A facile synthesis of 3,4-dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones and naphthoxazin-2-ones and their reactions with organolithium and Grignard reagents — Preparation of *N*-[1-(2′-hydroxyphenyl)alkyl]amides

Cristina Cimarelli, Gianni Palmieri, and Emanuela Volpini

Abstract: A facile and simple method for the preparation of 3,4-dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones or naphthoxazin-2-ones in high yields from aminoalkylphenols and aminoalkylnaphthols is described. The reactions of the products obtained with organolithium and Grignard reagents were studied, and a method for the preparation of *N*-[1-(2-hydroxyphenyl)alkyl]-*N*-alkylamides, which are of pharmaceutical interest, from benzoxazinones was developed. A possible reaction mechanism is also proposed. The relative configuration of chiral products was determined from conformational analysis of ^{1}H NMR spectra.

Key words: benzoxazinones, naphthoxazinones, organometallic reagents, amide preparation, aminoalkylphenols.

Résumé : On décrit une méthode simple et efficace de préparer avec des rendements élevés des 3,4-dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones ou naphtoxazin-2-ones à partir d'aminoalkylphénols ou d'aminoalkylnaphtols. On a étudié les réactions des produits avec les réactifs de Grignard et les organolithiens et on a mis au point une méthode de préparation de *N*-[1-(2-hydroxyphényl)alkyl]-*N*-alkylamides, des produits présentant un intérêt pharmaceutique, à partir de benzoxazinones. On propose une hypothèse de mécanisme réactionnel. La configuration relative des produits chiraux a été déterminée par une analyse conformationnelle appliquée aux spectres de résonance magnétique du proton.

Mots clés : benzoxazinones, naphtoxazinones, réactifs organométalliques, préparation d'amides, aminoalkylphénols.

[Traduit par la Rédaction]

Introduction

3,4-Dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones are a class of compounds studied because of their diverse biological properties as potential antimicrobial agents (1), as anti-inflammatory agents (2), as acetylcholinesterase inhibitors (3), and as analgesics, bactericides, and muscle relaxants (4). At the same time they are also known to originate from the photodegradation of pesticides such as ethiofencarb (5). Several synthesis methods for benzoxazinones have been reported in the literature (4, 6–9). All of these methods suffer from the same drawbacks, specifically the use of toxic solvents (benzene) or reagents (carbamyl chlorides, isocyanates, phosgene), or they require a two-step synthesis sequence.

On the other hand, 3,4-dialkyl-3,4-dihydro-2*H*-1,3-naphthoxazin-2-ones are known in the literature (10) for their activity against several bacterial species, and they have also been used as precursors in the preparation of phosphinic ligands for asymmetric catalysis (11); however, only very few methods for their preparation have been reported (10, 12).

Recently, we became interested in the synthesis of aminoalkylphenols (13) and aminoalkylnaphthols (14), two classes of compounds studied for their pharmaceutical properties (15) but also widely used as ligands in ligand-accelerated catalysis (LAC) (16), in particular in the asymmetric catalyzed addition of organozinc reagents to aldehydes (17). We have developed a series of synthetic procedures that lead to aminoalkylphenols and aminoalkylnaphthols in a simple and straightforward way.

Now we wish to report a new, direct, and mild method for the preparation of 3,4-disubstituted 3,4-dihydro-2*H*-1,3-benzoxazin-2-ones and naphthoxazin-2-ones that we have developed using aminoalkylphenols and aminoalkylnaphthols as precursors. Moreover, the results of the study of the reactions of these compounds with alkyllithium and Grignard reagents and a method for the preparation of *N*-[1-(2-hydroxyphenyl)alkyl]amides and of the corresponding naphthyl derivatives, which are known for their pharmaceutical properties (10, 18), are described.

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C. Cimarelli,[1] G. Palmieri, and E. Volpini. Dipartimento di Scienze Chimiche, Università di Camerino, Via S. Agostino 1, I-62032 Camerino, Italy.

[1]Corresponding author (e-mail: cristina.cimarelli@unicam.it).

Results and discussion

Aminoalkylphenols **(1)** and aminoalkylnaphthols **(4)**, when treated with carbonyldiimidazole (Im_2CO) in dichloro-

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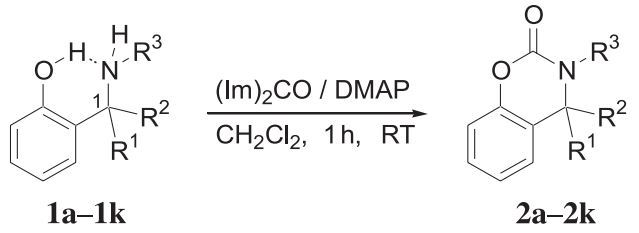
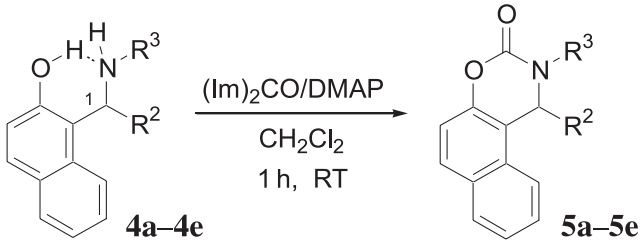
Scheme 1.



Scheme 2.



methane, in the presence of dimethylaminopyridine (DMAP) (19), produce the desired 3,4-dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones (**2**) (Scheme 1) and naphthoxazin-2-ones (**5**) (Scheme 2), respectively, in reasonable reaction times and in good yields. This procedure allows the one-step preparation of cyclized products in a mild and straightforward way. It is very simple and quick and does not require dangerous or expensive chemicals. Moreover, when the reaction is complete, simple filtration of the reaction mixture on a thin pad of silica gel provides a quick and easy method for obtaining a high yield of purified product. The silica gel isolates the excess carbonyldiimidazole and DMAP and the basic by-products. The absolute configuration of chiral centres remains unaltered under these reaction conditions. The results obtained for several aminoalkylphenols and aminoalkylnaphthols are reported in Tables 1 and 2, respectively.

Cyclization with carbonyldiimidazole was previously reported in the literature (22) for the preparation of 1-benzyl-4-(2-oxo-3,4-dihydro-2*H*-1,3-benzoxazine-3-yl)piperidine from 1-benzyl-4-(2-hydroxyphenylmethyl)aminopiperidine, a product unsubstituted at the C-4 carbon atom. The described methodology, without DMAP, requires heating of the reaction mixture in THF to reflux and a longer reaction time.

