

One-pot synthesis of thiocarbamidoalkyl naphthols

Zhong-Ping Zhang, Jian-Ming Wen, Jing-Hua Li* and Wei-Xiao Hu

College of Pharmaceutical Sciences, Zhejiang University of Technology, 310032, P. R. China

An efficient, inexpensive and mild method for the synthesis of α -thiocarbamidoalkyl- β -naphthols, catalysed by *p*-toluenesulfonic acid at room temperature is reported. A set of thiocarbamidoalkyl naphthols have been synthesised in high yields from aromatic aldehydes, β -naphthol and *N*-phenylthiourea or thiourea. The procedure involves a short reaction time and a simple experimental procedure.

Keywords: multicomponent reactions, thiocarbamidoalkyl naphthols, Betti base

Compounds bearing 1,3-amino oxygenated functional groups are found in biologically important natural products and drugs including a number of nucleoside antibiotics and HIV protease inhibitors, such as ritonavir and lipinavir.^{1–6} Amino naphthols exhibit antihypertensive, adrenoceptor blocking, and Ca²⁺ channel blocking activities.^{7–9}

Multicomponent reactions (MCRs) have attracted considerable attention since they do not require the isolation of intermediates saving time, energy and raw materials. Hence the discovery of new MCRs is still in demand.^{10–14}

Various methods have been reported for the straightforward synthesis of Betti base derivatives by the aminoalkylation of β -naphthol with aromatic aldehydes and heterocyclic amines,^{15,16} pyrrolidine,¹⁷ iminium salts^{18,19} and methyl carbamate.²⁰ Amidoalkyl naphthols can be prepared from the Betti base or by condensation of aromatic aldehydes, β -naphthol and amides as the ammonia source. To our knowledge, relatively few reports have appeared in this field.^{21–28} A straightforward synthesis of thiocarbamidoalkyl naphthols from thiourea and its derivatives has not been reported. We report here a mild, simple and efficient method for the one-pot three-component condensation of aromatic aldehydes, β -naphthol and thioureas.

In our initial search for appropriate reaction conditions, we chose the reaction of β -naphthol with benzaldehyde and *N*-phenylthiourea as a model with a variety of catalysts in CH₂Cl₂ at room temperature (Scheme 1 and Table 1, entries 1–7).

As shown in Table 1, the best result was obtained when *p*-toluenesulfonic acid (*p*-TSA) was used as a catalyst (Table 1, entry 7). We then examined the reaction in various solvents in the presence of 10% *p*-TSA (Table 1, entries 7–11). We found that 1,2-dichloroethane and CH₂Cl₂ gave high yields of the product. However, 1,2-dichloroethane is toxic and so we chose CH₂Cl₂ as a solvent for the reactions.

Under the reaction conditions established as above, various thiocarbamidoalkyl naphthols were then synthesised in good to excellent yields by the reaction of different aromatic aldehydes with β -naphthol and *N*-phenylthiourea or thiourea. The results are summarised in Table 2. Among them, **3a** was identified, by R_f value (on TLC), ¹H NMR and m.p., as the same compound as prepared from Betti base and isothiocyanatobenzene in toluene at room temperature. In all cases, aromatic aldehydes bearing either electron-donating or

Table 1 Effect of catalysts on the reaction of benzaldehyde, β -naphthol and *N*-phenylthiourea^a

Entry	Catalyst	Solvent	Yield/% ^b
1	Yb(OTf) ₃	CH ₂ Cl ₂	<30
2	La(OTf) ₃	CH ₂ Cl ₂	<30
3	Cu(OTf) ₂	CH ₂ Cl ₂	73
4	Zn(OTf) ₂	CH ₂ Cl ₂	Trace
5	HOTf	CH ₂ Cl ₂	52
6	CH ₃ SO ₃ H	CH ₂ Cl ₂	<30
7	CF ₃ COOH	CH ₂ Cl ₂	48
8	<i>p</i> -TSA	CH ₂ Cl ₂	90
9	<i>p</i> -TSA	ClCH ₂ CH ₂ Cl	93
10	<i>p</i> -TSA	Toluene	78
11	<i>p</i> -TSA	CH ₃ OH	85
12	<i>p</i> -TSA	C ₂ H ₅ OH	80

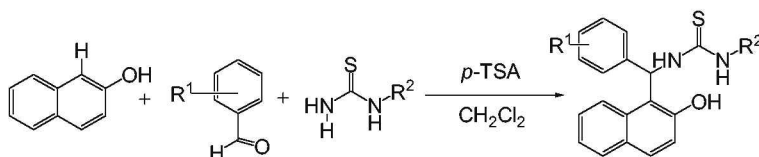
^aReaction conditions: solvent (5 mL), benzaldehyde (1 mmol), β -naphthol (1 mmol), *N*-phenylthiourea (1.1 mmol), cat. amount 10%, room temperature, 12 h. ^bIsolated yield.

electron-withdrawing groups reacted successfully. As expected aromatic aldehydes with electron-withdrawing groups reacted faster than the aromatic aldehydes with electron-donating groups. When thiourea was used as the amine source, the aminoalkylation of naphthol gave a lower yield and needed a longer reaction time.

