Synthesis and Antimicrobial Studies of a New Series of **Bis**-Heterocycles

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**Abstract:** Series of novel **bis**-heterocycles bearing isoxazole and imidazole moieties have been synthesized via 1,3-dipolar cycloaddition reactions. $^1\text{HNMR}$, $^{13}\text{CNMR}$, IR and elemental analyses characterized the newly synthesized compounds. All the synthesized compounds were evaluated for their antimicrobial activity and were compared with the standard drugs. The compounds demonstrated potent to weak antimicrobial activity.

**Keywords:** **Bis**-Heterocycles; Antimicrobial activity; Chloramine-T.

**Introduction**

Among five membered heterocycles, isoxazole and imidazole are represents a class of compounds of great importance in biological chemistry. For instance, isoxazole possesses biological activities like$^{1,2}$ (insecticidal, antibacterial, antibiotic, antitumour, antifungal). Isoxazole also serves as anti-influenza virus activity$^3$, inhibition of human leukocyte elastase and cathepsin G$^4$. In fact, Valdecoxb a isoxazole derivative is now widely used in the market as anti-inflammatory drug$^5$. Imidazole derivatives are gaining synthetic interest in recent years due to their broad spectrum of biological activities like anti-inflammatory$^6$, analgesic$^7$, antibacterial$^8$ and antifungal$^9$. 2-**n**-Butyl-4-chloro-5-farnyl-imidazole is a key intermediate for the synthesis of Losartan a nonpeptide angiotensin antagonist, which is an orally active antihypertensive drug$^{10}$. Literature survey reveals that **bis**-heterocycles bearing isoxazole$^{11,12}$ was synthesized via 1,3-dipolar cycloaddition of aldoxime to divinyl ketone / sulfone using chloramine-T as dehydrating agent.

1,3-Dipolar cycloaddition reactions are useful tools for constructing biologically potent five membered heterocycles$^2$ and nitrile oxides serves as excellent 1,3-dipoles. Cycloaddition of nitrile oxide to olefinic compounds are of synthetic interest, since the product isoxazole obtained are the versatile intermediate for the synthesis of bifunctional
compounds. Nitrile oxides can be generated by dehydrogenation of aryl aldoximes with mercuric acetate, manganese dioxide, tert-butyl hypo chlorite, chloramine-T etc. In our laboratory Rai et al. extensively used chloramine-T for the generation of nitrile oxide and nitrile imine from aldoxime and aldehyde hydrazone respectively. With this background, it is considered worthwhile to prepare bis-heterocycles starting from 2-n-butyl-4-chloro(N-substituted)–imidazole-5-carbaldehyde and screen them for antimicrobial activity.

![Scheme 1](image)

**Experimental**

$^1$H NMR spectra were recorded on a Bruker AM 300 MHz spectrometer using CDCl$_3$ as solvent and tetramethylsilane as internal standard. $^{13}$C NMR spectra were measured on Jeol 400 (100MHz) instrument. The chemical shifts are expressed in $\delta$ and following abbreviations were used: s = singlet, d = doublet, t = triplet and m = multiplet. Infrared (IR) spectra were measured on Shimadzu 8300 spectrometer. Elemental analyses were obtained on a Vaio-EL instrument. Thinlayer chromatography (TLC) was done with pre-coated silica gel G plates using chloroform-acetone as eluent.

**Antimicrobial activity**

All the synthesized compounds were evaluated for antimicrobial activity by the disc diffusion method and microdilution method. Five bacteria and five fungal species were used as the antimicrobial test strains namely: *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas fluorescens*, *Xanthomonas campestris* pvs, *Xanthomonas oryzae*, *Aspergillus niger*, *Aspergillus flavus*, *Fusarium oxysporum*, *Trichoderma species*, *Fusarium and monaliforme*. *Streptomycin* and *tetracycline* were used as standard drugs against bacteria and *nystatin* was used against fungi. In all the determinations tests were performed in triplicate and the results were taken as a mean of at least three determinations.
Preparation of 4’-(2-Butyl-4-chloro-5-formyl-imidazol-1-ylmethyl-4,5-dimethoxy-benzene (2)

