Tetrahedron Letters 50 (2009) 6693–6697

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

# $B(C_6F_5)_3$: an efficient catalyst for reductive alkylation of alkoxy benzenes and for synthesis of triarylmethanes using aldehydes

S. Chandrasekhar *, Sanjida Khatun, G. Rajesh, Ch. Raji Reddy

*Organic Division-I, Indian Institute of Chemical Technology, Hyderabad 500 007, India*

ARTICLE INFO

*Article history:*
Received 28 April 2009
Revised 11 September 2009
Accepted 16 September 2009
Available online 19 September 2009

*Keywords:*
Tris(pentafluorophenyl)borane
Polymethylhydrosiloxane
Reductive alkylation
Electron-rich arenes
Aldehyde

ABSTRACT

Tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] has been used as an efficient catalyst for reductive alkylation of alkoxy benzenes using aldehydes as an alkylating agent in the presence of polymethylhydrosiloxane (PMHS). Various alkylated trimethoxybenzene derivatives have been prepared in good to high yields. In addition, $B(C_6F_5)_3$ was also used as a catalyst for the reaction of electron-rich arenes with aldehydes to obtain triarylmethanes. The use of reductive alkylation protocol for the synthesis of an isochroman and tetrahydroisoquinoline derivatives has also been demonstrated.

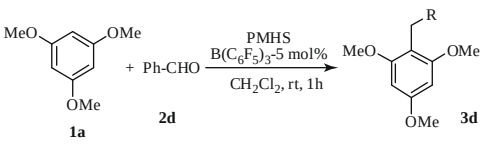


Friedel–Crafts alkylation of aromatic compounds is one of the important reactions, which has found significant applications in the synthesis of various biologically active compounds.[1] Common synthetic methods for the alkylation include the reaction of aromatic compounds with alkyl halides in the presence of Lewis acid activators.[2] The alternative methods used to obtain the alkylated aromatics are; acylation followed by reduction,[3] alkylation with alcohol or its derivatives,[4,5] and alkenylation with organometallic reagents.[6] Further, reductive alkylation of aromatic compounds can be achieved by using carbonyl compounds as alkylating agents,[7] which are very limited. Hence, there has been a considerable interest in the development of a mild and efficient method for reductive alkylation of aromatics.

The efficiency of tris(pentafluorophenyl)borane [$B(C_6F_5)_3$] catalyst has been revealed in combination with silanes for the various reduction procedures by us[8] and others.[9] In our continued interest in the development of new reduction procedures,[8,10] we envisioned that the reductive alkylation of electron-rich aromatics (**1**) with aldehydes (**2**) in the presence of PMHS–$B(C_6F_5)_3$ would proceed smoothly to give the alkylated products (**3**).

With this idea, we first attempted the reaction of trimethoxybenzene (**1a**) with benzaldehyde (**2d**) in $CH_2Cl_2$ using polymethylhydrosiloxane in the presence of 5 mol % of $B(C_6F_5)_3$ and the reaction was completed in 1 h to give the benzyl trimethoxybenzene (**3d**) in 90% yield (Scheme 1 and Table 1, entry 4). Further, the generality of this reaction was examined by using trimethoxybenzene (**1a**) as a representative aromatic compound. As can be seen from Table 1, varieties of aldehydes were used as alkylating agents to give the corresponding alkylated trimethoxybenzene in good yields. Aliphatic aldehydes **2a**, **2b,** and **2c**, successfully participated in the reductive alkylation of trimethoxybenzene under the present reaction conditions to provide the corresponding alkylated products **3a** to **3c** (Table 1, entries 1–3) without rearrangement. Further, substituted aromatic aldehydes such as 2-nitro, 4-fluoro, 3-hydroxy, and 2,5-dimethoxy benzaldehydes, **2e**, **2f**, **2g,** and **2h**, were well reacted with trimethoxybenzene under PMHS–$B(C_6F_5)_3$ reagent system to give the corresponding benzylated trimethoxybenzenes, **3e** to **3h** (Table 1, entries 5–8). To our delight, furanose aldehyde **2j** obtained from glucose di-acetonide, was also used as an alkylating agent to obtain trimethoxybenzyl furanose **3j** in 89% yield (Table 1, entry 10) which can be mimicked as *C*-aryl sugar. However, the reaction of trimethoxybenzene with acetophenone (**2k**) was unsuccessful even under reflux temperature and/or for longer reaction time (Table 1, entry 11).

