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AN EFFICIENT IONIC LIQUID MEDIATED MICROWAVE ASSISTED SYNTHESIS OF PYRAZOLES CHARACTERIZATION AND ITS BIOLOGICAL PROPERTIES.

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ABSTRACT:
Fluorinated Pyrazoles and its derivatives have evolved as crucial scaffolds in medicinal chemistry due to their diverse biological activities, and pharmaceutical properties. The series of pyrazoles and its derivatives typically involves the cyclocondensation of hydrazines with α, β-unsaturated carbonyl compounds under microwave irradiation in the presence of ionic liquid. The structure of the synthesized compounds was confirmed using IR, ^{1}H NMR, and LC-MS, and they were examined for antibacterial and antifungal activity. The major characteristics of this technique include operational simplicity, short reaction times, mild reaction conditions, and high yield. Importantly, NMPyTs (ionic liquid) can undergo up to three recycle runs without any noticeable loss of catalytic activity.

KEYWORDS: **Pyrazoles, Biological Properties, Microwave irradiation, Ionic liquid, Characterization.**

INTRODUCTION

Pyrazoles are an important class of five-membered nitrogen-containing heterocycles that have gained significant attention due to their broad spectrum of biological and pharmaceutical applications. The pyrazoles ring system consists of two adjacent nitrogen atoms at positions 1 and 2, which contribute to its unique electronic and chemical properties. These compounds are widely studied in medicinal chemistry, as they exhibit diverse pharmacological activities, including anti-inflammatory, antimicrobial, anticancer, analgesic, and enzyme inhibitory effects.[i-Ii] The synthesis of pyrazoles derivatives can be achieved through various methods, such as the cyclocondensation of hydrazines with 1,3-diketones, metal-catalyzed reactions, and environmentally friendly approaches using ionic liquids or microwave-assisted techniques. Advances in synthetic methodologies have enabled the development of highly functionalized pyrazole derivatives with improved pharmacokinetic and pharmacodynamics properties.[Iii] Beyond their pharmaceutical significance, pyrazoles also find applications in agrochemicals,

dyes, and materials science due to their stability and tunable properties.[Iv] The continuous exploration of pyrazoles chemistry has led to the discovery of novel derivatives with enhanced biological activity, making them valuable scaffolds for drug development.This review aims to provide an overview of the synthesis, biological importance, and recent advancements in pyrazoles chemistry, with a focus on their role in modern medicinal and material sciences.

Ionic liquids (ILs) are a unique class of organic salts that remain in the liquid state at or near room temperature. They consist of bulky organic cations, such as imidazolium, pyridinium, or phosphonium ions, paired with various anions, including halides, tetrafluoroborate, or bis(trifluoromethylsulfonyl)imide[v]. Unlike conventional solvents, ILs possess remarkable physicochemical properties, such as low volatility, high thermal stability, wide electrochemical windows, and tunable solubility, making them highly attractive for sustainable chemical processes.[Vi] Due to their unique characteristics, ILs have found widespread applications in organic synthesis, catalysis, electrochemistry, and separation processes. They have been particularly useful as green solvents in heterocyclic synthesis, including the preparation of bioactive pyrazoles, where they enhance reaction efficiency, selectivity, and recyclability. [Vii] Additionally, ILs have been explored in the development of task-specific ionic liquids (TSILs), which are designed to exhibit tailored functionalities for specific chemical transformations.[Viii] Recent advancements in IL research have focused on the development of biodegradable and bio-based ionic liquids, further improving their environmental compatibility and expanding their industrial applications. This review discusses the fundamental properties of ILs, their role in green chemistry, and their applications in modern organic synthesis, particularly in the preparation of heterocyclic compounds.

The progression and increasing importance of compounds containing pyrazoles in biological systems, especially in natural products, medicinal chemistry, and drug development, is referred to as the biological evolution of pyrazoles. Although pyrazoles itself is a synthetic heterocyclic compound, its derivatives have become essential in biological processes due to their unique structural and electronic characteristics. These compounds have gained significant relevance in various biological applications, despite pyrazoles being artificially created. The enhanced solubility of these compounds allows them to interact with a diverse array of enzymes and receptors in biological systems. The significance of N-heterocyclic compounds is evident, as nitrogen atoms are key components in over 50% of FDA-approved small molecule drugs.[Ix] In the realm of heterocyclic and medicinal chemistry, the pyrazole ring stands out as a fundamental structure. Its importance stems from its capacity to exhibit a broad spectrum of biological activities, including antimicrobial,[x] anti-inflammatory,[Xi] fever-reducing,[Xii]anticancer,[Xiii]antiviral,[Xiv]antitumor,[Xv] pain-relieving,[Xvi]fungistatic,[Xvii] and blood sugar-lowering effects.[Xviii]

Among the chemical elements, CF_3 is renowned for its extreme reactivity and high toxicity. However, in minuscule amounts, CF_3 serves a vital purpose in dental health, contributing to the prevention and treatment of dental cavities while also enhancing the strength of teeth and bones. CF_3 atoms exhibit several unique characteristics, including elevated electronegativity, minimal polarizability, diminutive atomic dimensions, and a bisected nuclear orientation. The formation of robust carbon-CF_3 bonds occurs when a CF_3 atom replaces carbon, oxygen, or hydrogen. Moreover, the presence of a CF_3 atom exerts a significant influence on the pKa values and hydrogen bonding potential of adjacent functional groups.