A mixture of 2-Butyl-5-chloro-3H-imidazole-4-carbaldehyde 1 (1.0 g, 5.37 mmol) and anhy. K$_2$CO$_3$ (0.90 g, 6.52 mmol) in dimethylformamide (10 mL) was stirred for 15 min at rt. Bromomethyl-4,5-dimethoxy-benzene (1.66 g, 5.35 mmol) was then added and the mixture was stirred at rt for 6 hr. After completion of the reaction (TLC toluene-ethylacetate; 7:3), the reaction mass was diluted with 25 mL water and the product was extracted with dichloromethane (25 mL). The extract was washed with water (10 mL) and then dried (Na$_2$SO$_4$), the solvent was evaporated and the remaining pale yellow oil was crystallized from ethanol to gave 2 as a white crystalline solid to yield 1.83 g (82%), m.p 86-87°C.

Synthesis of 4,5-dihydro-3-(substituted-imidazole)-5-phenylisoxazole (5a)

A mixture of substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4a (0.265 g, 2.55 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) in ethanol (20 mL) was warmed on a water bath for 2-3 hr. the progress of the reaction was monitored by TLC. After completion of the reaction the solvent was evaporated in vacuum. The residual mass was extracted into ether (25 mL), washed successively with water (2 x 20 mL), 5% NaOH (1x10 mL), brine solution (2 x 15 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent afforded crude oily substance, which was purified by column chromatography using chloroform-acetone (9:1) as eluent to gave the product as yellow solid (0.94 g, 69% yield), m.p.124-126°C.

4,5-Dihydro-3-(substituted-imidazole)-5-methyl-5-phenylisoxazole (5b)

Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4b (0.30 g, 2.55 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow solid (0.99 g, 71% yield), and m.p.130-132°C.

4,5-Dihydro-3-(substituted-imidazole)isoxazole-5-carbonitrile (5c)

Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4c (0.135 g, 2.55 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow oil (0.78 g, 62% yield).

5-(Chloromethyl)-4,5-dihydro-3-(substituted-imidazole)isoxazole (5d)

Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4d (0.194 g, 2.57 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow solid (0.84 g, 65% yield), m.p.138-140°C.

5-(Bromomethyl)-4,5-dihydro-3-(substituted-imidazole)isoxazole (5e)

Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4e (0.31 g, 2.56 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow solid (1.02 g, 73% yield), and m.p.144-146°C.

(4,5-Dihydro-3-(substituted-imidazole)isoxazol-5-yl)methanol (5f)

Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4f (0.148 g, 2.55 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow oil (0.78 g, 63% yield).

4,5-Dihydro-3-(substituted-imidazole)isoxazole-5-yl acetate (5g)

Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4g (0.22 g, 2.55 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow solid (1.0 g, 76% yield), m.p.148-150°C.
4,5-Dihydro-3-(substituted-imidazole)isoazole-5-yl propionate (5h)
Obtained from substituted-imidazole aldoxime 3 (1.0 g, 2.55 mmol), 4h (0.255 g, 2.55 mmol) and chloramine-T trihydrate (0.72 g, 2.56 mmol) as yellow solid (1.05 g, 78% yield), m.p.158-160 °C.

Results and Discussion
The general synthetic pathway discussed hereafter is depicted in Scheme. Compound 1 was alkylated using bromomethyl-4,5-dimethoxy benzene and potassium carbonate in DMF. Then formyl function of 2 was converted into the aldoxime 3. When oxidative dehydrogenation of 3 by chloramine-T (CAT) afforded nitrile oxide, which was in situ trapped by the different olefins 4 (a-h) under refluxing condition in ethanol. Thus produced compound was identified by NMR spectroscopy as 4,5-dihydro-3-(substituted-imidazole)-5-substituted-isoxazole 5 (a-h) in good quality and yield. The starting substrate 2-n-butyl-4-chloro-(N-substituted)-imidazole-5-carbaldehyde 1 was prepared according to literature procedure.20 Compound 3 was prepared by standard procedure21.

