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# An Efficient Synthesis of New Chiral Oxazolines

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Several new chiral oxazolines were prepared conveniently in good to high yields using a two-step synthesis involving formation of an optically active amide, *in situ* conversion of the amide into tosylate (OTs) and finally ring closing reaction under MW irradiation (800 W) in solvent free condition. A comparison of these results with those obtained from the ring closing reaction under classical conditions was also made.

**Keywords:** Oxazoline, Chiral, Microwave, Chiral amide, Ring closing, Solvent free

## INTRODUCTION

The construction of five-membered nitrogen-containing heterocycles such as oxazolines belongs to an important class of compounds. Oxazolines are versatile intermediates in the synthesis of β-substituted serines which are of significant importance because of their utility in the synthesis of various antibiotics [1]. On the other hand, chiral oxazolines have been extensively used in asymmetric synthesis, as both auxiliaries and ligands [2,3]. Optically active oxazolines exist in a variety of natural products and biologically active compounds [4,5] and they can easily be converted into optically active β-amino alcohols which are useful synthetic intermediates [6,7].

Numerous methods have been developed for the preparation of 2-substituted oxazolines from carboxylic acids using high temperatures of up to 200-220 °C [8], open vessel microwave-assisted synthesis starting from carboxylic acids [9], repeated use of $SOCl_2$ [10], phosphines together with harmful halogenated hydrocarbons such as $CCl_4$ or hexachloroethane [11], or under other drastic reaction conditions. Some other methods, starting from amino alcohols reaction with carboxylic acids [12], *ortho* esters [13], nitriles [14], iminoethers [15] and acyl benzotriazoles [16] have been reported. Other major synthetic methods start from β-hydroxy amides, with cyclisation attained with a number of reagents including Burgess' reagent [17], DAST [18], $PPh_3$/DIAD [19] and immobilized *p*-toluensulfonylchloride/$Et_3N$ [20].

In continuation of our recent research in the synthesis and use of *N*-heterocyclic compounds in organic synthesis [21], herein we report the synthesis of some new chiral oxazolines in high yields and short reaction times (1-3 min) using microwave irradiations under solvent free conditions. A comparison of this method with the classical conditions was also made.

## EXPERIMENTAL

### Apparatus and Chemicals

Melting points were measured on an Electrothermal 9100 apparatus. Optical rotations were measured in $CH_2Cl_2$ (c = 1) by Kruss digital polarimeter P 3002. IR spectra were determined on a Shimadzo IR-470 spectrometer. $^1H$ NMR and $^{13}C$ NMR spectra were recorded on a 500 MHz Bruker DRX-500 in $CDCl_3$ as solvent and TMS as internal standard.

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Preparative thin-layer chromatography was prepared from Merck Kieselgel 60 H, $F_{254}$, Art No 7730. For column chromatography, Merck Kieselgel 60, Art No 107733 was employed. Chemicals were purchased from Merck and Fluka. All solvents used were dried and distilled according to standard procedures.

### General Procedure for Preparation of Amides (2a-i)

Triethylamine (15.6 mmol) in dry dioxane (12 ml) was added to 2-amino-3-phenyl propanol (8.0 mmol) at 0 °C. Then, a solution of acyl chloride (7.6 mmol) in dry dioxane (10 ml) was added. The mixture was stirred for 1.5 h at this temperature. The product was filtered, the filterate was concentrated under vacuum and purified by column chromatography (silica gel, EtOAc/Ether: 1/1) to provide the desired amides **2** (86-95%) (Table 1).

### General Procedure for Preparation of 2-Aryl-4-benzyl-4,5-dihydroxazole (3a-i) Under Classical Conditions

*p*-TsCl (5.6 mmol) and 4-DAMP (2 mmol) were added into a solution of amide **2** (4 mmol) in triethylamine (20 mmol) and 1,2-dichloroethane (16 ml). The mixture was heated under reflux condition. The progress of the reaction was monitored by TLC (EtOAc/ether: 1/3). After completion of the reaction, the product was washed with water. The organic layer was separated, dried ($MgSO_4$) and the solvent was evaporated under vacuum. The residue was purified by preparative thin layer chromatography (silica gel, EtOAc/ ether: 1/3) to provide the desired 2-aryl-4-benzyl-4,5-dihydroxazole **3** ( 52-78%)(Table 2).

