CHAPTER-VII

A competent pot and atom efficient three component synthesis of 1-(α-aminoalkyl) naphthols (Betti bases) catalyzed by high surface area nanoporous MgO in aqueous media
INTRODUCTION

In this section the synthesis of α-aminoalkyl naphthols, commonly known as Betti bases has been discussed catalyzed over nanocrystalline MgO in aqueous conditions at room temperature.

![General structure of a Betti base](image)

Importance of Betti bases

Compounds bearing 1,3 arrangements of amino and oxygenated functional groups are frequently found in various biologically active natural products. The importance lies in their ability to bind Lewis acidic sites making a stable 6 membered ring. The 1-(α-aminoalkyl)-2-naphthols, the ‘so-called’ Betti bases belong to this class of compounds. These can be transformed into derivatives which exhibit antibacterial, hypotensive and bradycardiac activity. The phenolic hydroxyl and amino groups can be utilized in developing several synthetic building blocks. Optically active Betti bases can be used as ligands to chelate with organometallic reagents in different reactions to provide highly efficient asymmetric induction. Reaction of Betti bases with aldehydes produces 1,3-oxazines, an important biologically active scaffold.
A brief review on the synthesis of Betti bases

The classical synthesis of Betti bases generally involves a modified Mannich pathway by the condensation of 2-naphthol, aldehydes and ammonia. However, modifications have been made to prepare Betti base derivatives by using other naphthols, quillins, different aldehydes and alkyl or aryl amines replacing ammonia. A brief review on the synthesis of these aminoalkyl naphthols has been highlighted.

Ghandi et al\(^7\) reported the uncatalyzed one-pot, three-component reaction of 2-naphthol, aromatic aldehyde and heteroaryl amine in water at room temperature leading to the formation of the corresponding aminonaphthols (Betti bases). Variety of heteroaryl amines reacted with different aldehydes in water in very short time (25-50 min) generating excellent yields of the products (Scheme 1).

![Scheme 1](image)

Recently Kumar and his co workers\(^8\) developed an efficient non-ionic surfactant (Triton X-100) catalyzed multicomponent synthesis of Betti base from secondary amines, aromatic aldehydes, and \(\beta\)-naphthol using Mannich-type reaction in water. The reaction proceeds through initial imine formation, which is stabilized by colloidal dispersion of the surfactant and undergoes nucleophilic addition to afford the corresponding \(\text{N}_2\text{N}\)-dialkylated Betti base in excellent yields (Scheme 2).
Synthesis of Betti bases was carried out by Cardellicchio et al.\textsuperscript{9} in ethanol at room temperature by condensing benzaldehyde, ammonia/alkylamine and 2-naphthol without using any catalyst (Scheme 3). However it took 6 days to provide good yields of the products. In these reactions the Betti bases were used as a chiral auxiliary for the enantioselective addition of diethylzinc to different aldehydes.

Ammonium carbamate and ammonium hydrogen carbonate were used as very effective solid ammonia sources by Fulop and Szatmari\textsuperscript{10} to prepare different α-aminoalkynaphthols and α-aminoalkylquinolinols in ethanol and water as solvents under microwave irradiation. The products were obtained in excellent yields in one-pot three-component Mannich reactions (Scheme 4). Variety of aromatic and aliphatic aldehydes including heteroaryl aldehydes were used in the reaction.
Enantiopure 2-aminoalkylphenol derivatives, an interesting class of compounds, were synthesized by Cimarelli et al.\textsuperscript{11} applying practical and convenient methods for the determination of their configuration (Scheme 5). The uses of these compounds in metal catalysed asymmetric reactions in the addition of dialkyl zinc reagents to aldehydes and in the reduction of ketones with borane have been described.

Cameron and his co-workers\textsuperscript{12} carried out a novel two-step procedure involving the formation of 1-arylidene-2-tetralones from 2-tetralone and subsequent Michael addition of a cyclic secondary amine with an alkenone to produce the Betti bases. The three component reaction was performed under solventless and microwave condition catalyzed by PTSA. The reaction was complete within 1 min (Scheme 6).
A diastereoselective Yb(OTf)₃ catalyzed three-component synthesis of chiral aminoalkyl α-naphthols/phenols from an electron-rich α-naphthol/phenol, an amine, and a chiral α-Ν,Ν-dibenzylamino aldehyde was developed by Zhu et al.¹³. The diastereoselectivity of this Mannich reaction was temperature-dependent, and either anti or syn diastereomer could be prepared by controlling the reaction conditions (Scheme 7). Low reaction temperature (–20 °C) favored the predominate formation of anti adduct, whereas at higher temperature (60 °C) the syn isomer was the major product.

