A New Procedure for the Synthesis of 1-Arylmethyl-2-Naphthols

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Abstract

A novel and environmentally-friendly two-step procedure for the synthesis of 1-arylmethyl-2-naphthols in excellent yield is reported. It involves microwave-assisted facile formation of Mannich bases of 2-naphthol under solvent-free conditions and subsequent Pd-catalyzed deamination leading to formation of title compounds.

Keywords: 1-arylmethyl-2-naphthols, deamination, microwave, solvent-free, Pd-catalyzed.

Introduction

Naphthalene nucleus is commonly found in compounds of commercial importance. A number of pharmaceutical and agricultural agents have naphthalene framework. Some of the commonly known examples include LY326315 (a selective estrogen receptor modulator),[1] naproxen & nabumetone (non-steroidal anti-inflammatory drugs),[2,3] naphazoline & pronethalol (cardiovascular agents),[4,5] 1-naphthaleneacetic acid & 2-naphthoxyaceticacid (plant growth regulators),[6,7] terbinafine & naftifine (antifungal agents)[8,9] etc. In literature, 2-naphthol and 2-naphthol derivatives are also reported as bactericides[10] and antioxidants.[11]

Owing to the wide variety of practical application of naphthalene nucleus as building blocks, it is paramount to develop synthetic strategies around this nucleus to gain easy access to variety of naphthalene derivatives. Substitution at position 1 of the naphthalene ring, as seen in molecules like LY326315, naphazoline and terbinafine (Figure 1), is of particular interest to this group. We are using ambident nucleophile 2-naphthol in our studies.

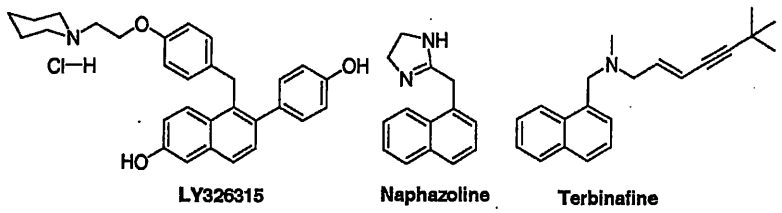
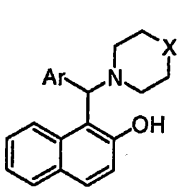


Fig 1: Molecular structures of representative 1-substituted naphthalene derivatives of pharmaceutical importance.

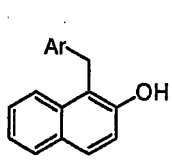
Various methods are known for substitution of 2-naphthol at position-1[12-27] including Zn-mediated thermal transfer of benzyl group from benzylaryl ether to 2-naphthol,[12] thermal rearrangement of 2-benzyloxynaphthalene,[12] nuclear arylmethylation of 2-naphthol alkali metal salts using corresponding halides,[13,16,18,19] Clemmensen reduction of aryl 1-(2-hydroxynaphthyl)ketone,[24] and other, more cumbersome procedures.[15,20-23] Many of these procedures have serious drawbacks, e.g. formation of side product(s), low yield, use of elevated temperature, long reaction time, etc.[12,13,15,16,19,20,22,23]

Over the past few years microwave irradiation has become a common and efficient energy source in the chemical and pharmaceutical industry.[28] The exorbitant increase in number of publications dealing with this subject emphasizes on the promising potential of microwave accelerated syntheses that has not yet been discovered completely. Microwave accelerated reactions still reveal fascinating opportunities concerning reaction course, rate and yield. Microwave chemistry is particularly effective in dry media reaction. Microwaves generate rapid intense heating of polar substances resulting in significantly reduced reaction times, cleaner reactions and, in many cases, higher yields.

We herein report a novel, convenient and highly efficient method for the preparation of 1-arylmethyl-2-naphthols in good to excellent yields involving two steps. It involves formation of 2-naphthol Mannich bases (**1-9**) followed by catalytic deamination leading to 1-arylmethyl-2-naphthols (**10-16**). Both steps can be carried out under microwave irradiation conditions with a total reaction time of less than three minutes.



