One–pot Strategy of Copper-catalyzed Synthesis of 1,2-Disubstituted Benzimidazoles

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1. Preparation of starting materials

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\begin{align*}
\text{NH}_2 & \quad \text{Br} \quad \text{R}_2 \\
\text{X} & \quad \text{NaHCO}_3 \\
\text{DMF, 50 °C} & \quad \text{R}_1 \\
\end{align*}
\]

Scheme 1

\(N\)-benzyl-2-halogen anilines were prepared according to a modified literature procedure.\(^1\) An oven-dried flask was charged with compounds A (5 mmol), the corresponding benzyl bromide B (6 mmol), NaHCO\(_3\) (10 mmol), and DMF (15 mL). The mixture was stirred at 50 °C until complete consumption of starting material was indicated by TLC. Then the mixture was cooled to room temperature and quenched with Brine and the organic layer extracted with ethyl acetate. The combined extracts were washed with brine and dried over Na\(_2\)SO\(_4\), concentrated under reduced pressure and purified by column chromatography to afford the pure product 1.

2. \(^1\)H NMR, \(^{13}\)C NMR and HRMS spectra

1-Benzyl-2-phenyl-1H-benzo[d]imidazole (3a).
1-Benzyl-5-chloro-2-phenyl-1H-benzo[d]imidazole (3b)
1-Benzyl-5-fluoro-2-phenyl-1H-benzo[d]imidazole (3c)
1-Benzyl-2-phenyl-5-(trifluoromethyl)-1H-benzo[d]imidazole (3d)
1-Benzyl-6-chloro-2-phenyl-1\textit{H}-benzo[\textit{d}]imidazole (3e)
1-Benzyl-5-methyl-2-phenyl-1H-benzo[d]imidazole (3f)
1-Benzyl-6-methyl-2-phenyl-1H-benzo[d]imidazole (3g).
1-Benzyl-5-bromo-2-phenyl-1H-benzo[d]imidazole (3h)
1-Benzyl-2-phenyl-1H-benzo[d]imidazole-5-carbonitrile (3i)
1-(4-Methylbenzyl)-2-phenyl-1\textit{H}-benzo[\textit{d}]imidazole (3j)
1-(3-Methylbenzyl)-2-phenyl-1H-benzo[d]imidazole (3k)
1-(4-(Tert-butyl)benzyl)-2-phenyl-1H-benzo[d]imidazole (3l)
1-(3-Fluorobenzyl)-2-phenyl-1H-benzo[d]imidazole (3m)
1-(2-Fluorobenzyl)-2-phenyl-1H-benzo[d]imidazole (3n)
1-(3-Chlorobenzyl)-2-phenyl-1H-benzo[d]imidazole (3o)
1-(4-Bromobenzyl)-2-phenyl-1H-benzo[d]imidazole (3p)
1-(Naphthalen-2-ylmethyl)-2-phenyl-1H-benzo[d]imidazole (3q)
1-([1,1'-Biphenyl]-4-ylmethyl)-2-phenyl-1H-benzo[d]imidazole (3r)
1-Hexyl-2-phenyl-1H-benzo[d]imidazole (3s)
1-(3-Methylbut-2-en-1-yl)-2-phenyl-1H-benzo[d]imidazole (3t)
5-Chloro-1-(3-chlorobenzyl)-2-phenyl-1H-benzo[d]imidazole (3u)
1-Benzyl-2-(p-tolyl)-1H-benzo[d]imidazole(3v)
1-Benzyl-2-(4-methoxyphenyl)-1H-benzo[d]imidazole (3w)
1-Benzyl-2-(4-chlorophenyl)-1H-benzo[d]imidazole (3x)
1-Benzyl-2-(4-fluorophenyl)-1H-benzo[d]imidazole (3y)
1-Benzyl-2-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazole (3z).
1-Benzyl-2-(3-chlorophenyl)-1H-benzo[d]imidazole (3aa).
1-Benzyl-2-(3-fluorophenyl)-1H-benzo[d]imidazole (3ab).
1-Benzyl-2-(thiophen-2-yl)-1H-benzo[\textit{d}]imidazole (3ac)
1-Benzyl-1H-benzo[d]imidazole (3ad)
1-Benzyl-2-methyl-1H-benzo[d]imidazole (3ae)
1-Benzyl-2-ethyl-1H-benzo[d]imidazole (3af)
2-(4-Fluorophenyl)-1-(naphthalen-2-ylmethyl)-1H-benzo[d]imidazole (3qa)
2-(4-Chlorophenyl)-1-(naphthalen-2-ylmethyl)-1H-benzo[d]imidazole (3qb)
2-(4-Methoxyphenyl)-1-(naphthalen-2-ylmethyl)-1H-benzo[d]imidazole (3qc)
1-([1,1’-Biphenyl]-4-ylmethyl)-2-(4-fluorophenyl)-1H-benzo[d]imidazole (3ra)
1-([1,1'-Biphenyl]-4-ylmethyl)-2-(4-chlorophenyl)-1H-benzo[d]imidazole (3rb)
1-[(1,1'-Biphenyl)-4-ylmethyl]-2-(4-methoxyphenyl)-1H-benzo[d]imidazole (3rc)
3. References