An organocatalytic enantioselective Friedel–Crafts reaction of α-naphthols with preformed aldimes leading to the formation of Betti base derivatives was developed by Wang et al.¹⁴ The method afforded a direct access to chiral aminoarylnaphthols in good yields and with good to high enantioselectivities (Scheme 8).
A procedure was reported by Xiong for the facile synthesis of bis-Betti bases with two chiral carbon centers. Coupling of 1 equiv of 2,6-dihydroxynaphthalene with 2 equiv of piperidine or morpholine and cyanobenzaldehyde at 100 °C produced the bis analog in good yield (Scheme 9). The reaction involved two sequential Betti reactions.

A procedure that could be considered as an extended Betti reaction was reported by Li et al. They reacted 2-naphthol with 3,4-dihydroisoquinoline, a cyclic imine molecule, thus forming 1-naphthoyl tetrahydroisoquinolines. The reaction involved an aza-Friedel Craft reaction under neat and heating condition (Scheme 10).
The diastereoselective synthesis of aminonaphthols from chiral aldehydes was reported by Palmieri et al (Scheme 11).¹⁷ The reaction occurred by treating 2-naphthol with primary or secondary amines and chiral aldehydes at room temperature in the absence of any solvents to afford the products in good yield.

Mukhopadhyay and her group¹⁸ developed an atom-economic methodology for the multi-component one-pot synthesis of (quinolinyl- and isoquinolinyl- amino) alkyl naphthols and their bis- analogs employing the ionic liquid [][bmim][Br] as a “dual reagent catalysis” at 25 °C. The approach possesses several advantages such as excellent yields, lower reaction times, mild reaction conditions, recyclability and easy purification processes (Scheme 12).
A different approach was proposed by Saidi et al\textsuperscript{19} in the preparation of aza analog of Betti bases. They coupled electron rich aromatic compounds with different aldehydes and trimethylsilyl dialkylamine as the amine source catalyzed over LiClO\textsubscript{4} in diethyl ether (Scheme 13). The Mannich type reaction occurred at room temperature affording good yield of the products.

\begin{center}
\textbf{Scheme 13}
\end{center}

Katritzky and his group\textsuperscript{20} developed a method for the preparation of Betti base analogs using \(N\)-[\(\alpha\)-amino(hetero)arylmethyl]benzotriazoles derived from a variety of (hetero)aromatic aldehydes. These were reacted with sodium phenolates to afford amino(hetero)arylmethylated phenols in high yields. In refluxing toluene 18-crown-6 was used as a promoter (Scheme 14).

\begin{center}
\textbf{Scheme 14}
\end{center}
"A competent pot and atom efficient three component synthesis of l-(α-aminoalkyl) naphthols (Betti bases) catalyzed by high surface area nanoporous MgO in aqueous media"

➤ RESULTS AND DISCUSSION
The candidate's synthesis of Betti bases involved a very simple procedure. A three component coupling involving 2-naphthol, an aldehyde and an amine in water catalyzed over nanocrystalline MgO at room temperature generated the α-aminoalkynaphthol derivatives, the 'so called' Betti bases.

➤ Advantage of the process
Betti bases are very important molecules in the asymmetric synthesis arena. These molecules and their derivatives have been used as chiral auxiliary in several chiral syntheses. So, their synthesis in an operationally simple and benign method has become important in recent years. Unfortunately, there has not been much effort for the synthesis of Betti bases using heterogeneously catalysts in an environmental friendly media. This is the first report for the application of nanocrystalline MgO in the synthesis of Betti bases. The main advantages of the processes developed by the candidate are, i) very fast reaction due to significant rate acceleration by nanocrystalline and high surface area MgO, ii) uses water as reaction media which is considered as a green solvent, iii) room temperature synthesis, iv) no need for creating an inert atmosphere and v) recyclability of the catalyst.
Physical characterization of nanocrystalline MgO

Nanocrystalline MgO has a polyhedral crystalline structure containing a number of anionic oxide Lewis basic (O²⁻, O¹⁻) and hydroxyl Bronsted base (OH) sites along with Mg²⁺ as Lewis acid site (Fig. 7.1). Moreover, the high surface concentrations of edge/corner and various exposed crystal planes, leads to inherently high surface reactivity per unit area.