1. Ar = Phenyl, X = CH_2
2. Ar = Phenyl, X = O
3. Ar = Phenyl, X = -
4. Ar = 4-Cl phenyl, X = CH_2
5. Ar = 4-Me phenyl, X = CH_2
6. Ar = 4-NO_2 phenyl, X = CH_2
7. Ar = 4-OMe phenyl, X = CH_2
8. Ar = 4-Pyridyl, X = CH_2
9. Ar = 2-Pyridyl, X = O



10. Ar = Phenyl
11. Ar = 4-Me phenyl
12. Ar = 4-NO_2 phenyl
13. Ar = 4-OMe phenyl
14. Ar = 4-Pyridyl
15. Ar = 2-Pyridyl

Fig 2: Molecular structures of 2-naphthol mannich base precursors (**1-9**) and 1-arylmethyl-2-naphthols (**10-15**).

Materials and Methods

2-Naphthol, cyclic secondary amines, aromatic aldehydes, *p*-toluenesulfonic acid, ammonium formate and 10% Pd/C were obtained from Aldrich Chemical Co. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker AV300 spectrophotometer at 300 MHz and 75 MHz, respectively. ^{1}H NMR and ^{13}C NMR for compounds **1-8** were recorded at 273K for better resolution of peaks. Melting points were recorded on a MEL-TEMP II apparatus and are uncorrected. EI-MS and HR-MS spectra were obtained on CEC 21-110B Sector instrument. UV-Vis and IR spectra were recorded on LKB Biochrom Ultraspec Plus 4054 and Nicolet Avatar 330FT-IR spectrophotometers respectively.

Domestic microwave oven manufactured by Kenmore was used for the microwave-assisted reactions at highest power (900 W) and 2450 MHz operating frequency.

Synthesis of 2-Naphthol Mannich Bases (1-9): 2-Naphthol Mannich bases were prepared by a recent modification[29] of a literature procedure[30] where catalytic amount of *p*-toluenesulfonic acid was used without solid support. Products were obtained in good to excellent yields. The reaction data is summarized in Table 1.

1-(Phenyl-piperidin-1-yl-methyl)-2-naphthol (1). ^{1}H and ^{13}C NMR were identical to those reported in literature.[31] IR, KBr Disc, ν: 3443, 3050, 2971, 1621, 1599, 1455, 1268, 1238 and 702 cm^{-1}. UV-Vis, MeOH, λ_{max}: 244, 280 and 336 nm. EI-MS (70 eV), *m/z* (% int.): 317 (M^+, 11), 231 (100), 200 (2) and 84 (41). HR-MS calcd. for $C_{22}H_{23}NO$: 317.1780; found: 317.1785.

1-(Morpholin-4-yl-phenylmethyl)-2-naphthol (2). ^{1}H and ^{13}C NMR were identical to those reported in literature.[31] IR, KBr Disc, ν: 3443, 3058, 2971, 2842, 1619, 1598, 1454, 1384, 1236 and 1116 cm^{-1}. UV-Vis, MeOH, λ_{max}: 242, 291 and 325 nm. EI-MS (70 eV), *m/z* (% int.): 319 (M^+, 7), 233 (4), 231 (100), 86 (1). HR-MS calcd. for $C_{21}H_{21}NO_2$: 319.1572; found: 319.1566.

