A novel and efficient synthesis of *bis*(benzofuranyl)methanes and 2-benzofuran-1-nitroalkanes catalyzed by $Bi(OTf)_3$

Ren Er Chen, Yan Li Wang, Zhi Wei Chen, and Wei Ke Su

Abstract: Bismuth (III) triflate-catalyzed Friedel–Crafts reactions between benzofuran and aldehydes in different solvents were investigated. Bis(benzofuranyl)methanes were obtained with good yields when acetonitrile was used as solvent, while in the case of nitromethane the multi-component reaction products, 2-benzofuran-1-nitroalkanes, were formed under similar conditions. A plausible mechanism is given.

Key words: benzofuran, aldehyde, bis(benzofuranyl)methanes, $Bi(OTf)_3$, 2-benzofuran-1-nitroalkane.

Résumé : On a étudié les réactions de Friedel–Crafts catalysées par le triflate de bismuth(III) et effectuées entre le benzofurane et les aldéhydes dans divers solvants. Avec l'acétonitrile comme solvant, on obtient de bons rendements de bis(benzofuranyl)méthanes alors que dans le nitrométhane, dans des conditions semblables, il y a formation de 2-benzofurane-1-nitroalcanes, des produits qui résultent de réactions entre plusieurs réactifs. On propose un mécanisme plausible.

Mots-clés : benzofurane, aldéhyde, bis(benzofuranyl)méthanes, $Bi(OTf)_3$, 2-benzofurane-1-nitroalcanes.

[Traduit par la Rédaction]

Introduction

Most natural and synthetic compounds with benzofuran moieties exhibit broad bioactivities (1, 2) such as antitumor, antifungal, antivirus activities, 5-lipoxygensase and 5α-reductase inhibitory activity (3–5). Moreover, they are also key intermediates for constructing some natural bioactive quinines (6). Though there are some reports of bis(benzofuranyl)methanones (7) and macrocyclic trimer (8), which were prepared from activated benzofurans, bis(benzofuranyl)methanes were only reported in one article (9). In that article, an environmentally harmful mineral acid was chosen as catalyst.

Recently, metal triflates have been widely used as Lewis acids that have low toxicity, low cost, high stability, are easy to handle and recover from water (10–13). In our ongoing green chemistry research program, investigating the use of environmentally friendly reagents, catalysts, and processes for organic reactions, we wish to study the activities of metal triflates in catalyzing the Friedel–Crafts alkylation and multi-component reaction. Herein, we wish to introduce $Bi(OTf)_3$ as a mild, highly efficient, and environmentally benign catalyst for the preparation of benzofuran derivatives. An effective, convenient, and economic method for the synthesis of bis(benzofuranyl)methanes was developed. Additionally, the first three-component synthetic procedure of 2-benzofuran-1-nitroalkane derivatives are reported here. The catalyst could be recovered easily after the reactions and reused without evident loss of activity.

Results and discussion

The condensation between benzofuran (2 equiv.) and benzaldehyde **1a** (1 equiv.) in CH_3NO_2 at refluxing temperature was used as a model reaction (Scheme 1) for the screening of a suitable metal triflate catalyst, and the results are summarized in Table 1. It can be seen that all metal triflates, with the exception of $Mg(OTf)_2$ and $Sr(OTf)_2$, showed good catalytic effects. $Sc(OTf)_3$ and $Bi(OTf)_3$ were particularly effective for this Friedel–Crafts alkylation reaction in short reaction times (Table 1, entries 1–8). Considering its low cost, $Bi(OTf)_3$ was chosen as reaction catalyst. The amounts of metal triflate were also examined in CH_3NO_2. When $Bi(OTf)_3$ and $Sc(OTf)_3$ were used as catalysts, 1 mol% was enough to finish the reaction in 1 h. There is no obvious influence on the yield on increasing the amount of $Bi(OTf)_3$ and $Sc(OTf)_3$ (Table 1, entries 6 and 9).