The present study we focused on the second step and describes the synthesis of nitrogen heterocycles from carbon trifluoride (CF_3) containing chalcones.In our efforts on the development of sustainable methodologies for the synthesis of pyrazoles and its derivatives in the presence of N-methyl pyridiniumtosylate (NMPyTs) ionic liquid as a highly efficient and green catalyst via condensation reactions of substituted chalcones and substituted hydrazine

hydrate under microwave irradiation at 70 to 80 ^{o}C. The synthesized pyrazoles derivatives confirmed by TLC, melting point and spectroscopic analysis and it's demonstrate the antibacterial and antifungal properties.

EXPERIMENTAL

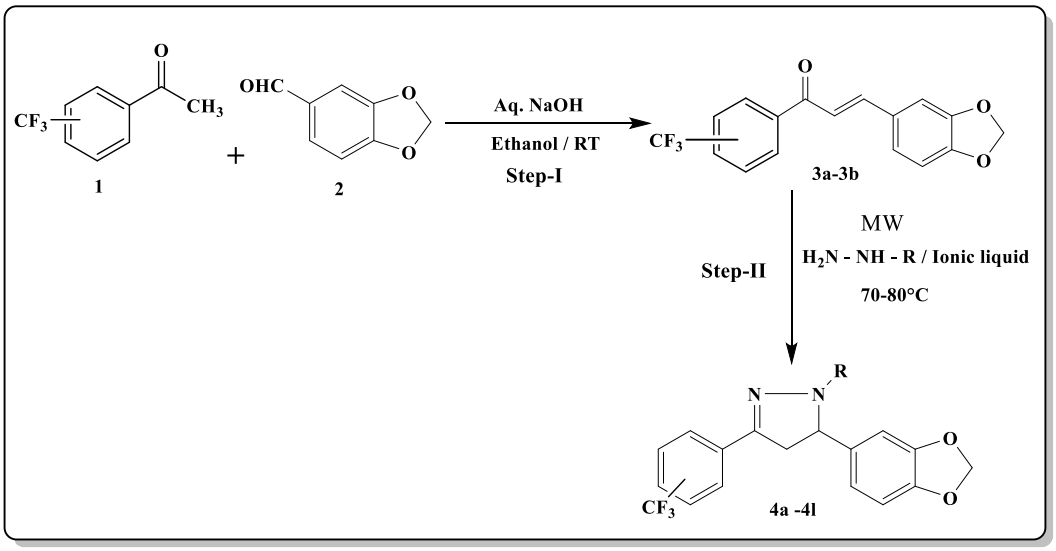
GENERAL

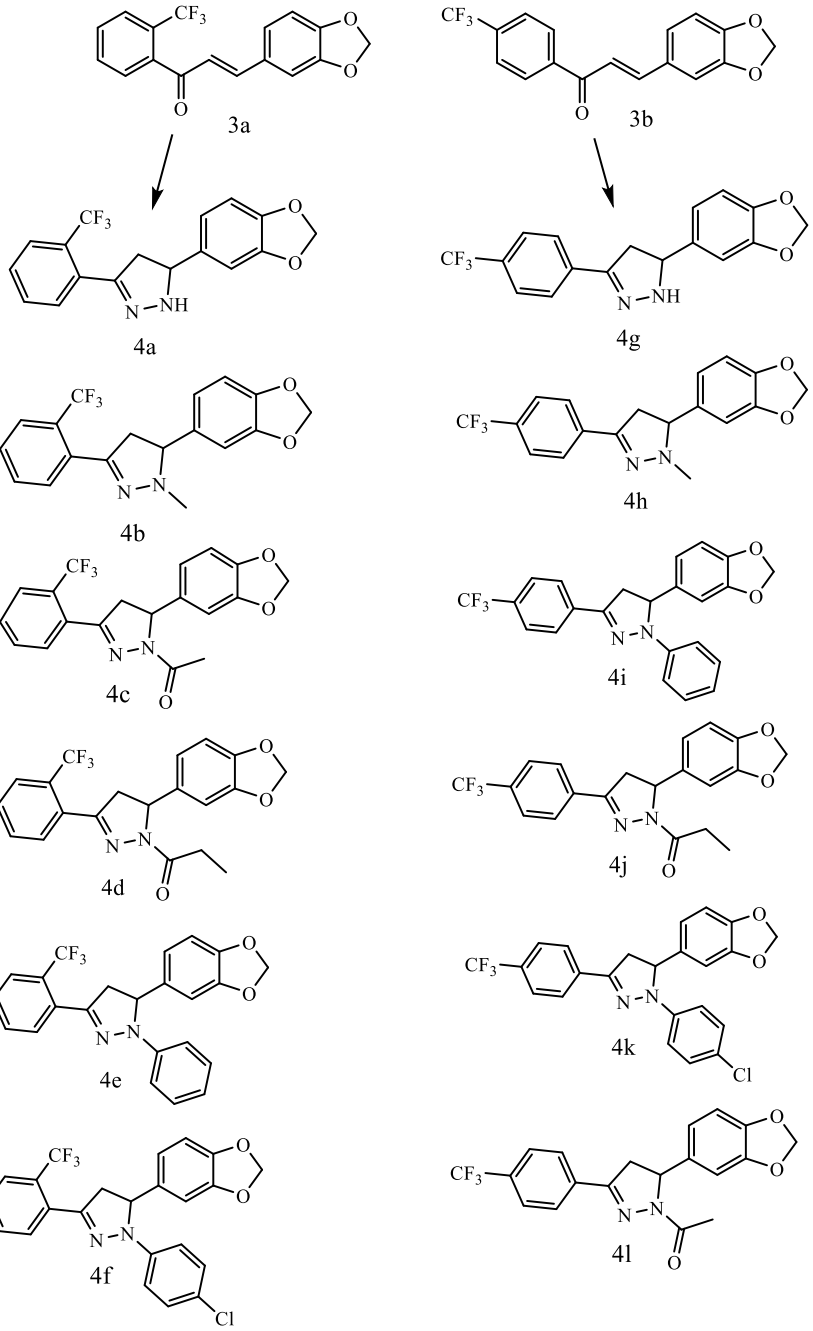
All of the synthetic grade reagents and chemicals were purchased from Merck Chemicals and Sigma Aldrich India. They weren't further purified before being used. A Buchi melting-point B-540 device was used to record melting points in open capillaries. A Bruker instrument (400 MHz) was used to obtain ^{1}H NMR spectra, and chemical shifts are reported in δppm. High-resolution LC–MS, Thermo spectrometers (70 eV) were used to measure the mass spectra. A microwave oven with an Erlenmeyer flask and model number LG MH 4048 ADROEIL (2450 MHz, 1200 W) was used to perform microwave irradiation.