1-(Phenyl-pyrrolidin-1-yl-methyl)-2-naphthol (3). ^{1}H NMR (300MHz, 293K, $CDCl_3$) δ: 1.86-1.91 (4H, m, 4 × CH), 2.10-2.73 (3H, m, 3 × NCH), 3.21-3.41 (1H, m, NCH), 5.15 (1H, s, Ar-CH-Ar'), 7.16-7.32 (5H, m, Ar'-H), 7.36-7.42 (1H, m, Ar-H), 7.61-7.74 (4H, m, Ar-H), 7.89-7.92 (1H, m, Ar-H) 13.90 (1H, bs, OH). ^{13}CNMR (75 MHz, 273K, $CDCl_3$) δ: 23.80, 52.79, 55.25, 71.18, 116.94, 117.01, 120.36, 121.53, 122.87, 126.86, 128.34, 128.90, 129.16, 129, 96, 130.02, 132.18, 141.49 and 155.82. IR, KBr Disc, ν: 3442, 3060, 2982, 1621, 1500, 1471, 1383, 1239 and 751 cm^{-1}. UV-Vis, MeOH. λmax : 245, 280, 290 and 335 nm. EI-MS (70 eV) m/z (% int.): 303 (M^+, 4), 233 (2), 232 (65), 231 (100), 70 (7). HR-MS calcd. for $C_{21}H_{21}NO$: 303.1623; found: 303.1626.

1-(4-Chlorophenyl)-piperidin-1-yl-methyl)-2-naphthol (4). ^{1}H NMR (300 MHz, 273 K, $CDCl_3$) δ: 1.27 (1H, bs, CH), 1.62-1.70 (5H, bs, 5 × CH), 1.97 (1H, bs, NCH), 2.03 (1H, bs, NCH), 2.73 (1H, bs, NCH), 3.36 (1H, bs, NCH), 5.07 (1H, s, Ar-CH-Ar'), 7.19-7.41 (4H, m, Ar-H), 7.43-7.46 (1H, m, Ar-H), 7.54-7.68 (2H, m, Ar-H), 7.71-7.81 (3H, m, Ar-H) and 13.12 (1H, bs, OH). ^{13}C NMR (75 MHz, 273 K, $CDCl_3$) δ: 24.35, 26.10, 26.30, 52.41, 55.14, 71.49, 117.13, 120.45, 121.20, 123.06, 127.08, 129.51, 129.77, 130.22 130.94, 131.16, 132.50, 134.21, 138.33 and 156.12. IR, KBr Disc, ν: 3440, 3080, 2951, 1620, 1519, 1474, 1384, 1104, 742 and 515 cm^{-1}. UV-Vis, MeOH, λ_{max}: 242, 291 and 336 nm. EI-MS (70 eV) *m/z* (% int.): 353 (M+2, 0.7), 350 (M^+, 2), 266 (2) , 264 (2), 231 (6), 84 (100). HR-MS calcd. for $C_{22}H_{22}ClNO$: 351.1390; found: 351.1387.

1-(4-Methylphenyl)-piperidin-1-yl-methyl)-2-naphthol (5). ^{1}HNMR (300 MHz, 273 K, $CDCl_3$) δ: 1.41 (1H, bs, CH), 1-50-1.91 (5H, m, 5× CH), 2.27-2.46 (4H, m, Ar-CH_3, NCH), 2.92 (1H, bs, NCH), 3.23 (1H, bs, NCH), 3.53 (1H, bs, NCH), 5.23 (1H, s, Ar-CH-Ar'), 7.01-7.08 (1H, m, Ar-H), 7.22-7.28 (2H, m, Ar-H), 7.37-7.42 (3H, m, Ar-H), 7.49-7.52 (2H, m, Ar-H), 7.68-7.75 (1H, m, Ar-H), 7.81-7.84 (1H, m, Ar-H) and 13.32 (1H, bs, OH). ^{13}CNMR (75 MHz, 273 K, $CDCl_3$) δ: 21.63, 24.03, 25.72, 26.00, 52.10, 55.20, 64.90, 109.00, 117.82, 120.33, 121.24, 123.06, 126.22, 127.10, 129.11, 129.47, 130.25, 130.87, 134.88 and 155.36. IR, KBr Disc, ν: 3439, 3060, 2963, 1621, 1595, 1384, 1359, 1261, 1231 and 821 cm^{-1}. UV-Vis, MeOH, λ_{max}: 244, 291 and 336 nm. EI-MS (70 eV), *m/z* (% int.): 331 (M^+, 14), 247 (10) and 231 (100). HR-MS calcd. for $C_{23}H_{25}NO$: 331.1936; found: 331.1930.

