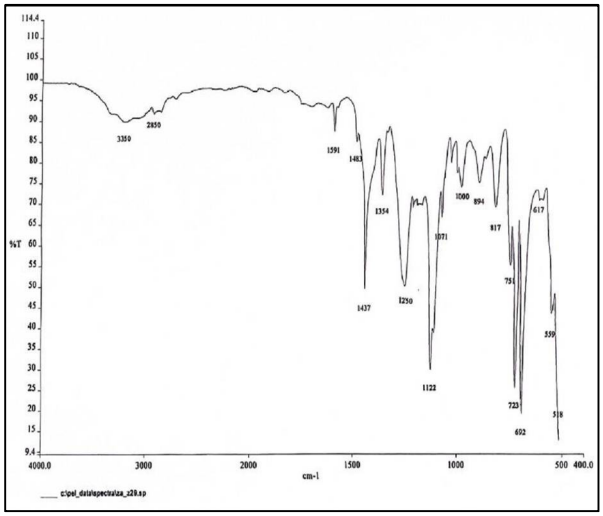


Figure 5. FTIR Spectrum of annulated epoxide derived from dpp-amino methyl ketone (c)

The formation of the final product obtained through cyclization of dpp-amino methyl ketone was confirmed through ^{1}H NMR shown in Fig. 6.

δ_H (300 MHz; $CDCl_3$) 3.04-3.07 (2 H, td, *J 13*.4, *7*.2, -CH*H*NH-), 2.73-2.75 (2 H, td, *J 13*.4, *7*.1, -C*H*HNH-),), 2.01 (1 H, s, -N*H*-), 1.32 (3 H, s, -CH_3).

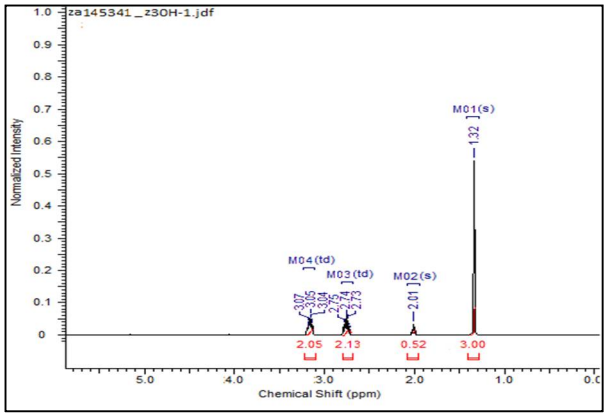


Figure 6 **.^{1}H NMR of annulated epoxide derived from dpp-amino ketone (c)**

δ_C (75 MHz; $CDCl_3$) 57.82 (-*C*H-O-), 56.53 (-*C*H_2NH-), 54.30 (-CH_3) *C*-O-), 52.33 (-*C*H_2NH-), 24.95 (-*C*H_3). All non-identical ^{13}C atoms showed different chemical shift values in the spectrum as FS-5.

DEPT (75 MHz; $CDCl_3$): Chemical shift values for methyl and methine groups for the synthesized compound are represented as FS-6 i.e 20.43 (-CH_3), 67.02 (-CH), Chemical shift values for methylene groups (-CH_2) are 49.14 and 50.08, respectively.