Table 2 One-pot synthesis of thiocarbamidoalkyl naphthols in the presence of *p*-TSA^a

No.	R ¹	R ²	Yield ^b /%	t/h
3a	H	Ph	90	12
3b	<i>p</i> -Cl	Ph	91	8
3c	<i>o</i> -Cl	Ph	88	10
3d	2,4-dichloro	Ph	86	10
3e	<i>m</i> -NO ₂	Ph	93	8
3f	<i>p</i> -F	Ph	92	9
3g	<i>p</i> -OH	Ph	78	24
3h	<i>p</i> -CH ₃ O	Ph	81	24
3i	3,4-dimethyl	Ph	74	24
3j	H	H	72	24
3k	<i>m</i> -NO ₂	H	78	18
3l	<i>o</i> -Cl	H	77	20
3m	3,4-dimethyl	H	58	24

^aReaction condition: CH₂Cl₂ as solvent (5 mL), aromatic aldehyde (1 mmol), β -naphthol (1 mmol), *N*-phenylthiourea or thiourea (1.1 mmol), cat. amount 10%, room temperature. ^bIsolated yield.



Scheme 1

* Correspondent. E-mail: lijh@zjut.edu.cn

In conclusion, we have developed an efficient and convenient synthesis of 1-thiocarbamidoalkyl-2-naphthol derivatives by a three-component condensation of aryl aldehydes, 2-naphthol and *N*-phenylthiourea or thiourea in the presence of *p*-TSA. This method offers several significant advantages: high conversions, mild reaction conditions and easy handling, which makes it a useful and attractive process for the convenient synthesis of substituted thiocarbamidoalkyl naphthols.

Experimental

Melting points were determined on a Büchi B-540 melting apparatus and are uncorrected. The NMR spectra were measured on a Bruker Avance III 500 instrument using DMSO-*d*₆ as the solvent with TMS as the internal standard. IR spectra were recorded using KBr pellets on a Nicolet 6700 FI-IR spectrophotometer. Mass spectra were measured with GCT Premier CAB 075. Elemental analyses were performed on Thermo Finnigan EA1112 elemental analyser.

General procedure for preparation of 3a-m

A mixture of aromatic aldehyde (1 mmol), β-naphthol (1 mmol), *N*-phenylthiourea or thiourea (1.1 mmol) and TsOH·H₂O (0.1 mmol) in CH₂Cl₂ (5 mL) was stirred at room temperature for the appropriate time (Table 2). The progress of the reaction was monitored by TLC (2:1 hexane: ethyl acetate). After completion of the reaction, as indicated by TLC, the reaction mixture was filtered and the precipitate washed thoroughly with CH₂Cl₂ and then with water. The crystalline product was collected without further purification. The physical and spectroscopic data of the compounds 3a-m are as follows.

3a: Colourless crystals; m.p. 178–180°C; IR (KBr) cm⁻¹: 3447, 3285, 3172, 3066, 1626, 1605, 1546, 1515, 1436, 1360, 1259, 1144, 811, 747; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.20 (s, 1H), 10.16 (s, 1H), 8.71–8.70 (ss, br, 1H), 8.16 (s, br, 1H), 8.00–7.98 (ss, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.5 Hz, 1H), 7.54–7.48 (m, 3H), 7.34 (q, *J* = 8 Hz, 3H), 7.28–7.13 (m, 7H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 180.7, 153.6, 142.8, 139.4, 133.0, 130.0, 129.3, 129.1, 128.6, 127.5, 126.8, 126.3, 125.0, 123.8, 123.2, 122.9, 119.1, 119.0, 53.8; MS (EI) *m/z* (%): 231 (100), 202 (20), 144 (75), 115 (29); Anal. Calcd for C₂₄H₂₀N₂O₂S: C, 74.97; H, 5.24; N, 7.29. Found: C, 74.87; H, 5.46; N, 7.47%.