1-(4-Nitrophenyl)-piperidin-1-yl-methyl)-2-naphthol (6). ^{1}HNMR (300 MHz, 273 K, $CDCl_3$) δ: 1.28 (1H, bs, CH), 1.58-1.73 (5H, m, 5 × CH), 2.02 (1H, bs, -NCH), 2.15 (1H, bs, -NCH), 2.65 (1H, bs, -NCH), 3.37 (1H, bs, -NCH), 5.23 (1H, s, Ar-CH-Ar'), 7.18-7.31 (2H, m, Ar-H), 7.42 (1H, t, J= 7.5 Hz, Ar-H), 7.70-7.81 (5H, m, Ar-H), 8.13-8.16 (2H, m, Ar-H) and 13.78 (1H, bs, OH). ^{13}C NMR (75 MHz, 273 K, $CDCl_3$) δ: 24.32, 26.10, 26.40, 52.78, 55.03, 71.45, 115.26, 120.48, 120.83, 123.22, 124.61, 127.26, 129.06, 129.61, 130.21, 130.62, 132.33, 147.61, 147.73 and 155.74. IR, KBr Disc, ν: 3439, 3080, 3060, 2926, 1621, 1514, 1441, 1414, 1346, 1265, 1231 and 830 cm^{-1}. UV-Vis, MeOH, λ_{max}: 244, 295 and 335 nm. EI-MS (70 eV), *m/z* (% int.): 362 (M^+, 14), 279 (9), 260 (61), 231 (39), 230 (100), 85 (54), 58 (14). HR-MS calcd. for $C_{22}H_{22}N_2O_3$: 362.1630; found: 362.1634.

1-[(4-Methoxyphenyl)piperidin-1-yl-methyl]-2-naphthol (7). ^{1}H NMR (300MHz, 273K, $CDCl_3$) δ: 1.29-140 (1H, m, CH), 1.66-1.86 (5H, m, 5 × CH), 1.92-2.41 (2H, m, 2 × NCH), 2.74-2.91 (1H, m, NCH), 3.35-3.49 (1H, m, NCH), 3.73 (3H, s, OCH_3), 5.13 (1H, s, Ar-CH-Ar'), 6.78-6.81 (1H, m, Ar-H), 7.22-7.27 (2H, m, Ar-H), 7.39-7.43 (1H, m, Ar-H), 7.49-7.52 (2H, m, Ar-H), 7.67-7.74 (3H, m, Ar-H), 7.82-7.86 (1H, m, Ar-H), 13.71 (1H, bs, OH). ^{13}CNMR (75 MHz, 273K, $CDCl_3$) δ: 22.83, 24.35, 26.07, 52.15, 55.02, 55.59, 71.56, 114.48, 116.33, 120.37, 121.39, 122.85., 126.87, 129.07, 129.34, 129.85, 130.68, 131.46, 132.63, 155.52, 159.63. IR, KBr Disc,ν: 3440, 3060, 2992, 1621, 1511, 1473, 1314, 1242, 1033 cm^{-1}.UV-Vis, MeOH. λmax : 244, 291 and 335 nm. EI-MS (70 eV) m/z (% int.): 347(1), 261(100), 247(2), 84(19). HR-MS calcd. for $C_{23}H_{25}NO_2$: 347.1885; found: 347.1874.