***R*$_f$:** 0.32 (MeOH-DCM, 5:95)

Successful dpp-protection of –NH_2 group in amino alcohol labelled as **(a)** was checked by observing a peak of stretching frequency 1005 cm^{-1} corresponds to N-P bond and the same was corroborated through ^{1}H NMR analysis. Aromatic protons (-Ar*H*) exhibited their existence in the ^{1}H NMR spectrum by showing signals in the aromatic region, i.e. 7.38-7.84 ppm. Methine group (-C*H*-) gave a multiplet on the higher field side because it is directly attached to an electronegative atom, *i.e.* oxygen in the compound. A broad singlet of -OH group can be seen at 3.62 ppm. In this molecule, a stereo-centre was found as a methylene group because both protons in –CH_2-are not identical. Each proton in this group gave its "td" with their different chemical shift values i.e. -CH*H*NH- at 2.99-3.07 and -C*H*HNH- at 2.79-2.88 ppm, respectively. Amino group (-NH-) showed its singlet at 2.77 ppm. Methyl protons gave their singlet on the downfield side at 1.11-1.12 ppm. ^{13}C NMR analysis of this compound showed the existence of seven non-identical carbon atoms in –dpp protected amino alcohol. In DEPT spectrum, one –CH_3 signal, one -CH- signal, and four -ArCH- signals appeared above the baseline and one -CH_2- signal appeared below the baseline. The position of these signals in the spectrum showed a good agreement with the structural framework of the compound.

Amino alcohol **(a)** was then oxidized to amino ketone labelled as **(b)** in which -OH stretching frequency disappeared and a prominent carbonyl peak appeared at 1720 cm^{-1}. The ketonic compound was further analysed through ^{1}H NMR analysis. Aromatic protons (-Ar*H*) appeared in the spectrum of aromatic range *i.e.* 7.91-7.47 ppm. Protons of -N*H*- group showed their singlet at 3.97 ppm. Methylene protons (-C*H*$_2$-) gave their doublet at 3.88-3.91 ppm. Methyl protons (-C*H*$_3$) showed their singlet on the downfield side at 2.18 ppm. Seven non-identical carbon atoms were verified in the amino ketone through ^{13}C NMR analysis. In the DEPT spectrum, one –CH_3 signal, four –ArCH signals were appeared above the baseline and one -CH_2- signal appeared below the baseline. In this spectrum, the –CH- was absent because of the oxidation of secondary alcohol into ketone. DEPT analysis proved a potential alternative in justifying the structure of synthesized amino ketone.

Annulation of methyl amino ketone **(b)** into epoxide **(c)** can be confirmed by observing 1250 cm^{-1} (C-O epoxide stretch) in IR spectrum. In this annulated epoxide, there is a stereo-centre, *i.e.* methylene carbon. In this group both protons on each (-C*H*$_2$) group

behaved differently. In NMR studies, both methylene protons showed their signals at different chemical shift values *i.e*3.04-3.07 (-CH*H*NH-) and 2.73-2.75 (-C*H*HNH-), respectively. Amino proton gave its weak signal at 2.01 ppm. Methyl protons showed their prominent singlet at 1.32 ppm. ^{13}C NMR analysis and DEPT analysis effectively confirmed the non-identical carbon atoms and the actual structure of methyl containing annulated epoxide. The same annulation reaction was performed by using ethyl amino ketone but could not succeed, which might be due to the steric hindrance of bulky ethyl ($-C_2H_5$) group.

Biological Activities

The biological activity of compounds labelled as **a, b,** and **c** have been evaluated, which showed good antibacterial and antifungal activities. These activities were evaluated using the well diffusion method [17] and DCM was used as a control in this study. The antibacterial properties were investigated against two Gram (+) strains i.e. *S. aureus* and *B. subtilis* and two Gram (-) strains *i.e*. *E. coli* and *K. pneumonia* because they cause multiple human diseases. *S. aureus* and *B. subtiliscause* multiple diseases in humans including skin infections, respiratory infections, bone joint infections, bloodstream infections wound infection, etc. Similarly, Gastroenteritis, urinary tract infection, pneumonia, and liver abscesses are mainly caused by *E. Coli* and *K. pneumoniae*. Likewise, antifungal properties were tested against *A. niger* and *A. flavus*as listed in Table 2. Inhibition zones were measured in mm for all microorganisms. MIC data was evaluated for the same species as shown in Table 3.