The reactivity of the synthesized 3,4-dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones (**2**) towards organometallic reagents has been studied, in particular with alkyllithium and Grignard reagents. 3,4-Dialkyl-3,4-dihydro-2*H*-1,3-benzoxazin-2-ones (**2**) react with organolithiums at 0 °C in toluene in reasonable times and give satisfactory yields of *N*-[1-(2-hydroxyphenyl)alkyl]-*N*-alkylamides (**3**) (Scheme 3). Naphthoxazin-2-one (**5a**), under the same reaction conditions, reacts with *n*-butyllithium to afford the corresponding amide **(6ab)** but only in poor yield (28%). The reaction gives satisfactory yields with methyllithium, isopropyllithium, *n*-butyllithium, and phenyllithium. Only allyl- and benzyl-Grignard reagents are reactive towards the substrates studied, while MeMgBr and PhMgCl are nonreactive.

Alkyllithiums and Grignard reagents have been used in a slight excess (10%) with respect to the starting material. With a large excess, the double addition of organometallic

Table 1. Synthesis of benzoxazinones **2**.

Entry	**1**	R^1	R^2	R^3	**2**	Yield (%)[a]
1	**1a**[b]	H	H	R*[c]	**2a**	72
2	**1b**[d]	H	Me	Bn	**2b**	91
3	(*l*)[e]-**1c**[f]	H	Me	R*[c]	(*l*)[e]-**2c**	69
4	(*u*)[e]-**1c**[f]	H	Me	R*[c]	(*u*)[e]-**2c**	64
5	(*l*)[e]-**1d**[f]	H	Et	R*[c]	(*l*)[e]-**2d**	65
6	**1e**	H	*n*-Bu	Me	**2e**	98
7	**1f**	H	*n*-Bu	Bn	**2f**	78
8	(*l*)[e]-**1g**[g]	H	*n*-Bu	R*[c]	(*l*)[e]-**2g**	93
9	(*u*)[e]-**1g**[g]	H	*n*-Bu	R*[c]	(*u*)[e]-**2g**	88
10	**1h**[h]	H	Ph	Bn	**2h**	76
11	(*l*)[e]-**1i**[f]	H	Ph	R*[c]	(*l*)[e]-**2i**	84
12	(*u*)[e]-**1i**[f]	H	Ph	R*[c]	(*u*)[e]-**2i**	87
13	**1j**	Me	Ph	Me	**2j**	85
14	**1k**	*n*-Bu	Ph	Bn	**2k**	78

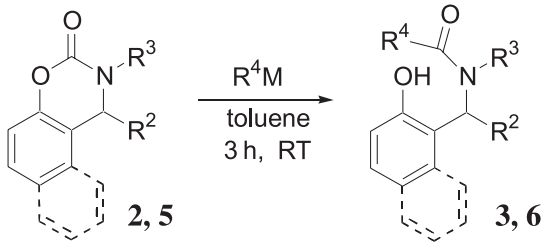
[a]Yields of the pure isolated compounds.
[b]Reference 20.
[c]R*–NH_2 = (±)-1-phenylethylamine.
[d]Reference 21.
[e](*l*) = like (*RR*, *SS*); (*u*) = unlike (*RS*, *SR*)
[f]Reference 13*a*.
[g]Reference 13*d*.
[h]Reference 17.

Table 2. Synthesis of naphthoxazinones **5**.

Entry	**4**	R^2	R^3	**5**	Yield (%)[a]
1	**4a**[b]	Ph	Bn	**5a**	98
2	(*l*)[c]-**4b**[d]	Ph	R*[e]	(*l*)[c]-**5b**	95
3	(*l*)[c]-**4c**[g]	Ph	R*[f]	(*l*)[c]-**5c**	95
4	(*l*)[c]-**4d**[h]	4-$MeOC_6H_4$	R*[e]	(*l*)[c]-**5d**	86
5	(*l*)[c]-**4e**[h]	2-Naphthyl	R*[e]	(*l*)[c]-**5e**	71

[a]Yields of the pure isolated compounds.
[b]Reference 22.
[c](*l*) = like (*RR*, *SS*); (*u*) = unlike (*RS*, *SR*).
[d]Reference 17.
[e]R*–NH_2 = (±)-1-phenylethylamine.
[f]R*–NH_2 = (±)-1-(1-naphthyl)ethylamine.
[g]Reference 13*a*.
[h]Reference 14*a*.

Scheme 3.



reagent to the carbonyl group of the starting benzoxazinone is observed, and the reaction produces the original aminoalkylphenol **1** and the corresponding symmetric ketone. In fact, GC–MS analysis of the crude mixtures of the reactions of **2b**, **2h**, and **2e** with 2.5 equiv. of phenyllithium and butyllithium reveals the chromatographic peaks and mass spectra of aminoalkylphenols **1b**, **1h**, and **1e** and of dibutylketone and benzophenone.

Scheme 4.

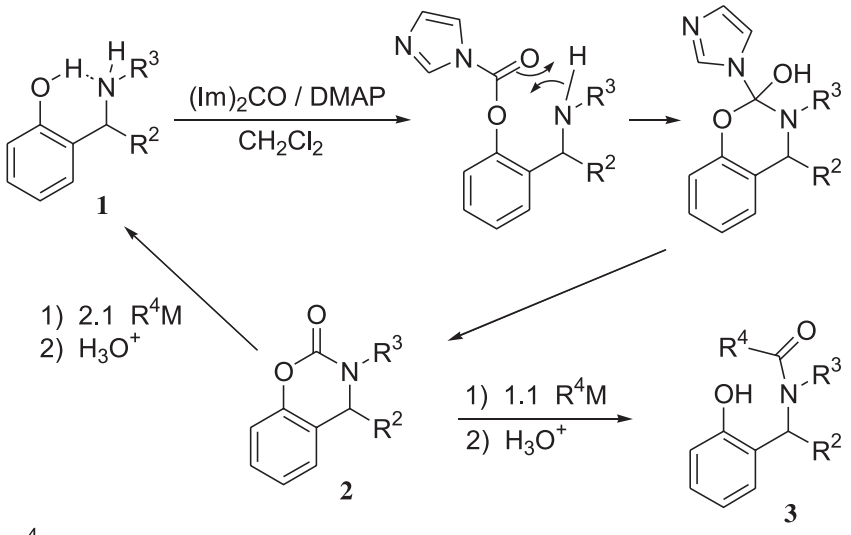


Table 3. Synthesis of *N*-[1-(2′-hydroxyphenyl)alkyl]amides.

