Res Chem Intermed (2013) 39:1153–1168
DOI 10.1007/s11164-012-0674-y

Synthesis of 5-alkoxy-4-amino-3-bromo-2(5*H*)-furanones containing benzene rings

Fu-Ling Xue · Jian-Xiao Li · Zhao-Yang Wang · Jin-Feng Xiong · Di Li

Received: 16 April 2012 / Accepted: 29 May 2012 / Published online: 27 June 2012

Abstract Using KF as base and THF as solvent, different 5-alkoxy-3,4-dibromo-2(5*H*)-furanones were reacted with amines containing a benzene ring structure by Michael addition–elimination reaction at room temperature or 40 °C to give twenty-three 5-alkoxy-4-amino-3-bromo-2(5*H*)-furanones containing benzene rings, with yields of 21–86 % (mostly over 64 %). The structures of all the newly synthesized compounds were elucidated and confirmed by FTIR, UV, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy, elemental analysis, and X-ray single-crystal diffraction. This rapid synthesis of the series of 2(5*H*)-furanones derivatives with different bioactive units is not only an important synthetic strategy for 2(5*H*)-furanone derivatives but also a basis for synthesis of potential drug molecules for activity testing.

Keywords 2(5*H*)-Furanone · Synthesis · Amine · Benzene ring structure · Michael addition–elimination reaction

Introduction

2(5*H*)-Furanones are important oxygen-containing heterocycles [1, 2]. 2(5*H*)-Furanone is an important structural subunit found in many natural products (Fig. 1) [3–6]. Many compounds containing the 2(5*H*)-furanone moiety have aroused great interest because of their significant biological activity [7], for example antifungal [8, 9], anti-inflammatory [10, 11], antiviral [12], and antitumor [13–15]. Furthermore,

Electronic supplementary material The online version of this article (doi: 10.1007/s11164-012-0674-y) contains supplementary material, which is available to authorized users.

F.-L. Xue · J.-X. Li · Z.-Y. Wang (✉) · J.-F. Xiong · D. Li
School of Chemistry and Environment, South China Normal University, Guangzhou 510006, People's Republic of China
e-mail: wangwangzhaoyang@tom.com

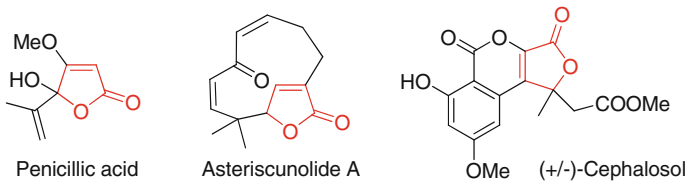


Fig. 1 Some biologically active natural products bearing the 2(5*H*)-furanone moiety

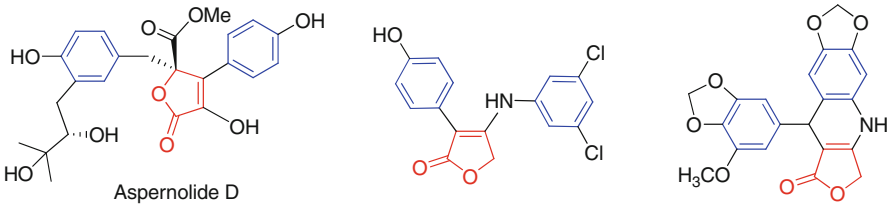


Fig. 2 Some biologically active natural or synthetic 2(5*H*)-furanone compounds containing benzene rings

relatively simple 2(5*H*)-furanone compounds are also important organic intermediates [13, 16–20]. As a result, many researchers have recently devoted much attention to 2(5*H*)-furanone chemistry [21–28].

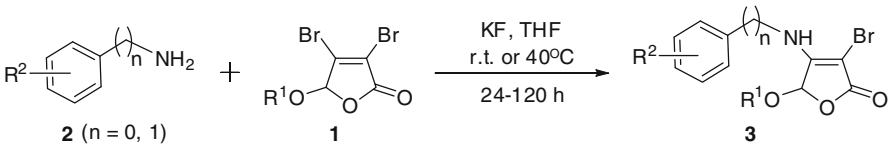
Many compounds containing the benzene ring structure have biological activity [29–32]. Some natural or synthetic 2(5*H*)-furanone compounds containing the benzene ring framework (Fig. 2) have especially important biological activity, including anti-inflammatory, antibacterial, antimitotic, and HIV-1 integrase inhibitory activity [9, 33–38]. Therefore, synthesis of 2(5*H*)-furanone derivatives containing benzene rings has been receiving substantial attention [9, 34–37, 39–41].

In this article, in order to design and synthesize novel 2(5*H*)-furanone derivatives with better biological activity, we tried to introduce benzene ring structures into 2(5*H*)-furanone molecules. On the basis of our previous studies on the syntheses of serial 5-alkoxy-4-amino-3-halo-2(5*H*)-furanones [38], we further investigated the reaction of 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1** with different amines **2** containing benzene rings, and synthesized a series of 5-alkoxy-4-amino-3-bromo-2(5*H*)-furanones, **3a**–**3w**, containing benzene rings (Scheme 1).

Results and discussion

Effects of different 2(5*H*)-furanone intermediates on yield

In our previous work [38] we investigated Michael addition–elimination reactions of 5-alkoxy-3,4-dihalo-2(5*H*)-furanone intermediates with different compounds containing nitrogen, for example amino acids, amino acid esters, aliphatic primary amines, and secondary amines. Therefore, after the intermediates 5-alkoxy-3,4-dibromo-2(5*H*)-furanones had been obtained [42], Michael addition–elimination



Scheme 1 Synthetic route to target compounds **3**

reactions with different amines containing benzene rings were performed in the presence of KF, under a protective N_2 atmosphere, in THF at room temperature or 40 °C (Scheme 1). The results are shown in Table 1.

It is apparent that all the 5-alkoxy-3,4-dibromo-2(5*H*)-furanones could be smoothly transformed into the desired products, and most isolated yields were equal to or better than 64 %. Of course, the steric effect of the 5-alkoxy group in the intermediates was obvious. When the 5-substituted group was methoxy, in the reaction with same amine **2** yields of the corresponding products were usually higher than those of products prepared from 5-benzyloxy-3,4-dibromo-2(5*H*)-furanones. For example, the biggest yield of the former was 86 % (Table 1, entry 10) whereas that of the latter was 83 % (entry 21).

Effects of different amines on yield

Similarly, when the same 5-alkoxy-3,4-dibromo-2(5*H*)-furanone was used it is apparent from Table 1 that different amines containing benzene rings notably affected the Michael addition–elimination reaction.

First, benzylamines reacted more easily than aromatic anilines with 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1**, providing the desired products. It is also apparent from Table 1 that not only were all yields better when benzylamines were used, reaction times (usually 24–48 h) of benzylamines with 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1** were also shorter than those for aromatic anilines (usually equal to or more than 72 h).