### General Procedure for Preparation of 2-Aryl-4-benzyl-4,5-dihydroxazole (3a-i) Using Microwave Irradiation Under Solvent Free Conditions

*p*-TsCl (2.8 mmol) and 4-DAMP (1 mmol) were added into a solution of amide **2** (2 mmol) in triethylamine (10 mmol). The mixture was heated under microwave irradiation (800 W) for 1-3 min. The progress of the reaction was monitored by TLC (EtOAc/ether: 1/3). After completion of the reaction, the product was purified by preparative thin layer chromatography (silica gel, EtOAc/ether: 1/3) to provide the desired 2-aryl-4-benzyl-4,5-dihydroxazole **3** (59-84%) (Table 2).

**2-Chloro-*N*-(1-hydroxy-3-phenyl propane-2-yl) benzamide (2a).** White solid, m.p.: 92-94 °C; IR (KBr, $cm^{-1}$): 3278 (vs), 3061 (w), 3026 (w), 2931 (w), 1645 (vs), 1600 (w), 1541 (s), 1450 (m), 1081 (s), 1063 (s), 748 (s), 698 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.52 (d, *J* = 7.6 Hz, 1H), 7.25-7.38 (m, 8H), 6.60 (d, *J* = 7.4 Hz, 1H), 4.42 (m, 1H), 3.78 (dd, *J* = 3.6, 11.1 Hz, 1H), 3.70 (dd, *J* = 4.6, 11.1 Hz, 1H), 3.0 (d, *J* = 7.2 Hz, 2H), 2.98 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 167.4, 137.9, 135.4, 131.7, 131.0, 130.5, 130.3, 129.7, 129.0, 127.4, 127.1, 64.0, 53.8, 37.3 ppm.

**4-Chloro-*N*-(1-hydroxy-3-phenyl propane-2-yl) benzamide (2b).** White crystal, m.p.: 168-169 °C; IR (KBr, $cm^{-1}$): 3298 (s), 3050 (w), 2967 (w), 1639 (vs), 1550 (s), 1486 (m), 1450 (m), 1053 (m), 842 (m), 682 (m); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.24 (t, *J* = 9.1 Hz, 3H), 7.14 (m, 4H), 7.04 (m, 1H), 4.16 (m, 1H), 3.58 (t, *J* = 6.4 Hz, 1H), 3.53 (dd, *J* = 3.5, 11.3 Hz, 1H), 3.46 (dd, *J* = 4.4, 11.3 Hz, 1H), 2.84 (d, *J* = 6.5 Hz, 2H), 2.59 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 166.5, 138.8, 137.5, 129.7, 129.1, 128.7, 128.6, 126.5, 63.02, 53.7, 37.1 ppm.

**2-Flouro-*N*-(1-hydroxy-3-phenyl propane-2-yl) benzamide (2c).** Yellow solid, m.p.: 124-126 °C; IR (KBr, $cm^{-1}$): 3317 (s), 3080 (m), 3024 (m), 2955 (w), 2929 (m), 2867 (w), 1643 (vs), 1614 (m), 1548 (s), 1483 (s), 1452 (s), 1218 (s), 1051 (s), 757 (s), 673 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 8.10 (m, 1H), 7.51 (m, 1H), 7.37-7.19 (m, 7H), 7.13 (dd, *J* = 8.3, 11.9 Hz, 1H), 7.0 (s, 1H), 4.4 (m, 1H), 3.84 (dd, *J* = 3.6, 11.06 Hz, 1H), 3.75 (dd, *J* = 5.1, 11.06 Hz, 1H), 3.05 (dd, *J* = 4.4, 7.0 Hz, 2H), 2.47 (s, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 160.0, 137.8, 133.9, 133.8, 132.4, 129.7, 129.1, 127.1, 125.2, 121.2, 116.5, 64.7, 54, 37.5 ppm.