GENERAL PROCEDURE FOR THE SYNTHESIS OF FLUORINATED PYRAZOLES DERIVATIVES:

In a Round bottom flask, mixture of fluronated aromatic ketone (1) and aromatic aldehyde (2)were in the presence of aqueous sodium hydroxide in ethanol. The reaction was stirred at room temperature for completion of reaction to produce chalcone in the first step(3a-3l). In the second step, chalcone 3a-3l(0.01mol) were cyclized with a substituted hydrazine hydrate (0.01mol) and catalytic amount of ionic liquid in an Erlenmeyer flask placed in microwave and irradiated until completion of the reaction at 70-80 ^{o}C. The reaction mixture was monitored by TLC (ethyl acetate-hexane, 2:8). After the completion of the reaction, the reaction mixture was poured on crushed ice and filtered it. The crude product was collected and recrystallized in ethanol and dried. The entire product was characterized by physical constant and spectroscopic techniques and compared with the standard method.

Scheme 1: Synthesis of pyrazoles derivatives





SPECTRAL ANALYSIS OF SYNTHESIZED DERIVATIVES 4a-4l.

IR spectra were recorded on Make Bruker FTIR spectrometer ranging from 4000 to 650 cm^{-1} using potassium bromide pellets. Mass spectra were recorded on Make: Agilent Technologies.^{1}H NMR spectra were recorded on Bruker Avance 400F (MHz) spectrometer (Bruker scientific Ltd Switzerland) where DMSO-d_6 and $CDCl_3$ as solvents and Tetramethylsilane (TMS) as internal standard were used. HPLC purity was performed using HPLC Make Waters. Open capillary method was used to determine melting points using Make: Metteler Toledo MP50. The progress of reactions and the purity of the isolated compounds were monitored by thin layer chromatography (TLC) on alumina plated coated with silica gel60 F_{254}, 0.25 mm thickness (Merck) plates using ethyl acetate–hexane (2:8) as eluent; visualization was done by treatment with iodine vapor and under UV light.

5-(1,3-benzodioxol-5-yl)-3-[2-(trifluoromethyl)phenyl]-4,5-dihydro-1*H*-pyrazole (4a): M.Pt.=156-159 °C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 3212 (N-H str.), 2922(Ar-H str.), 2853 (C-H str.), 1618 (C=N str.), 1581 (C=C str.), 1452 (C-H bend), 1335 (C-CF_3 str.), 1145 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 6.08 s (2H, O-CH_2-O piperonal), 6.80 s (1H, Ar-H), 7.13–7.28 d (1H, Ar-H, *J* = 6.8 Hz), 7.27–7.37 d (2H, Ar-H), 7.61–7.62 d (1H, Ar-H, *J* = 6.0 Hz), 7.68–7.73 d (1H, Ar-H, *J* = 13.6 Hz), 7.76 d (1H, Ar-H), 7.81–7.86 d (2H, Ar-H), mass spectrum (m/z) 334.70 $(M)^+$, HPLC purity=99.75%. Found %: C 61.02; H 3.92' F 17.05; N 8.38; O 9.57; $C_{17}H_{13}F_3N_2O_2$. Calculated, C 61.06; H 3.88; F 17.03; N 8.34; O 9.53.