Second, irrespective of the benzylamine or aromatic aniline, steric hindrance resulting from the positions of substituents was also obvious. For example, for benzylamines, when the substituent was at the 2-position of the benzene ring (e.g. substrate **2k**), the yield was reduced (Table 1, entries 22 and 23). Thus, lower reactivity aromatic anilines, for example *o*-chloroaniline, reacted slowly with 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1**, prolonging reaction time.

Third, the type of substituent on the benzene ring also affected the yield. Usually, electron-donating substituents were advantageous for the reaction (e.g. Table 1, entries 12 and 13). In contrast, electron-withdrawing substituents were disadvantageous. For the strongly electron-withdrawing nitro group ($-NO_2$), reaction of even *p*-nitroaniline, with low steric hindrance, did not occur.

When the substituent on the benzene ring was a halogen, all *p*-halo substituted amines could be smoothly transformed into the desired products. However, the yields of the products were low (21–64 %). For the same kinds of amine and 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1**, yields from *p*-fluoro-substituted amines

Table 1 Yields of the target compounds **3** obtained by reaction of 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1** with amines **2** containing benzene rings

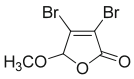
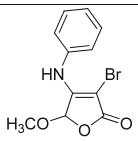
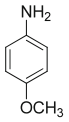
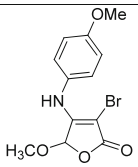
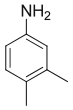
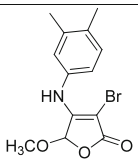
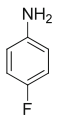
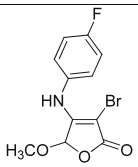
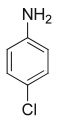
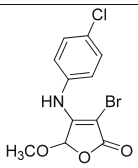
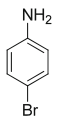
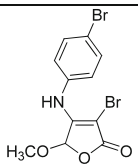
Entry	Intermedisates **1**	Amines **2**	Time (h)	Compounds **3**	Yield (%)
1	 **1a**	 **2a**	72	 **3a**	75
2	**1a**	 **2b**	60	 **3b**	80
3	**1a**	 **2c**	72	 **3c**	78
4	**1a**	 **2d**	96	 **3d**	64
5	**1a**	 **2e**	120	 **3e**	52
6	**1a**	 **2f**	120	 **3f**	36

Table 1 continued

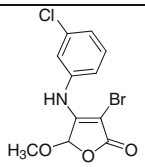
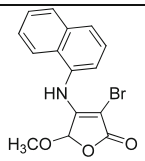
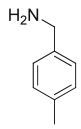
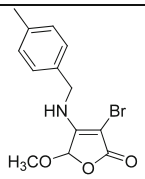
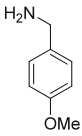
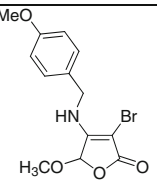
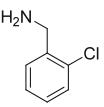
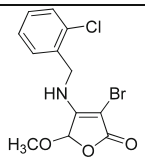
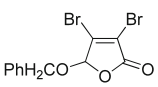
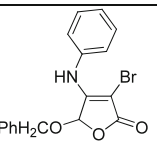
7	**1a**	 **2g**	120	 **3g**	46
8	**1a**	 **2h**	120	 **3h**	41
9	**1a**	 **2i**	24	 **3i**	84
10	**1a**	 **2j**	24	 **3j**	86
11	**1a**	 **2k**	24	 **3k**	67
12	 **1b**	**2a**	72	 **3l**	66

Table 1 continued

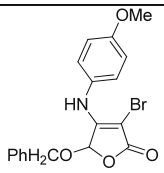
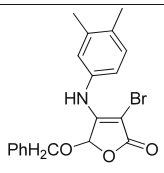
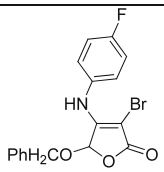
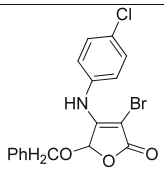
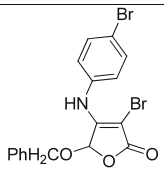
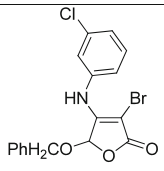
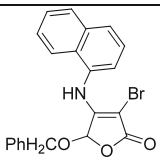
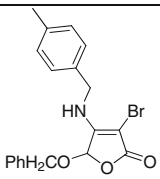
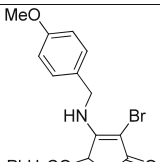
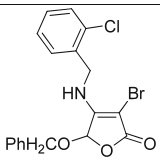
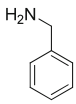
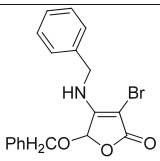
13	**1b**	**2b**	72	 **3m**	76
14	**1b**	**2c**	72	 **3n**	72
15	**1b**	**2d**	96	 **3o**	43
16	**1b**	**2e**	120	 **3p**	31
17	**1b**	**2f**	120	 **3q**	21
18	**1b**	**2g**	120	 **3r**	26

Table 1 continued

19	**1b**	**2h**	120	 **3s**	22
20	**1b**	**2i**	30	 **3t**	78
21	**1b**	**2j**	24	 **3u**	83
22	**1b**	**2k**	48	 **3v**	64
23	**1b**	 **2l**	48	 **3w**	76

were usually the best, and yields from *p*-bromo-substituted amines were the worst (Table 1, entries 4–6 and 15–17).

Characterization of the structures of the new compounds

In the IR spectra, stretching absorption of the N–H groups was observed in the region 3,300–3,100 cm^{-1} whereas stretching absorption bands of saturated C–H

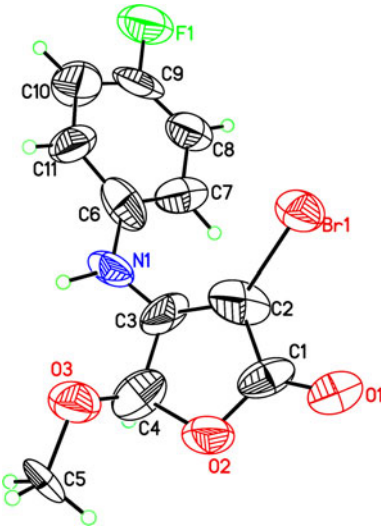


Fig. 3 X-ray structure of compound **3d**

were observed in the region 2,980–2,820 cm^{-1}. The strong C=O stretching band appeared at 1,760–1,720 cm^{-1} and the C=C stretching band occurred in the region 1,650–1,600 cm^{-1}.

The existence of C=O and C=C groups was also proved by UV spectroscopy—there were strong absorption peaks in the 240–300 nm region caused by the $\pi \rightarrow \pi^*$ transition of the C=C–C=O conjugated system in the 2(5*H*)-furanone ring.