***N*-(1-Hydroxy-3-phenyl propane-2-yl) 4-nitrobenzamide (2d).** Pall brown crystal, m.p.: 139-141 °C; IR (KBr, $cm^{-1}$): 3292 (s), 3075 (w), 2966 (m), 2925 (s), 2854 (m), 1646 (vs), 1600 (m), 1554 (s), 1515 (vs), 1450 (m), 1336 (s), 1029 (s), 837 (s), 746(s), 696 (s) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): δ 8.32 (d, *J* = 6.9 Hz, 2H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.31 (m, 3H), 6.46 (d, *J* = 6.64 Hz, 1H), 4.46 (m, 1H), 3.86 (m, 1H), 3.79 (m, 1H), 3.0 (d, *J* = 7.3 Hz, 2H), 2.20 (t, *J* = 5.8 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 163.2, 129.8, 129.4, 128.7, 127.6, 124.4, 64.2, 53.8, 37.6 ppm.

**Table 1.** Preparation of Amides **2a-i**

| Entry | Ar | Time (h) | Yield (%)[a,b] | Mp ($^oC$) | $[\alpha]_D^{25}$ |
|---|---|---|---|---|---|
| **a** | 2-$ClC_6H_5$ | 1.5 | 91 | 94-95 | -0.88 |
| **b** | 4-$ClC_6H_5$ | 1.5 | 93 | 168-169 | -2.08 |
| **c** | 2-$FC_6H_5$ | 1.5 | 93 | 124-126 | -10.02 |
| **d** | 4-$NO_2C_6H_5$ | 1.5 | 95 | 139-141 | -6.07 |
| **e** | $C_6H_5$ | 1.5 | 90 | 158-160 | +0.88 |
| **f** | $C_6H_5$-CH=CH | 1.5 | 89 | 141-142 | -1.65 |
| **g** | 2-Thienyl | 1.5 | 90 | 117-118 | -5.3 |
| **h** | 4-$MeC_6H_5$ | 1.5 | 88 | 148-150 | -4.37 |
| **i** | 4-$MeOC_6H_5$ | 1.5 | 86 | 142-143 | -1.32 |

[a]All products were characterized by IR, $^1$H NMR and $^{13}$C NMR. [b]Isolated yield.

**Table 2.** Synthesis of 4-Benzyl-2-aryl-4,5-dihydroxazoles (**3a-i**)

| Entry | Ar | Classical | | Microwave (800 W) | | | |
|---|---|---|---|---|---|---|---|
| | | Time (h) | Yield (%)[a,b] | Time (min) | Yield (%)[a,b] | Mp ($^oC$) | $[\alpha]_D^{25}$ |
| **a** | 2-$ClC_6H_5$ | 22 | 72 | 2 | 80 | - | +1.34 (+1.35)[c] |
| **b** | 4-$ClC_6H_5$ | 22 | 74 | 2 | 78 | 128-130 | -1.8 (-1.83)[c] |
| **c** | 2-$FC_6H_5$ | 22 | 74 | 2 | 82 | 86-88 | -4.8 (-4.82)[c] |
| **d** | 4-$NO_2C_6H_5$ | 20 | 78 | 1 | 84 | 73-74 | -0.36 |
| **e** | $C_6H_5$ | 24 | 70 | 2 | 73 | 61-63 | -2.38 |
| **f** | $C_6H_5$-CH=CH | 24 | 70 | 1 | 72 | - | -2.24 |
| **g** | 2-Thienyl | 24 | 55 | 3 | 62 | - | -2.36 |
| **h** | 4-$MeC_6H_5$ | 27 | 48 | 2 | 60 | 90-91 | +0.13 |
| **i** | 4-$MeOC_6H_5$ | 27 | 52 | 3 | 59 | - | -2.4 |

[a]All products were characterized by IR, $^1$H NMR and $^{13}$C NMR. [b]Isolated yield. [c]Optical activity was measured in MeOH (c 2).