5-(1,3-benzodioxol-5-yl)-1-methyl-3-[2-(trifluoromethyl)phenyl]4,5-dihydro-1*H*-pyrazole (4b) M.Pt.=66 to 69 °C, IR (KBr, $\gamma_{max,}$ cm^{-1}), 3047 (Ar-H str.), 2924 (C-H str.), 1636(C=N str.), 1548 (C=C str.), 1465 (C-H bend), 1334 (C-CF_3 str.), 1165 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 2.81s (3H, -CH_3), 2.95–3.04d (1H, -CH_2), 3.31–3.37d (1H, -CH_2), 4.08-4.14d (1H, -CH), 5.95–5.98d (2H, O-CH_2-O, *J* = 4.0 Hz), 6.79–6.89d (1H, Ar-H), 6.88–6.90d (1H, Ar-H, *J* = 8.0 Hz), 7.43–7.47 d (1H, Ar-H, *J* = 16 Hz), 7.29–7.35m (1H, Ar-H), 7.39–7.48d (1H, Ar-H), 7.54–7.57d (1H, Ar-H, *J* = 16 Hz), 7.58–7.63m (1H, Ar-H), mass spectrum (m/z) 348.65 $(M)^+$, HPLC purity=99.53 %, Anal. Calculated (%) for $C_{18}H_{15}F_3N_2O_2$ (348.3), C=62.07, H= 4.34, F=16.36, N=8.04, O=9.19, Actual, C=62.04, H=4.29, F=16.31, N=7.98, O=9.15.

1-{5-(1,3-benzodioxol-5-yl)-3-[2-(trifluoromethyl)phenyl]4,5-dihydro-1*H*-pyrazol-1-yl}ethanone (4c) M.Pt.=88-90 °C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 2981 (Ar-H str.), 2937 (C-H str.), 1724 (C=O str.), 1634 (C=N str.), 1605 (C=C str.), 1457 (C-H bend), 1375(C-CF_3 str.), 1157 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 2.22 s (3H, -CH_3), 3.02–3.07 d (1H, -CH_2, *J* = 22.8 Hz), 3.88–3.94 d (1H, -CH_2), 5.46–5.48 d (1H,-CH, *J* = 16 Hz), 5.99-6.03 s (2H, O-CH_2-O, *J* = 4.0 Hz), 6.68–6.74 m (2H, Ar-H, *J* = 19.2 Hz), 6.85–6.89 d (1H, Ar-H, *J* = 8.0 Hz), 7.65–7.71 d (1H, Ar-H, *J* = 16.0 Hz), 7.76–7.78 m (2H, Ar-H, *J* = 8.0 Hz), 7.89–7.91 d (1H, Ar-H, *J* = 8.0 Hz), mass spectrum (m/z) 376.55 $(M)^+$, HPLC purity=99.77 %, Found, %: C 60.64; H 4.02; F 15.15; N 7.44; O 12.76; $C_{19}H_{15}F_3N_2O_3$. Calculated, C 60.67; H 3.97; F 15.11; N 7.41; O 12.81.

1-{5-(1,3-benzodioxol-5-yl)-3-[2-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazol-1-yl}propan-1-one (4d)M.Pt.=81-83°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 2955 (Ar-H str.), 2855 (C-H str.), 1730 (C=O str.), 1635 (C=N str.), 1614 (C=C str.), 1449 (C-H bend), 1389 (C-CF_3), 1151 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 1.15–1.19 t (3H, -CH_3), 2.72–2.76 q (2H, Acetyl-CH_2, *J* = 23.7 Hz), 3.05–3.14 d (1H, -CH_2, *J* = 22.8 Hz), 3.71–3.79 d (1H, -CH_2-), 5.47–5.53 d (1H, -CH-, *J* = 16.0 Hz), 5.93 s (2H, O-CH_2-O), 6.70–6.72 d (1H, Ar-H, *J* = 8.0 Hz), 6.74–6.75 d (1H, Ar-H), 6.75–6.77 d (1H, Ar-H, *J* = 8.0 Hz), 7.52–7.55 d(1H, Ar-H, *J* = 14.8 Hz), 7.58–7.64 m (2H, Ar-H), 7.77–7.79 d (1H, Ar-H, *J* = 8.0 Hz), mass spectrum (m/z) 390.80 $(M)^+$, HPLC purity=99.62 %, Found %: C 61.54; H 4.39; F 14.6; N 7.18; O 12.30; $C_{20}H_{17}F_3N_2O_3$ Calculated C 61.57; H 4.34; F 14.56; N 7.14; O 12.24.