![Diagram of Reactive sites of nano MgO](image)

Fig. 7.1. Reactive sites of nano MgO

Nanocrystalline MgO was synthesized by a non-hydrothermal sol-gel approach involving a new method of synthesis for the porous and high surface area metal oxides. The material thus synthesized was characterized by SEM, TEM and X-ray diffraction study. Fig. 7.2A and 7.2B depicts the SEM image. The external morphology of the material is clearly evident from image 7.2A. 7.2B represents the highly porous structure of the nano MgO. The pores seem to be of uniform size. This high porosity is responsible for the high surface area. TEM analysis of the sample represents a clearer and closer view (Fig. 7.3). The particles are crystalline in nature and particle sizes range between 20-22 nm. X-ray powder diffraction analysis satisfies the overview (Fig. 7.4). The crystalline nature of the nanocatalyst is also evident from the peaks arising due to reflection at various exposed crystal planes (such as 002, 001 and 111) which is in close agreement with face centered cubic (fcc) MgO. With the application of Sherrer’s formula the crystallite sizes have been determined. Calculations using the FWHM values reveal the particle size to be 18-28 nm which is in close agreement with the TEM data.
Fig. 7.2. (A and B). Scanning Electron Micrograph (SEM) of nano MgO.
Fig. 7.3. Transmission Electron Micrograph (TEM) of nano MgO.

Fig. 7.4. X-ray Diffraction Study of nano MgO.
Optimization of reaction conditions

Feasibility of the reaction conditions were investigated by selecting a probe reaction involving the coupling of 2-naphthol, benzaldehyde and pyrrolidine. Optimization was done with variation of the reaction medium. The results have been summarized in Table 1. The difference in results indicated the influence of solvent on the reaction. Different conventional organic solvents like tetrahydrofuran, acetonitrile, dichloromethane and toluene afforded low to moderate yields (33-72%). In hexane no reaction was observed. The best result was achieved in aqueous condition when it furnished the coupled product in high yield (88%). The reaction failed in the absence of any catalyst. Optimization of catalysts was done by comparison of catalytic activity of bulk MgO, conventionally prepared MgO by heating MgCO₃ at high temperature and nanocrystalline MgO. The best result was achieved using nano MgO due to its high surface area and larger number of active sites. Notably, there was no need for creating an inert atmosphere and the reactions were carried out under ambient conditions only.

Table 1. Screening of solvents in the synthesis of Betti bases*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tetrahydrofuran</td>
<td>8</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>Acetonitrile</td>
<td>8</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>Dichloromethane</td>
<td>8</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>12</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>Hexane</td>
<td>12</td>
<td>n.r.</td>
</tr>
<tr>
<td>6</td>
<td>Water</td>
<td>2</td>
<td>88</td>
</tr>
</tbody>
</table>

*Reaction conditions: Benzaldehyde: pyrrolidine: 2-naphthol = 1:2: 1.0: 1.0, 50 mg catalyst, room temperature; isolated yield after purification.
In order to study the scope and limitations of this procedure, a series of reactions were carried out with 2-naphthol using variety of aromatic aldehydes and aliphatic amines. The results have been shown in Table 2. The reactions worked well with almost all the aldehydes. However aromatic aldehydes bearing groups like -NO$_2$, -CN and -Cl showed better reactivity due to their electron withdrawing effect and the reactions were completed in shorter time. Reaction of methoxyl aldehydes also showed very good result. Even the heteroaryl aldehyde, 2-furfural, afforded the desired product in high yield.