***N*-(1-Hydroxy-3-phenyl propane-2-yl) benzamide (2e).** White crystal, m.p.: 158-160 °C; IR (KBr, $cm^{-1}$): 3309 (vs), 3024 (w), 2927 (w), 1637 (vs), 1542 (s), 1488 (m), 1450 (m), 1031 (s), 746 (s), 696 (vs) $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.71 (d, *J* = 7.96 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.59 Hz, 2H), 7.31 (m, 3H), 6.38 (s, 1H), 4.41 (m, 1H), 3.86 (m, 1H), 3.77 (m, 1H), 3.0 (dd, *J* = 2.56, 7.2 Hz, 2H), 2.64 (t, *J* = 5.2 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 172.6, 144.2, 140.3, 136.5, 134.7, 133.6, 132.7, 131.5, 68.1, 54.7, 42.2 ppm.

***N*-(1-Hydroxy-3-phenyl propane-2-yl) cinamamide (2f).** White crystal, m.p.: 158-160 °C; IR (KBr, $cm^{-1}$): 3350 (s), 3296 (vs), 3025 (w), 2952 (w), 1656 (vs), 1623 (vs), 1546 (vs), 1485 (m), 1455 (m), 1054 (s), 746 (s), 700 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.65 (d, *J* = 15.6 Hz, 1H), 7.52 (m, 2H), 7.39 (m, 5H), 7.27-7.30 (m, 3H), 6.39 (d, *J* = 15.6 Hz, 1H),

5.87 (d, *J* = 6.90 Hz, 1H), 4.30 (m, 1H, CH), 3.81 (dd, *J* = 3.2, 11.0 Hz, 1H), 3.72 (dd, *J* = 15.1, 11.0 Hz, 1H), 3.0 (d, *J* = 7.2 Hz, 2H), 2.71 (s, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 167.0, 142.2, 138.1, 135.3, 130.4, 129.8, 129.4, 129.3, 128.4, 127.4, 120.9, 67.0, 53.8, 37.6 ppm.

***N*-(1-Hydroxy-3-phenyl propane-2-yl) thiophen-2-carboxamide (2g).** White crystal, m.p.: 117-118 °C; IR (KBr, $cm^{-1}$): 3294 (s), 3078 (w), 2952 (m), 2923 (w), 2856 (w), 1629 (vs), 1540 (s), 1492 (m), 1450 (m), 1046 (m), 719 (s), 696 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.49 (d, *J* = 4.4 Hz, 1H), 7.44 (d, *J* = 3.5 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.29 (m, 3H), 7.07 (t, *J* = 4.3 Hz, 1H), 6.35 (d, *J* = 6.8, 1H), 4.36 (m, 1H), 3.81 (dd, *J* = 3.59, 11.1 Hz, 1H), 3.73 (dd, *J* = 4.9, 11.1 Hz, 1H), 3.02 (d, *J* = 7.16 Hz, 2H), 2.86 (s, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 162.7, 139.0, 137.9, 130.6, 129.7, 129.1, 128.6, 128.0, 127.2, 64.3, 53.7, 37.4 ppm.

***N*-(1-Hydroxy-3-phenyl propane-2-yl) 4-methylbenzamide (2h).** Yellow solid, m.p.: 148-150 °C; IR (KBr, $cm^{-1}$): 3353 (vs), 3335 (vs), 3058 (s), 3026 (s), 2950 (s), 2925 (s), 2854 (s), 1650 (vs), 1600 (vs), 1560 (vs), 1487 (s), 1450 (s), 1332 (s), 1033 (s), 850 (w), 690 (vs); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.48 (d, *J* = 6.9 Hz, 2H), 7.36-7.26 (m, 8H), 6.54 (d, *J* = 6.8 Hz, 1H), 4.31 (m, 1H), 3.80 (dd, *J* = 3.56, 11.1 Hz, 1H), 3.72 (dd, *J* = 5.07, 11.1 Hz, 1H), 3.17 (s, 1H), 3.03 (dd, *J* = 2.2, 7.06 Hz, 2H), 2.38 (s, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ; 168.7, 138.1, 134.7, 132.7, 129.7, 129.1, 128.8, 128.1, 127.1, 64.0, 53.7, 37.4, 21.6 ppm.