The encouraging results described above for the reductive alkylation of 1,3,5-trimethoxybenzene spurred us to test the reactivity



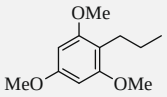
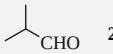
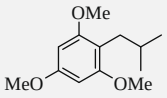
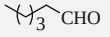
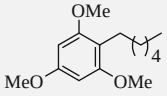
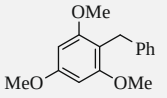
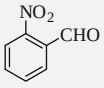
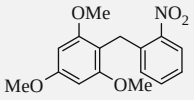
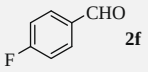
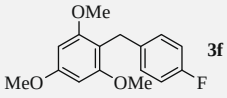
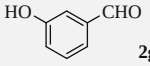
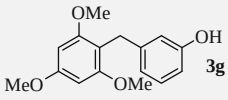
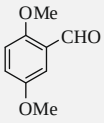
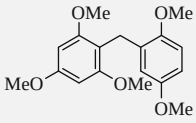
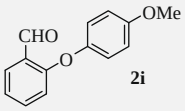
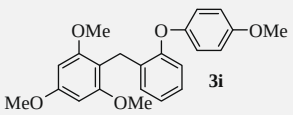
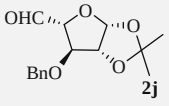
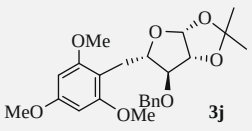

R = alkyl, aryl

**Scheme 1.** Reductive alkylation.

* Corresponding author. Tel.: +91 40 27193210; fax: +91 40 27160512.
*E-mail address:* srivaric@iict.res.in (S. Chandrasekhar).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.09.085

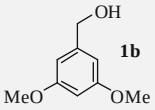
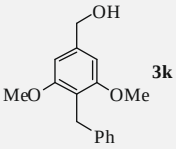
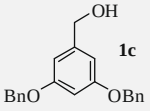
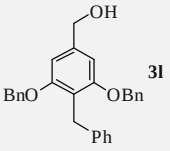
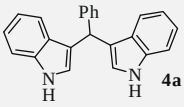
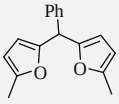
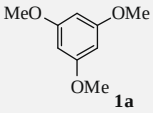
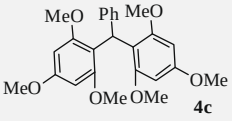
**Table 1**
Reductive alkylation of trimethoxybenzene (**1**) with aldehydes using PMHS–5 mol % of $B(C_6F_5)_3$

| Entry | Aldehyde (**2**) | Time (h) | Product (**3**) | Yield[a] (%) |
|---|---|---|---|---|
| 1 |  **2a** | 1 |  **3a** | 92 |
| 2 |  **2b** | 1.5 |  **3b** | 91 |
| 3 |  **2c** | 1.5 |  **3c** | 91 |
| 4 | PHCHO **2d** | 1 |  **3d** | 90 |
| 5 |  **2e** | 1 |  **3e** | 88 |
| 6 |  **2f** | 1.5 |  **3f** | 88 |
| 7 |  **2g** | 2.5 |  **3g** | 87 |
| 8 |  **2h** | 2 |  **3h** | 94 |
| 9 |  **2i** | 2 |  **3i** | 91 |
| 10 |  **2j** | 1.5 |  **3j** | 89 |
| 11[b] |  **2k** | 12 | No reaction | – |

[a] Isolated yield.
[b] Reaction was also carried at reflux temperature.

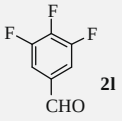
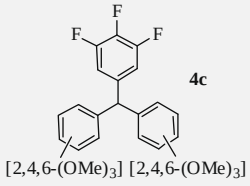
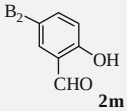
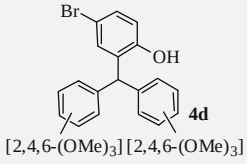
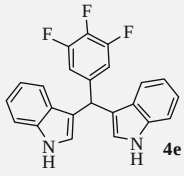
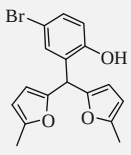
of other electron-rich arenes. Thus, the reaction of 3,5-dimethoxybenzyl alcohol (**1b**) and 3,5-dibenzyloxybenzyl alcohol (**1c**) with benzaldehyde (**2d**) in the presence of PMHS and 5 mol % of $B(C_6F_5)_3$ was tested, which gave the corresponding alkylated products **3k** and **3l** in good yields (Table 2, entries 1 and 2). On the other hand, the treatment of indole (**1d**) and 2-methylfuran (**1e**) with benzaldehyde under the described reductive alkylation conditions [PMHS–$B(C_6F_5)_3$] did not provide the expected reductive alkylative product, instead the triarylmethanes **4a** and **4b** were obtained (Table 2, entries 3 and 4). The formation of these products was observed within 15 min. This may be due to the more nucleophilic nature of indole and 2-methylfuran compared to the PMHS in the presence of $B(C_6F_5)_3$.[11] To obtain the triarylmethane product from 1,3,5-trimethoxybenzne (**1a**), the reaction of **1a** was carried out with benzaldehyde and 5 mol % of $B(C_6F_5)_3$ in the absence of PMHS and as expected the triarylmethane **4c** was obtained in

**Table 2**
Reaction of electron-rich arenes with benzaldehyde (**2d**) using PMHS–5 mol % of $B(C_6F_5)_3$

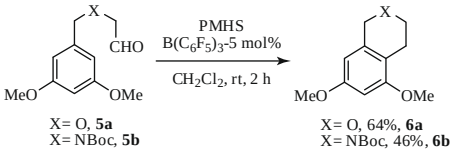
| Entry | Arene | Time (h) | Product | Yield[a] (%) |
|---|---|---|---|---|
| 1 |  **1b** | 2 |  **3k** | 78 |
| 2 |  **1c** | 2.5 |  **3l** | 73 |
| 3 |  **1d** | 0.25 |  **4a** | 94 |
| 4 |  **1e** | 0.25 |  **4b** | 92 |
| 5[b] |  **1a** | 3 |  **4c** | 85 |

[a] Isolated yield.
[b] Reaction was also carried out in the absence of PMHS.
[c] Yield calculated based on indole.