In ^{1}H NMR, there was a singlet at 5.65–6.03 ppm from the 5-H of 2(5*H*)-furanone. Furthermore, the molecular structure of product **3d** was confirmed by X-ray analysis (Fig. 3). Combined with data from other structure characterization, it was apparent the furanone ring was not opened under these experimental conditions.

This characterization not only proved the structures of the twenty-two newly synthesized compounds were as expected, it also showed that the concise and effective synthetic method for 2(5*H*)-furanone derivatives containing benzene rings had wide applicability and broad tolerance of different substituent groups.

Conclusion

In summary, twenty-three 5-alkoxy-4-amino-3-bromo-2(5*H*)-furanones containing benzene rings were designed and efficiently synthesized under very mild reaction conditions. These target compounds with multiple bioactive moieties will afford a basis for activity testing of potential drug molecules. Many conversions could be carried out by use of C–X in the benzene ring [11, 43–45]. Thus, these 5-alkoxy-4-amino-3-bromo-2(5*H*)-furanones are also important intermediates for more 2(5*H*)-furanone derivatives with polyfunctional groups.

Experimental

General

All melting points were determined on an X-5 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on a Bruker Vector 33 FT-IR instrument, by the liquid film method, in the absorption range 4,000–400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ on a Varian DRX-400 MHz spectrometer, and tetramethylsilane (TMS) was used as internal standard. UV absorption peaks were measured by use of a Shimazu UV-2550 ultraviolet absorption detector with dichloromethane as solvent. Elemental analysis was performed with a Thermo Flashea TM 112 elemental analyzer. Mass spectra (MS) were recorded on a Thermo LCQ DECA XP MAX mass spectrometer.

All reagents and solvents were commercially available and used as received. Using furfural, benzyl alcohol, and methanol as starting materials, the intermediate 5-alkoxy-3,4-dibromo-2(5*H*)-furanones **1a** and **1b** were prepared in accordance with the literature [38, 42].

Typical procedure for synthesis of target compounds **3a**–**3w**

5-Alkoxy-3,4-dibromo-2(5*H*)-furanone **1** (1 mmol) in THF (3 mL) was stirred with KF (3 mmol) under an atmosphere of N_2. Subsequently, the appropriate amine **2** containing a benzene ring was added at room temperature or 40 °C. After completion of the reaction, as indicated by TLC, the reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL), and then washed with saturated salt solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (10 mL × 2). The organic layers were combined and dried over $MgSO_4$. The solvent was removed under reduced pressure then the residue was purified by flash chromatography on silica gel to afford compounds **3a–3w** for analysis.

*3-Bromo-5-methoxy-4-phenylaminofuran-2(5H)-one (**3a**)*

Yellow solid, yield 75 %; m.p. 116.2–116.8 °C (115–117 °C [46]); UV–visible (CH_2Cl_2) λ_{max}: 288 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.41 (3H, *s*, CH_3O-6), 5.92 (1H, *s*, CH-5), 7.14 (1H, *s*, NH-7), 7.19 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13), 7.25 (1H, *t*, $J = 8.0$ Hz, ArH-11), 7.36–7.40 (2H, *m*, ArH-10, 12); ^{13}C NMR (100 MHz, $CDCl_3$-TMS), δ: 55.7, 78.7, 99.2, 123.6, 126.4, 129.3, 136.6, 156.8, 167.7; IR (film) *v*: 3265, 3059, 2936, 2841, 1748, 1644, 1595, 1536, 1498, 1450, 1320, 1191, 1127, 950, 747, 712, 577; ESI–MS *m*/*z* (%): 282 ($[M - H]^-$, 100.0); Anal. Calcd for $C_{11}H_{10}BrNO_3$: C 46.50, H 3.55, N 4.93, Found: C 46.22, H 3.72, N 4.66.

*3-Bromo-5-methoxy-4-(4-methoxyphenyl)aminofuran-2(5H)-one (**3b**)*

Reddish brown liquid, yield 80 %; UV–visible (CH_2Cl_2) λ_{max}: 286 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.39 (3H, *s*, CH_3O-6), 3.82 (3H, *s*, CH_3O-14), 5.80 (1H,

s, CH-5), 6.89 (2H, *d*, $J = 8.0$ Hz, ArH-10, 12), 7.05 (1H, *s*, NH-7), 7.14 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.5, 55.6, 77.0, 99.0, 114.2, 126.4, 129.1, 157.6, 158.3, 167.9; IR (film) *v*: 3266, 3049, 2936, 2839, 1754, 1644, 1513, 1463, 1443, 1324, 1246, 1190, 1129, 950, 830, 521; ESI–MS *m*/*z* (%): 312 ([M − H]$^-$, 95.3); Anal. Calcd for $C_{12}H_{12}BrNO_4$: C 45.88, H 3.85, N 4.46, Found: C 45.97, H 3.69, N 4.52.

*3-Bromo-4-(3,4-dimethylphenyl)amino-5-methoxyfuran-2(5H)-one (**3c**)*

White solid, yield 78 %; m.p. 115.7–116.1 °C; UV–visible (CH_2Cl_2) λ_{max}: 289 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 2.25 (3H, *s*, CH_3-14), 2.26 (3H, *s*, CH_3-15), 3.41 (3H, *s*, CH_3O-6), 5.89 (1H, *s*, CH-5), 6.90–6.94 (2H, *m*, ArH-9, 13), 6.96 (1H, *s*, NH-7), 7.12 (1H, *d*, $J = 8.0$ Hz, ArH-12); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 19.3, 19.9, 55.4, 78.1, 99.0, 120.9, 124.9, 130.2, 134.2, 135.0, 137.7, 157.0, 167.6; IR (film) *v*: 3280, 3027, 2921, 2852, 1748, 1642, 1610, 1505, 1446, 1325, 1196, 1127, 1008, 831, 746, 513; ESI–MS *m*/*z* (%): 310 ([M − H]$^-$, 67.3); Anal. Calcd for $C_{13}H_{14}BrNO_3$: C 50.02, H 4.52, N 4.49, Found: C 49.88, H 4.71, N 4.62.

*3-Bromo-4-(4-fluorophenyl)amino-5-methoxyfuran-2(5H)-one (**3d**)*

Yellow solid, yield 64 %; m.p. 140.1–140.4 °C; UV–visible (CH_2Cl_2) λ_{max}: 283 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.42 (3H, *s*, CH_3O-6), 5.84 (1H, *s*, CH-5), 7.04–7.11 (2H, *m*, ArH-9, 13), 7.17–7.23 (2H, *m*, ArH-10, 12), 7.28 (1H, *s*, NH-7); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.8, 77.8, 99.2, 116.0, 126.5, 132.4, 157.0, 161.0, 168.0; IR (film) *v*: 3263, 3054.9, 2921, 2849, 1750, 1645, 1604, 1509, 1446, 1325, 1221, 1189, 1128, 951, 835, 505; ESI–MS *m*/*z* (%): 300 ([M − H]$^-$, 97.3); Anal. Calcd for $C_{11}H_9BrFNO_3$: C 43.73, H 3.00, N 4.64, Found: C 43.86, H 3.24, N 4.41.

