CHAPTER 4
Greener and Efficient Protocol for the Synthesis of Novel Tetra-substituted Pyrazoles in Aqueous Medium

4.1 Results and Discussion
Several syntheses of pyrazoles have been developed and by far the most established method of choice is the reaction of $\beta$-ketoesters with hydrazines. Recently, a few efficient methods have been developed however; most of these utilize a circuitous route, carried out in organic solvents, and are often require longer reaction time. Since a large amount of waste in the environment is attributed to the use of organic solvents, there is a great interest in the development of organic reactions in environmentally benign media. Recently, water has been shown to induce unique reactivity and selectivity which cannot be attained for reactions in organic media. In addition, water as a solvent will reduce the use of harmful organic solvents and may lead to the development of eco-friendly chemical processes. Therefore, water as a reaction medium would be highly desirable if such reactions could be performed using reusable catalysts.

Further, heterogeneous catalysts have grabbed much focus recently for the synthesis of organic compounds from both economical and environmental perspectives. The use of reusable solid acid catalysts produces one of the most promising green, sustainable processes in organic synthesis and use of these solid catalysts provides various advantages over liquid catalyst which include easy experimental, reduced equipment corrosion and product isolation procedures. During the past decades there has been an exceptional growth in the application of heterogeneous catalysis to carry out organic transformations as a consequence of its importance in terms of economical, environmental and practical aspects. A greener and facile aqueous synthesis of pyrazoles using Amberlyst-70 as recyclable catalyst was reported (Chandak et al., 2012) recently and Nasseri et al. (2014) have reported the synthesis of pyrazoles in aqueous medium using cellulose sulfuric acid as a bio-supported and efficient solid acid catalyst. A Greener and rapid room temperature synthesis of pyrazoles in aqueous medium catalyzed by PSSA was also reported (Polshettiwar et al., 2009).
4.1.1 Synthesis of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)alkyl)anilines

In our continued efforts for designing greener synthetic pathways, herein, we report an expeditious synthetic protocol for the synthesis of pyrazoles by the reaction of β-amino carbonyls with hydrazines catalyzed by polystyrene supported sulfonic acid (PSSA), which proceeded efficiently in water in the absence of any organic solvent at room temperature within 10–15 min. Initially we have tried to synthesize the new pyrazole derivatives using different solid catalysts like CSA, Amberlyst-70, Silica-supported sulphuric acid catalysts and PSSA, along with some conventional acid catalysts like HCl, H$_2$SO$_4$ and CH$_3$COOH in different solvents and conditions. To optimize the reaction conditions and catalysts, synthesis of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline from 3-ethoxy-4-(phenylamino)hexan-2-one (1 mmol) and phenyl hydrazine (1.2 mmol) was chosen as a model reaction and performed under various catalysts (Scheme 4.1).

![Scheme 4.1 Synthesis of N-(1-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline](image)

During our initial efforts to optimize the reaction conditions, we have started with conventional inorganic acid catalysts such as HCl and H$_2$SO$_4$ in ethanol under reflux conditions. But failed to get the desired product, may be due to the temperature sensitive nature of the substrate. So in our next trial, we have run the reaction with the same catalysts at room temperature and succeeded to get the product, but with very poor yields. Then optimization of the reaction conditions was continued with different reusable solid acid catalysts in aqueous medium at room temperature. All the results were tabulated in the following table (Table 4.1). Among all the catalysts, PSSA was proven to be a better
catalyst for our reaction and afford the products with excellent yield than other catalysts CSA, Amberlyst-70, Silica-supported sulphuric acid, HCl and H$_2$SO$_4$.

**Table 4.1** Optimization of Synthesis of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline with Different Catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time</th>
<th>Yield (%) *</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PSSA</td>
<td>Water</td>
<td>RT</td>
<td>10-15 min</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td>CSA</td>
<td>Water</td>
<td>RT</td>
<td>20-30 min</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>Amberlyst-70</td>
<td>Water</td>
<td>RT</td>
<td>20-30 min</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>SiO$_2$.H$_2$SO$_4$</td>
<td>Solvent Free</td>
<td>RT</td>
<td>50-60 min</td>
<td>60</td>
</tr>
<tr>
<td>5</td>
<td>H$_2$SO$_4$</td>
<td>Ethanol</td>
<td>RT</td>
<td>3-4 hrs</td>
<td>45</td>
</tr>
<tr>
<td>6</td>
<td>HCl</td>
<td>Ethanol</td>
<td>RT</td>
<td>3-4 hrs</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>H$_2$SO$_4$</td>
<td>Ethanol</td>
<td>50-60</td>
<td>6-7 hrs</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>HCl</td>
<td>Ethanol</td>
<td>50-60</td>
<td>6-7 hrs</td>
<td>-</td>
</tr>
</tbody>
</table>

*after recrystallization

So, keep in view of the importance of convenient, efficient, inexpensive, and eco-friendly route for the synthesis of our pyrazole derivatives, we have chosen PSSA as best catalyst for the synthesis of our target compounds.

