# Microwave-assisted Synthesis of 2*H*-Benzo[*b*][1,4]oxazin-3(4*H*)-ones and 1*H*-Pyrido[2,3-*b*][1,4]oxazin-2(3*H*)-ones *via* Smiles Rearrangement

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Received February 21, 2008

Highly efficient synthesis of substituted benzo[1,4]oxazin-3-ones and pyrido[1,4]oxazin-2-ones under microwave irradiation *via* Smiles rearrangement is reported. Substituted benzo[1,4]oxazin-3-ones and pyrido[1,4]oxazin-2-ones were obtained by treatment of substituted 2-chlorophenols or 2-chloropyridols with *N*-substituted 2-chloroacetamide in the presence of potassium carbonate in MeCN and subsequent exposure to cesium carbonate in DMF. All the reactions which take 2-10 hours under conventional condition were completed successfully within a few minutes under microwave irradiation giving moderate to excellent yields.

Key Words : Microwave-assisted reaction, Benzo[1,4]oxazinone, Pyrido[1,4]oxazinone, Smiles rearrangement

### Introduction

The importance of [1,4]-oxazines in biological systems has attracted great interest due to their medicinal and pharmacological characteristics. Many compounds containing [1,4]-oxazine moiety have found wide biological activities such as being antiulcer,<sup>1</sup> antihypertensive,<sup>2</sup> antifungal,<sup>3</sup> anticancer,<sup>4</sup> and antithromobotic.<sup>5</sup> [1,4]-oxazines are also known as 5-HT<sub>6</sub> receptor antagonists,<sup>6</sup> bladder-selective potassium channel openers,<sup>7</sup> dual selective serotonin reuptake inhibitors (SSRIs) and 5-HT<sub>1A</sub> receptor,<sup>8</sup> dopamine agonists,<sup>9</sup> and inhibitors of PI3Kinase.<sup>10</sup> Some substituted [1,4]-oxazines are also related to blocking the TXA<sub>2</sub> receptor and activate the PGI<sub>2</sub> receptor.<sup>11</sup> Moreover, certain kinds of [1,4]-oxazines are of interest as photochromic compounds.<sup>12</sup> Typically, benzo-fused and pyrido-fused [1,4]oxazinones as one of the most important series among [1,4]oxazine derivatives and have received considerable attention. Substituted [1,4]-oxazinones are useful intermediates for the synthesis of corresponding [1,4]-oxazines via reduction method.<sup>13</sup> In particular, pyrido-fused[1,4]-oxazines are prepared from their [1,4]-oxazinones, since the general synthetic methods for obtaining 1,4-benzoxazines are not suitable for the pyridine derivatives.<sup>14</sup> Therefore, the synthesis of [1,4]-oxazinones is of importance, which can be

acquired *via* direct cyclization of 2-haloacetyl halide or alkyl 2-halo propionates with 2-aminophenols. They were also generated by several other methods.<sup>15</sup>

In view of the importance of substituted [1,4]-oxazinones, we have initiated a programme for the development of simpler and more convenient methods for preparing heterocyclic systems with high efficacy,<sup>16-17</sup> which leads to prepare diverse molecules especially benzo-fused and pyrido-fused-[1,4]oxazinones. In previous studies it was demonstrated that new method *via* Smiles rearrangement was applied to synthesize pyrido[2,3-*b*][1,4]oxazinones.<sup>16</sup> Our investigation of this system forms part of an ongoing study on more benzo- and pyrido-derivatives, initiated by the simple starting materials of substituted 2-chlorophenol and 2-chloro-3-pyridol.

However, the synthetic protocols for substituted benzo-[1,4]oxazin-3(4*H*)-ones or pyrido[1,4] oxazin-2(3*H*)-ones *via* Smiles rearrangement require a period of 2-10 hours under conventional condition.<sup>16</sup> Microwave-assisted organic synthesis is a new and rapidly growing area in synthetic organic chemistry. It was observed that some organic reactions proceed much more quickly and with higher yields under microwave irradiation than conventional heating. To the best of our knowledge, no example for the synthesis of benzo- and pyrido-fused [1,4]oxazinone under microwave



Scheme 1

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irradiation *via* Smiles rearrangement is reported. Herein, we studied the synthesis of benzo-fused [1,4]oxazin-3(4*H*)-ones and pyrido-fused [1,4]oxazin-2(3*H*)-ones series. It was found that microwave-assisted heating reproducibly resulted in high to excellent yields of the corresponding products within a few minutes.