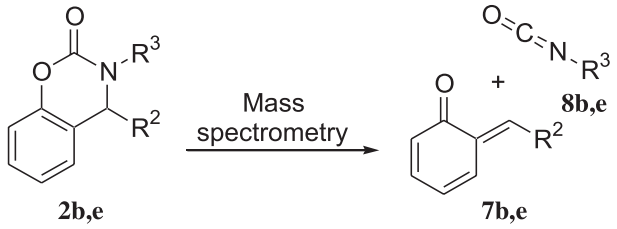
Entry	**2**	R^4M	**3**	Yield (%)[a]
1	**2b**	MeLi	**3ba**	69
2	**2b**	*n*-BuLi	**3bb**	90
3	**2b**	PhLi	**3bd**	75
4	**2b**	AllylMgCl	**3be**	79
5	**2b**	BnMgCl	**3bf**	50
6	(*l*)[b]-**2d**	*n*-BuLi	(*l*)[b]-**3db**	56
7	**2e**	*n*-BuLi	**3eb**	31
8	**2h**	*n*-BuLi	**3hb**	43
9	**2h**	*i*-PrLi	**3hc**	77
10	(*l*)[b]-**2i**	*n*-BuLi	(*l*)[b]-**3ib**	62
11	**5a**	*n*-BuLi	**6ab**	28

[a]Yields of the pure isolated compounds.
[b](*l*) = like (*RR*, *SS*); (*u*) = unlike (*RS*, *SR*).

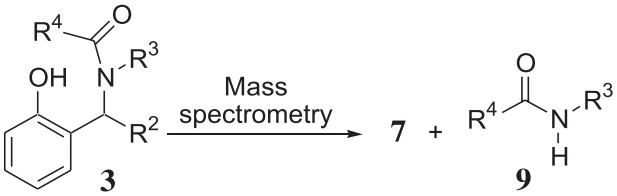
In several cases the reaction proceeds with comparable results in *n*-hexane, but when the starting materials are poorly soluble in this solvent, toluene gave the best results. The results obtained in the reactions of benzoxazinones **2b**, **2d**, **2e**, **2h**, and **2i** with some organolithiums and Grignard reagents are reported in Table 3.

A hypothesized mechanism for these reactions is presented in Scheme 4. Moreover, it is possible to make some observations for the behaviour of these compounds when they are subjected to GC–MS analysis. Within the mass spectra of pure benzoxazinones **2b** and **2e**, we observed the fragmentation pattern corresponding to the enone **7** and the isocyanate **8**, as depicted in Scheme 5. In a similar fashion, in 1,4-dihydro-2*H*-3,1-benzoxazin-2-one derivatives, under flash vacuum pyrolysis conditions, CO_2 extrusion was observed (23). Naphthoxazinones **5** under the same conditions decompose during the gas chromatographic analysis to give a complex mixture of unidentified products. The final amide **3** decomposes in a similar way, and it is possible to observe in the mass spectra the peaks corresponding to the enone **7**

Scheme 5.



Scheme 6.

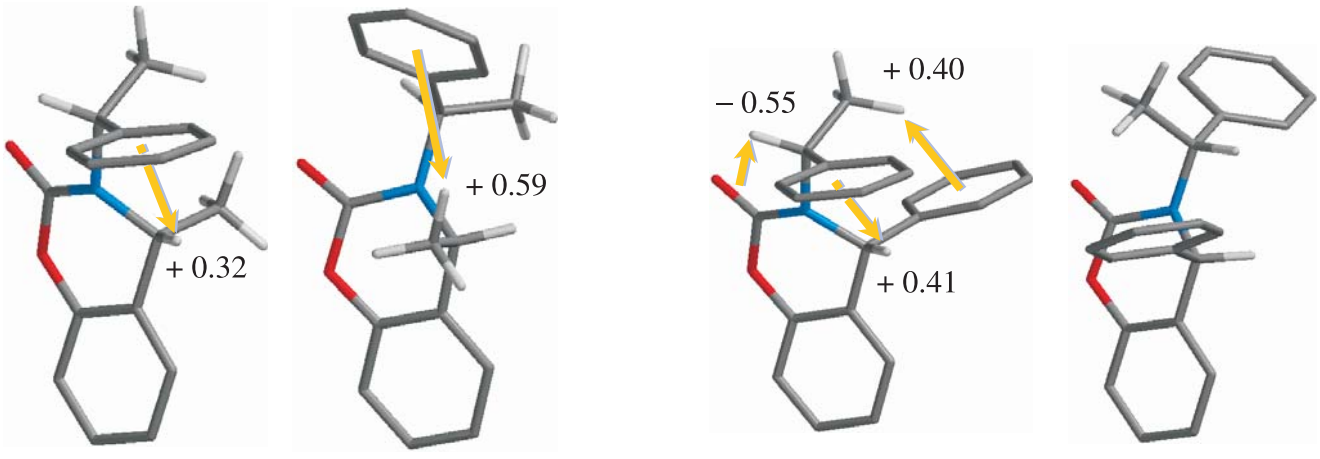


and the amide **9**, as depicted in Scheme 6 for **3bb**, **3db**, **3bd**, **3bf**, and **3eb**.

Stereochemistry

The relative configurations of benzoxazinones and naphthoxazinones were assigned by analogy with the chiral starting aminophenols. To confirm that cyclization took place with retention of configuration, the stereochemistry of the prepared oxazinones was confirmed by conformational analysis on the diastereomeric couples (*R*,*R*)-**2c**/(4*S*,1*R*)-**2c** and (*R*,*R*)-**2i**/(4*S*,1*R*)-**2i**. The more stable conformations for (*R*,*R*)- and (4*S*,1′*R*)-**2c** and (*R*,*R*)- and (4*S*,1′*R*)-**2i**, obtained by PM3 semi-empirical minimization, are reported in Fig. 1. A comparison of the differences in ^{1}H NMR chemical shifts ($\Delta\delta$) observed for the diastereomeric couples, resulting from the anisotropic effects of the phenyl and carbonyl groups, as indicated in Fig. 1, allowed us to assign relative configurations.

Fig. 1. Minimized conformations for the (*R,R*)- and (4*S*,1′*R*)-**2c** and the (*R,R*)- and (4*S*,1′*R*)-**2i** oxazinones with observed ^{1}H NMR Δδ (ppm) resulting from anisotropic effects.



(*R,R*)-**2c** (4*S*, 1′*R*)-**2c** (*R,R*)-**2i** (4*S*,1′*R*)-**2i**

Experimental

General methods

Proton and ^{13}C NMR spectra were recorded with a Varian VXR 300 instrument. Chemical shifts are given in ppm downfield from Me_4Si in $CDCl_3$ solution. Coupling constants are given in Hz. IR spectra were recorded with a Perkin-Elmer 257 spectrometer. GC–MS analyses were performed with a HP-59970 workstation consisting of a HP-5890 gas chromatograph equipped with a methyl silicone capillary column and a HP-5970 mass detector. All melting points are uncorrected. Toluene and hexane were dried by refluxing over sodium wires and then distilled into a dry receiver under a nitrogen atmosphere. All reagents were of commercial quality from freshly opened containers. Commercial alkyllithium and Grignard reagent solutions (Aldrich) were used in a dry atmosphere.