Solvents such as DMF, CH_3CN, EtOH, and PhMe (Table 1, entries 10–13) were also tested. Acetonitrile was found to give maximum yield followed by nitromethane. Reaction temperature was also explored in CH_3CN. No product was found at room temperature after 3 h. When the reaction temperature was increased to reflux, the yield was obviously improved. In light of this, subsequent studies were carried out under the following optimized conditions: 1 mol% $Bi(OTf)_3$ at refluxing temperature in CH_3CN. In this reac-

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R.E. Chen, Y.L. Wang, Z.W. Chen, and W.K. Su.[1] Key Laboratory of Pharmaceutical Engineering (Zhejiang University of Technology), Ministry of Education, College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China.

[1] Corresponding author (e-mail: suweike@zjut.edu.cn).

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Scheme 1.

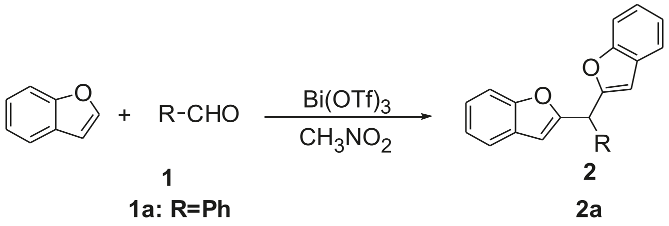


Table 1. The synthesis of bis(benzofuranyl)methanes under different reaction conditions.

Entry	Catalyst	Solvent	Loading (mol%)	Yield (%)[a]
1	$Cu(OTf)_2$	CH_3NO_2	10	65
2	$Zn(OTf)_2$	CH_3NO_2	10	55
3	$Mg(OTf)_2$	CH_3NO_2	10	0
4	$Yb(OTf)_3$	CH_3NO_2	10	46
5	$Sc(OTf)_3$	CH_3NO_2	1	75
6	$Sc(OTf)_3$	CH_3NO_2	5	76
7	$Sr(OTf)_2$	CH_3NO_2	10	0
8	$Bi(OTf)_3$	CH_3NO_2	1	76
9	$Bi(OTf)_3$	CH_3NO_2	5	77
10	$Bi(OTf)_3$	DMF[b]	1	0
11	$Bi(OTf)_3$	CH_3CN[b]	1	77
12	$Bi(OTf)_3$	EtOH[b]	1	65
13	$Bi(OTf)_3$	PhMe[b]	1	60
14	No catalyst	CH_3CN[b]	0	0

Note: General conditions: benzofuran (2 equiv.), benzaldehyde (1 equiv), and catalyst (0.01–0.1 equiv.) at 101 °C; reaction time 1.5 h.

[a] Isolate yields based on benzaldehyde.

[b] Reaction temperature: refluxing temperature.

Table 2. The Friedel–Crafts alkylation of benzofuran with aldehydes catalyzed by $Bi(OTf)_3$ in CH_3CN.

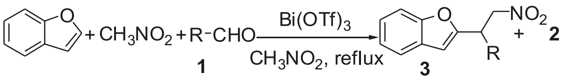
Entry	R	Compound **2**	Yield (%)[a]
1	*n*-C_6H_5	**2a**	77, 76, 75, 75[b]
2	4-OH-C_6H_4	**2b**	65
3	3-CH_3O-4-OH-C_6H_3	**2c**	63
4	4-CH_3O-C_6H_4	**2e**	70
5	4-Cl-C_6H_4	**2f**	70
6	3-Cl-C_6H_4	**2g**	80
7	3-F-C_6H_4	**2h**	83
8	2-F-6-Cl-C_6H_3	**2i**	81
9	3-NO_2-C_6H_4	**2j**	87
10	3-OH-C_6H_4	**2k**	78
11	3-Br-C_6H_4	**2l**	78
12	H	**2m**	70
13	*n*-C_4H_9	**2n**	73
14	2-NO_2-C_6H_4	**2o**	45
15	2-OH-C_6H_4	**2p**	38
16	2,4-$(CH_3O)_2$-C_6H_3	**2q**	0
17	2-OCH_3-C_6H_5	**2r**	0

Note: Reaction condition: aldehyde (1 mmol), benzofuran (2 mmol), and $Bi(OTf)_3$ (1 mol%) in acetonitrile at refluxing temperature.

[a] Isolated yields based on aldehyde.

[b] Catalyst was reused three times.