As shown in Scheme 1, the preparation of the benzo- and pyrido-fused [1,4]oxazinones begins with commercially available 2-chlorophenol or 2-chloro-3-pyridol (**1a-p**). Initially, the reaction of **1a-p** with *N*-substituted-2-chloro-

acetamide (**2a-p**) in the presence of potassium carbonate under microwave irradiation furnished the *N*-sustituted-2-(2chlorobenz-3-yloxy)acetamide or *N*-substituted-2-(2-chloro pyridin-3-yloxy) acetamide (**3a-p**). Subsequent exposure of **3a-p** to cesium carbonate in DMF under microwave irradiation led to cyclization and gave the corresponding [1,4]oxazinones (**4a-p**) *via* Smiles rearrangement. These reactions were extremely rapid compared with the reactions under conventional heating. All the products were confirmed by physical and spectral data. Detailed investigations of differ-

Table 1	L. (	Comparison	between	microwav	e irra	diation	(M.W.)	and	conventional	heating	(C.H.)	) in the s	ynthesis	of 3a-j	Í
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entry	phenols	products	C.H <sup><i>a</i></sup> M.W <sup><i>b</i></sup> <b>1a-h</b> to <b>3a-j 1a-h</b> to <b>3a-j</b>			W <sup>b</sup> 0 <b>3a-j</b>
2	1	1 <u> </u>	time (h)	yield (%)	time (min)	yield (%)
1	CI OH 1a	CI Sa	7	86	8	85
2	1a		10	82	8	90
3	1a		10	83	7	80
4	CI CI 1b	CI CI Sd	6	75	9	82
5	CI OH Ic	CI CI Se	6	95	8	92
6	CI OH CI 1d	$ \begin{array}{c} CI & O \\ H \\ CI & H \end{array} $ Bn H Bn	5	66	8	85
7	H <sub>3</sub> C CI 1e	H <sub>3</sub> C CI 3g	3	90	8	93
8	H <sub>3</sub> C OH If	$H_3C$	4	77	8	86
9	MeO CI 1g	MeO CI 3i	2	85	7	90
10	CI CI Ih	CI CI CI CI CI CI CI CI CI CI CI CI CI C	4	70	7	88

<sup>a</sup>Conversion of 1a-h to 3a-j with conventional heating (C.H). <sup>b</sup>Conversion of 1a-h to 3a-j with microwave irradiation (M.W)

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entry	pyridinol ( <b>1i</b> )	products	C.H <sup>a</sup> <b>1i</b> to <b>3k-p</b>		M.W <sup>b</sup> 1i to 3k-p	
		-	time (h)	yield (%)	time (min)	yield (%)
1		O N Cl Sk	3	90	4	92
2	1i		3	92	5	95
3	1i	O N CI 3m	5	92	5	90
4	1i		5	89	3	90
5	1i		4	90	5	93
6	1i		3	88	5	95

Table 2. Comparison between microwave irradiation (M.W.) and conventional heating (C.H.) in the synthesis of 3k-p

<sup>*a*</sup>Conversion of **1i** to **3k-p** with conventional heating (C.H). <sup>*b*</sup>Conversion of **1i** to **3k-p** with microwave irradiation (M.W)

Comparison between microwave irradiation	on (M.W.) and conventiona	l heating (C.H.) i	in the synthesis of <b>4a-j</b>
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entry	acetamide	products	С.Н <sup><i>a</i></sup> <b>3а-ј</b> to <b>4а-ј</b>			W <sup>b</sup> 5 <b>4a-j</b>
			time (h)	yield (%)	time (min)	yield (%)
1	CI Saturation of the second se	Bn N O Cl Cl	5	89	15	98
2			8	83	15	85
3		N O 4c	8	78	15	80
4	CI CI 3d	CI V Ad	5	67	15	84
5	CI CI 3e	CI O 4e	6	68	13	86