5-(1,3-benzodioxol-5-yl)-1-phenyl-3-[2-(trifluoromethyl)phenyl]-4, 5-dihydro-1*H*-pyrazole (4e) M.Pt.=147-150°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 2963 (Ar-H str.), 2884 (C-H str.), 1611 (C=N str.), 1562 (C=C str.), 1464 (C-H bend), 1385 (C-CF_3str.), 1208 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 3.07-3.13 d (1H, -CH_2), 3.91–3.99 d(1H, -CH_2), 5.45–5.48 d (1H,-CH-, *J* = 18.0 Hz), 5.98–5.99 s (2H, O-CH_2-O), 6.723–6.75 d (1H, Ar-H, *J* = 6.0 Hz), 6.79–6.81 d (1H, Ar-H, *J* = 4.0 Hz), 6.79–6.80 d (1H, Ar-H,), 6.81–6.90 t (1H, Ar-H), 6.96–6.96 d (1H, Ar-H), 6.89–6.91 d(1H, Ar-H), 7.14–7.19 d (2H, Ar-H), 7.58–7.62 d (1H, Ar-H, *J* = 15.9 Hz), 7.70–

7.73 d (2H, Ar-H, *J* = 12.4 Hz), 7.85–7.87 d (1H, Ar-H, *J* = 8.0 Hz), mass spectrum (m/z) 411.50 $(M)^+$, HPLC purity=97.32 %, Found %: C 67.31; H 4.18; F 13.89; N 6.83; O 7.80; $C_{23}H_{17}F_3N_2O_3$. Calculated C 67.26; H 4.16; F 13.86; N 6.80; O 7.84.

5-(1,3-benzodioxol-5-yl)-1-(4-chlorophenyl)-3-[2-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazole (4f)M.Pt.=138-141°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 3118 (Ar-H str.), 2848 (C-H str.), 1651 (C=N str.), 1522 (C=C str.), 1336 (C-CF_3str.)**,** 1115 (C-O str.),^{1}H NMR spectrum, δ, ppm: 3.11–3.18 d (1H,-CH_2), 3.81–3.88 d (1H,-CH_2), 5.22–5.26 s (1H, -CH-), 5.92–5.94 s (2H, O-CH_2-O, *J* = 8.0 Hz), 6.75–6.85 d (3H, Ar-H), 7.06–7.09 m (2H, Ar-H, *J* = 8.8 Hz), 7.18–7.22 m (2H, Ar-H), 7.44–7.47 d (1H, Ar-H, *J* = 15.2 Hz), 7.55–7.59d (1H, Ar-H, *J* = 16 Hz), 7.63–7.65 d (1H, Ar-H, *J* = 8.0 Hz), 7.75–7.78 d (1H, Ar-H, *J* = 8.4 Hz), mass spectrum (m/z) 446.60 $(M)^+$, HPLC purity=98.25 %, Found %: C 62.10; H 3.63; Cl 7.97; F 12.81; N 6.30; O 7.19; $C_{23}H_{16}ClF_3N_2O_2$. Calaclaued C 62.13; H 3.58; Cl 7.93; F 12.77; N 6.32; O 7.14.

5-(1,3-benzodioxol-5-yl)-3-[4-(trifluoromethyl)phenyl]-4,5-dihydro-1*H*-pyrazole (4g):M.Pt.=87- 89°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 3349 (N-H str.), 2902 (Ar-H str.), 2789 (C-H str.), 1616 (C=N str.), 1488 (C=C str.), 1444(C-H bend), 1326 (C-CF_3 str.), 1125 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 2.85–2.93 d (1H, -CH_2 pyrazole), 3.41–3.45 d(1H, -CH_2 pyrazole), 4.84–4.89 d (1H, -C-H pyrazole, *J* = 20.0 Hz), 6.01–6.05 d (1H, O-CH_2-O Piperonal, *J* = 20.0 Hz), 6.09 s(1H, -CH_2-), 6.76–7.41 m (3H, Ar-H piperonal), 7.74–7.88m (4H, Ar-H), mass spectrum (m/z) 334.40 $(M)^+$, HPLC purity=97.91 %, Found %: C 61.08; H 3.92; F 17.05; N 8.38; O 9.57; $C_{17}H_{13}F_3N_2O_2$. Calculated C 61.11; H 3.93; F 17.01; N 8.32; O 9.61.

5-(1,3-benzodioxol-5-yl)-1-methyl-3-[4-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazole (4h) M.Pt. = 107-109°C, IR (KBr, $\gamma_{max,}$ cm^{-1}), 2957 (Ar-H str.), 2865 (C-H str.), 1614 (C=N str.), 1686 (C=C str.), 1443 (C-H bend), 1327 (C-CF_3 str.), 1114 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 2.71–2.75 s (3H, -CH_3), 2.85–2.99 d (1H, -CH_2 pyrazole), 3.52–3.55 d (1H, -CH_2 pyrazole, *J* = 6.4 Hz), 4.17-4.19 d (1H, -CH pyrazole, *J* = 5.2 Hz), 6.01–6.04 s (2H, O-CH_2-O piperonal, *J* = 5.2 Hz), 6.87–7.04m (3H, Ar-H piperonal), 7.74–7.78 d (4H, Ar-H CF_3 Benzene), mass spectrum (m/z) 348.50 $(M)^+$, HPLC purity=98.29%, Found %: C 62.07; H 4.34; F 16.36; N 8.04; O 9.19; $C_{18}H_{15}F_3N_2O_2$ Calculated C 62.11; H 4.30; F 16.30; N 7.96; O 9.13.