The reactions were studied with a variety of aliphatic amines like pyrrolidine, piperidine, morpholine, butylamine and benzylamine. Excellent reactivity was observed with different aldehydes and 2-naphthol resulting in good yields. Surprisingly, the reaction was not successful with aromatic amines which might be due to its reduced nucleophilicity. Similarly, proline also failed to produce the corresponding Betti base. After the reaction, the crude reaction mixtures were purified through column chromatography using neutral alumina and appropriate mixtures of EtOAc/Hexane as eluents. The isolated products were then characterized from $^1$H NMR, $^{13}$C NMR, IR spectrometry and elemental analysis.
Table 2. Synthesis of Betti bases over nanocrystalline MgO catalyst*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>Amine</th>
<th>Product</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH$_2$CHO</td>
<td>U</td>
<td>4a</td>
<td>2.0</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>CH$_2$CHO</td>
<td>H</td>
<td>4b</td>
<td>3.0</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>CH$_2$CHO</td>
<td>NH</td>
<td>4c</td>
<td>2.5</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>CH$_2$CHO</td>
<td>CH$_2$NH$_2$</td>
<td>4d</td>
<td>3.5</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>CH$_2$CHO</td>
<td>CH$_2$NH$_2$</td>
<td>4e</td>
<td>3.0</td>
<td>78</td>
</tr>
<tr>
<td>6</td>
<td>CH$_2$CHO</td>
<td>CH$_2$NH$_2$</td>
<td>4f</td>
<td>3.0</td>
<td>81</td>
</tr>
<tr>
<td>7</td>
<td>CH$_2$CHO</td>
<td>CH$_2$NH$_2$</td>
<td>4g</td>
<td>2.5</td>
<td>87</td>
</tr>
<tr>
<td>8</td>
<td>MeCH$_2$CHO</td>
<td>U</td>
<td>4h</td>
<td>3.5</td>
<td>84</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4i</td>
<td>3.0</td>
<td>88</td>
</tr>
<tr>
<td>10</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4j</td>
<td>2.0</td>
<td>92</td>
</tr>
<tr>
<td>11</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4k</td>
<td>4.0</td>
<td>86</td>
</tr>
<tr>
<td>12</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4l</td>
<td>3.5</td>
<td>82</td>
</tr>
<tr>
<td>13</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4m</td>
<td>3.0</td>
<td>85</td>
</tr>
<tr>
<td>14</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4n</td>
<td>2.0</td>
<td>90</td>
</tr>
<tr>
<td>15</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4o</td>
<td>3.0</td>
<td>88</td>
</tr>
<tr>
<td>16</td>
<td><img src="" alt="Chemical Structure" /></td>
<td><img src="" alt="Chemical Structure" /></td>
<td>4p</td>
<td>3.0</td>
<td>89</td>
</tr>
</tbody>
</table>
Mechanistic study of the reaction

At high temperature calcination (600 °C) the nanocrystalline MgO catalyst contains large number of anionic oxide Lewis basic (O$^{2-}$, O$^-$) along with hydroxylic Bronsted basic (OH) sites and few number of Lewis acidic Mg$^{2+}$ ions. As a result the catalyst is highly alkaline in nature. The enhanced surface area due to small particle size is an added advantage for its reactivity. All these important factors are responsible for the high accessibility of the substrate molecules on the catalyst surface. The reaction involves the initial formation of imines by condensation of aldehydes and amines promoted by Lewis acid Mg$^{2+}$ site. The basic sites converts the 2-naphthol into corresponding anion and this then reacts with the imine at the α-position following a Mannich type pathway to produce the 1-(α-aminoalkyl)-2-naphthols.

*Reaction conditions: aldehyde: amine: 2-naphthol = 1.2 : 1.0 : 1.0, 50 mg MgO, water; rt; isolated yield after purification.

| 17 | CH$_2$=CHO | 4r | 2.5 | 87 |
| 18 | CH$_2$=CHO | 4s | 4.0 | <20 |
| 19 | CH$_2$=CHO | 4u | 6.0 | n.r |
EXPERIMENTAL

• General

$^{1}$H NMR (300 MHz) and $^{13}$C NMR (75 MHz) spectral analysis was carried out on a Bruker-Avance Digital 300 MHz Spectrometer. TMS was used as internal standard. Infrared spectra were recorded in KBr pellet in reflection mode on a Perkin Elmer RX-1 FTIR spectrophotometer. Melting points (uncorrected) were determined on a Kofler Block apparatus. E. Merck aluminium-backed silica gel plates coated with silica gel G were used for analytical TLC and monitored under UV light (254 and 360 nm) and also by dipping in alkaline KMnO$_4$ solution and being charred. Synthetic grade chemicals were used from Spectrochem for carrying out the organic reactions. For preparation of the catalyst, fine A. R. grade chemicals from Fischer and Sigma were used. For column chromatography 100-200 mesh silica gel (E-Merck) was used. All the solvents used in the reaction were distilled and dried over Na$_2$SO$_4$.