1-(Piperidin-1-yl-pyridin-4-yl-methyl)-2-naphthol (8). ^{1}H NMR (300 MHz, 273 K, $CDCl_3$) δ: 1.61 (1H, bs, CH), 1.72-1.88 (5H, bs, 5 × -CH), 2.10 (1H, bs, -NCH), 2.71 (1H, bs, -NCH), 3.16 (1H, bs, -NCH), 3.35 (1H, bs, -NCH), 5.07 (1H, s, Ar-CH-Ar'), 7.15-7.82 (8H, m, Ar-H), 8.50-8.52 (2H, d, J= 8 Hz, Ar-H) and 13.75 (1H, bs, OH). ^{13}C NMR (75 MHz, 273 K, $CDCl_3$) δ: 24.40, 26.42, 26.44, 52.71, 54.94, 71.26, 115.17, 120.41, 120.94, 123.15, 124.12, 127.17, 129.01, 129.55, 130.48, 132.39, 149.11, 150.67 and 155.87. IR, KBr Disc, ν: 3442, 3044, 2944, 1621, 1598, 1451, 1384, 1267, 1236 and 816 cm^{-1}. UV-Vis, MeOH, λ_{max}: 241 and 298 nm. EI-MS (70 eV) m/z (% int.): 318 (M^+, 5), 235 (4), 233 (100), 232 (51). HR-MS calcd. for $C_{21}H_{22}N_2O$: 318.1732; found: 318.1727.

1-(Morpholin-1-yl-pyridin-2-yl-methyl)-2-naphthol (9). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.31-2.44 (2H, m, 2 × –NCH), 2.69-2.90 (2H, m, 2 × –NCH), 3.73- 3.89 (4H, m, 4 × –OCH), 5.45 (1H, s, Ar-CH-Ar'), 7.13-7.18 (2H, m, Ar-H), 7.25-7.31 (1H, m, Ar-H), 7-40-7.46 (1H, m, Ar-H), 7.55-7.74 (4H, m, Ar-H), 8.06-8.10 (1H, d, J= 8.4 Hz, Ar-H), 8.57-8.60 (1H, d, J= 4.8 Hz, Ar-H) and 12.98 (1H, bs, OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 52.96, 67.25, 73.94, 114.45, 120.16, 122.06, 123.22, 123.39, 123.79, 127.16, 129.16, 130.47, 133.02, 137.79, 149.42, 155.34 and 159.32. IR, KBr Disc, ν: 3439, 3040, 2934, 1621, 1592, 1451, 1384, 1262, 1236 and 819 cm^{-1}. UV-Vis, MeOH, λ_{max}: 242 and 296 nm.

Synthesis of 1-arylmethyl -2-naphthols (10-16)

Method A: A mixture of appropriate 2-naphthol Mannich base (0.7 mmol), ammonium formate (7 mmol), Pd/C (40 mg, cat.) in methanol (15 ml) was refluxed for 2 hours. The reaction mixture was filtered on a celite bed, the methanol was concentrated and the product was extracted with ethyl acetate and water. The dried (anhydrous Na_2SO_4) organic layer was rotary evaporated to yield solid product which was washed with ice-cold dichloromethane (3 ml). The product thus obtained was found to be pure on TLC examination.

Method B: A mixture of appropriate 2-naphthol Mannich base (0.7 mmol), ammonium formate (7 mmol) and 10% Pd/C (40 mg, cat.) was irradiated by microwave in methanol (10 ml) for 1 minute (2 × 30 sec); methanol evaporated completely. TLC was checked after dissolving the material in methanol (5 ml) which showed appreciable conversion (~70-80%). It was then filtered on a celite bed; the methanol was rotary evaporated and the product was extracted with ethyl acetate and water. The dried organic layer to vacuum concentrated to dryness and resulting solid product was washed with ice-cold dichloromethane (3 ml). It was found to be pure on TLC.

1-Benzyl-2-naphthol (10). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.50 (2H, s, Ar-CH_2-Ar'), 7.05-7.24 (5H, m, Ar-H), 7.28-7.50 (2H, m, Ar-H), 7.74 (1H, d, J= 9 Hz, Ar-H), 7.84 (1H, d, J= 8.1 Hz, Ar-H), 7.94-7.97 (2H, m, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 31.11, 118.31, 118.58, 123.68, 123.78, 126.58, 127.13, 128.64, 128.97, 128.99, 129.02, 129.90, 134.09, 140.40 and 151.61. IR, KBr Disc, ν: 3423, 3060, 3027, 2938, 1630, 1602, 1474, 718 cm^{-1}. EI-MS (70 eV) m/z (% int.): 234 (M^+, 100), 91 (5). HR-MS calcd. for $C_{17}H_{14}O$: 234.1045; found: 234.1044.