Preparation of starting aminoalkylphenols 1a–1i and aminoalkylnaphthols 4a–4e

Starting aminoalkylphenols and aminoalkylnaphthols were prepared according to previously reported procedures (11) using (±)-phenylethylamine as the chiral starting material instead of the (*R*) enantiomer. Spectral data for the unknown starting materials **1e, 1f**, **1j**, and **1k** follow.

2-[1-(Methylamino)pentyl]phenol (1e)

Yield 98%. Oil. IR ν_{max} (liquid film) (cm^{-1}): 2950, 2836, 1482, 1447, and 1270. ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, 3H, *J* = 6.6 Hz), 1.10–1.50 (m, 4H), 1.60 (bs, 1H), 1.60–1.90 (m, 2H), 2.43 (s, 3H), 3.61 (t, 1H, *J* = 7.0 Hz), 6.70–7.30 (m, 4 H), and 9.00 (s, 1H). Anal. calcd. (%) for $C_{12}H_{19}NO$, MW 193.288: C 74.45, H 9.91, N 7.25; found: C 74.56, H 10.04, N 7.27.

2-[1-(Benzylamino)pentyl]phenol (1f)

Yield 80%. Oil. IR ν_{max} (liquid film) (cm^{-1}): 2968, 2943, 2870, 1527, 1488, and 1243. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.83 (t, 3H, *J* = 7.0 Hz), 1.09–1.34 (m, 4H), 1.62–1.85 (m, 3H), 3.60 (d, 1H, *J* = 12.8 Hz), 3.74 (t, 1H, *J* = 7.2 Hz), 3.83 (d, 1H, *J* = 12.8 Hz), 6.80–7.20 (m, 9H), and 13.40 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.9, 22.6, 28.4, 35.7, 51.8, 63.6, 116.8, 118.9, 127.5, 128.4, 128.5, 128.7, 129.2, 132.4, 157.4, and 165.6. Anal. calcd. (%) for $C_{18}H_{23}NO$, MW 269.386: C 80.26, H 8.61, N 5.20; found: C 80.21, H 8.86, N 5.37.

2-[1-(Methylamino)-1-phenylethyl]phenol (1j)

Yield 91%. Oil. IR ν_{max} (liquid film) (cm^{-1}): 3308, 2981, 1494, 1262, 820, 754, and 720. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.86 (s, 3H), 2.29 (s, 3H), 2.65 (s, 1H), 6.66–7.44 (m, 9H), and 12.30 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.6, 28.9, 64.7, 117.4, 118.8, 126.7, 127.5, 128.5, 128.6, 129.1, 129.8, 144.7, and 158.3. Anal. calcd. (%) for $C_{15}H_{17}NO$, MW 227.30: C 79.26, H 7.54, N 6.16; found: C 79.48, H 7.32, N 6.27.

2-[1-(Benzylamino)-1-phenylpentyl]phenol (1k)

Yield 84%. Oil. IR ν_{max} (liquid film) (cm^{-1}): 2954, 1606, 1455, 1295, 753, and 699. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.99 (t, 3H, *J* = 7.0 Hz), 1.20–1.60 (m, 4H), 2.30–2.70 (m, 3H), 3.62 (bs, 2H), 6.70–7.70 (m, 14H), and 12.20 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.4, 23.3, 25.4, 36.1, 47.0, 55.8, 117.5, 118.9, 126.7, 127.1, 128.0, 128.4, 129.0, 129.1, 129.2, 139.0, 143.8, 158.1, 163.5, and 175.1. Anal. calcd. (%) for $C_{24}H_{27}NO$, MW 345.48: C 83.44, H 7.88, N 4.05; found: C 83.30, H 7.57, N 4.23.

Preparation of benzoxazinones 2a–2k and naphthoxazinones 5a–5e

Aminoalkylphenols **1b**–**1i** (2 mmol) or aminoalkylnaphthols **3a**–**3e** (2 mmol), in a 50-mL round-bottom flask equipped with a magnetic stirring bar, were dissolved in 10 mL CH_2Cl_2 at room temperature (RT) to which was added DMAP (0.2 mmol) and carbonyldiimidazole (3 mmol). The reaction mixture was allowed to stand at RT for 1 h and then the mixture was filtered on a thin pad of silica gel, affording almost pure **2a**–**2k** or **5a**–**5e.** When necessary, the final benzoxazinones or naphthoxazinones were purified further by recrystallization or chromatographic separation.

Spectral data for the products obtained follow. In the numerical designations of the compounds below, the prefixes *(l)* and *(u)* mean *like* (*RR*, *SS*) and *unlike* (*RS*, *SR*), respectively.

3-(1′-Phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2a)

White crystals; mp 98–100 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 2930, 1712, 1500, 1415, 1238, 797, and 734. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.68 (d, 3H, *J* = 7.0 Hz), 3.91 (d, 1H, *J* = 14.3 Hz), 4.30 (d, 1H, *J* = 14.6 Hz), 5.92 (q, 1H, *J* = 7.2 Hz), and 6.95–7.43 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.2, 41.3, 53.8, 116.3, 117.8, 124.3, 125.7, 127.6, 128.1, 128.9, 129.0, 138.8, 149.7, and 151.3. MS (EI) *m/z* (%): 253 (M^+, 10), 148 (7), 105 (100), and 77 (18). Anal. calcd. (%) for $C_{16}H_{15}NO_2$, MW 253.30: C 75.87, H 5.97, N 5.53; found: C 75.92, H 6.21, N 5.79.

3-Benzyl-4-methyl-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2b)

White crystals; mp 110–112 °C (*n*-hexane). IR ν_{max} (Nujol) (cm^{-1}): 2924, 1709, 1497, 1423, 1371, 1253, 761, and 746. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.44 (d, 3H, *J* = 6.6 Hz), 4.28 (d, 1H, *J* = 15.4 Hz), 4.39 (q, 1H, *J* = 6.6 Hz), 5.26 (d, 1H, *J* = 15.4 Hz), and 7.00–7.50 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.5, 50.1, 52.9, 116.7, 124.1, 124.5, 125.4, 128.1, 128.2, 129.0, 129.1, 136.2, 149.4, and 151.8. MS (EI) *m/z* (%): 253 (M^+, 9), 238 (20), 162 (11), 120 (48), and 91 (100). Anal. calcd. (%) for $C_{16}H_{15}NO_2$, MW 253.30: C 75.87, H 5.97, N 5.53; found: C 75.78, H 5.90, N 5.64.