• Representative procedure for the synthesis of Betti bases

A mixture of 2-naphthol (1.0 eq), an amine (1.0 eq), and an aldehyde (1.2 eq) was stirred at room temperature in water in presence of 50 mg MgO catalyst for certain periods (as indicated in Table 2). After completion of the reaction as indicated by TLC, the reaction mixture was extracted with ethyl acetate (3 × 10 mL). The extract was concentrated under reduced pressure and purified by column chromatography using 100-200 mesh silica gel with ethyl acetate/hexane (6-10%) as eluents. The isolated compounds were characterized from their mp, IR, $^{1}$H NMR, $^{13}$C NMR spectral analysis and elemental analysis.

• Typical procedure for the synthesis of nanocrystalline MgO

A non-hydrothermal sol-gel procedure was followed in the process. Anhydrous MgCO$_3$ was used as the Mg source. 1.0 gm of the salt was dissolved in 0.5 gm triethanolamine solvent with stirring at room temperature. Deionised water (0.3 gm) was added dropwise to form a
clear gel. The gel was stirred for 1 h at room temperature. Then triethyl ammonium hydroxide (0.2 ml) was added to the mixture to maintain pH 12. This was aged at room temperature for 24 h to obtain a white gel. The gel was dried at 120 °C for another 24 h and finally the cake was calcined at 600 °C for 6 h to obtain a fine white powder. The powder was characterized by SEM, TEM and XRD analysis.

➤ CONCLUSION
An efficient, clean, step economic and one pot procedure for the synthesis of Betti bases has been developed by the three component coupling of aldehyde, amine and 2-naphthol over the high surface area nanocrystalline MgO catalyst under aqueous condition. Mild reaction conditions, short reaction time, excellent yields of the products makes this methodology highly significant.

➤ PUBLICATION
“A competent pot and atom-efficient synthesis of Betti bases over nanocrystalline MgO involving a modified Mannich type reaction”
Bikash Karmakar, Julie Banerji*
SPECTROSCOPIC DATA OF SOME CHARACTERISTIC COMPOUNDS

1-(α-N-pyrroloidobenzyl)-2-naphthol
White solid; mp 180 °C; IR (KBr): 3449.9, 2967.0, 1841.3, 1510.3, 1591.8, 1456.9, 1236.0, 1095.6, 950.5, 823.5, 748.8, 699.5 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): δ 1.83 (bs, 4H), 2.3–2.5 (m, 4H), 5.11 (s, 1H), 7.13 (d, $J$ = 8.7 Hz, 1H), 7.16–7.25 (m, 5H), 7.34 (1H, $J$ = 7.7 Hz, 1H), 7.58 (d, $J$ = 7.0 Hz, 1H), 7.64 (d, $J$ = 9.3 Hz, 1H), 7.67 (d, $J$ = 9.3 Hz, 1H), 7.85 (d, $J$ = 8.4 Hz, 1H); $^{13}$C NMR (CDCl$_3$, 75.5 MHz): δ 23.4, 53.5, 70.8, 116.6, 119.9, 121.09, 122.36, 126.37, 127.85, 128.49, 128.59, 128.69, 128.87, 129.5, 131.87, 141.15, 155.5; Anal. Calcd for C$_{21}$H$_{21}$NO: C, 83.17; H, 6.93; N, 4.62%. Found: C, 83.08; H, 6.87; N, 4.69%.

1-(α-N-piperidobenzyl)-2-naphthol
White solid; mp 172 °C; IR (KBr): 3437.3, 2934.4, 2565.2, 1592.2, 1450.2, 1539.2, 1235.1, 1077.6, 942.5, 815.4, 739.6, 699.9 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): δ 1.69–2.3 (m, 10H), 5.08 (s, 1H), 7.14–7.28 (m, 5H), 7.36 (t, $J$ = 7.7 Hz, 1H), 7.54 (s, 2H), 7.67 (t, $J$ = 9.4 Hz, 2H), 7.84 (d, $J$ = 8.7 Hz, 1H), 14.0 (bs, 1H); $^{13}$C NMR (CDCl$_3$, 75.5 MHz): δ 24.09, 25.97, 52.44, 72.03, 119.98, 121.01, 122.35, 126.37 (2C), 127.94, 128.66, 128.89, 129.43, 132.36, 139.47, 155.43; Anal. Calcd for C$_{22}$H$_{22}$NO: C, 83.28; H, 7.26; N, 4.42%. Found: C, 83.19; H, 7.32; N, 4.53%.