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# Table 3. Continued

entry	acetamide	products	C.H <sup>a</sup> <b>3a-j</b> to <b>4a-j</b>		M.W <sup>b</sup> <b>3a-j</b> to <b>4a-j</b>	
		-	time (h)	yield (%)	time (min)	yield (%)
6	CI O N <sup>r</sup> Bn CI 3f	CI Bn N O 4f	7	92	13	95
7	H <sub>3</sub> C CI 3g	H <sub>3</sub> C 4g	5	66	13	84
8	H <sub>3</sub> C Cl 3h	H <sub>3</sub> C U O 4h	5	70	15	88
9	MeO CI 3i	MeO 4i	3	74	15	82
10	CI O N Bn CI CI 3j	Cl C	5	63	15	90

<sup>a</sup>Conversion of **3a-j** to **4a-j** with conventional heating (C.H). <sup>b</sup>Conversion of **3a-j** to **4a-j** with microwave irradiation (M.W)

Table 4. Compariso	on between microway	ve irradiation (	M.W.) and	conventional heating	(C.H.) in the s	vnthesis of ox	azinone 4k-p

entry	acetamide	products	С <b>3k-р</b> 1	C.H <sup><i>a</i></sup> <b>3k-p</b> to <b>4k-p</b>		W <sup>b</sup> 5 <b>4k-p</b>
			time (h)	yield (%)	time (min)	yield (%)
1	O N Cl 3k	Bn N N O 3k	3	90	4	92
2			3	92	5	95
3	N CI 3m	N O 3m	5	92	5	90
4		N S S S S S S S S S S S S S S S S S S S	5	89	3	90
5		N O 30	4	90	5	93
6		N O 3p	3	88	5	95

<sup>a</sup>Conversion of **3k-p** to **4k-p** with conventional heating (C.H). <sup>b</sup>Conversion of **3k-p** to **4k-p** with microwave irradiation (M.W)

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ent substitutions of  $R_1$  on benzyl group or diverse  $R_2$  group on the reaction time and yields of the intermediates and products were studied and the data of the results were illustrated in Table 1-4.

As indicated, with the aim of increasing compound diversity through the integration of diverse skeletons, different substituted benzyl groups including different dichlorophenol, trichlorophenol, methyl chlorophenol, methoxy chlorophenols were used in the synthesis of benzo-fused [1,4]-oxazinones. The difference of substituted groups on benzyl ring did not have significant influence on the reaction time and yields. To study the influence of *N*-substituted-2-chloroacetamide on the rearrangement reaction, diverse  $R_2$  groups were studied. Table 2 & 4 shows pyridine derivatives reacted more rapidly compared to benzene derivatives under the same conditions. All the reactions which take 2-10 hours under conventional heating were completed in 3-15 minutes under microwave irradiation.

Moreover,  $K_2CO_3$  in MeCN was the most effective system for the synthesis of **3a-p**, and  $Cs_2CO_3$  in DMF was found to be the most suitable reagent system for the preparation of **4a-p** according to our investigation of the base and solvent effects on the synthesis. Based on our previous work,<sup>16,17</sup> we proposed the overall annulation is best explained by the process involved with Smiles rearrangement as shown in Scheme 2.

In summary, a novel and highly efficient synthesis of substituted benzo [b][1,4]oxazin-3(4*H*)-ones and pyrido-[2,3-b]oxazin-2(3*H*)-ones under microwave irradiation *via* Smiles rearrangement was established. Higher yields and shorter reaction time are the notable advantages of this method. The further work including expansion of new compound series and biological activity is underway in our laboratory.

#### **Experimental Section**

Typical procedure for the synthesis of N-benzyl-2-(2,3dichlorophenoxy)acetamide 3a. The solution of 2,3-dichlorophenol 1a (1.00 g, 6.14 mmol), N-benzyl-2-chloroacetamide (1.13 g, 6.14 mmol), K<sub>2</sub>CO<sub>3</sub> (1.02 g, 7.36 mmol) in dry CH<sub>3</sub>CN was placed into microwave oven (KMIC-1.5 kW) at 85 °C and irradiated for the period listed in Table 1. The solvent was evaporated under reduced pressure. The residue was poured into water and then adjusted to pH = 7. It was then extracted by ethyl acetate. The combined organic layers were dried over anhydrous MgSO<sub>4</sub> and solvent was removed under vacuum to obtain the crude product. Pure product was obtained by further recrystallization as white solid 3a (1.62 g, 85%). mp 129-130 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.57 (d, J = 6.8 Hz, 2H), 4.59 (s, 2H), 6.83 (dd, J = 7.6, 2 Hz, 1H), 7.13 (br s, 1H), 7.14-7.20 (m, 2H), 7.26-7.37 (m, 5H);  ${}^{13}$ C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  43.1, 68.4, 111.8, 122.1, 123.9, 127.6, 127.7, 128.8, 134.2, 137.6, 154.0, 167.1; MS (m/z): 309 (M<sup>+•</sup>).