*3-Bromo-4-(4-chlorophenyl)amino-5-methoxyfuran-2(5H)-one (**3e**)*

White oil, yield 52 %; UV–visible (CH_2Cl_2) λ_{max}: 293 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.45 (3H, *s*, CH_3O-6), 5.88 (1H, *s*, CH-5), 6.84 (1H, *s*, NH-7), 7.13 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13), 7.36 (2H, *d*, $J = 8.0$ Hz, ArH-10, 12); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.7, 79.8, 99.0, 124.8, 129.4, 131.9, 135.1, 156.3, 167.1; IR (film) *v*: 3263, 3049, 2921, 2849, 1750, 1642, 1593, 1523, 1492, 1468, 1320, 1190, 1128, 977, 820, 746, 501; ESI–MS *m*/*z* (%): 316 ([M − H]$^-$, 89.7); Anal. Calcd for $C_{11}H_9BrClNO_3$: C 41.47, H 2.85, N 4.40, Found: C 41.62, H 2.61, N 4.29.

*3-Bromo-4-(4-bromophenyl)amino-5-methoxyfuran-2(5H)-one (**3f**)*

Yellowish solid, yield 36 %; m.p. 117.0–117.5 °C; UV–visible (CH_2Cl_2) λ_{max}: 294 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.45 (3H, *s*, CH_3O-6), 5.88 (1H, *s*, CH-5), 6.98 (1H, *s*, NH-7), 7.07 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13), 7.50 (2H, *d*, $J = 8.0$ Hz, ArH-10, 12); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.8, 79.8, 99.1,

119.6, 125.1, 132.3, 135.7, 156.2, 167.3; IR (film) *v*: 3266, 3055, 2921, 2846, 1747, 1640, 1587, 1534, 1489, 1324, 1188, 1127, 1010, 817, 502; ESI–MS *m*/*z* (%): 360 ([M − H]$^-$, 57.7); Anal. Calcd for $C_{11}H_9Br_2NO_3$: C 36.40, H 2.50, N 3.86, Found: C 36.58, H 2.59, N 4.00.

*3-Bromo-4-(3-chlorophenyl)amino-5-methoxyfuran-2(5H)-one (**3g**)*

Yellow solid, yield 46 %; m.p. 139.5–140.5 °C; UV–visible (CH_2Cl_2) λ_{max}: 291 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.48 (3H, *s*, CH_3-6), 5.92 (1H, *s*, CH-5), 6.88 (1H, *s*, NH-7), 7.07 (1H, *d*, $J = 8.0$ Hz, ArH-13), 7.19–7.25 (2H, *m*, ArH-9, 11), 7.29–7.35 (1H, *m*, ArH-12); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.8, 80.7, 99.1, 121.1, 123.2, 126.3, 130.3, 134.9, 137.8, 156.0, 167.0; IR (film) *v*: 3263, 3060, 2933, 2841, 1751, 1643, 1593, 1536, 1480, 1329, 1191, 1128, 955, 778, 746, 688, 543; ESI–MS *m*/*z* (%): 316 ([M − H]$^-$, 86.3); Anal. Calcd for $C_{11}H_9BrClNO_3$: C 41.47, H 2.85, N 4.40, Found: C 41.31, H 3.00, N 4.59.

*3-Bromo-5-methoxy-4-(naphthalen-1-ylamino)furan-2(5H)-one (**3h**)*

Brown solid, yield 41 %; m.p. 143.5–144.3 °C; UV–visible (CH_2Cl_2) λ_{max}: 296 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.30 (3H, *s*, CH_3O-6), 5.77 (1H, *s*, CH-5), 6.80 (1H, *s*, NH-7), 7.42 (1H, *d*, $J = 8.0$ Hz, ArH-9), 7.47–7.53 (1H, *m*, ArH-10), 7.56–7.64 (2H, *m*, ArH-16, 17), 7.87 (1H, *d*, $J = 8.0$ Hz, ArH-11), 7.93 (2H, *d*, $J = 8.0$ Hz, ArH-14, 15); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.7, 77.2, 99.1, 121.7, 123.9, 125.2, 126.9, 127.4, 128.3, 128.7, 129.8, 132.1, 134.2, 157.9, 167.2; IR (film) *v*: 3358, 3038, 2922.68, 2852, 1747, 1644, 1597, 1575, 1506, 1331, 1202, 1128, 1005, 793, 773, 747, 522; ESI–MS *m*/*z* (%): 332 ([M − H]$^-$, 100.0); Anal. Calcd for $C_{15}H_{12}BrNO_3$: C 53.91, H 3.62, N 4.19, Found: C 53.84, H 3.75, N 4.27.

*3-Bromo-5-methoxy-4-(4-methylbenzyl)aminofuran-2(5H)-one (**3i**)*

Colorless liquid, yield 84 %; UV–visible (CH_2Cl_2) λ_{max}: 275 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 2.35 (3H, *s*, CH_3-15), 3.48 (3H, *s*, CH_3O-6), 4.59 (2H, *s*, CH_2-8), 5.65 (2H, *s*, CH-5, NH-7), 7.19 (4H, *s*, ArH-10, 11, 13, 14); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 21.2, 47.3, 55.2, 77.4, 98.2, 127.5, 129.7, 133.8, 138.0, 159.2, 167.6; IR (film) *v*: 3319, 3093, 3005, 2922, 2846, 1751, 1645, 1578, 1516, 1445, 1324, 1202, 1126, 977, 805, 508; ESI–MS *m*/*z* (%): 310 ([M − H]$^-$, 40.8); Anal. Calcd for $C_{13}H_{14}BrNO_3$: C 50.02, H 4.52, N 4.49, Found: C 50.13, H 4.48, N 4.35.

*3-Bromo-5-methoxy-4-(4-methoxybenzyl)aminofuran-2(5H)-one (**3j**)*

Yellowish oil, yield 86 %; UV–visible (CH_2Cl_2) λ_{max}: 277 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.48 (3H, *s*, CH_3O-6), 3.81 (3H, *s*, CH_3O-15), 4.57 (2H, *s*, CH_2-8), 5.62 (1H, *s*, NH-7), 5.66 (1H, *s*, CH-5), 6.91 (2H, *d*, $J = 8.0$ Hz, ArH-11, 13), 7.24 (2H, *d*, $J = 8.0$ Hz, ArH-10, 14); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 47.1, 55.2, 55.4, 77.4, 98.4, 114.3, 128.8, 129.0, 159.4, 167.7; IR (film) *v*:

3315, 3082, 2922, 2839, 1749, 1642, 1586, 1513, 1442, 1322, 1249, 1176, 1124, 975, 819, 515; ESI–MS *m/z* (%): 326 ($[M - H]^-$, 100.0); Anal. Calcd for $C_{13}H_{14}BrNO_4$: C 47.58, H 4.30, N 4.27, Found: C 47.64, H 4.49, N 4.13.