(l)-(±)-4-Methyl-3-(1′-phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one ((l)-2c)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2932, 1715, 1503, 1423, 1369, 1248, 760, and 744. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.43 (d, 3H, *J* = 6.6 Hz), 1.81 (d, 3H, *J* = 7.3 Hz), 4.15 (q, 1H, *J* = 6.6 Hz), 5.65 (q, 1H, *J* = 7.0 Hz), and 7.00–7.60 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.4, 29.9, 50.5, 55.7, 116.6, 124.4, 124.5, 126.5, 127.5, 128.0, 128.7, 128.9, 139.6, 149.8, and 152.2. Anal. calcd. (%) for $C_{17}H_{17}NO_2$, MW 267.322: C 76.38, H 6.41, N 5.24; found: C 76.29, H 6.54, N 5.18.

(u)-(±)-4-Methyl-3-(1′-phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one ((u)-2c)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2930, 1712, 1428, 1243, 763, and 748. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.83 (d, 3H, *J* = 6.6 Hz), 1.66 (d, 3H, *J* = 7.0 Hz), 4.47 (q, 1H, *J* = 6.6 Hz), 5.70 (q, 1H, *J* = 7.1 Hz), and 7.00–7.60 (m, 9H). Anal. calcd. (%) for $C_{17}H_{17}NO_2$, MW 267.322: C 76.38, H 6.41, N 5.24; found: C 76.22, H 6.63, N 5.20.

(l)-(±)-4-Ethyl-3-(1′-phenylethyl)-3,4-dihydro-benzo[e][1,3]oxazin-2-one ((l)-2d)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2948, 1690, 1607, 1412, 1350, 760, and 695. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.75 (t, 3H, *J* = 7.4 Hz), 1.79 (d, 3H, *J* = 7.3 Hz), 1.64–1.88 (m, 2H), 3.97 (dd, 1H, *J* = 3.7, 7.4 Hz), 5.62 (q, 1H, *J* = 7.3 Hz), and 6.78–7.60 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.5, 18.2, 30.7, 55.6, 55.9, 116.2, 123.7, 123.9, 125.5, 127.5, 127.9, 128.7, 128.8, 139.3, 150.2, and 152.4. MS (EI) *m/z* (%): 281 (M^+, 1), 252 (41), 148 (87), 105 (100), and 77 (18). Anal. calcd. (%) for $C_{18}H_{19}NO_2$, MW 281.349: C 76.84, H 6.81, N, 4.98; found: C 76.63, H 6.90, N, 5.14.

4-Butyl-3-methyl-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2e)

White crystals; mp 127–129 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 2924, 1712, 1463, 1230, and 757. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.86 (t, 3H, *J* = 6.8 Hz), 1.00–1.40 (m, 4H), 1.65–2.00 (m, 2H), 3.12 (s, 3H), 4.41 (dd, 1H, *J* = 3.7, 6.2 Hz), and 7.00–7.40 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 22.7, 25.5, 34.9, 35.3, 60.4, 116.4, 122.1, 124.2, 125.7, 129.0, 150.1, and 151.7. MS (EI) *m/z* (%): 219 (M^+, 1), 162 (100), 118 (7), and 91 (19). Anal. calcd. (%) for $C_{13}H_{17}NO_2$, MW 219.280: C 71.21, H 7.81, N 6.39; found: C 70.97, H 7.68, N 6.45.

3-Benzyl-4-butyl-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2f)

White crystals; mp 48–50 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 2982, 2914, 1741, 1438, 1255, 757, and 743. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.79 (t, 3H, *J* = 6.7 Hz), 1.00–1.60 (m, 4H), 1.50–1.90 (m, 2H), 4.20 (d, 1H, *J* = 15.3 Hz), 4.28 (dd, 1H, *J* = 3.5, 6.9 Hz), 5.24 (d, 1H, *J* = 15.3 Hz), and 6.92–7.18 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.9, 22.4, 25.5, 34.6, 50.1, 56.7, 116.3, 122.3, 124.0, 125.6, 127.9, 127.9, 1278.0, 128.7, 128.8, 136.0, and 149.9. MS (EI) *m/z* (%): 295 (M^+, 2), 238 (100), 155 (17), and 91 (98). Anal. calcd. (%) for $C_{19}H_{21}NO_2$, MW 295.376: C 75.87, H 5.97, N 5.53; found: C 75.77, H 5.91, N 5.63.

(l)-(±)-4-Butyl-3-(1′-phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one ((l)-2g)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2930, 1718, 1500, 1429, 1364, 1251, 762, and 743. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.82 (t, 3H, *J* = 6.2 Hz), 0.87–1.30 (m, 4H), 1.60–1.80 (m, 2H), 1.80 (d, 3H, *J* = 7.3 Hz), 4.01 (dd, 1H, *J* = 3.7, 8.0 Hz), 5.63 (q, 1H, *J* = 7.3 Hz), and 6.80–7.60 (m, 9H). Anal. calcd. (%) for $C_{16}H_{23}NO_2$, MW 309.402: C 77.64, H 7.49, N 4.53; found: C 77.63, H 7.61, N, 4.43.

(u)-(±)-4-Butyl-3-(1′-phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one ((u)-2g)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2935, 1720, 1432, 1231, and 762. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.63 (t, 3H, *J* = 6.8 Hz), 0.87–1.30 (m, 4H), 1.60–1.80 (m, 2H), 1.65 (d, 3H, *J* = 7.3 Hz), 4.33 (d, 1H, *J* = 8.4 Hz), 5.66 (q, 1H, *J* = 7.0 Hz), and 6.80–7.60 (m, 9H). Anal. calcd. (%) for $C_{16}H_{23}NO_2$, MW 309.402: C 77.64, H 7.49, N 4.53; found: C 77.51, H 7.63, N 4.71.

3-Benzyl-4-phenyl-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2h)

White crystals; mp 130–134 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 2937, 1705, 1599, 1424, 1356, 745, and 698. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.76 (d, 1H, *J* = 15.2 Hz), 5.26 (s, 1H), 5.40 (d, 1H, *J* = 15.2 Hz), and 6.83–7.45 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 49.7, 60.9, 116.7, 121.7, 124.6, 127.0, 127.3, 128.2, 128.6, 128.9, 129.1, 129.2, 129.5, 135.7, 140.7, 148.6, and 151.2. MS (EI) *m/z* (%): 315 (M^+, 7), 224 (9), 181 (100), 132 (13), 106 (14),

and 91 (34). Anal. calcd. (%) for $C_{21}H_{17}NO_2$, MW 315.365: C 79.98, H 5.43, N 4.44; found: C 80.05, H 5.62, N 4.64.