1-{5-(1,3-benzodioxol-5-yl)-3-[4-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazol -1-yl}ethanone (4i)M.Pt.=162-164°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 3066 (Ar-H str.), 2898 (C-H str.), 1653 (C=O str.), 1596 (C=N str.), 1495 (C=C str.), 1445 (C-H bend), 1329 (C-CF_3 str.), 1118 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 2.32 s (3H, -CH_3), 3.16–3.22 d (1H, -CH_2 pyrazole), 3.82–3.89 d (1H, -CH_2 pyrazole, *J* = 30.0 Hz), 5.48–5.52 d(1H,-CH pyrazole, *J* = 16.0 Hz), 5.97 s (2H, O-CH_2-O), 6.68–6.86m (3H, Ar-H piperonal), 7.82–7.97 d (4H, Ar-H CF_3 Benzene), mass spectrum (m/z) 376.55 $(M)^+$, HPLC purity=99.95%, Found %: C 60.64; H 4.02; F 15.15; N 7.44; O 12.76; $C_{19}H_{15}F_3N_2O_3$. Calculated C 60.69; H 3.98; F 15.21; N 7.40; O 12.80.

1-{5-(1,3-benzodioxol-5-yl)-3-[4-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazol-1-yl}propan-1-one (4j) M.Pt.= 146-148°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 2986 (Ar-H str.), 2947 (C-H str.), 1673 (C=O str.), 1596 (C=N str.), 1493 (C=C str.), 1435 (C-H bend), 1327 (C-CF_3), 1121(C-O str.), ^{1}H NMR spectrum, δ, ppm:1.05–1.07 t (3H, -CH_3), 2.72–2.76 q (2H, Acetyl-CH_2, *J* = 13.2 Hz), 3.15–3.18 d (1H, -CH_2 pyrazole, *J* = 22.8 Hz), 3.81–3.89 d (1H, -CH_2 pyrazole, *J* = 29.6 Hz), 5.48–5.52 d (1H, -CH- pyrazole, *J* = 15.6 Hz), 5.98 s (2H, O-CH_2-O piperonal), 6.67–6.84 d (3H, Ar-H piperonal), 7.81–7.99m (4H, Ar-H CF_3 Benzene), mass spectrum (m/z)

390.50 $(M)^+$, HPLC purity=99.71%, Found %: C 61.54; H 4.39; F 14.60; N 7.18; O 12.30; $C_{20}H_{17}F_3N_2O_3$. Calculated C 61.60; H 4.37; F 14.58; N 7.21; O 12.24.

5-(1,3-benzodioxol-5-yl)-1-phenyl-3-[4-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazole (4k) M.Pt.=155-157°C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 2925 (Ar-H str.), 1595 (C=N str.), 1497 (C=C str.), 1446 (C-H bend), 1328 (C-CF_3str.), 1119 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 3.12-3.18 d (1H,-CH_2 pyrazole, *J* = 23.6 Hz), 3.86–3.94 d (1H, -CH_2 pyrazole), 5.48–5.42 d(1H,-CH pyrazole, *J* = 18.4 Hz), 5.93–5.98 s (2H, O-CH_2-O piperonal,), 6.75–6.79 m (3H, Ar-H), 6.84–6.87 d (1H, Ar-H, *J* = 7.6 Hz), 7.03–7.07 d (2H, Ar-H), 7.17–7.21 d (2H, Ar-H), 7.76–7.78 d (2H, Ar-H), 7.91–7.95 d (2H, Ar-H), mass spectrum (m/z) 412.55 $(M)^+$, HPLC purity=98.78 %, Found %: C 67.31; H 4.18; F 13.89; N 6.83; O 7.80; $C_{23}H_{17}F_3N_2O_3$. Calculated C 67.39; H 4.13; F 13.84; N 6.77; O 7.74.

5-(1,3-benzodioxol-5-yl)-1-(4-chlorophenyl)-3-[4-(trifluoromethyl)phenyl]- 4, 5-dihydro-1*H*-pyrazole (4l)M.Pt.=137-139 °C, IR (KBr, $\gamma_{max,}$ cm^{-1}) 2887 (Ar-H str.), 1592 (C=N str.), 1492 (C=C str.), 1446 (C-H str.), 1325 (C-CF_3str.)**,** 1126 (C-O str.), ^{1}H NMR spectrum, δ, ppm: 3.14–3.20 d (1H,-CH_2 pyrazole, *J* = 23.2 Hz), 3.88–3.95 d (1H,-CH_2 pyrazole), 5.49–5.55 s (1H, -CH- pyrazole, *J* = 20.0 Hz), 5.96–5.97 s (2H, O-CH_2-O piperonal), 6.76–6.79 d (2H, Ar-H, *J* = 11.2 Hz), 6.86–6.88 d (1H, Ar-H, *J* = 7.6 Hz), 7.04–7.08 d (2H, Ar-H, *J* = 8.8 Hz), 7.22–7.25 d (2H, Ar-H, *J* = 9.2 Hz), 7.74–7.77 d (2H, Ar-H, *J* = 8.4 Hz), 7.92–7.95 d (2H, Ar-H, *J* = 8.0 Hz), mass spectrum (m/z) 446.60 $(M)^+$, HPLC purity=99.95%, Found %: C 62.10; H 3.63; Cl 7.97, F 12.81; N 6.30; O 7.19; $C_{23}H_{16}ClF_3N_2O_2$. Calculated C 62.16; H 3.58; Cl 8.04; F 12.87; N 6.23; O 7.16.