***N*-(1-Hydroxy-3-phenyl propane-2-yl) 4-methoxybenzamide (2i).** White solid, m.p.: 142-143 °C; IR (KBr, $cm^{-1}$): 3303 (vs), 3026 (m), 2920 (m), 2845 (m), 1633 (vs), 1627 (vs), 1541 (s), 1506 (s), 1454 (m), 1334 (m), 1257 (s), 1029 (s), 842 (s), 750 (m), 696 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.58 (dd, *J* = 2.48, 8.8 Hz, 2H), 7.17 (m, 4H), 7.01 (m, 1H), 6.71 (dd, *J* = 2.7, 8.8 Hz, 2H), 4.19 (t, *J* = 5.2 Hz, 1H), 4.11 (m, 1H), 3.65 (s, 3H), 3.42 (m, 2H), 2.79 (dd, *J* = 3.02, 7.1 Hz, 2H), 2.63 (s, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 167.1, 162.2, 139.0, 129.7, 129.2, 128.6, 127.4, 126.4, 113.7, 63.1, 55.6, 53.5, 37.2 ppm.

**4-Benzyl-2-(2-chlorophenyl)-4,5-dihydroxazole (3a).** Colourless liquid, IR (KBr, $cm^{-1}$): 3062 (w), 3025 (w), 2960 (w), 2925 (m), 2854 (w), 1649 (vs), 1596 (m), 1475 (s), 1244 (m), 1033 (s), 765 (s), 732 (s), 702 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.77 (dd, *J* = 1.3, 7.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.40-7.26 (m, 8H), 4.69 (m, 1H), 4.39 (t, *J* = 8.9 Hz, 1H), 4.20 (t, *J* = 7.8 Hz, 1H), 3.28 (dd, *J* = 5.2, 13.7 Hz, 1H), 2.85 (dd, *J* = 8.4, 13.7 Hz, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 163.0, 138.1, 133.8, 132.0, 131.7, 131, 129.8, 129.0, 127.9, 127.0, 126.9, 72.1, 68.6, 42.0 ppm.

**4-Benzyl-2-(4-chlorophenyl)-4,5-dihydroxazole (3b).** White crystal, m.p.: 128-130 °C; IR (KBr, $cm^{-1}$): 3025 (w), 2956 (w), 2925 (m), 2854 (w), 1639 (vs), 1548 (s), 1487 (s), 1452 (m), 1332 (m), 1087 (s), 1155 (s), 840 (s), 698 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.91 (d, *J* = 7.3 Hz, 2H), 7.73 (d, *J* = 8.12 Hz, 2H), 7.37 (m, 3H), 7.27 (m, 3H), 4.61 (m, 1H), 4.39 (m, 2H), 3.04 (d, *J* = 7.26, 2H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 166.4, 137.3, 133.6, 129.6, 129.5, 129.1, 128.8, 127.1, 126.4, 72.7, 68.9, 53.7 ppm.

**4-Benzyl-2-(2-flouro phenyl)-4,5-dihydroxazole (3c).** White solid, m.p.: 86-88 °C; IR (KBr, $cm^{-1}$): 3062 (w), 2963 (w), 2925 (w), 2854 (w), 1649 (vs), 1596 (m), 1475 (s), 1244 (s), 1099 (s), 962 (s), 766 (s), 702 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 7.89 (t, *J* = 7.4 Hz, 1H), 7.47 (m, 1H), 7.33 (m, 3H), 7.26 (m, 4H), 7.18 (m, 1H), 4.66 (m, 1H), 4.36 (t, *J* = 8.9 Hz, 1H), 4.18 (t, *J* = 7.8 Hz, 1H), 3.31 (dd, *J* = 4.8, 13.7 Hz, 1H), 2.79 (dd, *J* = 8.9, 13.7 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 163.8, 138.1, 131.5, 129.76, 129.74, 129.1, 129.0, 126.9, 124.4, 124.3, 71.8, 68.3, 42.0 ppm.