Antimicrobial activity
Antimicrobial activity of all the compounds was shown in Table 1 and 2. Among the series of synthesized compounds, 5d and 5e shown better inhibition. Remaining compounds shown moderate inhibition. The better inhibition shown by 5d and 5e may be due to the presence of chloro and bromo group in the compound.

Table 1. Minimal inhibitory concentration in µg mL\(^{-1}\)[X] and Inhibitory zone in (diameter) mm [Y] of the synthesized compounds against tested bacterial strains by micro dilution method and disc diffusion method respectively

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bacillus substilis</th>
<th>Escherichia coli</th>
<th>Pseudomonas fluorescens</th>
<th>Xanthomonas campestris pvs</th>
<th>Xanthomonas oryzae</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>21 07 26 13</td>
<td>23 16 25 12</td>
<td>23 12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5b</td>
<td>22 11 26 08</td>
<td>23 10 25 07</td>
<td>21 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5c</td>
<td>19 10 17 11</td>
<td>20 13 19 10</td>
<td>23 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5d</td>
<td>17 14 14 12</td>
<td>13 15 11 09</td>
<td>15 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5e</td>
<td>18 10 15 12</td>
<td>15 13 12 10</td>
<td>15 09</td>
<td></td>
<td></td>
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<td>23 10 25 07</td>
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<tr>
<td>5g</td>
<td>21 07 26 13</td>
<td>23 16 25 12</td>
<td>23 12</td>
<td></td>
<td></td>
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<tr>
<td>5h</td>
<td>22 10 21 11</td>
<td>25 14 22 11</td>
<td>24 11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>19 13 13 14</td>
<td>12 17 -   -</td>
<td>- -</td>
<td>- -</td>
<td></td>
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<tr>
<td>Tetracycline</td>
<td>- - - - -</td>
<td>- - - - -</td>
<td>09 12</td>
<td>13 12</td>
<td></td>
</tr>
</tbody>
</table>

Streptomycin sulfate (25 µg per disc); Tetracycline (25 µg per disc) were used as positive reference standard antibacterial discs, Synthesized compounds (25 µg per disc).
Table 2. Minimal inhibitory concentration in µg mL⁻¹ [X] and Inhibitory zone in (diameter) mm [Y] of the synthesized compounds against tested fungal strains by micro dilution method and disk diffusion method respectively

<table>
<thead>
<tr>
<th>Compound</th>
<th>Aspergillus niger</th>
<th>Aspergillus flavus</th>
<th>Fusarium oxysporium</th>
<th>Trichoderma species</th>
<th>Fusarium monalifome</th>
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<tbody>
<tr>
<td></td>
<td>X Y mm</td>
<td>X Y mm</td>
<td>X Y mm</td>
<td>X Y mm</td>
<td>X Y mm</td>
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<tr>
<td>5a</td>
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<td>18 09</td>
<td>14 12</td>
<td>15 14</td>
<td>14 11</td>
</tr>
<tr>
<td>5b</td>
<td>19 07</td>
<td>18 11</td>
<td>17 12</td>
<td>15 09</td>
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</tr>
<tr>
<td>5c</td>
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<td>16 13</td>
<td>13 13</td>
<td>14 15</td>
<td>11 11</td>
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<tr>
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<td>12 10</td>
<td>16 11</td>
<td>10 14</td>
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<tr>
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<td>15 11</td>
<td>13 14</td>
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<td>10 12</td>
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<tr>
<td>5f</td>
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<td>18 11</td>
<td>17 12</td>
<td>15 09</td>
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<tr>
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<td>17 07</td>
<td>16 15</td>
<td>16 13</td>
<td>13 10</td>
<td></td>
</tr>
<tr>
<td>5h</td>
<td>20 06</td>
<td>17 16</td>
<td>18 11</td>
<td>14 08</td>
<td></td>
</tr>
<tr>
<td>Nystatin</td>
<td>15 08</td>
<td>15 10</td>
<td>11 14</td>
<td>12 16</td>
<td>09 12</td>
</tr>
</tbody>
</table>

Nystatin (25 µg per disc) was used as positive reference standard antifungal discs, Synthesized compounds (25 µg per disc).