Scheme 2.



tion, $Bi(OTf)_3$ could be reused three times without obvious loss of activity (Table 2, entry 1).

To extend the scope of the metal triflate-catalyzed method for the synthesis of bis(benzofuranyl)methanes, a series of aldehydes were investigated (Table 2). Both aromatic and aliphatic aldehydes were applicable to this reaction, except for **1q** and **1r**. The results indicated that a spacial steric effect had an obvious influence on the reaction (Table 2, entries 14–17). Furthermore, the substituted groups on the aromatic ring also had evident influence on the reaction. The aromatic ring-bearing electron-withdrawing groups only required short times with high yields, excluding the sterically hindered 2-nitrobenzaldehyde **1o**. The *m*-substituted benzaldehyde with electron-withdrawing groups were more beneficial to the reactions (Table 2, entries 6, 7, 9, and 11). To our surprise, good yield was also obtained when 3-hydroxybenzaldehyde was used as substrate (Table 2, entry 10). Considering the good reaction activity of aldehydes, benzophenone, acetone, and cyclohexanone were chosen as substrates. Trace reactions took place as indicated by TLC.

The formation of 2-benzofuran-1-nitroalkane derivatives was discovered serendipitiously. During the preparation of bis(benzofuranyl)methanes in nitromethane, another product was detected by TLC and identified as compound **3** (Scheme 2) by ^1H NMR, ^{13}C NMR, and MS. Thus, the catalytic activity of $Bi(OTf)_3$ was explored for the multicomponent condensation using 4-hydroxybenzaldehyde as model substrate. 4-Hydroxybenzaldehyde, benzofuran, and nitromethane were stirred at room temperature for 4 h at the molar ratio of 1:1:1 in CH_3CN. No product was found, as monitored by TLC. But when it was heated to refluxing temperature, contrary to our expectation, compound **2** were obtained instead of compound **3**. We also carried out the condensation of 4-hydroxybenzaldehyde, benzofuran, and nitromethane in CH_3NO_2. Interestingly, compound **3** was obtained as major product along with compound **2** as minor product (Table 3, entry 2). To extend the scope of the metal triflate-catalyzed method for the synthesis of 2-benzofuran-1-nitroalkane derivatives, we also tried other aldehydes. The results are summarized in Table 3. It can be seen that this condensation was only suitable for the aromatic aldehydes bearing strong electron-donating groups (Table 3, entries 2–5).

A possible mechanism for the formation of bis(benzofuranyl)methanes and 2-benzofuran-1-nitroalkane derivatives is proposed in Scheme 3 (paths A and B). When CH_3CN was used as reaction solvent, intermediate [**a**] was formed, which was easily attacked by another benzofuran in the presence of $Bi(OTf)_3$ (14). Furthermore, the aromatic ring-bearing electron-withdrawing group was more beneficial to the formation of compound **2,** except for 3-hydroxybenzaldehyde. To our surprise, when CH_3NO_2 is utilized as reaction media there may exist another reaction mechanism

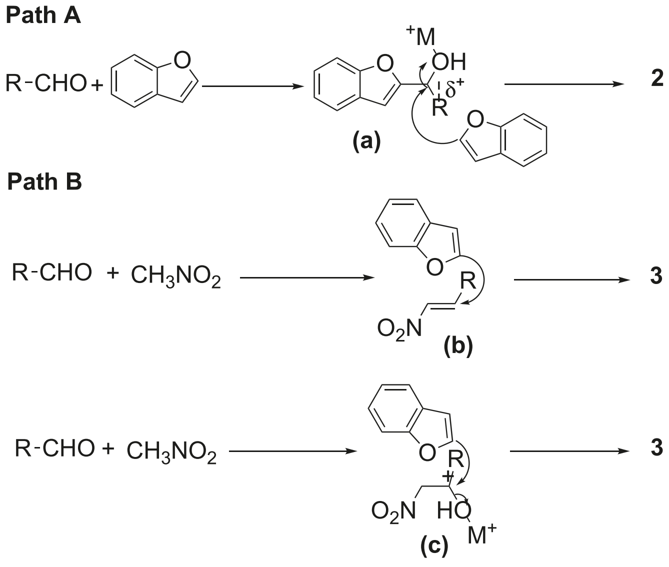
Table 3. The synthesis of 2-benzofuran-1-nitroalkane derivatives catalyzed by $Bi(OTf)_3$ in CH_3NO_2.