RESULT AND DISCUSSION

The synthesis of CF_3-containing pyrazoles was efficiently carried out using an ionic liquid as a green and recyclable catalyst. The reaction proceeded in microwave smoothly under mild conditions, yielding the desired pyrazoles derivatives in excellent yields (80–95%) Table 1. The catalytic efficiency of the ionic liquid was demonstrated by its ability to be reused up to five cycles with minimal loss in catalytic activity. Spectral analysis confirmed the successful formation of CF_3-substituted pyrazoles without any detectable by-products, indicating a high selectivity of the reaction.

Table1. Synthesized Derivatives of fluorinated pyrazoles

Entry	Derivatives (R)	Time in min	% of Yield	Melting Point in °C
3a+4a	-H	5.30	85	156-159
3a+4b	-CH_3	4.30	90	66-69
3a+4c	-$COCH_3$	8.30	83	88-90
3a+4d	-$COCH_2CH_3$	6.30	85	81-83
3a+4e	-Ph	6.00	87	147-150
3a+4f	-C_6H_5-p-Cl	7.00	89	138-141
3b+4g	-H	5.00	91	87- 89
3b+4h	-CH_3	4.00	92	106-109
3b+4i	-Ph	5.30	90	162-164
3b+4j	-$COCH_2CH_3$	6.00	87	146-148
3b+4k	-C_6H_5-p-Cl	6.30	91	155-157
3b+4l	-$COCH_3$	7.00	85	137-139

The synthesized CF_3-containing pyrazoles were subjected to biological evaluation to determine their potential pharmacological activity. The antimicrobial assay revealed significant inhibitory

activity against Gram-positive and Gram-negative bacterial strains, with minimum inhibitory concentration (MIC) values. The antibacterial and antifungal properties of the synthesized compounds were examined good antibacterial activity was demonstrated by the synthesized derivatives, 4b, 4c, 4g, and 4j. When compared to common medications such as isoniazid and rifampicin, compounds 4a and 4f exhibited the same antifungal activity as griseofulvin.

Antibacterial activity: For E. Coli, compound 4c activity MIC-50 µg/ml is comparable to standard chloramphenicol (MIC-50 µg/ml) but roughly half that standard ciprofloxacin (MIC-25 µg/ml). For P.Aeruginosa, compounds 4g and 4j each have an activity MIC-60.5µg/ml, which is lower than that of chloramphenicol (MIC-50µg/ml) and ciprofloxacin (MIC-25µg/ml). For S. Aureus, compounds 4c and 4h have an activity MIC of 60.5 µg/ml, which is also less than that of both popular drugs. For S. Pyogenus, compound 4g (MIC-50 µg/ml) is equivalent to standard chloramphenicol (MIC-50 ug/ml) but less than standard ciprofloxacin (MIC-25 µg/ml). Table 2 displays the antibacterial activity data.

Table 02: Antibacterial Activity of compounds 4a-4l

Antibacterial Activity					
Sr. No	Entry	*E.Coli*	*P. Aeruginosa*	*S. Aureus*	*S. Progenies*
1	4a	125	100	200	100
2	4b	**60.5**	100	100	**60.5**
3	4c	**50**	100	**60.5**	100
4	4d	100	250	100	250
5	4e	250	100	250	250
6	4f	200	125	125	200
7	4g	100	**60.5**	100	**50**
8	4h	100	125	**60.5**	100
9	4i	100	200	100	100
10	4j	125	**60.5**	100	125
11	4k	100	100	125	125
12	4l	100	125	100	250
Chloramphenicol		50	50	50	50
Ciprofloxacin		25	25	50	50

Antifungal activity: Compound 4e activity MIC-250 µg/ml for Candida albicans is lower than that of standard Nystatin (MIC-100 µg/ml) but double that of standard Griseofulvin (MIC-500 µg/ml). Standards for Griseofulvin (MIC-500 µg/ml) and Compounds 4a, 4f, 4j, and 4l) have the same activity (MIC-500 µg/ml). Compounds 4(a-l) had less action against A. Niger and A. Clavatus than standard Nystatin (MIC-100 µg/ml) and Griseofulvin (MIC-100 µg/ml). The antifungal result is shown in Table 3.