Spectral data of the compounds

**Compound 2**: ¹H NMR CDCl₃; δ 0.94 (t, 3H, CH₃), 1.32 (m, 2H, CH₂), 2.61 (t, 2H, CH₂), 3.64 (s, 6H, OCH₃) 4.86 (s, 2H, CH₂), 6.45 (s, 1H, ArH), 6.82 (s, 1H, ArH), 9.50 (s, 1H, CH), ¹³C NMR CDCl₃: δ 13.9 (C), 23.2 (C), 24.5 (C), 33.1 (C), 33.9 (C), 57.5 (2C), 116.1 (C), 117.6 (C), 118.2 (C), 134.2 (C), 136.6 (C), 140.9 (C), 147.2 (C), 148.4 (C), 156.2 (C), 189.2 (C). IR (KBr pellets cm⁻¹) v 3069, 2961, 1764, 1667, 1485. Anal.Calcd. For C₁₇H₂₀BrClN₂O₃: C, 49.12, H, 4.85, N, 6.74%. Found: C, 49.19, H, 4.87, N 6.70 %.

**Compound 5a**: ¹H NMR CDCl₃; δ 0.97 (t, 3H, CH₃), 1.35 (m, 2H, CH₂), 1.64 (m, 2H, CH₂), 2.57 (t, 2H, CH₂), 3.21 (dd, 1H, J =8.2, 4-H), 3.28 (dd, 2H, J =8.2, 4-H), 3.74 (s, 6H, OCH₃), 5.02 (s, 2H, CH₂), 5.02 (dd, 1H, J=4.0, 5-H), 6.42 (s, 1H, ArH), 6.78 (s, 1H, ArH), 7.21 (m, 5H, ArH), ¹³C NMR CDCl₃: δ 14.2 (C), 23.0 (C), 25.7 (C), 33.4 (C), 34.8 (C), 41.6 (C), 56.3 (2C), 81.1 (C), 116.3 (C), 117.7 (C), 118.5 (C), 122.2 (C), 126.2 (C), 127.2 (2C), 127.8 (C), 128.9 (2C), 134.5 (C), 140.7 (C), 148.0 (C), 148.7 (C), 149.0 (C), 164.7 (C). Anal.Calcd. For C₂₅H₂₇BrClN₃O₃: C, 56.35; H, 5.11; N, 7.89; Found: C, 56.37; H, 5.13; N, 7.87 %.

**Compound (5b)**: ¹H NMR CDCl₃; δ 0.95 (t, 3H, CH₃), 1.35 (m, 2H, CH₂), 2.61 (m, 2H, CH₂), 3.18 (s, 2H, 4-CH₂), 3.74 (s, 6H, OCH₃), 5.02 (s, 2H, CH₂), 5.02 (dd, 1H, J=8.0, 4-H), 5.02 (s, 1H, CH₃), ¹³C NMR CDCl₃: δ 14.2 (C), 23.1 (C), 25.6 (C), 29.7 (C), 33.5 (C), 37.7 (C), 56.3 (2C), 87.1 (C), 116.3 (C), 117.5 (C), 118.6 (C), 122.2 (C), 126.1 (2C), 126.2 (2C), 126.4 (C), 128.5 (2C), 134.3 (C), 148.2 (C), 148.7 (C), 149.0 (C), 150.1 (C), 164.6 (C). Anal.Calcd. For C₂₅H₂₇BrClN₃O₃: C, 57.10; H, 5.11; N, 7.89; Found: C, 56.37; H, 5.13; N, 7.87 %.