Entry	R	Compound	Yield (%)[a]
1	*n*-C_6H_5	**3a**	0
		2a	38
2	4-OH-C_6H_4	**3b**	83
		2b	8
3	3-CH_3O-4-OH-C_6H_3	**3c**	80
		2c	7
4	2,4-$(CH_3O)_2$-C_6H_3	**3d**	85
		2d	0
5	4-CH_3O-C_6H_4	**3e**	82
		2e	8
6	3-Cl-C_6H_4	**3g**	0
		2g	40
7	3-NO_2-C_6H_5	**3j**	0
		2j	43
8	3-OH-C_6H_4	**3k**	0
		2k	40
9	H	**3m**	0
		2m	36
10	*n*-C_4H_9	**3n**	0
		2n	38

Note: Reaction condition: aldehyde (1 mmol), benzofuran (1 mmol), and $Bi(OTf)_3$ (1 mol%) in nitromethane at refluxing temperature.

[a] Isolated yields based on aldehyde.

Scheme 3.



(path B). Compound **3** was synthesized via two possible processes. Intermediate [**b**] was attacked by benzofuran to obtain the Michael adduct **3**. Intermediate [**c**] suffered a nucleophilic attack by benzofuran to give compound **3**. We predicted the mechanism by performing the following reactions. The condensation of **1** and nitromethane in CH_3CN at the molar ratio of 1:1 at refluxing temperature, catalyzed by $Bi(OTf)_3$, gave no product. But when this reaction proceeded in CH_3NO_2 at refluxing temperature, a henry product was obtained with high yield. The aromatic ring-bearing electron-donating groups were apt for the synthesis of the henry product. This may be explained because the electron-donating groups are crucial to the stability of intermediate [**b**]. We also tried the condensation of benzofuran and the henry reaction. Only the aromatic ring-bearing strong electron-donating groups can react easily, which helped us explain the result in Table 3.

Conclusion

In summary, we have developed a simple, convenient, and efficient synthetic protocol for bis(benzofuranyl)methanes using a catalytic amount of $Bi(OTf)_3$ in CH_3CN. Additionally, $Bi(OTf)_3$ efficiently promotes three-component coupling reactions of aldehyde, benzofuran, and nitromethane. The simplicity, efficiency, easy work-up, and the need for only a small amount of $Bi(OTf)_3$ makes it the preferred procedure for the preparation of different kinds of 2-benzofuran-1-nitroalkane derivatives. This class of compounds may be used to construct some bioactive compounds.

Experimental section[2]

General method

All reagents are commercially available. Bismuth(III) triflate was prepared from triphenylbismuth and triflic acid (15). Melting points were measured on a digital melting point apparatus WR-1B and were uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a Varian 400 MHz or Bruker Anance III (500 MHz) instrument using $CDCl_3$ as the solvent, and chemical shifts were expressed in parts per million (ppm) using TMS as an internal standard. Mass spectra were measured with a Trace Finnigan DSQ. High-resolution mass spectral (HRMS) analyses were measured on an Agilent 6210 TOF LC/MS using APCI and EI (electrospray ionization) techniques. IR measurements were carried out with a Nicolet Aviatar-370 instrument. Elemental analysis was performed on a VarioEL-III instrument. All spectral data of the products were identical to authentic samples.

General procedure for the preparation of bis(benzofuranyl)methanes

A mixture of benzofuran (2 mmol), benzaldehyde (1 mmol), and $Bi(OTf)_3$ (0.01 mmol) in CH_3CN (1 mL) was heated at refluxing temperature for 1 h. Then water was added, and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography (silica gel, petroleum ether / methylene chloride *v*/*v* 16:1) to afford the adduct. The aqueous layer was washed by ethyl acetate and concentrated in vacuo to give white crystals $[Bi(OTf)_3]$,

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[2] Supplementary data for this article are available on the journal Web site (canjchem.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0R6, Canada. DUD 3773. For more information on obtaining material refer to cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml.

which was finally heated at 180 °C for 48 h in vacuo to afford $Bi(OTf)_3$ as a colorless crystal.