3b: Colourless crystals; m.p. 164–166°C; IR (KBr) cm⁻¹: 3363, 3191, 3018, 1629, 1543, 1518, 1489, 1328, 1267, 812, 747; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.23 (s, 2H), 8.68–8.67 (ss, br, 1H), 8.14 (s, br, 1H), 7.97–7.95 (ss, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 9.0 Hz, 1H), 7.54–7.33 (m, 8H), 7.24–7.22 (ss, 1H), 7.19–7.13 (m, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 180.4, 153.2, 141.5, 139.0, 132.4, 130.9, 129.8, 128.8, 128.7, 128.2, 128.1, 127.7, 127.1, 125.5, 124.6, 123.3, 122.8, 122.3, 118.5, 118.2, 52.8; MS (EI) *m/z* (%): 384 (M-34, 1), 267 (28), 231 (100), 202 (30), 144(60), 115 (23); Anal. Calcd for C₂₄H₁₉ClN₂O₂S: C, 68.81; H, 4.57; N, 6.69. Found: C, 68.70; H, 4.56; N, 6.54%.

3c: Colourless crystals; m.p. 174–176°C; IR (KBr) cm⁻¹: 3382, 3186, 3009, 1629, 1592, 1540, 1515, 1435, 1371, 1331, 1266, 811, 747; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.04 (s, 1H), 9.99 (s, 1H), 8.47 (d, *J* = 8.5 Hz, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 7.82 (d, *J* = 8 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.65–7.64 (ss, 1H), 7.63–7.48 (m, 3H), 7.34–7.22 (m, 6H), 7.14 (d, *J* = 9.0 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 179.7, 153.7, 139.5 × 2, 132.7, 132.1, 130.0, 129.8, 129.2, 128.6, 128.5, 128.2, 128.1, 126.6, 126.2, 124.0, 123.1, 122.6, 122.5, 118.5, 117.2, 52.4; MS (EI) *m/z* (%): 384 (M-34, 1), 231 (100), 202 (15), 144(60), 115 (36); Anal. Calcd for C₂₄H₁₉ClN₂O₂S: C, 68.81; H, 4.57; N, 6.69. Found: C, 68.84; H, 4.59; N, 6.62%.

3d: Colourless crystals; m.p. 152–154°C; IR (KBr) cm⁻¹: 3380, 3160, 1628, 1541, 1517, 1266, 1195, 814, 744; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.06 (s, 1H), 9.98 (s, 1H), 8.48 (d, *J* = 8.5 Hz, 1H), 8.24 (d, *J* = 9.0 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.74–7.73 (ss, 1H), 7.67–7.65 (m, 3H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.47–7.45 (m, 2H), 7.33–7.29 (m, 3H), 7.13–7.17 (m, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 180.3, 154.3, 139.9, 139.5, 133.1, 133.0, 132.1, 131.8, 130.6, 129.1, 129.0, 128.9, 128.6, 127.2, 126.8, 124.5, 123.3, 123.1, 123.0, 118.9, 117.0, 52.5; MS (EI) *m/z* (%): 418 (M-34, 2), 265 (100), 202 (13), 144(42), 115 (15); Anal. Calcd for C₂₄H₁₈Cl₂N₂O₂S: C, 63.58; H, 4.00; N, 6.18. Found: C, 63.64; H, 4.15; N, 6.22%.

3e: (Yellow crystals); m.p. 142–144°C; IR (KBr) cm⁻¹: 3422, 3334, 3165, 1628, 1522, 1475, 1352, 1319, 1245, 1190, 807, 744; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.37 (s, 1H), 10.31 (s, 1H), 8.77–

8.76 (ss, 1H), 8.21 (s, br, 1H), 8.11–8.06 (m, 3H), 7.89 (t, *J* = 9.0 Hz, 2H), 7.63–7.55 (m, 5H), 7.39–7.35 (m, 3H), 7.26 (d, *J* = 8.5 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 181.2, 153.8, 148.2, 145.6, 139.5, 133.2, 132.7, 130.7, 130.2, 129.3, 129.2, 128.7, 127.9, 125.1, 123.8, 123.5, 122.7, 122.0, 120.7, 118.9, 118.1, 53.3; MS (EI) *m/z* (%): 348 (3), 231 (50), 202 (25), 144 (100), 115 (17); Anal. Calcd for C₂₄H₁₉N₃O₃S: C, 67.12; H, 4.46; N, 9.78. Found: C, 67.15; H, 4.45; N, 9.81%.