*3-Bromo-4-(2-chlorobenzyl)amino-5-methoxyfuran-2(5H)-one (**3k**)*

Yellowish solid, yield 67 %; m.p. 131.4–133.1 °C; UV–visible (CH_2Cl_2) λ_{max}: 274 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.50 (3H, *s*, CH_3O-6), 4.60–4.85 (2H, *m*, CH_2-8), 5.54 (1H, *s*, NH-7), 5.73 (1H, *s*, CH-5), 7.29–7.44 (4H, *m*, ArH-11, 12, 13, 14); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 45.4, 55.1, 77.3, 98.2, 127.5, 129.3, 129.7, 129.9, 133.3, 134.4, 158.7, 167.3; IR (film) *v*: 3301, 3073, 2933, 2841, 1752, 1646, 1573, 1528, 1444, 1323, 1202, 1128, 977, 748, 514; ESI–MS *m/z* (%): 332 ($[M - H]^-$, 100.0); Anal. Calcd for $C_{12}H_{11}BrClNO_3$: C 43.34, H 3.33, N 4.21, Found: C 43.21, H 3.15, N 4.38.

*5-Benzyloxy-3-bromo-4-phenylaminofuran-2(5H)-one (**3l**)*

Yellow solid, yield 66 %; m.p. 142.3–143.4 °C; UV–visible (CH_2Cl_2) λ_{max}: 290 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.50–4.74 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 6.03 (1H, *s*, CH-5), 6.87 (1H, *s*, NH-7), 7.01 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13), 7.07–7.17 (3H, *m*, ArH-10, 11, 12), 7.25–7.29 (3H, *m*, ArH-16, 17, 18), 7.33–7.37 (2H, *m*, ArH-15, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 71.1, 79.4, 97.1, 123.5, 126.4, 128.5, 128.5, 128.7, 129.5, 135.0, 136.8, 157.5, 167.4; IR (film) *v*: 3264, 3055, 3034, 2921, 2851, 1747, 1638, 1595, 1497, 1449, 1319, 1191, 1130, 1026, 746, 698, 496; ESI–MS *m/z* (%): 382 ($[M + Na]^+$, 93.7); Anal. Calcd for $C_{17}H_{14}BrNO_3$: C 56.68, H 3.92, N 3.89, Found: C 56.52, H 4.01, N 4.01.

*5-Benzyloxy-3-bromo-4-(4-methoxyphenyl)aminofuran-2(5H)-one (**3m**)*

Brown liquid, yield 76 %; UV–visible (CH_2Cl_2) λ_{max}: 288 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.82 (3H, *s*, CH_3O-20), 4.47–4.72 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 5.90 (1H, *s*, CH-5), 6.82 (2H, *d*, $J = 12.0$ Hz, ArH-10, 12), 6.85 (1H, *s*, NH-7), 6.99–7.05 (2H, *m*, ArH-16, 18), 7.07 (2H, *d*, $J = 12.0$ Hz, ArH-9, 13), 7.16–7.31 (3H, *m*, ArH-15, 17, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 55.6, 71.0, 77.6, 96.9, 114.4, 126.5, 128.5, 128.5, 128.6, 129.3, 135.1, 158.3, 158.4, 167.7; IR (film) *v*: 3265, 3035, 2921, 2850, 1748, 1641, 1588, 1513, 1455, 1326, 1246, 1192, 1130, 948, 829, 746, 699, 514; ESI–MS *m/z* (%): 390 ($[M + H]^+$, 27.3), 412 ($[M + Na]^+$, 95.0); Anal. Calcd for $C_{18}H_{16}BrNO_4$: C 55.40, H 4.13, N 3.59, Found: C 55.54, H 4.29, N 3.39.

*5-Benzyloxy-3-bromo-4-(3,4-dimethylphenyl)aminofuran-2(5H)-one (**3n**)*

Yellow oil, yield 72 %; UV–visible (CH_2Cl_2) λ_{max}: 290 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 2.21 (3H, *s*, CH_3-20), 2.27 (3H, *s*, CH_3-21), 4.47–4.73 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 5.98 (1H, *s*, CH-5), 6.75 (1H, *s*, NH-7), 6.86

(1H, *d*, $J = 8.0$ Hz, ArH-9), 6.89 (1H, *s*, ArH-13), 6.96–7.02 (2H, *m*, ArH-16, 18), 7.09 (1H, *d*, $J = 8.0$ Hz, Ar–H-10), 7.24–7.36 (3H, *m*, Ar–H-15, 17, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 19.4, 19.9, 71.0, 78.4, 97.0, 121.3, 125.2, 128.4, 128.4, 128.6, 130.4, 134.3, 135.1, 135.3, 137.9, 157.9, 167.5; IR (film) *v*: 3265, 3027, 2925, 2852, 1749, 1641, 1612, 1505, 1454, 1322, 1198, 1129, 956, 823, 746, 698, 513; ESI–MS *m*/*z* (%): 388 ($[M + H]^+$, 8.3), 410 ($[M + Na]^+$, 100.0); Anal. Calcd for $C_{19}H_{18}BrNO_3$: C 58.78, H 4.67, N 3.61, Found: C 58.88, H 4.80, N 3.52.

*5-Benzyloxy-3-bromo-4-(4-fluorophenyl)aminofuran-2(5H)-one (**3o**)*

White solid, yield 43 %; m.p. 150.4–152.2 °C; UV–visible (CH_2Cl_2) λ_{max}: 283 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.51–4.75 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 5.92 (1H, *s*, CH-5), 6.77 (1H, *s*, NH-7), 7.00 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13), 7.04 (2H, *d*, $J = 8.0$ Hz, ArH-10, 12), 7.05–7.21 (3H, *m*, ArH-16, 17, 18), 7.28–7.33 (2H, *m*, ArH-15, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 71.1, 78.9, 96.7, 116.2, 126.4, 128.6, 128.6, 128.7, 132.5, 134.9, 157.6, 161.1, 167.4; IR (film) *v*: 3274, 3060, 2922, 2852, 1748, 1643, 1603, 1510, 1454, 1325, 1223, 1191, 1133, 949, 834, 747, 698, 505; ESI–MS *m*/*z* (%): 376 ($[M - H]^-$, 100.0); Anal. Calcd for $C_{17}H_{13}BrFNO_3$: C 53.99, H 3.45, N 3.70, Found: C 53.78, H 3.37, N 3.84.