General procedure for the preparation of 2-benzofuran-1-nitroalkane derivatives

$Bi(OTf)_3$ (0.01 mmol) was added to a solution of benzofuran (1 mmol), 4-hydroxybenzaldehyde (1 mmol) in 2 mL of nitromethane. The reaction mixture was stirred at 101 °C for 2 h and then cooled to room temperature. Water (10 mL) was added and the mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic phases were dried over Na_2SO_4, evaporated, and the crude product was purified by flash chromatography (silica gel, petroleum ether / ethyl acetate *v*/*v* 4:1) to afford the corresponding products. The aqueous layer was washed by ethyl acetate and concentrated in vacuo to give white crystals [$Bi(OTf)_3$], which was finally heated at 180 °C for 48 h in vacuo to afford $Bi(OTf)_3$ as a colorless crystal.

2a

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3133, 1637, 1400, 1253, 748. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.49–7.16 (m, 13H, ArH), 6.46 (s, 2 H, furan-H), 5.70 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.1, 154.3, 138.1, 128.8, 127.7, 127.5, 124.5, 124.1, 123.9, 120.9, 111.3, 105.2, 45.9. MS (EI) *m*/*z* (%): 324 (100), 247 (64). HRMS (EI) calcd. for $C_{23}H_{16}O_2$: 324.1150; found: 324.1151.

2b

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3412, 3132, 1614, 1400, 1252, 748. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.48 (d, J = 8.0 Hz, 2H, ArH), 7.42 (d, J = 7.5 Hz, 2H, ArH), 7.27–7.17 (m, 6H, ArH), 6.81 (d, J = 7.5 Hz, 2H, ArH), 6.45 (s, 2H, furan-H), 5.64 (s, 1H, CH), 5.42 (s, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 157.1, 155.3, 155.1, 130.1, 129.9, 128.4, 124.0, 122.8, 120.8, 115.6, 111.2, 105.0, 45.1. MS (EI) *m*/*z* (%): 340 (100), 247 (35). HRMS (APCI) calcd. for (M – 1) $C_{23}H_{16}O_3$: 339.1021; found: 339.1016.

3b

Light yellow crystal, mp 92.8–94.6 °C. IR (KBr, cm^{-1}) ν_{max}: 3410, 3171, 1614, 1551, 1337, 1210, 749. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, J = 8.0 Hz, 1H, ArH), 7.43 (d, J = 8.4 Hz, 1H, ArH), 7.28–7.18 (m, 4H, ArH), 6.82 (d, J = 8.8 Hz, 2H, ArH), 6.48 (s, 1H, furan-H), 5.15–5.10 (m, 1H, $CHNO_2$), 5.00 (t, J = 7.6 Hz, 1H, CH), 4.89–4.83 (m, 1H, $CHNO_2$), 1.58 (s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.5, 155.1, 154.9, 129.3, 128.2, 127.9, 124.3, 123.0, 120.9, 116.0, 111.1, 104.3, 77.8, 43.1. MS (EI) *m*/*z* (%): 283 (5), 236 (100). $C_{16}H_{13}NO_4$: calcd. C 67.84, H 4.63, N 4.94; found C 67.89, H 4.70, N 4.94.

2c

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3416, 3132, 1617, 1400, 1253, 747. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.49 (d, J = 7.5 Hz, 2H, ArH), 7.42 (d, J = 8.0 Hz, 2H, ArH), 7.28–7.20 (m, 4H, ArH), 6.92–6.87 (m, 3H, ArH), 6.47 (s, 2H, furan-H), 5.63 (s, 1H, CH), 5.60 (s, 1H, OH), 3.84 (s, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 157.0, 155.1, 146.7, 145.2, 129.9, 128.3, 124.4, 124.0, 122.8, 121.6, 120.8, 114.6, 111.2, 105.0, 56.0, 45.6. MS (EI) *m*/*z* (%): 370 (100), 247 (48). HRMS (APCI) calcd. for (M – 1) $C_{24}H_{18}O_4$: 369.1127; found: 369.1130.