**Scheme 4.2** Synthesis of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)alkyl)anilines (3a-l)

After the optimization of reaction conditions, we turned our attention for studying the scope of this method and treated various substituted β-amino carbonyls with different hydrazines under mild reaction conditions (Scheme 4.2). The results are summarized in Table 4.2. In all cases, the reaction proceeded readily at room temperature to afford the corresponding pyrazoles in good to excellent yields (75–90%).
Table 4.2 Synthesis of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)alkyl)anilines (3a-l)

<table>
<thead>
<tr>
<th>Product</th>
<th>R</th>
<th>(^1) R</th>
<th>(^2) R</th>
<th>Time (min.)</th>
<th>Yield (%) (^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>H</td>
<td>CH(_3)</td>
<td>C(_6)(_5)</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>3b</td>
<td>4-F</td>
<td>CH(_3)</td>
<td>C(_6)(_5)</td>
<td>15</td>
<td>80</td>
</tr>
<tr>
<td>3c</td>
<td>4-CH(_3)</td>
<td>CH(_3)</td>
<td>C(_6)(_5)</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>3d</td>
<td>H</td>
<td>C(_2)(_5)</td>
<td>C(_6)(_5)</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>3e</td>
<td>4-CH(_3)</td>
<td>C(_2)(_5)</td>
<td>C(_6)(_5)</td>
<td>10</td>
<td>85</td>
</tr>
<tr>
<td>3f</td>
<td>4-Cl</td>
<td>C(_2)(_5)</td>
<td>C(_6)(_5)</td>
<td>15</td>
<td>75</td>
</tr>
<tr>
<td>3g</td>
<td>4-F</td>
<td>C(_2)(_5)</td>
<td>C(_6)(_5)</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>3h</td>
<td>4-F</td>
<td>CH(_3)</td>
<td>H</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>3i</td>
<td>H</td>
<td>C(_2)(_5)</td>
<td>H</td>
<td>15</td>
<td>85</td>
</tr>
<tr>
<td>3j</td>
<td>H</td>
<td>CH(_3)</td>
<td>H</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>3k</td>
<td>4-Cl</td>
<td>C(_2)(_5)</td>
<td>H</td>
<td>15</td>
<td>87</td>
</tr>
<tr>
<td>3l</td>
<td>4-F</td>
<td>C(_2)(_5)</td>
<td>H</td>
<td>10</td>
<td>90</td>
</tr>
</tbody>
</table>

\(^a\)after recrystallization

4.1.2 Spectral Characterization of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline (3d)

The compound 3d has been chosen as a representative example and its spectral characterization was described by using different spectroscopic techniques like \(^1\)H NMR, \(^{13}\)C NMR and HRMS. According to \(^1\)H NMR spectrum of the compound, presence of different set of equivalent protons were described as follows: Two triplet signals centered at \(\delta = 0.96\) and \(\delta = 1.29\) equivalents to 3H each represents the presence of two methyl (CH\(_3\)) groups attached to adjacent methylene groups and present in two different chemical environments. Further, a singlet at \(\delta = 2.31\) equivalents to 3H indicates the
presence of another methyl group attached to an aromatic nucleus. Two multiplet signals observed at \( \delta = 1.50-1.53 \) and \( \delta = 1.69-1.73 \) equivalents to 1H each denotes the presence of two diasteriotopic protons attached to the same carbon atom and adjacent to a chiral carbon. A quartet signal centered at \( \delta = 4.34 \) equivalents to 2H represents the presence of a methylene group attached to a methyl group and appeared at down field as it is adjacent to a more electronegative oxygen atom. Further signals at \( \delta = 6.65-7.47 \) equivalents to 10H represent the presence of two mono substituted phenyl groups.

According to \(^{13}\)C NMR spectrum, a signal at \( \delta = 156.81 \) represents the C5-carbon of the pyrazole ring which is attached to an ethoxy group and another downfield signal observed at \( \delta = 154.84 \) denotes the C3-carbon of the pyrazole nucleus. Further another significant signal at \( \delta = 146.61 \) represents the ipso carbon of phenyl ring attached to NH group and the other signal at \( \delta = 138.97 \) indicates the ipso carbon of another phenyl ring attached to the nitrogen atom (position-1) of the pyrazole nucleus. Other important diagnostic signals at \( \delta = 59.06 \) and \( \delta = 62.67 \) represents the aliphatic carbons attached to more electronegative N and O atoms respectively.