1-(α-N-morpholinobenzyl)-2-naphthol
White solid; IR (KBr): 3458.3, 2839.4, 1590.1, 1455.7, 1238.2, 1111.6, 942.7, 824.9, 747.7, 698.8 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz): δ 2.46 (s, 4H), 3.82 (s, 4H), 4.65 (s, 1H), 7.18 (t, $J$ = 7.3 Hz, 1H),
7.22–7.31 (m, 4H), 7.4 (t, J = 7.0 Hz, 1H), 7.58 (d, J = 6.9 Hz), 7.70 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 13.14 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz): \(\delta\) 66.85, 72.01 (2C), 115.08, 119.75, 121.0, 122.59, 126.53 (2C), 128.18, 128.82, 128.89, 129.09, 129.75, 132.33, 138.61, 154.73; Anal. Calcd for C\(_{21}\)H\(_{21}\)NO: C, 79.0; H, 6.58; N, 4.39%. Found: C, 79.12; H, 6.49; N, 4.50%.

\(\triangleright\) \(l\)-(\(\alpha\)-N-butylaminobenzyl)-2-naphthol

Crystalline white solid; mp 131-133 °C; IR (KBr): 3311.9, 3054.6, 2922.9, 1592.9, 1460.3, 1238.1, 1085.8, 975.8, 827.9, 747.8, 698.8 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 0.92 (m, 3H), 1.39 (m, 2H), 1.55–1.66 (m, 2H), 2.8–2.86 (m, 2H), 3.64 (m, 1H), 5.68 (s, 1H), 7.14 (d, J = 9.04 Hz, 1H), 7.24–7.29 (m, 5H), 7.31 (m, 2H), 7.36 (d, J = 7.5 Hz, 2H), 7.47–7.74 (m, 3H); \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz): \(\delta\) 13.85, 20.32, 48.96, 64.42, 109.4, 113.4, 120.12, 121.14, 122.35, 123.32, 126.39, 127.73, 128.06, 128.26, 128.6, 128.82, 129.09, 129.63, 130.54, 141.7, 156.84; Anal. Calcd for C\(_{21}\)H\(_{21}\)NO: C, 82.59; H, 7.59; N, 4.59%. Found: C, 82.71; H, 7.53; N, 4.51%.

\(\triangleright\) \(l\)-(\(\alpha\)-N-pyrrolido-4-nitrobenzyl)-2-naphthol

Yellow solid; IR (KBr): 3435.2, 3077.4, 2960.5, 2844.2, 2612.8, 1935.6, 1597.2, 1516.3, 1344.8, 1244.5, 1106.4, 828.9, 745.1 cm\(^{-1}\); \(^{1}\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) 1.9 (s, 4H), 2.51 (bs, 4H), 5.15 (s, 1H), 7.16 (d, J = 8.7 Hz, 1H), 7.26 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 7.5 Hz, 1H), 7.7 (t, J = 8.0 Hz, 2H), 7.82 (t, J = 7.0 Hz, 3H), 8.12 (d, J = 8.4 Hz, 2H); \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz): \(\delta\) 23.4, 53.66, 69.9, 115.4, 119.96, 120.46, 122.73, 124.02, 126.77, 128.66, 129.11, 129.2, 130.19, 131.5, 147.4, 148.4, 155.46; Anal. Calcd for C\(_{21}\)H\(_{20}\)N\(_2\)O\(_3\): C, 72.41; H, 5.74; N, 8.04%. Found: C, 72.51; H, 5.62; N, 8.11%.
> 1-(α-N-pyrrolido-4-methylbenzyl)-2-naphthol