Table 3: Antifungal activity of compounds 4a-4l

Antifungal Activity				
Sr. No	**Entry**	**C. Albicans**	**A. Niger**	**A. Clavatus**
1	4a	**500**	500	500
2	4b	1000	500	500
3	4c	1000	500	500
4	4d	1000	1000	1000
5	4e	**250**	1000	1000
6	4f	**500**	1000	1000
7	4g	1000	500	500

8	4h	1000	500	500
9	4i	1000	1000	1000
10	4j	500	1000	1000
11	4k	1000	500	500
12	4l	500	1000	1000
13	Nystatin	100	100	100
14	Griseofulvin	500	100	100

CONCLUSION:

The ionic liquid-catalyzed synthesis of CF_3-containing pyrazoles under microwave irradiation presents a sustainable and efficient approach. The method provides high yields, reduced reaction times, and an environmentally friendly alternative. The synthesized compounds exhibit promising biological activities, making them potential candidates for further pharmaceutical and agricultural applications. Molecules 4c and 4g could be promising antibacterial drugs. The fungal activity of prepared series is low except 4e which had twice activity in comparison with Griseofulvin as antifungal standard drug.

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REFERENCES

i Kaur, H.; Singh, R.; Mehta, S.; Advances in the medicinal chemistry of pyrazole derivatives; Bioorg. Chem.; 2020, **95**, 103476.

Ii Kumar, A.; Verma, P.; Sharma, N.; Pyrazole-based compounds as therapeutic agents; A review; Eur. J. Med. Chem.; 2022, **229**, 114056.

Iii Singh, P.; Sharma, V.; Green synthesis of pyrazoles using ionic liquids and microwave irradiation.; Journal of Heterocyclic Chemistry; 2019, **56**(2), 367–379.

Iv Patel, R.; Shah, D.; Bhatt, P.; Applications of pyrazole derivatives in pharmaceuticals and materials science. Current. Organic Chemistry; 2021, **25**(7), 982–995.

v Wasserscheid, P.; Welton, T.; Ionic liquids in synthesis; Wiley-VCH; 2008.

Vi Zhao, H.; Xia, S.; Ma, P.; Use of ionic liquids as 'green' solvents for extractions; J. Chem. Technol. Biotechnol; 2019, **94**(2), 31–49.

Vii Parveen, S.; Kumar, A.; Singh, R.; Recent advances in ionic liquid-mediated synthesis of heterocyclic compounds; Molecules; 2021, **26**(5), 1352.

Viii Plechkova, N. V.; Seddon, K. R.; Applications of ionic liquids in the chemical industry; Chemical Society Review; 2014, **43**(2), 155–174.

Ix Kerru, N.; Gummidi, L.; Maddila, S.; Gangu, K. K.; Jonnalagadda, S. B.; A review on recent advances in nitrogen-containing molecules and their biological applications; Molecules; 2020, **25**, 1909–1951.

x Isloor, A. M.; Kalluraya, B.; Shetty, P.; Synthesis and antimicrobial activity of some new pyrazole derivatives; European Journal of Medicinal Chemistry; 2009, **44**(9), 3784–3787.

Xi Szabo, G.; Fischer, J.; Kis-Varga, A.; Gyires, K.; Synthesis and pharmacological evaluation of novel pyrazole derivatives with anti-inflammatory activity; Journal of Medicinal Chemistry; 2008, **51**, 142–147.

Xii Padmini, T.; Kamal, B.; Synthesis and characterization of some novel pyrazole derivatives; Asian Journal of Chemistry; 2019, **31**(6), 1225–1229.

Xiii Zhang, Y.; Wu, C.; Zhang, N.; Fan, R.; Ye, Y.; Xu, J.; Design,synthesis and biological evaluation of novel pyrazole derivatives; International Journal of Molecular Science; 2023, **24**(11), 12724.

Xiv Manfredini, S.; Bazzanini, R.; Baraldi, P. G.; Guarneri, M.; Simoni, D.; Marongiu, M. E.; Pani, A.; et al.; Design and synthesis of pyrazole derivatives as potential antitumor agents; Journal of Medicinal Chemistry; 1992, **35**(6), 917–924.

Xv Rhim, H.; Lee, Y. S.; Park, S. J.; Choung, B. Y.; Lee, J. Y.; Design, synthesis and pharmacological evaluation of novel pyrazole derivatives; Bioorganic and Medicinal Chemistry Letters; 2005, **15**(2), 283–286.

Xvi Bekhit, A. A.; Nasralla, S. N.; El-Agroudy, E. J.; Hamouda, N.; Bekhit, S. A.; Amagase, K.; Ibrahrim, T. M.; Synthesis and anticancer evaluation of some new heterocyclic compounds derived from pyrazoles; European Journal of Pharmaceutical Science; 2002, **168**, 106080.

Xvii Liang, Z.; Rong, Z.; Cong, H.; Ying, D. Q.; Crystal structure and biological activity of novel pyrazole-based molecules; Journal Molecular Structure; 2023, **1277**, 134881.

Xviii Ahmed, A.; Zaib, S.; Bhat, M. A.; Saeed, A.; Altaf, M. Z.; Zahra, F. T.; Shabir, G.; Rana, N.; Khan, I.; Recent developments in pyrazole-based hybrid compounds for medicinal chemistry; Frontiers in Chemistry; 2021, **12**, 1380523.

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