*N*-Cyclohexyl-2-(2,3-dichlorophenoxy)acetamide (3b): White solid, mp 163-164 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 1.23-1.31 (m, 3H), 1.37-1.47 (m, 2H), 1.60-1.64 (m, 1H), 1.70-1.76 (m, 2H), 1.92-1.96 (m, 2H), 3.85-3.94 (m, 1H), 4.51 (s, 1H), 6.75 (br s, 1H), 6.81 (dd, J = 6.8, 2 Hz, 1H), 7.15-7.27 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 24.6, 25.5, 32.9, 47.8, 68.3, 111.7, 122.0, 123.7, 127.8, 134.1, 154.1, 166.1; MS (m/z): 303 (M<sup>++</sup>), 267(M<sup>++</sup>-Cl).

**2-(2,3-Dichlorophenoxy)-***N***-hexylacetamide (3c):** White solid, mp 96-98 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 0.89 (t, *J* = 6.8 Hz, 3H), 1.26-1.39 (m, 6H), 1.53-1.61 (m, 2H), 3.37 (dd, *J* = 13.2, 6.8 Hz, 2H), 4.53 (s, 2H), 6.82 (dd, *J* = 7.6, 2 Hz, 2H), 7.15-7.27 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  14.0, 22.6, 26.5, 29.4, 31.4, 39.1, 68.3, 111.6, 121.9, 123.7, 127.8, 134.2, 154.1, 167.0; MS (m/z): 305 (M<sup>++</sup>), 269 (M<sup>++-</sup>Cl).

*N*-Benzyl-2-(2,4-dichlorophenoxy)acetamide (3d): Colorless crystal, mp 124-125 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.54-4.56 (d, 4H), 6.82 (d, J = 8.8 Hz, 1H), 7.11 (br s, 1H), 7.19 (dd, J = 8.8, 2.4 Hz, 1H), 7.26-7.37 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  43.1, 68.5, 114.8, 123.8, 127.5, 127.6, 128.0, 128.8, 130.2, 137.6, 151.6, 167.1; MS (m/z): 309 (M<sup>++</sup>).

*N*-Benzyl-2-(2,5-dichlorophenoxy)acetamide (3e): White solid, mp 97-99 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.54 (s, 2H), 4.56 (d, J = 6 Hz, 2H), 6.89 (d, J = 2 Hz, 1H), 6.96 (dd, J = 8.4, 2 Hz, 1H), 7.12 (br s, 1H), 7.26-7.36 (m, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  43.1, 68.2, 114.6, 121.4, 123.0, 127.6, 127.7, 128.8, 131.0, 133.5, 137.6, 153.1, 167.0, 169.3; MS (m/z): 309 (M<sup>++</sup>).

*N*-Benzyl-2-(2,6-dichlorophenoxy)acetamide (3f): Colorless crystal, mp 94-96 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.58-4.60 (t, 4H), 7.03 (t, J = 8 Hz, 1H), 7.26-7.38 (m, 7H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  43.1, 71.5, 126.0, 127.6, 127.8, 128.8, 129.0, 137.7, 150.2, 167.6; MS (m/z): 309 (M<sup>++</sup>). 1384 Bull. Korean Chem. Soc. 2008, Vol. 29, No. 7

*N*-Benzyl-2-(2-chloro-4-methylphenoxy)acetamide (3g): Light yellow-brown crystal, mp 94-95 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 2.25 (s, 3H), 4.52 (s, 2H), 4.54 (d, *J* = 6 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 6.98-7.00 (dd, *J* = 4.4, 2 Hz, 1H), 7.16 (d, *J* = 2 Hz, 1H), 7.22 (br, 1H), 7.26-7.35 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ 20.4, 43.0, 68.5, 114.1, 122.6, 127.6, 128.5, 128.8, 130.9, 132.9, 137.8, 150.7, 167.8; MS (m/z): 289 (M<sup>++</sup>).