White solid; IR (KBr): 3450.1, 2959.4, 2838.6, 1592.3, 1449.5, 1395.3, 1227.4, 1109.2, 946.6, 811.9 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 1.86 \text{ (s, 4H)}, 2.17-2.44 \text{ (m, 4H)}, 2.26 \text{ (s, 3H)}, 5.11 \text{ (s, 1H)}, 7.07 \text{ (d, } J = 7.8 \text{ Hz, 1H)}, 7.14-7.24 \text{ (m, 3H)}, 7.37 \text{ (t, } J = 7.6 \text{ Hz, 1H)}, 7.49 \text{ (d, } J = 7.8 \text{ Hz, 2H)}, 7.65 \text{ (d, } J = 9.0 \text{ Hz, 1H)}, 7.69 \text{ (d, } J = 9.0 \text{ Hz, 1H)}, 7.87 \text{ (d, } J = 8.7 \text{ Hz, 1H}); ^{13}\text{C NMR (CDCl}_3, 75.5 MHz): \(\delta 21.0, 23.4, 70.47, 116.6, 119.86, 121.03, 122.29, 126.32, 128.33, 128.6, 128.8, 129.4, 131.8, 137.53, 138.0, 155.4\); Anal. Calcd for C\(_{21}\)H\(_{23}\)NO: C, 83.28; H, 7.26; N, 4.42% Found: C, 83.22; H, 7.35; N, 4.29%

> 1-(α-N-pyrrolido-3-nitrobenzyl)-2-naphthol

Yellow solid; IR (KBr): 3434.7, 3058.4, 2953.5, 2618.5, 1836.9, 1593.2, 1497.8, 1347.0, 1248.5, 1106.4, 821.8 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 1.65 \text{ (s, 4H)}, 2.49 \text{ (s, 4H)}, 5.1 \text{ (s, 1H)}, 7.18 \text{ (d, } J = 9.0 \text{ Hz, 1H)}, 7.26 \text{ (t, } J = 7.5 \text{ Hz, 1H)}, 7.43 \text{ (t, } J = 7.85 \text{ Hz, 2H)}, 7.71 \text{ (d, } J = 7.8 \text{ Hz, 2H)}, 7.84 \text{ (d, } J = 8.7 \text{ Hz, 1H)}, 7.99 \text{ (d, } J = 7.8 \text{ Hz, 1H)}, 8.07 \text{ (d, } J = 7.5 \text{ Hz, 1H)}, 8.47 \text{ (s, 1H)}; ^{13}\text{C NMR (CDCl}_3, 75.5 MHz): \(\delta 23.42, 53.5, 69.9, 115.52, 120.04, 120.5, 122.76, 123.36, 126.85, 128.65, 129.1, 129.97, 130.18, 131.5, 134.5, 143.37, 148.27, 155.53\); Anal. Calcd for C\(_{21}\)H\(_{20}\)N\(_2\)O\(_3\): C, 72.41; H, 5.74; N, 8.04% Found: C, 72.38; H, 5.76; N, 8.17%.

> 1-(α-N-piperido-4-chlorobenzyl)-2-naphthol

White solid; \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta 1.64 \text{ (m, 6H)}, 2.2 \text{ (s, 4H)}, 5.05 \text{ (s, 1H)}, 7.14 \text{ (d, } J = 9.0 \text{ Hz, 1H)}, 7.51 \text{ (d, } J = 8.4 \text{ Hz, 4H)}, 7.67 \text{ (t, } J = 9.0 \text{ Hz, 2H)}, 7.77 \text{ (d, } J = 8.6 \text{ Hz, 1H)}, 7.82
(d, \( J = 8.6 \text{ Hz}, 2H \)); \(^{13}\text{C} \text{NMR} \text{(CDCl}_3, \text{75.5 MHz)}): \delta \ 24.1, 26.0, 48.3, 71.26, 115.74, 119.97, 120.74, 122.44, 126.45, 128.95, 129.45, 129.56, 130.42, 130.9, 132.17, 133.65, 140.95, 155.41; \text{Anal. Calcd for C}_{22}\text{H}_{22}\text{NOCI: } \text{C, 75.11%; H, 6.26%; N, 3.98%; Found: C, 75.03; H, 6.37; N, 4.12%}.