**4-Benzyl-4,5-dihydro-2-(4-nitrophenyl) oxazole (3d).** Yellow solid, m.p.: 71-74 °C; IR (KBr, $cm^{-1}$): 3000 (w), 2957 (s), 2927 (s), 2858 (m), 1645 (s), 1608 (s), 1521 (vs), 1500 (m), 1452 (m ), 1342 (vs), 1068 (s), 962 (s), 856 (m), 752 (m), 702 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 8.26 (m, 2H), 8.11 (d, *J* = 2.7 Hz, 2H), 7.34-7.21 (m, 5H), 4.65 (m, 1H), 4.21 (m, 2H), 3.23 (dd, *J* = 5.3, 13.75 Hz, 1H), 2.78 (dd, *J* = 8.25, 13.75 Hz, 1H) ppm; $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 163.4, 137.9, 134, 131.3, 129.7, 129.6, 129.2, 129, 127.1, 72.8, 68.5, 42.0 ppm.

**4-Benzyl-4,5-dihydro-2-phenyl oxazole (3e).** White solid, m.p.: 61-63 °C; IR (KBr, $cm^{-1}$): 3050 (w), 2958 (w), 2927 (w), 1639 (vs), 1541 (s), 1475 (w), 1470 (m), 1284 (vs), 1130 (s), 760 (w), 705 (s); $^1$H NMR ($CDCl_3$, 500 MHz): δ 8.04 (m, 2H), 7.70 (m, 3H), 7.56-7.38 (m, 2H), 7.39-7.25 (m, 3H), 4.74 (m, 1H), 4.44 (m, 2H), 3.16 (dd, *J* = 5.6, 13.7 Hz, 1H), 2.99 (dd, *J* = 8.1, 13.7 Hz, 1H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ 167.5, 133.7, 132.0, 131.3, 130.1, 129.8, 129.2, 129.1, 128.9, 68.5, 65.6, 51.0 ppm.

**4-Benzyl-4,5-dihydro-2-acetryloxazole (3f).** Colorless liquid, IR (KBr, $cm^{-1}$): 3020 (m), 3050 (m), 2923 (m), 1650 (vs), 1600 (s), 1515 (m), 1450 (s), 985 (s), 759 (s), 698 (s); $^1H$ NMR ($CDCl_3$, 500 MHz): δ 7.52 (d, *J* = 7.5 Hz, 2H), 7.42-7.33 (m, 4H), 7.30-7.16 (m, 4H), 6.7 (d, *J* = 15.9 Hz, 1H), 6.38 (d, *J* = 15.9 Hz, 1H), 4.56 (m, 1H), 4.34 (m, 2H), 3.20 (dd, *J* = 5.49, 13.7 Hz, 1H), 2.76 (dd, *J* = 8.7, 13.7 Hz, 1H) ppm; $^{13}C$ NMR ($CDCl_3$, 125 MHz): δ 166.3, 138.2, 130.0, 129.8, 129.7, 129.5, 129.2, 129.1, 128.9, 71.8, 68.2, 53.0 ppm.

**4-Benzyl-4,5-dihydro-2-(thiophen-2-yl) oxazole (3g).** Colourless liquid, IR (KBr, $cm^{-1}$): 3025 (m), 2954 (s), 2925 (vs), 2854 (s), 1647 (vs), 1540 (w), 1500 (w), 1458 (m), 1085 (s), 705 (s) $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz): δ 7.62 (m, 1H), 7.49 (d, J = 3.9 Hz, 1H), 7.43 (t, *J* = 6.8 Hz, 1H), 7.32 (m, 2H), 7.28 (m, 2H), 7.11 (m, 1H), 4.60 (m, 1H), 4.37 (m, 1H), 4.17 (m, 1H), 3.29 (dd, *J* = 4.8, 13.7 Hz, 1H), 2.76 (dd, *J* = 9.1, 13.7 Hz, 1H) ppm; $^{13}C$ NMR ($CDCl_3$, 125 MHz): δ 164.7, 130.7, 130.2, 129.6, 129.0, 128.0, 126.9, 72.6, 68.4, 42.1 ppm.