1-(4-Methylbenzyl)-2-naphthol (11). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.32 (3H, s, Ar-CH_3), 4.45 (2H, s, Ar-CH_2-Ar'), 7.08-7.16 (4H, m, Ar-H), 7.34-7.48 (3H, m, Ar-H), 7.70-7.98 (3H, m, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.43, 30.70, 118.36, 118.75, 123.62, 123.76, 126.78, 126.93, 127.08, 128.50, 128.87, 128.96, 129.74, 129.87, 134.08 and 151.66. IR, KBr Disc, ν: 3435, 3026, 3017, 2972, 1615, 1600, 1468, 709 cm^{-1}. EI-MS (70 eV) m/z (% int.): 248 (M^+, 100), 156 (4), 144 (5), 105 (5). HR-MS calcd. for $C_{18}H_{16}O$: 248.1201; found: 248.1195.

1-(4-Aminobenzyl)-2-naphthol (12). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.58 (2H, bs, NH_2), 4.16 (2H, s, Ar-CH_2-Ar'), 6.40 (2H, m, Ar'-H), 6.87 (2H, m, Ar'-H), 7.21-7.39 (3H, m, Ar-H), 7.64-7.85 (3H, m, Ar-H), 9.63 (1H, bs, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 29.89, 49.46, 114.70, 119.01, 119.73, 123.00, 124.09, 126.79, 128.24, 129.10, 129.19, 129.42, 134.18, 147.07 and 153.17. IR, KBr Disc, ν: 3420, 3359, 3298, 1631, 1613, 1512, 1384, 807, 745 cm^{-1}. EI-MS (70 eV) m/z (% int.): 249 (M^+, 7), 144 (100), 115 (5), 93 (7). HR-MS calcd. for $C_{17}H_{15}NO$: 249.1154; found: 249.1148.

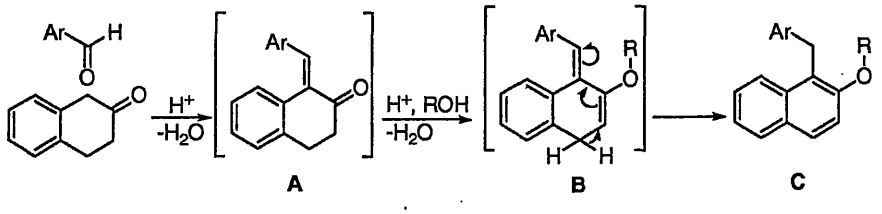
1-(4-Methoxybenzyl)-2-naphthol (13). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.65 (3H, s, O-CH_3), 4.29 (2H, s, Ar-CH_2-Ar'), 6.77 (2H, d, J= 8.2 Hz, Ar'-H), 7.08-7.41 (5H, m, Ar-H), 7.65-7.87 (3H, m, Ar-H), 9.72 (1H, bs, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 29.82, 55.76, 114.43, 118.99, 119.19, 123.08, 123.90, 126.96, 128.53, 128.95, 129.11, 129.15, 129.90, 134.08, 153.28 and 157.04. IR, KBr Disc, ν: 3367, 2926, 1630, 1607, 1584, 1510, 1384, 808, 745 cm^{-1}. EI-MS (70 eV) m/z (% int.): 264 (M^+, 100), 108 (54). HR-MS calcd. for $C_{18}H_{16}O_2$: 264.1150; found: 264.1152.