3f: Colourless crystals; m.p. 166–168°C; IR (KBr) cm⁻¹: 3368, 3170, 3016, 1630, 1544, 1520, 1506, 1439, 1330, 1269, 1186, 835, 751; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.22 (s, 1H), 10.20 (s, 1H), 8.70 (s, br, 1H), 8.13 (s, br, 1H), 7.96–7.95 (ss, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.55–7.33 (m, 6H), 7.24–7.09 (m, 6H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 180.3, 161.9, 160.0, 153.2, 139.0, 138.4, 132.3, 129.7, 128.8, 128.7, 128.2, 127.8, 127.7, 127.1, 125.5, 124.6, 123.3, 122.8, 122.3, 118.5, 118.3, 114.9, 114.8, 52.8; MS (EI) *m/z* (%): 251 (7), 249 (100), 231 (6), 144 (50), 115 (20); Anal. Calcd for C₂₄H₁₉FN₂O₂S: C, 71.62; H, 4.76; N, 6.96. Found: C, 71.53; H, 4.85; N, 6.83%.

3g: Pale yellow crystals; m.p. 162–164°C; IR (KBr) cm⁻¹: 3527, 3369, 3190, 3016, 1629, 1546, 1513, 1437, 1331, 1258, 1176, 832, 747; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.14 (s, 1H), 10.11 (s, 1H), 9.21 (br, 1H), 8.71 (s, br, 1H), 8.12 (s, br, 1H), 7.89–7.79 (m, 3H), 7.52–7.31 (m, 6H), 7.22 (d, *J* = 9 Hz, 1H), 7.21–7.10 (m, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 180.2, 156.5, 153.5, 139.4, 132.9, 132.7, 129.7, 129.3, 129.0, 128.6 × 2, 127.7, 127.3, 125.0, 123.8, 123.2, 119.2, 119.0, 115.3, 53.6; MS (EI) *m/z* (%): 249 (4), 247 (42), 231 (16), 144 (100), 115 (35); Anal. Calcd for C₂₄H₁₉N₂O₂S: C, 71.98; H, 5.03; N, 6.99. Found: C, 71.94; H, 4.92; N, 6.81%.

3h: Colourless crystals; m.p. 174–176°C; IR (KBr) cm⁻¹: 3364, 3195, 30156, 1628, 1543, 1511, 1327, 1246, 1177, 830, 747; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.16 (s, 1H), 10.14 (s, 1H), 8.71 (s, br, 1H), 8.12 (s, br, 1H), 7.92–7.90 (ss, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.52–7.31 (m, 6H), 7.22 (d, *J* = 9.0 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.85–6.82 (dd, *J* = 9.0 Hz, *J* = 2.0 Hz, 2H), 3.68 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 158.4, 153.5, 139.4, 134.6, 132.8, 129.8, 129.3, 129.1, 128.6, 128.5, 127.6, 127.4, 125.0, 123.8, 123.2, 119.0 × 2, 114.0, 55.5, 53.5; MS (EI) *m/z* (%): 380 (M-34, 2), 263 (10), 261 (100), 231 (78), 144 (73) 115 (28); Anal. Calcd for C₂₅H₂₂N₂O₂S: C, 72.44; H, 5.35; N, 6.76. Found: C, 72.24; H, 5.33; N, 6.72%.

3i: Colourless crystals; m.p. 168–170°C; IR (KBr) cm⁻¹: 3363, 3186, 3012, 1630, 1544, 1518, 1438, 1265, 822, 745; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.14 (s, 1H), 10.11 (s, 1H), 8.67 (s, br, 1H), 8.15 (s, br, 1H), 7.92–7.90 (ss, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.51–7.31 (m, 6H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.96 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 2.14 (s, 3H), 2.11 (s, 3H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 180.4, 153.6, 140.2, 139.5, 136.1, 134.7, 132.9, 129.8, 129.7, 129.3, 129.1, 128.6, 128.5, 127.4, 127.3, 126.0, 125.0, 123.9, 123.7, 123.2, 123.0, 119.3, 119.0, 53.6, 20.1, 19.4; MS (EI) *m/z* (%): 412 (M, 2), 262 (2), 245 (100), 144 (31); Anal. Calcd for C₂₆H₂₄N₂O₂S: C, 75.70; H, 5.86; N, 6.79. Found: C, 75.64; H, 5.85; N, 6.75%.