3c

Yellow crystal, mp 83.5–84.2 °C. IR (KBr, cm^{-1}) ν_{max}: 3410, 3130, 1610, 1400, 1253, 746. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, J = 8.4 Hz, 1H, ArH), 7.42 (d, J = 8.0 Hz, 1H, ArH), 7.27–7.18 (m, 2H, ArH), 6.90–6.82 (m, 3H, ArH), 6.49 (s, 1H, furan-H), 5.68 (s, 1H, OH), 5.13–5.08 (m, 1H, $CHNO_2$), 4.97 (t, J = 7.8 Hz, 1H, CH), 4.88–4.83 (m, 1H, $CHNO_2$), 3.85 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.2, 154.9, 146.8, 145.6, 127.9, 127.8, 124.3, 123.0, 122.7, 120.9, 120.8, 114.9, 111.1, 104.3, 77.8, 55.9, 43.6. MS (EI) *m*/*z* (%): 313 (14), 266 (100). $C_{17}H_{15}NO_5$: calcd. C 65.17, H 4.83, N 4.47; found C 65.21, H 4.85, N 4.47.

3d

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3130, 2925, 2851, 1613, 1554, 1377, 1254, 752. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, J = 8.0 Hz, 1H, ArH), 7.42 (d, J = 8.0 Hz, 1H, ArH), 7.27–7.18 (m, 2H, ArH), 7.05 (d, J = 8.8 Hz, 1H, ArH), 6.53 (s, 1H, ArH), 6.49 (s, 1H, furan-H), 6.43 (d, J = 8.0 Hz, 1H, ArH), 5.42–5.38 (m, 1H, $CHNO_2$), 5.01 (t, J = 7.6 Hz, 1H, CH), 4.93–4.88 (m, 1H, $CHNO_2$), 3.84 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 160.8, 157.8, 155.4, 154.8, 129.6, 128.2, 124.0, 122.8, 120.8, 116.8, 111.1, 104.6, 104.2, 99.0, 77.3, 55.6, 55.4, 37.6. MS (EI) *m*/*z* (%): 327 (10), 280 (74), 265 (100), 131 (50). $C_{18}H_{17}NO_5$: calcd. C 66.05, H 5.23, N 4.28; found C 66.10, H 5.26, N 4.28.

2e

White crystal. mp 106.9– 107.1 °C. IR (KBr, cm^{-1}) ν_{max}: 3128, 1632, 1400, 1250, 752. ^1H NMR (500 MHz, $CDCl_3$) δ: 7.48 (d, J = 7.5 Hz, 2H, ArH), 7.47–7.13 (m, 8H, ArH), 6.88 (t, J = 7.5 Hz, 2H, ArH), 6.45 (s, 2H, furan-H), 5.65 (s, 1H, CH), 3.78 (s, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 159.2, 157.3, 155.2, 130.3, 129.8, 128.5, 124.1, 122.9, 121.0, 114.3, 111.4, 105.2, 55.3, 45.3. MS (EI) *m*/*z* (%): 354 (100), 247 (20). $C_{24}H_{18}O_3$: calcd. C 81.34, H 5.12; found C 81.40, H 5.16.

3e

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3130, 2920, 2850, 1615, 1550, 1345, 748. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.49 (d, J = 7.2 Hz, 1H, ArH), 7.43 (d, J = 8.0 Hz, 1H, ArH), 7.31–7.19 (m, 4H, ArH), 6.90 (d, J = 8.8 Hz, 2H, ArH), 6.48 (s, 1H, furan-H), 5.16–5.11 (m, 1H, $CHNO_2$), 5.01 (t, J = 7.6 Hz, 1H, CH), 4.89–4.84 (m, 1H, $CHNO_2$), 3.80 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.2, 155.1, 154.7, 129.0, 128.2, 127.9, 124.3, 123.1, 120.8, 115.8, 111.1, 104.3, 77.6, 54.7, 43.1. MS (EI) *m*/*z* (%): 297 (15), 250 (100). $C_{17}H_{15}NO_4$: calcd. C 68.68, H 5.09, N 4.71; found C 68.64, H 5.15, N 4.72.