1-((Pyridine-4-yl)methyl)-2-naphthol (14). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 4.36 (2H, s, Ar-CH_2-Ar'), 7.18-7.39 (5H, m, Ar-H), 7.72-7.81 (3H, m, Ar-H), 8.37-8.38 (2H, m, Ar-H), 10.10 (1H, bs, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 30.19, 117.02, 118.92, 123.28, 123.53, 124.56, 127.30, 129.06, 129.16, 129.29, 133.99, 150.17, 151.34 and 153.70. IR, KBr Disc, ν: 3448, 3051, 2967, 2937, 1607, 1576, 1438, 1332, 1277, 808, 519 cm^{-1}. EI-MS (70 eV) m/z (% int.): 235 (M^+, 100), 157 (2). HR-MS calcd. for $C_{16}H_{13}NO$: 235.0997; found: 235.0993.

1-((Pyridine-2-yl)methyl)-2-naphthol (15). Prepared by methods A and B. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 4.49 (2H, s, CH_2), 7.02-7.45 (5H, m, Ar-H), 7.53-8.00 (4H, m, Ar-H), 8.48 (1H, d, J= 8.2 Hz, Ar'-H), 9.98 (1H, bs, OH). ^{13}C NMR (75 MHz, DMSO-d_6) δ: 34.14, 117.71, 119.17, 122.07, 123.16, 123.21, 123.97, 127.09, 128.23, 128.91, 129.10, 134.26, 137.55, 149.47, 153.59 and 161.88. IR, KBr Disc, ν: 3444, 3058, 2953, 2923, 1631, 1618, 1596, 1384, 750 cm^{-1}. EI-MS (70 eV) m/z (% int.): 235 (M^+, 100), 218 (83), 217 (18), 157 (2). HR-MS calcd. for $C_{16}H_{13}NO$: 235.0997; found: 235.0992.

Results and Discussion

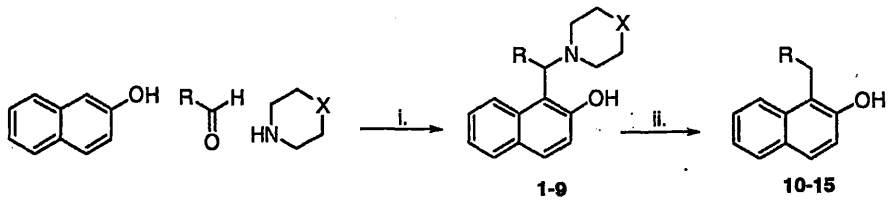
The interest of this laboratory lies in use of 2-naphthol and its dihydro derivative 2-tetralone as versatile building block for generation of molecular framework of medicinal importance.[32-34] In our previous work,[32,33] we devised an excellent procedure to prepare 1-arylmethyl-2-alkoxynaphthalenes (**C**) from 2-tetralone, aromatic aldehydes and alcohols under anhydrous acidic conditions (Scheme 1). It appeared quite logical that replacement of alcohol (ROH) with water (HOH) in this synthetic scheme should lead to formation of 1-arylmethyl-2-naphthol (**C**, R=H). But such an attempt failed to produce any result. 1-Arylmethyl-2-naphthols (**C**, R=H) can also be viewed as constitutional isomers of 1-arylidene-2-tetralones (**A**). Since 1-arylmethyl-2-naphthols (**C**, R=H) are aromatic, a conversion from **A** to **C** (R=H) should be rather facile; but after numerous attempts, including reaction via formation of easily cleavable silyl enol ethers (**B**, R=$SiMe_3$) and enol esters (**B**, R=$COCF_3$), we failed to achieve this.[32]



Scheme 1: Synthesis of 1-arylmethyl-2-alkoxynaphthalene.