The antibacterial activity of the synthesized compound and all intermediates was explored in detail and calculated against various pathogens. All compounds exhibited good to moderate activity for different bacterial strains, however, compound **c** showed good antibacterial activity for different Gram (+) (MIC 4.8 and 5.1 for *S. Aureus* and *B. Subtilis)* and Gram (–) strains (MIC 3.6 and 8.1 for *E. Coli* and *K. pneumoniae*). In this study, Sulfamethoxazole was used as a reference compound for comparison to assess the reliability of the method used. It is evident from Table 2 that compound **c** has comparable antibacterial activity with the reference compound. Bacterium *K. pneumoniae* is highly pathogenic to humans, however, MIC values depicted that this pathogen has lower microbial susceptibility compared to other tested microorganisms against compound **c.**

All synthesized intermediates and compounds (**a, b, and c)** were also examined for antifungal action against *Aspergillus nigar* and *Aspergillus flavus*. It is obvious from Table 3 that these compounds effectively inhibit the growth of fungal species. Among them, compound **c** exhibited remarkable activity against fungal strains (MIC 8.4 for *Aspergillus nigar* and 7.3 for *Aspergillus flavus*). It is also noticed that compound **c** proved to be more effective against *Aspergillus nigar*.

Table 2. **Inhibition zones and MIC of synthesized compounds against pathogenic bacterial strain.**

Name of compound	Bacterial strains							
	Gram Positive				Gram Negative			
	S. aureus		*B. subtilis*		*E. coli*		*K. pneumoniae*	
	[a]*ZI (mm)*	[b]*MIC (µg/mL)*	*ZI(mm)*	*MIC (µg/mL)*	*ZI(mm)*	*MIC (µg/mL)*	*ZI(mm)*	*MIC (µg/mL)*
a	18±0.10	7.5	15±1.50	7.1	17±0.30	8.4	12±0.13	9.8
b	16±1.10	11.6	16±0.12	6.9	15±0.20	6.8	12±0.10	9.9
c	24±0.12	4.8	19±0.11	5.1	22±0.21	3.6	13±0.15	8.1
Sulfamethoxazole	30±0.15	0.2	28±0.11	0.14	31±0.05	0.12	27±0.20	0.18

[a]ZI (Zone of inhibition) [b]MIC (Minimum Inhibitory concentration)

Table 3. **Inhibition zones and MIC of synthesized compounds against fungal strains.**

Name of compound	Fungal strains			
	Aspergillus nigar		*Aspergillus flavus*	
	ZI (mm)	*MIC (µg/mL)*	*ZI (mm)*	*MIC (µg/mL)*
a	17±0.19	11.3	15±0.21	9.3
b	13±1.17	15.7	11±1.19	13.6
c	20±0.12	7.3	19±0.15	8.5
Isoconazole	29.5±0.10	0.77	30±0.08	0.52

It is reported that some natural products and synthetic compounds containing pyrrolidine nuclei show good antimicrobial activities [18-20] and this fact is quite obvious in the above comparison Table 4 with sulphonamide derivatives [21]. Therefore, this remarkable antibacterial and antifungal activity of compound **c** might be due to the presence of a pyrrolidine nucleus in its structure.

Table 4. **MIC comparison of synthesized compounds with sulphonamide derivatives.**

Name of compound	Fungal strains	
	Aspergillus nigar	*Aspergillus flavus*
	MIC(µg/mL)	*MIC(µg/mL)*
a	11.3	9.3
b	15.7	13.6
c	7.3	8.5
HR7 [21]	30	12.5
HR8 [21]	65.5	50
Isoconazole	0.77	0.52

Conclusion

In the present study, novel alkylated pyrrolidine derivatives were successfully synthesized through various intermediates and explored their antimicrobial activities. The study revealed that the synthesized compound (c) has good antimicrobial activity against selected bacterial and fungal strains. In synthesis ethyl pyrrolidine derivative could not be synthesized which might be due to the steric hindrance. On behalf of the results, it can be concluded that **compound (c)** is a promising candidate for pharmaceutical and toiletry formulations against the tested microorganisms.

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Conflict of Interest

This research work is our original and collaborative work and there is no conflict of interest among authors.

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