![Fig. 4.1 \(^{1}\)H NMR Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline (3d)](image-url)
Finally the structure of the compound was confirmed by HRMS spectrum of the compound, the molecular ion peak observed at (m/z): 335.1980 were exactly coincides with the exact molecular weight of the compound (3d).
4.2 Experimental Section

4.2.1 Materials and Method

All reagents and solvents were prepared by using the systematic procedure already reported in the literature or were purchased from commercially available suppliers and used without further purification. \(^{1}\)H NMR and \(^{13}\)C NMR spectra were recorded on JEOL RESONANCE 400-MHz spectrometer using TMS as internal standard (chemical shifts \(\delta\) in ppm). HR-mass spectra (EI) were obtained with V.G. Micromass 7035. TLC visualization was made with iodine chamber. Column chromatography was performed on silica gel (60–120 mesh).

4.2.2 General Procedure for the Synthesis of Pyrazoles (3a-l)

To a mixture of \(\beta\)-keto Ester (1 mmol) and hydrazine (1.2 mmol), 0.1 mL of 20\% PSSA solution in water was added and stirred for 10-15 min. at room temperature. The products were then extracted into ethyl acetate and washed with dilute sodium bicarbonate solution. After drying the organic layer over sodium sulfate and evaporation of the solvent, the product was isolated by passing the crude reaction mixture over short silica gel column.

4.2.2.1 N-(1-(5-ethoxy-3-methyl-1-phenyl-1\(\text{H}\)-pyrazol-4-yl)ethyl)aniline (3a)

Yellowish liquid; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) – 1.33-1.29 (m, 6H); 2.29 (s, 3H); 3.52-3.55 (q, \(J\) = 4 Hz, 1H); 4.33-4.34 (q, \(J\) = 8 Hz, 2H); 6.56-6.59 (m, 2H); 6.65-6.67 (d, \(J\) = 8 Hz, 2H); 6.73-6.77 (m, 1H); 7.06-7.08 (d, \(J\) = 8 Hz, 1H); 7.15-7.16 (m, 2H); 7.22-7.25 (m, 2H); 7.32-7.35 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) - 13.71, 14.68, 21.78, 57.34, 59.14, 113.11, 115.21, 118.50, 123.23, 125.16, 129.10, 129.35, 137.32, 146.66, 151.58, 154.90; HRMS (M\(^+\)), (m/z): 321.1835.

4.2.2.2 N-(1-(5-ethoxy-3-methyl-1-phenyl-1\(\text{H}\)-pyrazol-4-yl)ethyl)-4-fluoroaniline (3b)

Yellowish liquid; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) – 0.84-0.86 (m, 3H); 1.19 (d, \(J\) = 8 Hz, 3H); 1.30-1.44 (m, 6H); 3.46-3.48 (q, \(J\) = 8 Hz, 2H); 4.31 (q, \(J\) = 8 Hz, 2H); 6.54-6.56 (m, 2H); 6.56-6.60 (d, \(J\) = 8 Hz, 2H); 1.01-1.07 (m, 2H); 7.02-7.05 (m, 1H); 7.13-7.38 (m, 2H); 7.44-7.47 (m, 2H). \(^{13}\)C NMR
4.2.2.3 N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-methylaniline (3c)
Reddish yellow liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 1.25 (d, $J = 8$ Hz, 3H); 1.35 (t, $J = 8$ Hz, 3H); 2.05 (s, 3H); 3.47 (q, $J = 8$ Hz, 1H); 4.32 (q, $J = 8$ Hz, 2H); 6.56-6.58 (m, 2H); 6.92-6.94 (m, 2H); 6.96 (m, 1H); 7.35-7.37 (m, 2H); 7.38-7.47 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 12.66, 14.51, 18.14, 20.52, 59.86, 65.93, 113.13, 115.37, 120.08, 125.75, 128.58, 129.29, 129.83, 138.84, 143.90, 144.64, 151.57; HRMS (M$^+$), (m/z): 335.1998.

4.2.2.4 N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline (3d)
Yellowish liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 0.96 (t, $J = 8$ Hz, 3H); 1.29 (t, $J = 4$ Hz, 3H); 1.50-1.53 (m, 1H); 1.69-1.73 (m, 1H); 2.31 (s, 3H); 3.57-3.59 (m, 1H); 4.34 (q, $J = 4$ Hz, 2H); 6.65-6.73 (m, 2H); 6.75-6.77 (m, 1H); 7.13-7.17 (m, 2H); 7.22-7.24 (m, 1H); 7.25-7.47 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 9.84, 13.76, 14.68, 21.93, 59.06, 62.67, 113.16, 115.19, 118.52, 123.03, 125.82, 129.03, 129.34, 138.97, 146.61, 154.84, 156.81; HRMS (M$^+$), (m/z): 335.1987.