(l)-(±)-4-Phenyl-3-(1′-phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one ((l)-2i)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2944, 1689, 1610, 1404, 1352, 758, and 696. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.28 (d, 3H, *J* = 7.2 Hz), 5.02 (s, 1H), 5.81 (q, 1H, *J* = 7.2 Hz), and 6.83–7.48 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.3, 56.1, 58.5, 116.7, 123.8, 124.6, 125.9, 126.3, 128.1, 128.3, 128.5, 128.9, 129.0, 129.4, 138.9, 143.6, 148.6, and 151.7. MS (EI) *m/z* (%): 329 (M^+, 11), 224 (7), 182 (40), 181 (85), 146 (27), 105 (100), and 77 (19). Anal. calcd. (%) for $C_{22}H_{19}NO_2$, MW 329.392: C 80.22, H 5.81, N 4.25; found: C 80.37, H 5.90, N 4.43.

(u)-(±)-4-Phenyl-3-(1′-phenylethyl)-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one ((u)-2i)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2951, 1692, 1413, 1332, and 760. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.67 (d, 3H, *J* = 7.3 Hz), 5.26 (q, 1H, *J* = 7.3 Hz), 5.43 (s, 1H), and 6.80–7.40 (m, 14H). MS (EI) *m/z* (%): 329 (M^+, 9), 182 (37), 181 (82), 105 (100), and 77 (16). Anal. calcd. (%) for $C_{22}H_{19}NO_2$, MW 329.392: C 80.22, H 5.81, N 4.25; found: C 80.31, H 5.69, N 4.15.

3,4-Dimethyl-4-phenyl-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2j)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 1710, 1414, 1377, 1232, 778, 745, and 700. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.98 (s, 3H), 2.77 (s, 3H), and 6.60–7.20 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.6, 32.0, 64.8, 116.3, 124.5, 127.0, 127.3, 127.4, 128.3, 129.0, 129.1, 143.5, 147.9, and 150.9. MS (EI) *m/z* (%): 253 (M^+, 4), 238 (10), 195 (89), 181 (40), 165 (23), and 152 (29). Anal. calcd. (%) for $C_{16}H_{15}NO_2$, MW 253.30: C 75.87, H 5.97, N 5.53; found: C 75.24, H 5.72, N, 5.46.

3-Benzyl-4-butyl-4-phenyl-3,4-dihydro-1,3-benzo[e][1,3]oxazin-2-one (2k)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 2957, 1713, 1455, 1389, 1231, 748, and 704. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.67 (t, 3H, *J* = 6.4 Hz), 0.75–1.30 (m, 4H), 2.00–2.40 (m, 2H), 4.07 (d, 1H, *J* = 15.0 Hz), 4.62 (d, 1H, *J* = 15.0 Hz), and 6.50–7.42 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.9, 22.4, 25.4, 38.6, 49.1, 69.2, 115.8, 124.4, 125.5, 127.3, 128.0, 128.2, 128.3, 128.5, 128.6, 128.7, 129.3, 138.3, 144.1, 148.8, and 152.0. MS (EI) *m/z* (%): 371 (M^+, 1), 314 (100), 222 (13), and 91 (95). Anal. calcd. (%) for $C_{25}H_{25}NO_2$, MW 371.47: C 80.83, H 6.78, N 3.77; found: C 80.57, H 6.53, N 3.84.

2-Benzyl-1-phenyl-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (5a)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3063, 3030, 1709, 1635, 1446, 1218, 1085, 994, 826, 743, and 703. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.93 (d, 1H, *J* = 15.4 Hz), 5.40 (d, 1H, *J* = 15.4 Hz), 5.73 (s, 1H), and 7.20–7.90 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 49.3, 58.8, 114.4, 117.2, 122.5, 125.3, 127.6, 128.2, 128.3, 128.4, 129.1, 129.1, 129.2, 129.4, 129.8, 130.6, 131.1, 135.7, 139.5, 147.1, and 151.1. MS (EI) *m/z* (%): 365 (M^+, 11), 288 (6), 260 (5), 231 (100), 202 (14), and 91 (20). Anal. calcd. (%) for $C_{25}H_{19}NO_2$, MW 365.424: C 82.17, H 5.24, N 3.83; found: C 82.38, H 4.97, N 3.62.

(l)-(±)-1-Phenyl-2-(1′-phenylethyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one ((l)-5b)

White crystals; mp 174–176 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 3064, 3027, 1712, 1628, 1588, 1517, 1438, 1158, 1029, 959, 882, 768, and 614. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.38 (d, 3H, *J* = 7.2 Hz), 5.69 (s, 1H), 5.86 (q, 1H, *J* = 7.2 Hz), and 7.20–7.80 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.9, 55.6, 56.4, 116.6, 117.1, 121.9, 125.0, 127.3, 127.4, 128.1, 128.3, 128.5, 128.6, 129.0, 129.1, 129.2, 130.1, 131.0, 138.6, 142.4, 146.8, and 151.5. Anal. calcd. (%) for $C_{26}H_{21}NO_2$; MW 379.45: C 82.30, H 5.58, N 3.69; found: C 82.28, H 5.72, N 3.40.

(l)-(±)-2-(1′-Naphthalen-2-yl-ethyl)-1-phenyl-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one ((l)-5c)

White crystals; mp 142–144 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 3060, 1712, 1420, 1222, 1184, 804, and 730. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.41 (d, 3H, *J* = 7.2 Hz), 5.37 (s, 1H), 6.46 (q, 1H, *J* = 7.2 Hz), and 7.20–8.00 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.2, 53.2, 55.1, 116.1, 116.8, 121.6, 123.1, 124.6, 124.7, 126.1, 126.2, 126.9, 127.2, 127.3, 127.5, 128.4, 128.7, 128.8, 129.0, 129.7, 129.8, 130.7, 131.9, 133.2, 133.9, 142.4, 146.1, and 152.0. Anal. calcd. (%) for $C_{30}H_{23}NO_2$, MW 429.51: C 83.89, H 5.40, N 3.26; found: C 83.72, H 5.28, N 3.35.

(l)-(±)-1-(4-Methoxy-phenyl)-2-(1′-phenylethyl)-1,2-dihydro-naphtho[1,2-e][1,3]-oxazin-3-one ((l)-5d)

White crystals; mp 151–153 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 3061, 2935, 1716, 1512, 1223, 1183, 1032, 814, 736, and 699. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.38 (d, 3H, *J* = 7.3 Hz), 3.71 (s, 3H), 5.62 (s, 1H), 5.81 (q, 1H, *J* = 7.3 Hz), and 6.75–7.80 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.1, 55.2, 55.4, 56.5, 114.6, 116.9, 117.0, 117.1, 122.0, 125.1, 127.5, 128.2, 128.4, 128.7, 129.1, 129.4, 130.1, 131.1, 134.6, 138.8, 146.7, 151.6, and 159.7. Anal. calcd. (%) for $C_{27}H_{23}NO_3$, MW 409.476: C 79.20, H 5.66, N 3.42; found: C 79.02, H 5.43, N, 3.15.