*5-Benzyloxy-3-bromo-4-(4-chlorophenyl)aminofuran-2(5H)-one (**3p**)*

White solid, yield 31 %; m.p. 109.1–110.3 °C; UV–visible (CH_2Cl_2) λ_{max}: 292 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.54–4.77 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 5.97 (1H, *s*, CH-5), 6.69 (1H, *s*, NH-7), 7.00–7.08 (4H, *m*, ArH-9, 10, 12, 13), 7.26–7.36 (*5H*, *m*, ArH-15, 16, 17, 18, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 71.2, 80.2, 96.6, 125.0, 128.6, 128.7, 128.8, 129.5, 132.0, 134.7, 135.2, 157.1, 167.1; IR (film) *v*: 3266, 3060, 3034, 2926, 2852, 1748, 1642, 1593, 1493, 1455, 1325, 1191, 1128, 1014, 822, 746, 698, 672, 507; ESI–MS *m*/*z* (%): 392 ($[M - H]^-$, 74.9); Anal. Calcd for $C_{17}H_{13}BrClNO_3$: C 51.74, H 3.32, N 3.55, Found: C 51.59, H 3.50, N 3.49.

*5-Benzyloxy-3-bromo-4-(4-bromophenyl)aminofuran-2(5H)-one (**3q**)*

Yellow solid, yield 21 %; m.p. 102.9–103.6 °C; UV–visible (CH_2Cl_2) λ_{max}: 292 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.55–4.77 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 5.98 (1H, *s*, CH-5), 6.67 (1H, *s*, NH-7), 6.95 (2H, *d*, $J = 8.0$ Hz, ArH-9, 13), 7.05 (2H, *d*, $J = 8.0$ Hz, ArH-10, 12), 7.30–7.37 (3H, *m*, ArH-16, 17, 18), 7.42 (2H, *d*, $J = 8.0$ Hz, ArH-15, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 71.2, 80.4, 96.6, 119.7, 125.1, 128.7, 128.7, 128.8, 132.5, 134.7, 135.8, 157.0, 167.0; IR (film) *v*: 3265, 3027, 2924, 2853, 1748, 1641, 1587, 1528, 1490, 1454, 1323, 1190, 1128, 1011, 817, 746, 698, 498; ESI–MS *m*/*z* (%): 436 ($[M - H]^-$, 49.7); Anal. Calcd for $C_{17}H_{13}Br_2NO_3$: C 46.50, H 2.98, N 3.19, Found: C 46.39, H 3.04, N 3.38.

*5-Benzyloxy-3-bromo-4-(3-chlorophenyl)aminofuran-2(5H)-one (**3r**)*

Yellow solid, yield 26 %; m.p. 118.0–119.2 °C; UV–visible (CH_2Cl_2) λ_{max}: 289 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.57–4.81 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2-6), 6.02 (1H, *s*, CH-5), 6.62 (1H, *s*, NH-7), 6.98 (1H, *d*, $J = 8.0$ Hz, ArH-9), 7.07–7.12 (2H, *m*, ArH-10, 11), 7.14 (1H, *s*, ArH-13), 7.21–7.26 (2H, *m*, ArH-16, 18), 7.29–7.34 (3H, *m*, ArH-15, 17, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 71.3, 81.1, 96.8, 121.3, 123.4, 126.4, 128.7, 128.7, 128.7, 130.4, 134.7, 135.1, 137.9, 156.7, 166.8; IR (film) *v*: 3352, 3060, 3033, 2922, 2851, 1748, 1638, 1592, 1534, 1479, 1322, 1191, 1127, 951, 746, 698, 505; ESI–MS *m*/*z* (%): 392 ($[M - H]^-$, 80.0); Anal. Calcd for $C_{17}H_{13}BrClNO_3$: C 51.74, H 3.32, N 3.55, Found: C 51.54, H 3.52, N 3.39.

*5-Benzyloxy-3-bromo-4-(naphthalen-1-ylamino)furan-2(5H)-one (**3s**)*

Brown solid, yield 22 %; m.p. 51.6–53.2 °C; UV–visible (CH_2Cl_2) λ_{max}: 294 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.27–4.62 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2O-6), 5.83 (1H, *s*, CH-5), 6.68 (1H, *d*, $J = 8.0$ Hz, ArH-9), 6.75 (1H, *s*, NH-7), 7.08–7.14 (2H, *m*, ArH-16, 18), 7.18–7.22 (1H, *m*, ArH-10), 7.33–7.45 (3H, *m*, ArH-15, 17, 19), 7.55–7.61 (2H, *m*, ArH-22, 23), 7.88 (1H, *d*, $J = 8.0$ Hz, Ar–H-11), 7.91–7.96 (2H, *m*, Ar–H-20, 21); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 71.2, 79.1, 96.8, 121.9, 123.9, 125.3, 126.9, 127.4, 128.3, 128.4, 128.4, 128.6, 129.9, 132.4, 134.2, 134.7, 158.9, 167.2; IR (film) *v*: 3359, 3032.9, 2922, 2852, 1763, 1640, 1575, 1506, 1470, 1331, 1209, 1122, 954, 774, 747, 697, 514; ESI–MS *m*/*z* (%): 408 ($[M - H]^-$, 100.0); Anal. Calcd for $C_{21}H_{16}BrNO_3$: C 61.48, H 3.93, N 3.41, Found: C 61.65, H 4.10, N 3.37.

*5-Benzyloxy-3-bromo-4-(4-methylbenzyl)aminofuran-2(5H)-one (**3t**)*

White solid, yield 78 %; m.p. 125.9–126.2 °C; UV–visible (CH_2Cl_2) λ_{max}: 276 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 2.34 (3H, *s*, CH_3-21), 4.48 (2H, *s*, CH_2-8), 4.64–4.82 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2O-6), 5.42 (1H, *s*, NH-7), 5.76 (1H, *s*, CH-5), 7.09 (2H, *d*, $J = 8.0$ Hz, ArH-10, 14), 7.15 (2H, *d*, $J = 8.0$ Hz, ArH-11, 13), 7.28–7.38 (*5H*, *m*, ArH-15, 16, 17, 18, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 21.2, 47.4, 70.4, 77.3, 96.3, 127.4, 128.7, 128.7, 129.7, 133.7, 135.3, 138.1, 159.8, 167.6; IR (film) *v*: 3300, 3027, 2921, 2851, 1747, 1637, 1547, 1514, 1495, 1451, 1322, 1215, 1122, 923, 801, 745, 697, 502; ESI–MS *m*/*z* (%): 410 ($[M + Na]^+$, 100.0); Anal. Calcd for $C_{19}H_{18}BrNO_3$: C 58.78, H 4.67, N 3.61, Found: C 58.75, H 4.72, N 3.42.