4.2.2.5 N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)-4-methylaniline (3e)
Yellowish liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 0.94 (t, $J = 8$ Hz, 3H); 1.28 (t, $J = 4$ Hz, 3H); 1.52-1.55 (m, 1H); 1.68-1.75 (m, 1H); 2.34 (s, 6H); 3.53-3.57 (m, 1H); 4.32 (q, $J = 4$ Hz, 2H); 6.63-6.74 (m, 2H); 7.14-7.18 (m, 2H); 7.23-7.26 (m, 1H); 7.32-7.37 (m, 2H); 7.41-7.43 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 12.73, 13.66, 15.35, 21.9, 25.64, 59.86, 65.94, 113.14, 115.38, 119.40, 125.80, 128.51, 129.29, 129.81, 138.93, 143.95, 144.72, 156.81; HRMS (M$^+$), (m/z): 349.2164.
4.2.2.6 4-chloro-N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)aniline (3f)

Yellowish liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 0.95 (t, $J = 8$ Hz, 3H); 1.27 (t, $J = 4$ Hz, 3H); 1.52-1.55 (m, 1H); 1.68-1.75 (m, 1H); 2.34 (s, 3H); 3.53-3.58 (m, 1H); 4.34 (q, $J = 4$ Hz, 2H); 6.49-6.54 (m, 2H); 7.14-7.18 (m, 2H); 7.23-7.26 (m, 1H); 7.32-7.37 (m, 2H); 7.41-7.43 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 12.68, 13.58, 14.41, 25.56, 59.82, 65.94, 116.04, 119.44, 120.14, 122.23, 125.72, 129.17, 138.83, 144.60, 155.12, 156.42, 157.56; HRMS (M$^+$), (m/z): 369.1628.

4.2.2.7 N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)-4-fluoroaniline (3g)

Yellowish liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 0.96 (t, $J = 8$ Hz, 3H); 1.24 (t, $J = 4$ Hz, 3H); 1.54-1.58 (m, 1H); 1.72-1.81 (m, 1H); 2.32 (s, 3H); 3.51-3.56 (m, 1H); 4.36 (q, $J = 4$ Hz, 2H); 6.47-6.56 (m, 2H); 7.12-7.19 (m, 2H); 7.25-7.30 (m, 1H); 7.34-7.39 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 12.71, 13.62, 14.43, 25.61, 59.85, 65.91, 116.09, 119.42, 120.04, 122.29, 125.79, 129.27, 138.93, 144.70, 155.28, 156.79, 157.62; HRMS (M$^+$), (m/z): 353.1912.

4.2.2.8 N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)ethyl)-4-fluoroaniline (3h)

Yellowish liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 1.28 (d, $J = 8$ Hz, 3H); 1.37 (t, $J = 8$ Hz, 3H); 2.23 (s, 3H); 2.59 (s, 3H); 3.56 (q, $J = 8$ Hz, 1H); 4.39 (q, $J = 8$ Hz, 2H); 7.02 (m, 2H); 7.05 (m, 2H); 12.62 (bs, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 12.71, 13.62, 14.43, 25.61, 58.46, 64.6, 113.4, 116.37, 118.9, 139.84, 143.80, 155.64, 163.7; HRMS (M$^+$), (m/z): 263.1434.

4.2.2.9 N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)propyl)aniline (3i)

Yellowish liquid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ - 0.9 (t, $J = 8$ Hz, 3H); 1.32 (t, $J = 4$ Hz, 3H); 1.52-1.55 (m, 1H); 1.78-1.84 (m, 1H); 2.10 (s, 3H); 3.48-3.52 (m, 1H); 4.39 (q, $J = 4$ Hz, 2H); 6.77 (m, 1H), 6.83 (m, 2H); 7.23 (m, 2H); 12.64 (bs, 1H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ - 10.71, 13.52, 14.83, 28.61, 56.85, 64.91, 113.45, 113.85, 120.8, 129.42, 138.93, 147.6, 163.62; HRMS (M$^+$), (m/z): 259.1685.
4.2.2.10 N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)ethyl)aniline (3j)

Yellowish liquid; ¹H NMR (400 MHz, CDCl₃) δ - 1.28 (t, J = 8 Hz, 3H); 1.42 (d, J = 8 Hz, 3H); 2.05 (s, 3H); 4.08 (q, J = 8 Hz, 1H); 4.38 (q, J = 8 Hz, 2H); 6.77 (m, 1H); 6.83 (m, 2H); 7.23 (m, 2H); 12.60 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ - 12.74, 14.75, 21.85, 54.65, 64.65, 113.5, 113.87, 120.9, 129.84, 147.80, 163.85; HRMS (M⁺), (m/z): 245.1528.