(l)-(±)-1-Naphthalen-2-yl-2-(1′-phenylethyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one ((l)-5e)

White crystals; mp 139–141 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 3058, 1712, 1717, 1634, 1517, 1222, 1184, 814, 739, and 699. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.31 (d, 3H, *J* = 7.3 Hz), 5.81 (s, 1H), 5.85 (q, 1H, *J* = 7.3 Hz), and 7.30–7.90 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.1, 55.9, 55.4, 56.6, 116.4, 117.2, 122.0, 125.0, 125.1, 126.4, 126.7, 129.8, 127.5, 127.9, 128.2, 128.3, 128.4, 128.7, 129.1, 129.1, 129.7, 130.3, 131.1, 133.3, 138.7, 139.7, 146.9, and 151.6. Anal. calcd. (%) for $C_{30}H_{23}NO_2$, MW 429.509: C 83.89, H 5.40, N 3.26; found: C 83.67, H 5.58, N 3.44.

Reaction of oxazinones 2b, 2d, 2e, 2h, 2i, and 5a with organolithiums and Grignard reagents

Oxazinones **2** or **5** (3 mmol) in a three-necked round-bottom flask, equipped with a magnetic stirring bar and rub-

ber septum, were dissolved in anhydrous toluene (10 mL) under a nitrogen atmosphere at 0 °C and were then treated with 3.3 mmol of a commercial solution of alkyllithium or Grignard reagent. The reaction was monitored by TLC using *n*-hexane/ethyl acetate (80/20) as an eluent. After a variable time (2–3 h) at RT, when the starting material was consumed, the reaction was quenched with a NH_4Cl saturated solution (5 mL) and the brine was extracted with CH_2Cl_2 (2 × 20 mL). The solution was dried with anhydrous Na_2SO_4 then filtered, and the solvent was evaporated under reduced pressure. Chromatographic separation of the crude oil obtained, with cyclohexane/ethyl acetate (80/20) as an eluent afforded products **3** and **6** in yields of 28% and 90%, respectively. Spectral data follow.

N-*Benzyl*-N-*[1-(2-hydroxyphenyl)ethyl]acetamide (3ba)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3138, 2966, 1630, 1484, 1445, 1223, and 758. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.49 (d, 3H, *J* = 7.1 Hz), 2.04 (s, 3H), 4.47 (s, 2H), 6.11 (q, 1H, *J* = 7.1 Hz), 6.80–7.40 (m, 9H), and 9.20 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.4, 22.5, 27.1, 47.3, 47.5, 117.9, 119.6, 125.9, 126.8, 127.6, 129.1, 129.8, 137.4, 156.0, and 174.9. Anal. calcd. (%) for $C_{17}H_{19}NO_2$, MW 269.34: C 75.81, H 7.11, N 5.20; found: C 75.58, H 7.38, N 5.32.

N-*Benzyl*-N-*[1-(2-hydroxyphenyl)ethyl]pentanamide (3bb)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3165, 2948, 1620, 1493, 1448, 1238, and 740. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.81 (t, 3H, *J* = 7.1 Hz), 1.12–1.34 (m, 2H), 1.46 (d, 3H, *J* = 7.0 Hz), 1.50–1.68 (m, 2H), 2.21 (dt, 2H, *J* = 3.2, 15.0 Hz), 4.45 (s, 2H), 6.12 (q, 1H, *J* = 7.2 Hz), 6.80–7.20 (m, 9H), and 9.10 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 22.6, 22.7, 26.2, 42.7, 51.9, 58.7, 117.1, 119.4, 125.9, 127.8, 128.5, 128.6, 128.9, 129.0, 129.8, 138.8, and 157.5. Anal. calcd. (%) for $C_{20}H_{25}NO_2$, MW 311.42: C 77.14, H 8.09, N 4.50; found: C 77.11, H 8.06, N 4.49.

N-*Benzyl*-N-*[1-(2-hydroxyphenyl)ethyl]benzamide (3bd)

White crystals; mp 160–162 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 3138, 2966, 1630, 1484, 1445, 1223, and 758. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.71 (d, 3H, *J* = 7.3 Hz), 4.50 (s, 2H), 6.03 (q, 1H, *J* = 7.3 Hz), 6.60–7.40 (m, 14H), and 9.50 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.9, 27.1, 49.4, 117.7, 119.6, 125.3, 126.9, 127.0, 127.2, 127.4, 127.8, 128.5, 128.5, 128.7, 129.9, 130.1, 156.1, and 175.4. Anal. calcd. (%) for $C_{22}H_{21}NO_2$, MW 331.41: C 79.73, H 6.39, N, 4.23; found: C 79.48, H 5.58, N 4.32.

N-*Benzyl*-N-*[1-(2-hydroxyphenyl)ethyl]but-3-enamide (3be)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3138, 2966, 1630, 1484, 1445, 1223, and 758. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.49 (d, 3H, *J* = 7.1 Hz), 2.90–3.20 (m, 2H), 4.47 (s, 2H), 4.96 (d, 1H, *J* = 17.2 Hz), 5.11 (d, 1H, *J* = 9.9 Hz), 5.77–6.03 (m, 1H), 6.12 (q, 1H, *J* = 7.1), 6.80–7.40 (m, 9H), and 9.10 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.4, 39.3, 46.8, 47.6, 117.8, 118.5, 119.7, 125.4, 125.9, 126.9, 127.8, 129.1, 129.9, 131.0, 137.4, 155.8, and 175.2. Anal. calcd. (%) for $C_{19}H_{21}NO_2$, MW 295.38: C 77.26, H 7.17, N 4.74; found: C 79.43, H 7.28, N 4.51.

N-*Benzyl*-N-*[1-(2-hydroxyphenyl)ethyl]-2-phenylacetamide (3bf)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3138, 2966, 1630, 1484, 1445, 1223, and 758. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.51 (d, 3H, *J* = 7.2 Hz), 3.54 (d, 1H, *J* = 15.4 Hz), 3.66 (d, 1H, *J* = 15.4 Hz), 4.46 (s, 2H), 6.16 (q, 1H, *J* = 7.2 Hz), 6.70–7.40 (m, 14H), and 9.13 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 17.4, 41.4, 46.8, 47.8, 117.8, 119.6, 125.9, 126.9, 127.3, 127.7, 128.9, 129.0, 129.2, 129.9, 134.3, 137.5, 142.8, 156.0, and 175.3. Anal. calcd. (%) for $C_{23}H_{23}NO_2$, MW 345.434: C 79.97, H 6.71, N 4.05; found: C 79.78, H 6.90, N 4.23.