*5-Benzyloxy-3-bromo-4-(4-methoxybenzyl)aminofuran-2(5H)-one (**3u**)*

White solid, yield 83 %; m.p. 107.4–108.6 °C; UV–visible (CH_2Cl_2) λ_{max}: 276 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 3.78 (3H, *s*, CH_3O-21), 4.46 (2H, *s*, CH_2-8), 4.64 $\sim$ 4.81 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2O-6), 5.44 (1H, *s*, NH-7), 5.77 (1H, *s*, CH-5), 6.86 (2H, *d*, $J = 8.0$ Hz, ArH-11, 13), 7.13 (2H, *d*, $J = 8.0$ Hz,

ArH-10, 14), 7.29–7.39 (*5H*, *m*, ArH-15, 16, 17, 18, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 47.1, 55.4, 70.4, 77.3, 96.4, 114.3, 128.5, 128.6, 128.7, 128.9, 129.3, 135.0, 159.5, 167.7; IR (film) *v*: 3357, 3066, 3027, 2922, 2851, 1748, 1639, 1586, 1513, 1455, 1322, 1249, 1176, 1126, 937, 818, 745, 698, 595; ESI–MS *m/z* (%): 426 ($[M + Na]^+$, 100.0); Anal. Calcd for $C_{19}H_{18}BrNO_4$: C 56.45, H 4.49, N 3.46, Found: C 56.38, H 4.70, N 3.27.

*5-Benzyloxy-3-bromo-4-(2-chlorobenzyl)aminofuran-2(5H)-one (**3v**)*

Yellowish solid, yield 64 %; m.p. 46.7–47.9 °C; UV–visible (CH_2Cl_2) λ_{max}: 274 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.59 (2H, *s*, CH_2-8), 4.66–4.81 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2O-6), 5.67 (1H, *s*, NH-7), 5.81 (1H, *s*, CH-5), 7.16–7.25 (3H, *m*, ArH-12, 13, 14), 7.29–7.36 (*5H*, *m*, ArH-15, 16, 17, 18, 19), 7.38 (1H, *d*, $J = 8.0$ Hz, ArH-11); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 45.5, 70.5, 77.3, 96.3, 126.2, 127.4, 128.7, 128.8, 129.0, 129.6, 129.9, 133.1, 134.5, 135.2, 159, 167.5,; IR (film) *v*: 3314, 3067, 3027, 2922, 2852, 1749, 1643, 1574, 1528, 1444, 1324, 1217, 1131, 947, 747,699, 524; ESI–MS *m/z* (%): 408 ($[M + H]^+$, 8.5), 430 ($[M + Na]^+$, 68.7); Anal. Calcd for $C_{18}H_{15}BrClNO_3$: C 52.90, H 3.70, N 3.43, Found: C 52.78, H 3.66, N 3.60.

*4-Benzylamino-5-benzyloxy-3-bromofuran-2(5H)-one (**3w**)*

Yellow solid, yield 76 %; m.p. 78.4–79.3 °C; UV–visible (CH_2Cl_2) λ_{max}: 275 nm; ^{1}H NMR (400 MHz, $CDCl_3$-TMS) δ: 4.53 (2H, *s*, CH_2-8), 4.64–4.82 (2H, *dd*, $J_1 = 12.0$ Hz, $J_2 = 12.0$ Hz, CH_2O-6), 5.47 (1H, *s*, NH-7), 5.76 (1H, *s*, CH-5), 7.21 (2H, *d*, $J = 8.0$ Hz, ArH-10, 14), 7.29–7.37 (8H, *m*, ArH-11, 12, 13, 15, 16, 17, 18, 19); ^{13}C NMR (100 MHz, $CDCl_3$-TMS) δ: 47.5, 70.5, 77.3, 96.3, 127.4, 128.2, 128.7, 128.8, 129.0, 135.3, 136.8, 159.6, 167.5; IR (film) *v*: 3359, 3060, 3027, 2921, 2851, 1748, 1638, 1531, 1495, 1455, 1322, 1215, 1120, 933, 746, 697, 573; ESI–MS *m/z* (%): 374 ($[M + H]^+$, 8.5), 396 ($[M + Na]^+$, 87.4); Anal. Calcd for $C_{18}H_{16}BrNO_3$: C 57.77, H 4.31, N 3.74, Found: C 57.89, H 4.38, N 3.85.

Acknowledgments The authors' are grateful to the National Natural Science Foundation of China (no. 20772035), the Third Talents Special Funds of Guangdong Higher Education (no. Guangdong-Finance-Education [2011]431) and the Natural Science Foundation of Guangdong Province (no. S2011010001556) for financial support.

References

1. X. Cheng, X.-F. Jiang, Y.-H. Yu, S.-M. Ma, J. Org. Chem. **73**, 8960 (2008)
2. S. Kim, P.H. Lee, J. Org. Chem. **77**, 215 (2012)
3. E. Lattmann, D. Kinchington, S. Dunn, H. Singh, W.O. Ayuko, M.J. Tisdale, J. Pharm. Pharmacol. **56**, 1163 (2004)
4. B.M. Trost, A.C. Burns, M.J. Bartlett, T. Tautz, A.H. Weiss, J. Am. Chem. Soc. **134**, 1474 (2012)
5. Y.-Z. Xie, N. Wang, B. Cheng, H.-B. Zhai, Org. Lett. **14**, 3 (2012)
6. K.R. Prasad, V.R. Gandi, Tetrahedron **21**, 275 (2010)
7. V.E.J. Hikawczuk, J.R. Saad, O.S. Giordano, C. García, T. Martín, V.S. Martín, M.E. Sosa, C.E. Tonn, J. Nat. Prod. **71**, 190 (2008)