**Compound (5c)**: ¹H NMR CDCl₃; δ 0.94 (t, 3H, CH₃), 1.32 (m, 2H, CH₂), 1.60 (m, 2H, CH₂), 3.42 (dd, 1H, J=8.0, 4-H), 3.49 (dd, 2H, J=8.0, 4-H), 3.79 (s, 6H, OCH₃), 4.96 (s, 2H, CH₂), 5.24 (dd, 1H, J=4.0, 5-H), 6.34 (s, 1H, ArH), 6.70 (s, 1H, ArH), ¹³C NMR CDCl₃: δ 14.2 (C), 23.0 (C), 25.7 (C), 33.4 (C), 33.7 (C), 40.8 (C), 56.3 (2C), 68.8
(C), 116.4 (C), 117.4 (C), 118.2 (C), 118.6 (C), 122.1 (C), 126.7 (C), 134.5 (C), 148.2 (C), 148.6 (C), 149.1 (C), 164.7 (C). Anal. Calcd. For C_{19}H_{25}BrClN_{2}O_{3}; C, 49.86; H, 4.60; N, 11.63; Found: C, 49.89, H, 4.67, N, 11.53 %.

**Compound (5d):** ¹H NMR CDCl₃: δ 0.97 (t, 3H, CH₃), 1.34 (m, 2H, CH₂), 1.64 (m, 2H, CH₂), 2.56 (t, 2H, CH₂), 3.38 (dd, 1H, J=8.4, 4-H), 3.42 (dd, 2H, J=8.4, 4-H), 3.46 (dd, 1H, J=7.6, CH₂Cl), 3.69 (dd, 1H, J=7.6, CH₂Cl), 3.75 (s, 6H, OCH₃), 5.02 (s, 2H, CH₂), 5.12 (m, 1H, 5-H), 6.40 (s, 1H, ArH), 6.78 (s, 1H, ArH). ¹³C NMR CDCl₃: δ 14.1 (C), 22.8 (C), 25.5 (C), 33.4 (C), 33.7 (C), 37.8 (C), 51.8 (C), 56.2 (2C), 69.8 (C), 116.4 (C), 117.5 (C), 118.6 (C), 121.9 (C), 126.2 (C), 134.5 (C), 148.1 (C), 148.6 (C), 149.1 (C), 164.7 (C). Anal. Calcd. For C_{19}H_{23}BrClN_{2}O_{3}; C, 47.55; H, 4.78; N, 8.32; Found: C, 47.53, H, 4.78, N, 8.35 %.

**Compound (5e):** ¹H NMR CDCl₃: δ 0.95 (t, 3H, CH₃), 1.33 (m, 2H, CH₂), 1.62 (m, 2H, CH₂), 2.55 (t, 2H, CH₂), 3.35 (dd, 1H, J=8.4, 4-H), 3.40 (dd, 2H, J=8.4, 4-H), 3.44 (dd, 1H, J=7.2, CH₂Br), 3.64 (dd, 1H, J=7.2, CH₂Br), 3.73 (s, 6H, OCH₃), 5.00 (s, 2H, CH₂), 5.04 (m, 1H, 5-H), 6.38 (s, 1H, ArH), 6.75 (s, 1H, ArH). ¹³C NMR CDCl₃: δ 14.3 (C), 22.8 (C), 25.6 (C), 33.6 (C), 33.8 (C), 38.8 (C), 41.0 (C), 56.4 (2C), 70.9 (C), 116.4 (C), 117.4 (C), 118.7 (C), 122.2 (C), 126.3 (C), 134.4 (C), 148.2 (C), 148.8 (C), 149.1 (C), 164.7 (C). Anal. Calcd. For C_{19}H_{25}BrClN_{2}O_{3}; C, 43.70; H, 4.40; N, 7.64; Found: C, 43.71, H, 4.42, N, 7.62 %.