2f

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3124, 1637, 1402, 1253, 747. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.50–7.21 (m, 12H, ArH), 6.47 (s, 2H, furan-H), 5.67 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.0, 143.6, 136.6, 133.6, 130.0, 129.0, 128.2, 124.2, 122.9, 120.9, 111.3, 105.4, 45.3. MS (EI) *m/z* (%): 360 (33), 358 (100), 247 (47). $C_{23}H_{15}ClO_2$: calcd. C 76.99, H 4.21; found C 76.94, H 4.26.

2g

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3125, 1632, 1400, 1252, 756. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (t, *J* = 7.0 Hz, 2H, ArH), 7.43 (t, *J* = 8.0 Hz, 2H, ArH), 7.37 (s, 1H, ArH), 7.30– 7.23 (m, 5H, ArH), 7.21–7.19 (m, 2H, ArH), 6.50 (s, 2H, furan-H), 5.68 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.8, 155.1, 140.0, 134.6, 130.0, 128.8, 128.2, 127.9, 126.9, 124.2, 122.9, 120.9, 111.3, 105.4, 45.5. MS (EI) *m/z* (%): 360 (34), 358 (100), 247 (100). $C_{23}H_{15}ClO_2$: calcd. C 76.99, H 4.21; found C 76.94, H 4.25.

2h

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3123, 1614, 1590, 1400, 1253, 748. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52–7.50 (m, 2H, ArH), 7.44 (d, *J* = 7.5 Mz, 2H, ArH), 7.35–7.16 (m, 6H, ArH), 7.12–7.08 (m, 1H, ArH), 7.04–7.02 (m, 1H, ArH), 6.50 (s, 2H, furan-H), 5.71 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 163.0 (*J* = 250 Hz), 155.9, 155.1, 143.6, 130.3, 130.2, 128.2, 124.3, 122.9, 120.9, 115.7 (*J* = 22.5 Hz), 114.7 (*J* = 21.0 Hz), 111.2, 105.3, 45.5. MS (EI) *m/z* (%): 342 (98), 247 (100). $C_{23}H_{15}FO_2$: calcd. C 80.69, H 4.42; found C 80.62, H 4.48.

2i

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3117, 1636, 1400, 1249, 745. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50–7.10 (m, 11H, ArH), 6.61 (s, 2H, furan-H), 6.34 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 162.0 (*J* = 250.0 Hz), 154.8, 154.3, 135.4, 129.7, 129.6, 128.4, 125.9, 124.0, 122.8, 120.8, 115.2 (*J* = 23.7 Hz), 111.2, 104.9, 39.3. MS (EI) *m/z* (%): 378 (33), 376 (100), 247 (76). $C_{23}H_{14}ClFO_2$: calcd. C 73.31, H 3.74; found C 73.28, H 3.78.

2j

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3120, 1616, 1529, 1400, 1348, 1252, 747. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.29 (s, 1H, ArH), 8.18 (d, *J* = 7.2 Hz, 1H, ArH), 7.73 (d, *J* = 8.8 Hz, 1H, ArH), 7.53 (d, *J* = 7.6 Hz, 3H, ArH), 7.44 (d, *J* = 7.6 Hz, 2H, ArH), 7.29–7.21 (m, 4H, ArH), 6.56 (s, 2H, furan-H), 5.81 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.1, 154.9, 148.5, 140.2, 134.7, 129.7, 128.0, 124.5, 123.7, 123.1, 122.8, 121.1, 111.3, 105.7, 45.5. MS (EI) *m/z* (%): 369 (100), 247 (63). $C_{23}H_{15}NO_4$: calcd. C 74.79, H 4.09, N 3.79; found C 74.75, H 4.12, N 3.75.

2k

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3415, 3128, 1630, 1400, 1250, 753. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 7.5 Hz, 2H, ArH), 7.42 (d, *J* = 8.0 Hz, 2H, ArH), 7.29–7.17 (m, 5H, ArH), 6.93 (d, *J* = 7.5 Hz, 1H, ArH), 6.83 (s, 1H, ArH), 6.82–6.75 (m, 1H, ArH), 6.48 (s, 2H, furan-H), 5.65 (s, 1H, CH), 5.17 (s, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 156.5, 155.9, 155.1, 139.8, 130.0, 128.3, 124.1, 122.8, 121.1, 120.9, 115.6, 114.7, 111.3, 105.2, 45.7. MS (EI) *m/z* (%): 340 (100), 247 (40). $C_{23}H_{16}O_3$: calcd. C 81.16, H 4.74; found C 81.12, H 4.80.