4.2.2.11 4-chloro-N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)propyl)aniline (3k)

Yellowish liquid; ¹H NMR (400 MHz, CDCl₃) δ - 0.92 (t, J = 8 Hz, 3H); 1.34 (t, J = 4 Hz, 3H); 1.54-1.58 (m, 1H); 1.76-1.80 (m, 1H); 1.93 (s, 3H); 3.92 (m, 1H); 4.37 (q, J = 4 Hz, 2H); 6.54 (m, 2H); 7.27 (m, 2H); 12.61 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ - 10.74, 12.52, 14.80, 28.64, 56.15, 64.61, 114.45, 126.2, 129.62, 139.93, 145.6, 163.52; HRMS (M⁺), (m/z): 293.1295.

4.2.2.12 N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)propyl)-4-fluoroaniline (3l)

Yellowish liquid; ¹H NMR (400 MHz, CDCl₃) δ - 0.90 (t, J = 8 Hz, 3H); 1.31 (t, J = 4 Hz, 3H); 1.53-1.56 (m, 1H); 1.77-1.82 (m, 1H); 1.91 (s, 3H); 3.97 (m, 1H); 4.35 (q, J = 4 Hz, 2H); 7.04 (m, 2H); 7.07 (m, 2H); 12.64 (bs, 1H). ¹³C NMR (100 MHz, CDCl₃) δ - 10.71, 12.54, 14.75, 28.61, 56.11, 64.54, 116.45, 118.9, 139.93, 143.6, 155.7, 163.42; HRMS (M⁺), (m/z): 277.1590.

4.3 Conclusion

In conclusion, herein we have reported an efficient and greener protocol for the synthesis of new pyrazole compounds which gets completed in 10–15 min. at room temperature with excellent yields and may provide a useful route for rapid drug discovery. The use of polystyrene supported, relatively low toxic, and inexpensive PSSA as a catalyst and the water as a reaction medium are additional eco-friendly attributes of this synthetic protocol.
4.4 Spectral Evidence for \( N-(1-(5\text{-ethoxy-3-methyl-1-phenyl-1}H\text{-pyrazol-4-yl})\text{alkyl anilines (3a-l)}} \)

**Fig. 4.4** \(^1\text{H} \) NMR Spectrum of \( \text{N-(1-(5\text{-ethoxy-3-methyl-1-phenyl-1}H\text{-pyrazol-4-yl})ethyl)aniline (3a)} \)

**Fig. 4.5** \(^{13}\text{C} \) NMR Spectrum of \( \text{N-(1-(5\text{-ethoxy-3-methyl-1-phenyl-1}H\text{-pyrazol-4-yl})ethyl)aniline (3a)} \)
Fig. 4.6 HRMS Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)aniline (3a)

Fig. 4.7 $^1$H NMR Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-fluoroaniline (3b)
Fig. 4.8 $^{13}$C NMR Spectrum of $N$-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-fluoroaniline (3b)

Fig. 4.9 HRMS Spectrum of $N$-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-fluoroaniline (3b)
Fig. 4.10 $^1$H NMR Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-methylaniline (3c)

Fig. 4.11 $^{13}$C NMR Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-methylaniline (3c)
Fig. 4.12 HRMS Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)ethyl)-4-methylaniline (3c)

Fig. 4.13 HRMS Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)propyl)-4-methylaniline (3e)
Fig. 4.14 HRMS Spectrum of 4-chloro-N-(1-(5-ethoxy-3-methyl-1-phenyl-1\text{H}-pyrazol-4-yl)propyl)aniline (3f)

Fig. 4.15 HRMS Spectrum of N-(1-(5-ethoxy-3-methyl-1-phenyl-1\text{H}-pyrazol-4-yl)propyl)-4-fluoroaniline (3g)
Fig. 4.16 HRMS Spectrum of N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)ethyl)-4-fluoroaniline (3h)

Fig. 4.17 HRMS Spectrum of N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)propyl)aniline (3i)
Fig. 4.18 HRMS Spectrum of 4-chloro-N-(1-(5-ethoxy-3-methyl-1H-pyrazol-4-yl)propyl)aniline (3k)