3j: Colourless crystals; m.p. 180–182°C; IR (KBr) cm⁻¹: 3417, 3302, 3191, 1614, 1514, 1435, 1350, 1262, 1210, 1173, 811, 697; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.02 (s, 1H), 8.41–8.39 (ss, 1H), 8.13 (s, br, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.76–7.74 (ss, 1H), 7.50–7.47 (m, 3H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.25–7.20 (m, 4H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 183.7, 153.7, 143.4, 133.0, 129.8, 129.0, 128.6, 128.4, 127.2, 126.6, 126.2, 123.2, 123.0, 119.7, 119.0, 54.3; MS (EI) *m/z* (%): 274 (M-34, 2), 231 (55), 202 (14), 144 (100), 115 (33); Anal. Calcd for C₁₈H₁₆N₂O₂S: C, 70.10; H, 5.23; N, 9.08. Found: C, 69.97; H, 5.25; N, 9.13%.

3k: Yellow crystals; m.p. 168–170°C; IR (KBr) cm⁻¹: 3422, 3356, 3096, 1626, 1529, 1437, 1350, 1267, 1210, 1171, 813, 749; ¹H NMR (500 MHz, DMSO-*d*₆): δ 10.09 (s, 1H), 9.17 (s, br, 1H), 8.13 (s, 2H), 8.12 (s, 1H), 8.03–8.02 (ss, 1H), 7.84–7.80 (dd, *J* = 11 Hz, *J* = 2.5 Hz, 2H), 7.63–7.49 (m, 3H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 9.0 Hz, 1H); ¹³C NMR (125 MHz, DMSO-*d*₆): δ 184.3, 153.9, 148.2, 146.3, 133.0, 132.8, 130.6, 130.1, 129.2, 128.7, 127.5, 123.2, 121.7, 120.7, 118.8, 118.3, 53.6; MS (EI) *m/z* (%): 319 (M-34, 3), 276 (20), 202 (3), 144 (100), 115 (19); Anal. Calcd for C₁₈H₁₅N₃O₃S: C, 61.18; H, 4.28; N, 11.89. Found: C, 61.26; H, 4.30; N, 11.97%.

3l: Colourless crystals; m.p. 166–168°C; IR (KBr) cm⁻¹: 3447, 3285, 3172, 3066, 1605, 1546, 1515, 1436, 1360, 1260, 1144, 811, 747; ¹H NMR (500 MHz, DMSO-*d*₆): δ 9.85 (s, 1H), 8.33 (d, *J* = 5 Hz, 1H), 8.31 (d, *J* = 4.5 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.74 (d,

$J = 9.0$ Hz, 1H), 7.60 (t, $J = 9.0$ Hz, 2H), 7.48 (t, $J = 7.5$ Hz, 1H), 7.33–7.20 (m, 6H), 7.09 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR (125 MHz, DMSO- d_6): δ 183.1, 154.0, 140.8, 133.3, 132.3, 130.4, 130.1, 129.4, 128.9, 128.6, 128.3, 126.9, 126.4, 123.8, 122.9, 119.0, 118.1, 53.5; MS (EI) m/z (%): 308 (M-34, 3), 231 (100), 202 (20), 144 (53), 115 (20); Anal. Calcd for $\text{C}_{18}\text{H}_{15}\text{ClN}_2\text{O}_5$: C, 63.06; H, 4.41; N, 8.17. Found: C, 63.14; H, 4.45; N, 8.26%.

3m: Colourless crystals; m.p. 164°C; IR (KBr) cm^{-1} : 3439, 3230, 3145, 1600, 1541, 1514, 1438, 1351, 1267, 1211, 1145, 813, 732; ^1H NMR (500 MHz, DMSO- d_6): δ 9.97 (s, 1H), 8.39–8.37 (ss, 1H), 8.15 (s, br, 1H), 7.82 (d, $J = 8.0$ Hz, 1H), 7.78 (d, $J = 9$ Hz, 1H), 7.71–7.69 (ss, 1H), 7.47 (br, 3H), 7.30 (t, $J = 7.5$ Hz, 1H), 7.21 (d, $J = 9.0$ Hz, 1H), 6.98 (d, $J = 8.0$ Hz, 1H), 6.92 (s, 1H), 6.83 (d, $J = 7.5$ Hz, 1H), 2.13 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, DMSO- d_6): δ 183.5, 153.6, 140.8, 135.8, 134.3, 133.1, 129.6, 129.5, 128.6, 127.3, 127.1, 123.8, 123.3, 123.0, 120.0, 119.1, 54.1, 20.1, 19.4; MS (EI) m/z (%): 302 (M-34, 3), 259 (19), 245 (100), 202 (5), 144 (100) 115 (41); Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_5$: C, 71.40; H, 5.99; N, 8.33. Found: C, 71.51; H, 6.05; N, 8.32%.