*N*-Benzyl-2-(2-chloro-5-methylphenoxy)acetamide (3h): Light brown crystal, mp 113-114 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.32 (s, 3H), 4.55 (s, 2H), 4.56 (d, *J* = 6 Hz, 2H), 6.71 (s, 1H), 6.77 (dd, *J* = 8, 0.8 Hz, 1H), 7.20 (br, 1H), 7.22-7.36 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  21.3, 43.0, 68.2, 114.9, 120.0, 123.6, 127.6, 126.8, 130.0, 137.7, 138.5, 152.5, 167.7; MS (m/z): 289 (M<sup>++</sup>).

*N*-Benzyl-2-(2-chloro-4-methoxyphenoxy)acetamide (3i): White solid, mp 88-89 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  3.75 (s, 3H), 4.52 (s, 2H), 4.55 (d, 2H), 6.75 (dd, J = 9.2, 2.8 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 6.93 (d, J = 2.8 Hz, 1H), 7.21 (br, 1H), 7.27-7.36 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ 43.0, 55.9, 69.2, 113.2, 115.7, 116.1, 123.8, 127.6, 128.8, 137.8, 147.1, 155.0, 167.9; MS (m/z): 305 (M<sup>++</sup>).

*N*-Benzyl-2-(2,4,5-trichlorophenoxy)acetamide (3j): White crystal, mp 137-138 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 4.53 (s, 2H), 4.55 (d, *J* = 6 Hz, 2H), 6.99 (s, 1H), 7.06 (br, 1H), 7.27-7.36 (m, 5H), 7.45 (s, 1H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$ 43.2, 68.5, 115.6, 122.1, 126.0, 127.6, 127.8, 128.9, 131.1, 131.7, 137.5, 151.7, 166.6; MS (m/z): 343 (M<sup>++</sup>).

Typical procedure for the synthesis of 4-benzyl-7-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one 4a (Table 3). The solution of N-benzyl-2-(2,3-dichlorophenoxy) acetamide 3a (0.6 g, 1.93 mmol), Cs<sub>2</sub>CO<sub>3</sub> (0.76 g, 2.32 mmol) in dry DMF was placed into microwave oven at 130 °C and irradiated for 15 min. The solvent was evaporated under reduced pressure. The residue was added into water and then adjusted to pH =7 and the mixture was extracted by ethyl acetate. The combined organic layers were dried over anhydrous MgSO<sub>4</sub> and the solvent was removed under vacuum to obtain crude product. Flash column chromatography on silica gel, eluting with hexanes/ethyl acetate yielded 4a as white solid (0.46 g, 88%). Mp 98-99 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.80 (s, 2H), 5.14 (s, 2H), 6.76-6.83 (m, 2H), 7.00-7.03 (dd, J = 7.6, 2 Hz, 1H), 7.21-7.33 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ45.2, 67.8, 114.2, 122.4, 122.8, 124.9, 126.6, 127.7, 129.0, 130.0, 135.5, 141.5, 164.2; MS (m/z): 273 (M<sup>+•</sup>).

**8-Chloro-4-cyclohexyl-2H-benzo**[*b*][1,4]oxazin-3(4H)one (4b): Light pink solid, mp 74-76 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  1.22-1.43 (m, 3H), 1.71 (t, 1H), 1.79-1.91 (m, 4H), 2.30-2.40 (m, 2H), 4.10-4.18 (m, 1H), 4.56 (s, 1H), 6.95 (t, *J* = 8 Hz, 1H), 7.06-7.09 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  25.3, 26.4, 29.4, 57.5, 68.9, 114.8, 122.6, 122.7, 124.7, 131.3, 142.8, 165.7; MS (m/z): 265 (M<sup>++</sup>).

**8-Chloro-4-hexyl-2H-benzo**[*b*][**1,4**]**oxazin-3**(**4***H*)-**one** (**4c**): Colorless liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 0.89 (t, J = 6.8 Hz, 3H), 1.31-1.39 (m, 6H), 1.60-1.68 (m, 2H), 3.91 (t, J = 7.6 Hz, 2H), 4.67 (s, 2H), 6.89 (dd, J = 1.6 Hz, 1H), 6.96 (t, J = 8 Hz, 1H), 7.05 (dd, J = 8, 1.6 Hz); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ14.0, 22.6, 26.5, 27.0, 41.5, 67.7, 113.4, 122.5, 122.7, 124.5, 130.0, 141.5, 163.6; MS (m/z): 267 (M<sup>++</sup>).