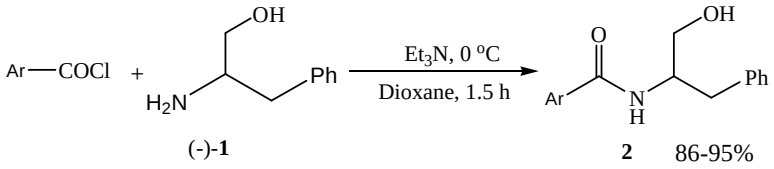
**4-Benzyl-4,5-dihydro-2-*p*-tolyloxazole (3h).** Brown solid, m.p.: 90-91 °C; IR (KBr, $cm^{-1}$): 3056 (m), 3028 (m), 2952 (m), 2923 (s), 2858 (m), 1639 (s), 1541 (s), 1492 (s), 1452 (s), 1275 (vs), 790 (w), 744 (s), 702 (s); $^1H$ NMR ($CDCl_3$, 500 MHz): δ 7.99 (t, *J* = 7.2 Hz, 2H), 7.39 (m, 2H), 7.34-7.23 (m, 6H), 4.47 (d, *J* = 10.1 Hz, 1H), 4.35 (dd, *J* = 5.6, 12.2 Hz, 1H), 3.77 (m, 1H), 3.35 (dd, *J* = 4.4, 13.4, 1H), 3.02 (dd, *J* = 3, 13.14 Hz, 1H), 2.35 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): δ 166.5, 138.6, 131.1, 129.7, 129.6, 129.3, 129, 128.7, 128.6, 127.8, 63.0, 52.0, 36, 21.6 ppm.

**4-Benzyl-4,5-dihydro-2-(4-metoxyphenyl) oxazole (3i).** Colorless liquid, IR (KBr, $cm^{-1}$): 3060 (w), 3026 (w), 2927 (m), 2900 (m), 2839 (w), 1647 (vs), 1608 (vs), 1514 (vs), 1454 (s), 1425 (m), 1359 (s), 1256 (vs), 1170 (vs), 1027 (s), 842 (s), 742 (s), 700 (s); $^1H$ NMR ($CDCl_3$, 500 MHz): δ 7.93 (d, *J* = 8.6 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.26 (m, 3H), 6.95 (d, *J* = 8.6 Hz, 2H), 4.59 (m, 1H), 4.35 (t, *J* = 8.8 Hz, 1H), 4.15 (t, *J* = 7.8 Hz, 1H), 3.88 (s, 3H), 3.27 (dd, *J* = 5.0, 13.7 Hz, 1H), 2.75 (dd, *J* = 9.0, 13.7 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 125 MHz): δ 164.2, 162.5, 138.5, 130.4, 129.6, 129.5, 128.9, 126.8, 114.1, 72.2, 68.2, 55.7, 42.3 ppm.

## RESULTS AND DISCUSSION

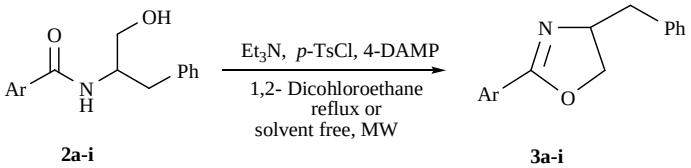
In the context of our study, 2-amino-3-phenyl propanol **1** was prepared by the reduction of L-phenylalanine. The preparation of amides (**2a-i**) (Table 1) was made by a chemoselective acylation of 2-amino-3-phenyl propanol **1** in the presence of $Et_3N$ at 0 °C (Scheme 1). At elevated temperatures, both amino and hydroxyl groups were acylated.

Finally, all the synthesized amides were used in a cyclisation reaction for preparation of the related chiral 2-substituted oxazolines (**3a-i**) under both classical conditions in refluxing 1,2-dichloroethane (Scheme 2) (Table 2) and microwave irradiation (800 W) in solvent free condition (Table 3). The structures of all products were established by




(-)-**1** **2** 86-95%

*Scheme 1*




**2a-i** **3a-i**

*Scheme 2*

spectroscopic (IR, $^{1}H$ NMR and $^{13}C$ NMR) analyses and optical activities were measured in $CH_2Cl_2$ (c 1).

In conclusion, this work describes an efficient synthesis of chiral oxazolines by the ring closing of amides under both classical and microwave conditions. The result of this study revealed that the cyclisation reaction under microwave irradiation gives the higher yields of products in shorter reaction times (1-3 min). However, the best result was achieved by the arylaldehydes having an electron withdrawing group.

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