(l)-(±)-[1-(2-Hydroxyphenyl)propyl]-(1′-phenylethyl)-pentanamide ((l)-3db)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3138, 2965, 1624, 1487, 1451, 1232, and 760. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.70 (t, 3H, *J* = 6.8 Hz), 0.90–1.14 (m, 2H), 1.02 (t, 3H, *J* = 7.1 Hz), 1.36–1.58 (m, 2H), 1.66–1.90 (m, 2H), 1.85 (d, 3H, *J* = 7.0 Hz), 1.94–2.34 (m, 2H), 4.80 (m, 1H), 5.90 (bs, 1H), 6.60–7.40 (m, 9H), and 9.45 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 11.8, 13.8, 19.5, 22.4, 24.3, 27.6, 35.8, 51.1, 55.3, 117.6, 119.6, 124.0, 125.9, 126.4, 127.2, 128.6, 129.7, 141.3, 156.8, and 178.0. Anal. calcd. (%) for $C_{22}H_{29}NO_2$, MW 339.471: C 77.84, H 8.61, N 4.13; found: C 77.58, H 8.34, N 3.92.

N-*[1-(2-Hydroxyphenyl)pentyl]*-N-*methylpentanamide (3eb)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3172, 2957, 1603, 1488, 1457, 1242, and 754. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.92 (t, 3H, *J* = 7.0 Hz), 0.93 (t, 3H, *J* = 7.0 Hz), 1.18–1.50 (m, 6H), 1.56–1.74 (m, 2H), 1.78–2.16 (m, 2H), 2.36 (dt, 2H, *J* = 3.7, 7.5 Hz), 2.79 (s, 3H), 5.79 (dd, 1H, *J* = 6.2, 9.5 Hz), 6.80–6.98 (m, 2H), 7.16–7.29 (m, 2H), and 9.22 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 14.2, 22.6, 22.7, 27.3, 28.8, 29.1, 29.2, 33.8, 50.7, 117.7, 119.3, 124.7, 126.8, 129.5, 156.4, and 176.4. MS (EI) *m/z* (%): 277 (M^+, 27), 220 (12), 162 (40), 136 (100), 133 (60), 116 (35), and 107 (43). Anal. calcd. (%) for $C_{17}H_{27}NO_2$, MW 277.402: C 73.61, H 9.81, N 5.05; found: C 73.48, H 9.47, N 5.24.

N-*Benzyl*-N-*[(2-hydroxyphenyl)phenylmethyl]pentanamide (3hb)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3142, 2956, 1626, 1487, 1454, 1229, and 761. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.85 (t, 3H, *J* = 7.3 Hz), 1.22–1.38 (m, 2H), 1.53–1.75 (m, 2H), 2.22–2.38 (m, 1H), 2.42–2.56 (m, 1H), 4.57 (d, 1H, *J* = 16.9 Hz), 4.84 (d, 1H, *J* = 16.9 Hz), 6.65–7.40 (m, 15H), and 8.90 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 22.7, 27.6, 34.09, 50.5, 58.0, 118.1, 119.9, 124.3, 126.2, 127.4, 127.8, 128.2, 128.7, 129.0, 130.0, 130.4, 136.9, 137.8, 156.7, and 177.5. Anal. calcd. (%) for $C_{25}H_{27}NO_2$, MW 373.487: C 80.40, H 7.29, N 3.75; found: C 80.18, H 7.43, N 3.57.

N-*Benzyl*-N-*[(2-hydroxyphenyl)phenylmethyl]isobutyramide (3hc)

White crystals; mp 166–167 °C (*n*-hexane/CH_2Cl_2). IR ν_{max} (Nujol) (cm^{-1}): 3138, 2966, 1630, 1484, 1445, 1223, and 758. ^1H NMR (300 MHz, $CDCl_3$) δ: 0.92 (d, 3H, *J* = 6.1 Hz), 1.26 (d, 3H, *J* = 7.0 Hz), 2.67–2.82 (m, 1H), 4.61

(d, 1H, *J* = 17.5 Hz), 4.84 (d, 1H, *J* = 17.5 Hz), 6.60–7.40 (m, 15H), and 9.00 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 18.9, 20.8, 32.3, 50.2, 57.5, 118.2, 119.9, 124.0, 126.0, 127.4, 127.7, 128.6, 128.7, 129.3, 130.1, 130.3, 137.4, 137.7, 157.0, and 182.0. Anal. calcd. (%) for $C_{24}H_{25}NO_2$, MW 359.46: C 80.19, H 7.01, N 3.90; found: C 79.97, H 7.23, N 3.69.

(l)-(±)*-N-*[(2-Hydroxyphenyl)phenylmethyl]*-N-*(1-phenylethyl)pentanamide ((l)-3ib)

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3140, 2961, 1626, 1486, 1451, 1229, and 761. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.96 (t, 3H, *J* = 7.3 Hz), 1.38–1.60 (m, 2H), 1.65–1.87 (m, 2H), 1.81 (d, 3H, *J* = 7.0 Hz), 2.68 (t, 2H, *J* = 7.5 Hz), 5.50 (q, 1H, *J* = 7.0 Hz), 5.60 (m, 1H) 6.30–7.40 (m, 14H), and 9.85 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 18.0, 22.8, 27.7, 35.2, 56.7, 62.2, 118.9, 124.6, 126.2, 126.5, 126.9, 128.0, 128.4, 128.8, 129.4, 129.6, 133.0, 138.5, 139.36, 156.3, and 174.8. Anal. calcd. (%) for $C_{26}H_{29}NO_2$, MW 387.514: C 80.59, H 7.54, N 3.61; found: C 80.32, H 7.76, N 3.48

N-*Benzyl-[(2-hydroxynaphthalen-1-yl)phenylmethyl]-pentanamide (6ab)*

Oil. IR ν_{max} (liquid film) (cm^{-1}): 3138, 2966, 1630, 1484, 1445, 1223, and 758. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.89 (t, 3H, *J* = 7.1 Hz), 1.26–1.43 (m, 2H), 1.60–1.78 (m, 2H), 2.38–2.67 (m, 2H), 4.54 (d, 1H, *J* = 16.8 Hz), 4.91 (d, 1H, *J* = 16.8), 6.90–7.70 (m, 17H), and 8.63 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.1, 22.7, 27.7, 34.3, 51.7, 57.4, 114.4, 120.6, 122.3, 123.0, 126.5, 126.6, 127.0, 127.5, 127.6, 128.6, 129.1, 129.1, 129.3, 131.3, 134.3, 136.4, 137.9, 155.2, and 176.2. Anal. calcd. (%) for $C_{29}H_{29}NO_2$, MW 423.55: C 82.24, H 6.90, N 3.31; found: C 79.47, H 5.78, N 3.54.

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