2l

Viscous oil. IR (neat, cm^{-1})ν_{max}: 3120, 1615, 1525, 1400, 1347, 1250, 745. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54–7.50 (m, 3H, ArH), 7.46–7.43 (m, 3H, ArH), 7.32 (s, 1H, ArH), 7.28–7.19 (m, 5H, ArH), 6.50 (s, 2H, furan-H), 5.67 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 155.8, 155.1, 140.3, 131.6, 130.9, 130.3, 128.2, 127.3, 124.2, 122.9, 122.8, 120.9, 111.3, 105.4, 45.5. MS (EI) *m/z* (%): 404 (26), 402 (26), 248 (46), 247 (100). $C_{23}H_{15}BrO_2$: calcd. C 68.50, H 3.75; found C 68.48, H 3.78.

2m

Melting point 70.1–71.2 °C. (lit. value (16) 73–74 °C). IR (KBr, cm^{-1}) ν_{max}: 3120, 2930, 1600, 1252, 750. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50–7.18 (m, 8H, ArH), 6.57 (s, 2H, furan-H), 4.29 (s, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ: 154.9, 153.7, 128.6, 123.8, 122.7, 120.6, 111.0, 104.1, 28.4. MS (EI) *m/z* (%): 248 (100), 247 (80).

2n

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3127, 2956, 2928, 2860, 1617, 1453, 1400, 1252, 747. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.57–7.17 (m, 8H, ArH), 6.56 (s, 2H, furan-H), 4.30 (t, *J* = 8.0 Hz, 1H), 2.23–2.18 (m, 2H, CH_2), 1.39–1.36 (m, 4H, 2 CH_2), 0.89 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 157.9, 154.7, 128.6, 123.6, 122.6, 120.6, 111.1, 103.2, 39.8, 32.1, 22.5, 22.4, 13.9. MS (EI) *m/z* (%): 304 (15), 247 (100). HRMS (EI) calcd. for: $C_{21}H_{20}O_2$ 304.1463; found: 304.1466.

2o

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3128, 1617, 1400, 1347, 1252, 748. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 7.0 Hz, 1H, ArH), 7.59 (t, *J* = 7.5 Hz, 1H, ArH), 7.53–7.47 (m, 4H, ArH), 7.43 (t, *J* = 8.0 Hz, 2H, ArH), 7.31–7.27 (m, 2H, ArH), 7.23–7.20 (m, 2H, ArH), 6.63 (s, 1H, ArH), 6.54 (s, 2H, furan-H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 155.1, 154.8, 148.5, 133.4, 132.7, 131.3, 128.7, 128.1, 125.3, 124.3, 123.0, 121.1, 111.3, 105.6, 40.8. MS (EI) *m/z* (%): 369 (100), 247 (60). $C_{23}H_{15}NO_4$: calcd. C 74.79, H 4.09, N 3.79; found C 74.82, H 4.11, N 3.79.

2p

Viscous oil. IR (neat, cm^{-1}) ν_{max}: 3413, 3130, 1617, 1400, 1252, 748. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 7.0 Hz, 2H, ArH), 7.43 (t, *J* = 8.0 Hz, 2H, ArH), 7.26–7.18 (m, 6H, ArH), 6.93 (t, *J* = 7.5 Hz, 1H, ArH), 6.83 (d, *J* = 7.0 Hz, 1H, ArH), 6.50 (s, 2H, furan-H), 6.09 (s, 1H, ArH), 5.08 (s, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ: 156.2, 155.1, 153.2, 129.9, 129.0, 128.3, 124.6, 124.0, 122.8, 121.3, 120.8, 116.1, 111.2, 105.2, 39.6. MS (EI) *m/z* (%): 340 (100), 247 (45). $C_{23}H_{16}O_3$: calcd. C 81.16, H 4.74; found C 81.13, H 4.79.

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