**Compound (5f):** ¹H NMR CDCl₃: δ 0.97 (t, 3H, CH₃), 1.34 (m, 2H, CH₂), 1.63 (m, 2H, CH₂), 2.32 (dd, 1H, OH), 2.57 (t, 2H, CH₂), 3.28 (dd, 1H, J=8.0, 4-H), 3.34 (dd, 1H, J=8.0, 4-H), 3.52-3.79 (m, 2H, CH₂), 3.74 (s, 6H, OCH₃), 4.98 (s, 2H, CH₂), 5.04 (m, 1H, 5-H), 6.41 (s, 1H, ArH), 6.77 (s, 1H, ArH). ¹³C NMR CDCl₃: δ 14.2 (C), 23.0 (C), 25.7 (C), 33.5 (C), 33.8 (C), 36.8 (C), 56.3 (2C), 70.6 (C), 77.5 (C), 116.3 (C), 117.4 (C), 118.4 (C), 121.9 (C), 126.2 (C), 134.5 (C), 148.1 (C), 148.7 (C), 149.0 (C), 164.7 (C). Anal. Calcd. For C_{19}H_{25}BrClN_{2}O_{3}; C, 49.35; H, 5.18; N, 8.63; Found: C, 49.33, H, 5.19, N, 8.64 %.

**Compound (5g):** ¹H NMR CDCl₃: δ 0.94 (t, 3H, CH₃), 1.35 (m, 2H, CH₂), 1.64 (m, 2H, CH₂), 2.04 (s, 3H, CH₃), 2.57 (t, 2H, CH₂), 3.30 (dd, 1H, J=8.2, 4-H), 3.37 (dd, 1H, J=8.2, 4-H), 3.78 (s, 6H, OCH₃), 5.02 (s, 2H, CH₂), 5.68 (dd, 1H, J=3.8, 5-H), 6.39 (s, 1H, ArH), 6.77 (s, 1H, ArH). ¹³C NMR CDCl₃: δ 14.3 (C), 21.1 (C), 23.0 (C), 25.6 (C), 33.4 (C), 33.8 (C), 56.3 (2C), 69.5 (C), 96.3 (C), 116.3 (C), 117.5 (C), 118.6 (C), 121.9 (C), 126.2 (C), 134.4 (C), 148.0 (C), 148.6 (C), 149.1 (C), 164.6 (C), 170.4 (C). Anal. Calcd. For C_{19}H_{25}BrClN_{2}O_{3}; C, 48.99; H, 4.89; N, 8.16; Found: C, 48.99, H, 4.88, N, 8.17 %.

**Compound (5h):** ¹H NMR CDCl₃: δ 0.95 (t, 3H, CH₃), 1.13 (t, 3H, CH₃), 1.33 (m, 2H, CH₂), 1.64 (m, 2H, CH₂), 2.28 (q, 2H, CH₂), 3.34 (t, 2H, CH₂), 3.31 (dd, 1H, J=8.0, 4-H), 3.38 (dd, 1H, J=8.0, 4-H), 3.75 (s, 6H, OCH₃), 4.99 (s, 2H, CH₂), 5.66 (dd, 1H, J=4.0, 5-H), 6.35 (s, 1H, ArH), 6.74 (s, 1H, ArH). ¹³C NMR CDCl₃: δ 9.5 (C), 14.1 (C), 22.8 (C), 25.6 (C), 30.1 (C), 33.4 (C), 33.7 (C), 56.3 (2C), 69.4 (C), 96.5 (C), 116.4 (C), 117.4 (C), 118.4 (C), 122.0 (C), 126.3 (C), 134.3 (C), 148.0 (C), 148.7 (C), 149.1 (C), 164.5 (C), 173.4 (C). Anal. Calcd. For C_{22}H_{27}BrClN_{2}O_{3}; C, 49.97; H, 5.15; N, 7.95; Found: C, 49.99, H, 5.13, N, 7.93 %.

**References**

2. Caramella P and Gruinger P in 1,3-Dipolar Cycloaddition Chemistry, vol 1, Edited by Padwa A (wiley interscience, New york) 1984, 337.
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