\( \text{1-(a-N-piperido-4-cyanobenzyl)-2-naphthol} \)

\text{White solid; } \text{\(^{1}\text{H} \text{NMR} \text{(CDCl}_3, \text{300 MHz): } \delta  \ 1.74 \text{ (bs, 6H), 1.92–2.2 (s, 4H), 5.17 (s, 1H), 7.17 (d, } J = 9.0 \text{ Hz, 1H), 7.28 (t, } J = 7.2 \text{ Hz, 1H), 7.43 (t, } J = 7.7 \text{ Hz, 1H), 7.59 (d, } J = 8.1 \text{ Hz, 2H), 7.71–7.76 (m, 4H), 7.81 (d, } J = 8.7 \text{ Hz, 1H); } \text{\(^{13}\text{C} \text{NMR} \text{(CDCl}_3, \text{75.5 MHz): } \delta  \ 30.9, 54.11, 74.7, 114.42, 119.35, 121.52, 122.73, 123.31, 126.62, 127.5, 127.78, 127.88, 128.38, 128.95, 129.25, 129.35, 139.11, 152.51; \text{Anal. Calcd for C}_{23}\text{H}_{23}\text{N}_2\text{O: C, 80.70%; H, 6.43%; N, 8.19%; Found: C, 80.61; H, 6.37; N, 8.27%}.)}

\( \text{1-(a-N-pyrrolido-3,4,5-trimethoxybenzyl)-2-naphthol} \)

\text{White solid; } \text{\(^{1}\text{H} \text{NMR} \text{(CDCl}_3, \text{300 MHz): } \delta  \ 1.87 \text{ (s, 4H), 2.5 (s, 4H), 3.75 (s, 3H), 3.82 (s, 6H), 5.05 (s, 1H), 6.67 (d, } J = 8.7 \text{ Hz, 1H), 6.86 (s, 2H), 7.15 (d, } J = 9.0 \text{ Hz, 1H), 7.24 (t, } J = 7.1 \text{ Hz, 1H), 7.40 (t, } J = 7.5 \text{ Hz, 1H), 7.72 (d, } J = 8.1 \text{ Hz, 1H), 7.89 (d, } J = 8.4 \text{ Hz, 1H); } \text{\(^{13}\text{C} \text{NMR} \text{(CDCl}_3, \text{75.5 MHz): } \delta  \ 23.4, 56.2, 56.2, 60.7, 71.0, 105.5, 116.57, 119.91, 121.09, 122.37, 126.3, 128.6, 128.9, 129.5, 131.86, 136.92, 153.17, 155.57; \text{Anal. Calcd for C}_{24}\text{H}_{27}\text{NO}_4: C, 73.28; H, 6.87; N, 3.56%; Found: C, 73.14; H, 6.77; N, 3.51%})}
Fig. 7.5.1. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of l-(α-N-pyrrolidobenzyl)-2-naphthol
Fig. 7.5.2. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 1-(α-N-piperidobenzyl)-2-naphthol
Fig. 7.5.3. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectra of 1-(α-N-morpholinobenzyl)-2-naphthol
Fig. 7.5.4. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectra of 1-(α-N-butylaminobenzyl)-2-naphthol
Fig. 7.5.5. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 1-(α-N-pyrrolido-4-nitrobenzyl)-2-naphthol
Fig. 7.5.6. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of l-(a-N-pyrrolido-4-methylbenzyl)-2-naphthol
Fig. 7.5.7. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 1-(α-N-pyrroldo-3-nitrobenzyl)-2-naphthol
Fig. 7.5.8. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 1-(α-N-piperido-4-chlorobenzyl)-2-naphthol
Fig. 7.5.9. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 1-(α-N-piperido-4-cyanobenzyl)-2-naphthol
Fig. 7.5.10. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of l-(α-N-pyrrolido-3,4,5-trimethoxybenzyl)-2-naphthol
Fig. 7.5.11. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectra of 1-(α-N-cyclohexylamino benzyl)-2-naphthol
Fig. 7.5.12. $^1$H NMR (A) (CDCl$_3$) and IR (B) (KBr) spectra of l-(α-N-pyrrolido-4-methoxybenzyl)-2-naphthol
Fig. 7.5.13. $^1$H NMR (A) and $^{13}$C NMR (B) (CDCl$_3$) spectra of 1-(α-N-pyrrolido-4-chlorobenzyl)-2-naphthol
References