We then decided to utilize an alternate and novel procedure to make 1-arylmethyl-2-naphthols (**C**, R=H) starting from 2-naphthol (Scheme 2). This involved facile formation of 2-naphthol Mannich bases (**1-9**) followed by reductive cleavage of C-N bond furnishing desired compounds (**10-15**). We employed a modified a literature procedure[30] which involved use of microwave to prepare a Mannich bases of 2-naphthol expeditiously. Instead of acidic alumina used in the literature procedure,[30] we utilized catalytic quantities of *p*-toluenesulfonic acid under solvent-free conditions.[29] We achieved moderate to excellent yields (Table-1) of 2-naphthol Mannich bases (**1-9**) and were able to reduce the reaction time from 5 minutes to 1 minute. The use of Pd catalyzed hydrogenolysis is widely used procedure for reductive deamination of benzylic amines.[35] The Mannich bases were subjected to Pd/C catalyzed reductive deamination in methanol utilizing ammonium formate as source of hydrogen gas under conventional heating conditions. It took between 1-2 hours for the reaction to go to completion as witnessed by TLC. The isolated yield and the purity of the products (**10-15**) were excellent. Chloro- and nitro- substituents on compounds **4** and **6** were also reduced during hydrogenation as expected yielding compounds **10** and **12**, respectively.

This type of reductive deamination is known under microwave conditions as well.[35] So we carried out a few representative reactions under microwave irradiation and the reaction indeed worked as efficiently in 1 minute. The results are appended in Table 1 as footnotes.



Scheme 2: Synthetic route followed for the preparation of 2-naphthol Mannich bases (**1-9**) and 1-arylmethyl-2-naphthols (**10-15**).

Formation of these products was easily confirmed by disappearance of aliphatic protons of N-heterocycle in NMR and shifting of -OH signal from δ 12-14 range for 2-naphthol Mannich bases (**1-9**) to ~ δ 9 for 1-arylmethyl-2-naphthols (**12-15**), where DMSO-d_6 was used as solvent; this peak did not appear in case of $CDCl_3$ as solvent. The shifting of OH signal indicated that there was H-bonding between -OH and heterocyclic N in Mannich bases which disappeared after hydrogenation. Also, the benzylic proton in 1-arylmethylnaphthols (**10-15**) integrated for 2 protons as opposed to 1 proton in case of 2-naphthol Mannich bases (**1-9**).

Table 1: Reaction data for the preparation of 2-naphthol Mannich bases (**1-9**) and 1-arylmethyl-2-naphthols (**10-15**).

2-Naphthol Mannich bases				1-Arylmethyl-2-naphthols			
Compd.	**Time in min.**	**% yield**	**Mp (lit. mp) in °C**	**Compd.**	**time in min.**	**% yield**	**mp (lit. mp) in °C**
1	1	79.7	192-194 (198-199)[31]	**10**	120	82.0	109-111 (111-112)[27]
2	1	85.8	177-179 (181-183)[31]	**10**[a]	60	92.9	110-111 (111-112)[27]
3	1	77.0	172-174	**10**	120	72.8	109-110 (111-112)[27]
4	1	72.0	165-166	**10**	120	59.3	107-108 (111-112)[27]
5	1	82.7	144-146	**11**	120	64.1	-
6	1	83.3	186-188	**12**	90	58.6	176-182
7	1	62.0	137-140	**13**[a]	120	54.2	129-130 (130-131)[26]
8	1	82.4	185-187	**14**	120	84.0	213-216
9	1	61.1	168-170	**15**[a]	120[a]	84.0	97-99

[a]Also carried out by microwave irradiation (cf. Materials and Methods; Method B). Data obtained is as under (Compound, reaction time in minute, % yield): **10**, 1, 71; **13**, 1, 77; **15**, 1, 65.

Conclusion

In conclusion, we have devised an elegant procedure for the synthesis of 1-arylmethyl-2-naphthols starting from 2-naphthol, an economical and readily available starting material, involving two extremely efficient microwave-assisted reactions. This constitutes as novel procedure where secondary amines were used to aid the selective insertion of arylmethyl group at position 1 of 2-naphthol. Chemical modification of 1-arylmethyl-2-naphthol framework is in progress to produce compounds of medicinal interest.

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