Received 17 November 2008; accepted 19 January 2009

Paper 08/0298 doi: [10.3184/030823409X416910](https://doi.org/10.3184/030823409X416910)

Published online: 6 April 2009

References

- 1 E. Juaristi, *Enantioselective synthesis of β -amino acids*; Wiley, New York, 1997.
- 2 S. Knapp, *Chem. Rev.*, 1995, **95**, 1859.
- 3 Y.F. Wang, T. Izawa, S. Kobayashi and M. Ohno, *J. Am. Chem. Soc.*, 1982, **104**, 6465.
- 4 T. Dingermann, D. Steinhilber and G. Folkers, *Molecular biology in medicinal chemistry*, Wiley-VCH, 2004.
- 5 A.Y. Shen, C.T. Tsai and C.L. Chen, *Eur. J. Med. Chem.*, 1999, **34**, 877.
- 6 A.Y. Shen, C.L. Chen and C.I. Lin, *Chin. J. Physiol.*, 1992, **35**, 45.
- 7 K.S. Atwal, B.C. O'Reilly, E.P. Ruby, C.F. Turk, G. Abcrg, M.M. Asaad, J.L. Bergey, S. Moreland and J.R. Powell, *J. Med. Chem.*, 1987, **30**, 627.
- 8 M. Grundke, H.M. Himmcl, E. Wettwer, H.O. Borbe and U. Ravens, *J. Cardiovasc. Pharmacol.*, 1991, **18**, 918.
- 9 K.F. Jim and W.D. Matthews, *J. Pharmacol. Exp. Ther.*, 1985, **234**, 161.
- 10 I. Devi and P.J. Bhuyar, *Tetrahedron Lett.*, 2004, **45**, 8625.
- 11 S.H. Mashraqui, M.B. Patil, H.D. Mistry, S. Ghadigaonkar and A. Meetsma, *Chem. Lett.*, 2004, **33**, 1058.
- 12 A. Chetia, C.J. Saikia, K.C. Lckhok and R.C. Boruah, *Tetrahedron Lett.*, 2004, **45**, 2649.
- 13 J. Zhu and H. Bicnaimé, *Multicomponent reactions*, Wiley-VCH, Weinheim, Germany, 2005.
- 14 A. Dömling and I. Ugi, *Angew. Chem. Int. Ed.*, 2000, **39**, 3168.
- 15 N.K. Paul, L. Dietrich and A. Jha, *Synth. Commun.*, 2007, **37**, 877.
- 16 A. Jha, N.K. Paul, S. Trikha and T.S. Camcron, *Can. J. Chem.*, 2006, **84**, 843.
- 17 M. Periasamy, M.N. Reddy and S. Anwar, *Tetrahedron: Asymmetry*, 2004, **15**, 1809.
- 18 M.R. Saidi, N. Azizi and M.R. Naimi-Jamal, *Tetrahedron Lett.*, 2001, **42**, 8111.
- 19 M.R. Saidi and N. Azizi, *Tetrahedron: Asymmetry*, 2003, **14**, 389.
- 20 M. Dabiri, A.S. Delbari and A. Bazgir, *Heterocycles*, 2007, **71**, 543.
- 21 M.M. Khodaci, A.R. Khosropour and H. Moghanian, *Synlett.*, 2006, 916.
- 22 S.B. Patil, P.R. Singh, M.P. Surpur and S.D. Samant, *Synth. Commun.*, 2007, **37**, 1659.
- 23 S. Kantevari, S.V.N. Vuppapapati and L. Nagarapu, *Catal. Commun.*, 2007, **8**, 1857.
- 24 N.P. Selvam and P.T. Perumal, *Tetrahedron Lett.*, 2006, **47**, 7481.
- 25 B. Das, K. Laxminarayana, B. Ravikanth and B.R. Rao, *J. Mol. Catal. A: Chem.*, 2007, **261**, 180.
- 26 L. Nagarapu, M. Basceruddin, S. Apuri and S. Kantevari, *Catal. Commun.*, 2007, **8**, 1729.
- 27 G. Srihari, M. Nagaraju and M.M. Murthy, *Helv. Chim. Acta*, 2007, **90**, 1497.
- 28 H.R. Shaterian and H. Yarahmadi, *ARKIVOC*, 2008 (ii) 105.