**4-Benzyl-7-chloro-2***H***-benzo[b]**[**1,4**]**oxazin-3**(*4H*)**-one** (**4d**): White-off solid, mp 98-100 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 4.72 (s, 2H), 5.13 (s, 2H), 6.76-6.78 (d, *J* = 8.4 Hz, 1H), 6.83-6.86 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.98-6.99 (d, *J* = 2.4 Hz, 1H), 7.21-7.33 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  45.0, 67.6, 116.5, 117.4, 122.7, 126.6, 127.7, 128.9, 129.0, 135.5, 145.9, 164.1; MS (m/z): 273 (M<sup>++</sup>).

**4-Benzyl-6-chloro-2H-benzo[b]**[1,4]oxazin-3(4H)-one (4e): White solid, mp 113-114 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$ 4.71 (s, 2H), 5.11 (s, 2H), 6.87-6.91 (m, 3H), 7.23-7.35 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  45.0, 76.8, 115.8, 118.0, 123.7, 126.7, 127.8, 129.0, 129.8, 135.3, 143.9, 164.4; MS (m/z): 273 (M<sup>++</sup>).

**4-Benzyl-5-chloro-2H-benzo[b][1,4]oxazin-3(4H)-one** (**4f):** Colorless liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ4.54 (s, 2H), 5.51 (s, 2H), 6.87-6.98 (m, 3H), 7.13-7.23 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ47.0, 69.2, 115.8, 123.9, 125.5, 126.0, 127.0, 127.7, 128.4, 136.4, 150.9, 167.3; MS (m/z): 273 (M<sup>++</sup>).

**4-Benzyl-7-methyl-2H-benzo[b][1,4]oxazin-3(4H)-one** (**4g**): White solid; mp 90-91 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.24 (s, 3H), 4.69 (s, 2H), 5.13 (s, 2H), 6.67-6.80 (m, 3H), 7.23-7.32 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  20.7, 45.0, 67.8, 115.5, 117.6, 123.3, 126.2, 126.6, 127.5, 128.9, 134.1, 136.1, 145.1, 164.6; MS (m/z): 253 (M<sup>++</sup>).

**4-Benzyl-6-methyl-2***H***-benzo**[*b*][**1,4**]**oxazin-3**(*4H*)**-one** (**4h**): White solid; mp 117-119 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.20 (s, 3H), 4.68 (s, 2H), 5.14 (s, 2H), 6.69 (s, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 7.24-7.34 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  45.0, 55.6, 67.8, 103.2, 107.9, 116.3, 122.2, 126.6, 127.5, 128.9, 136.0, 146.3, 156.4, 164.1; MS (m/z): 253 (M<sup>++</sup>).

**4-Benzyl-7-methoxy-2H-benzo**[*b*][1,4]oxazin-3(4H)-one (**4i**): Light pink solid; mp 71-74 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  3.71 (s, 3H), 4.69 (s, 2H), 5.12 (s, 2H), 6.41-6.44 (dd, *J* = 8.8, 2.8 Hz, 1H), 6.56 (d, *J* = 2.8 Hz, 1H), 6.76 (d, *J* = 12.8 Hz, 1H), 7.23-7.32 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  45.0, 55.6, 67.8, 103.2, 107.9, 116.3, 122.2, 126.6, 127.5, 128.9, 136.1, 146.3, 156.4, 164.1; MS (m/z): 269 (M<sup>++</sup>).

**4-Benzyl-6,7-dichloro-2H-benzo**[*b*][**1,4**]**oxazin-3(4H)-one** (**4j**): White solid; mp 157-159 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.72 (s, 2H), 5.10 (s, 2H), 6.94 (s, 1H), 7.07 (s, 1H), 7.22-7.36 (m, 5H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  45.1, 67.6, 116.9, 118.6, 126.1, 126.7, 126.9, 128.0, 128.5, 129.1, 135.0, 144.3, 163.9; MS (m/z): 307 (M<sup>++</sup>).

The physical and spectral data of known compounds pyrido[2,3-*b*] $\infty$ azin-2(3*H*)-ones **4k-4p** are in accordance with literature.<sup>18</sup>

**Acknowledgments.** The work is supported by Changwon National University in 2007.

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