8. R.W.S. Weber, R. Kappe, T. Paululat, E. Mosker, H. Anke, Phytochemistry **68**, 886 (2007)
9. Z.-P. Xiao, T.-W. Ma, M.-L. Liao, Y.-T. Feng, X.-C. Peng, J.-L. Li, Z.-P. Li, Y. Wu, Q. Luo, Y. Deng, X. Liang, H.-L. Zhu, Eur. J. Med. Chem. **46**, 4904 (2011)
10. V.J. Majo, J. Prabhakaran, N.R. Simpson, R.L. Van Heertum, J.J. Mann, J.S.D. Kumar, Bioorg. Med. Chem. Lett. **15**, 4268 (2005)
11. M.D. Guerrero, M. Aquino, I. Bruno, M.C. Terencio, M. Paya, R. Riccio, L. Gomez-Paloma, J. Med. Chem. **50**, 2176 (2007)
12. X. Luo, Y.-M. Shi, R.-H. Luo, S.-H. Luo, X.-N. Li, R–.R. Wang, S.-H. Li, Y.-T. Zheng, X. Du, W.-L. Xiao, J.-X. Pu, H.-D. Sun, Org. Lett. **14**, 1286 (2012)
13. M.-X. Wei, L. Feng, X.-Q. Li, X.-Z. Zhou, Z.-H. Shao, Eur. J. Med. Chem. **44**, 3340 (2009)
14. A. Kamal, P. Suresh, A. Mallareddy, B.A. Kumar, P.V. Reddy, P. Raju, J.R. Tamboli, T.B. Shaik, N. Jain, S.V. Kalivendi, Bioorg. Med. Chem. **19**, 2349 (2011)
15. M.-T. Liu, S. Lin, M.-L. Gan, M.-H. Chen, L. Li, S.-J. Wang, J.-C. Zi, X.-N. Fan, Y. Liu, Y.-K. Si, Y.-C. Yang, X.-G. Chen, J.-G. Shi, Org. Lett. **14**, 1004 (2012)
16. J.R. Cucarull-Gonzalez, J. Hernando, R. Alibes, M. Figueredo, J. Font, L. Rodriguez-Santiago, M. Sodupe, J. Org. Chem. **75**, 4392 (2010)
17. R. Jahjah, A. Gassama, V. Bulach, C. Suzuki, M. Abe, N. Hoffmann, A. Martinez, J.-M. Nuzillard, Chem. Eur. J. **16**, 3341 (2010)
18. M. Fleck, T. Bach, Chem. Eur. J. **16**, 6015 (2010)
19. N.F. Devyatova, L.S. Kosolapova, A.R. Kurbangalieva, E.A. Berdnikov, O.A. Lodochnikova, I.A. Litvinov, G.A. Chmutova, Russ. J. Org. Chem. **44**, 1225 (2008)
20. A.R. Kurbangalieva, N.F. Devyatova, L.S. Kosolapova, O.A. Lodochnikova, E.A. Berdnikov, I.A. Litvinov, G.A. Chmutova, Russ. Chem. Bull. Int. Ed. **58**, 126 (2009)
21. L.-H. Zhou, X.-Q. Yu, L. Pu, J. Org. Chem. **74**, 2013 (2009)
22. R. Surmont, G. Verniest, N. De Kimp, J. Org. Chem. **75**, 5750 (2010)
23. A. Gassama, C. Ernenwein, N. Hoffmann, Green Chem. **12**, 859 (2010)
24. J. Ren, D–.D. Ma, Y. Sha, F. Li, M.-S. Cheng, Heterocycles **81**, 1427 (2010)
25. E. Gondela, K.Z. Walczak, Eur. J. Med. Chem. **45**, 3993 (2010)
26. Y.-Q. Jiang, Y.-L. Shi, M. Shi, J. Am. Chem. Soc. **130**, 7202 (2008)
27. M. Perez, D. I. Perez, A. Martinez, A. Castro, G. Gomez, Y. Fall, Chem. Commun. 3252 (2009)
28. H.-L. Cui, J.-R. Huang, J. Lei, Z.-F. Wang, S. Chen, Y.-C. Chen, Org. Lett. **12**, 720 (2010)
29. A.R. Carroll, P.C. Healy, R.J. Quinn, C.J. Tranter, J. Org. Chem. **64**, 2680 (1999)
30. C.M. Clavel, O. Zava, F. Schmitt, B.H. Kenzaoui, A.A. Nazarov, L. Juillerat-Jeanneret, P.J. Dyson, Angew. Chem. Int. Ed. **50**, 7124 (2011)
31. Z.-K. Guo, T. Yan, Y. Guo, Y.-C. Song, R.-H. Jiao, R.-X. Tan, H.-M. Ge, J. Nat. Prod. **75**, 15 (2012)
32. S. Sanchez-Tena, M.L. Fernandez-Cachon, A. Carreras, M.L. Mateos-Martín, N. Costoya, M.P. Moyer, M.J. Nunez, J.L. Torres, M. Cascante, J. Nat. Prod. **75**, 26 (2012)
33. P. Nuclear, D. Sommit, N. Boonyuen, K. Pudhom, Chem. Pharm. Bull. **58**, 1221 (2010)
34. R. Labruere, B. Gautier, M. Testud, J. Seguin, C. Lenoir, S. Desbene-Finck, P. Helissey, C. Garbay, G.G. Chabot, M. Vidal, S. Giorgi-Renault, ChemMedChem **5**, 2016 (2010)
35. B. Wackler, P. Schneider, J.M. Jacobs, J. Pauly, C. Allen, M. Nett, D. Hoffmeister, Chem. Biol. **18**, 354 (2011)
36. M.N. Semenova, A.S. Kiselyov, D.V. Tsyganov, L.D. Konyushkin, S.I. Firgang, R.V. Semenov, O.R. Malyshev, M.M. Raihstat, F. Fuchs, A. Stielow, M. Lantow, A.A. Philchenkov, M.P. Zavelevich, N.S. Zefirov, S.A. Kuznetsov, V.V. Semenov, J. Med. Chem. **54**, 7138 (2011)
37. F. Shi, X.-N. Zeng, G. Zhang, N. Ma, B. Jiang, S.-J. Tu, Bioorg. Med. Chem. Lett. **21**, 7119 (2011)
38. Y.-Q. Mo, Z.-Y. Wang, W.-J. Mei, J.-H. Fu, Y.-H. Tan, S.-H. Luo, Monatsh. Chem. **143**, 443 (2012)
39. H.B. Borate, S.P. Sawargave, S.P. Chavan, M.A. Chandavarkar, R. Iyer, A. Tawte, D. Rao, J.V. Deore, A.S. Kudale, P.S. Mahajan, G.S. Kangire, Bioorg. Med. Chem. Lett. **21**, 4873 (2011)
40. F. Shi, S. Zhang, S.-S. Wu, Y. Gao, S.-J. Tu, Mol. Divers. **15**, 497 (2011)
41. A. Bhardwaj, Z.-J. Huang, J. Kaur, E.E. Knaus, ChemMedChem **7**, 62 (2012)
42. J.-X. Li, F.-L. Xue, Y.-H. Tan, S.-H. Luo, Z.-Y. Wang, Acta Chim. Sinica **69**, 1688 (2011)
43. F. Bellina, C. Anselmi, F. Martina, R. Rossi, Eur. J. Org. Chem. 2290 (2003)
44. J. Boukouvalas, L.C. McCann, Tetrahedron Lett. **51**, 4636 (2010)
45. B.-X. Tang, Y.-H. Zhang, R.-J. Song, D.-J. Tang, G.-B. Deng, Z.-Q. Wang, Y.-X. Xie, Y.-Z. Xia, J.-H. Li, J. Org. Chem. **77**, 2837 (2012)
46. Y. Hachihama, T. Shono, O. Ikeda, J. Org. Chem. **29**, 1371 (1964)