**Table 3**
$B(C_6F_5)_3$-catalyzed reaction of electron-rich arenes with aldehydes

| Entry | Arene | Aldehyde | Time (h) | Product | Yield[a] (%) |
|---|---|---|---|---|---|
| 1 | **1a** |  **2l** | 3 |  **4c** | 82 |
| 2 | **1a** |  **2m** | 2.5 |  **4d** | 78 |
| 3 | **1d** | **2l** | 0.5 |  **4e** | 93 |
| 4 | **1e** | **2m** | 0.5 |  **4f** | 92 |

[a] Isolated yield.




X= O, **5a**
X= NBoc, **5b**

X= O, 64%, **6a**
X= NBoc, 46%, **6b**

**Scheme 2.** Intramolecular reductive alkylation.

85% yield (Table 2, entry 5). This observation of triarylmethane formation[12–14] in the presence of $B(C_6F_5)_3$ prompted us to examine the diversity in the aldehyde part. Table 3 describes the reaction of electron-rich arenes **1a**, **1d,** and **1e** with different aldehydes to obtain the corresponding alkylated products **4c** to **4f** in good yields (Table 3, entries 1–5).

Next, we set out to expand this method to application for the intramolecular reductive alkylation (Scheme 2). Consequently, treatment of **5a** and **5b** with PMHS–$B(C_6F_5)_3$ reagent system afforded the corresponding intramolecular alkylated products, isochroman derivative **6a** (64%) and tetrahydroisoquinoline derivative **6b** (46%) without effecting the Boc protection. All the products obtained were fully characterized by $^1H$, $^{13}C$ NMR, mass, and IR spectra.[15]

In summary, an efficient $B(C_6F_5)_3$-catalyzed reductive alkylation of alkoxybenzenes using aldehyde as alkylating agents is successfully established in the presence of PMHS. Further, $B(C_6F_5)_3$-catalyzed reaction of electron-rich arenes with aldehydes to obtain triarylmethanes has also been demonstrated. The reaction described here is mild, efficient, general, and gives good yield of the product. The utility of the present method was successfully demonstrated for the synthesis of isochroman and tetrahydroisoquinoline derivatives.

*Representative experimental procedure for reductive alkylation:* To a stirred solution of trimethoxybenzene (**1a**, 1 mmol) in dichloromethane, benzaldehyde (**2d**, 1 mmol) was added. To this stirred solution, polymethylhydrosiloxane (3 mmol) and 5 mol % of $B(C_6F_5)_3$ were added at room temperature and the reaction progress was monitored by TLC analysis. After the completion of the reaction (1 h), the solvent was evaporated under vacuum and the residue was purified by column chromatography on silica gel using ethyl acetate and hexanes (10:90) as eluent to give the benzyl trimethoxybenzene **3d** in 90% yield.

*Representative experimental procedure for the synthesis of triarylmethanes*: To a stirred solution of indole (**1d**, 1 mmol) in dichloromethane, trifluoromethyl benzaldehyde (**2l**, 0.5 mmol) and 5 mol % of $B(C_6F_5)_3$ were added at room temperature and the reaction progress was monitored by TLC analysis. After the completion of the reaction (0.5 h), the solvent was evaporated under vacuum and the residue was purified by column chromatography on silica gel using ethyl acetate and hexanes (15:85) as eluent to give the triarylmethane **4e** in 93% yield.

## Acknowledgments

S.K. thanks CSIR, New Delhi and G.R. thanks UGC, New Delhi, for the award of research fellowships. The authors thank the referees for their valuable suggestions.

## References and notes

1. (a) *Nat. Prod. Chem*; Nakanishi, K., Goto, T., Ito, S., Natori, S., Nozoe, S., Eds.; Kodansha Scientific: Tokyo, 1975; p 131; (b) Olah, G. A.; Krishnamurti, R.; Prakash, G. K. S.. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, p 293; (c) Roberts, R. M.; Khalaf, A. A.. *Friedel–Crafts Alkylation Chemistry*. In *A Century of Discovery*; Dekker: New York, 1984.
2. (a) Ackermann, W.; Heesing, A. *Chem. Ber.* **1977**, *110*, 3126; (b) Inoue, M.; Umaki, N.; Sugita, T.; Ichikawa, K. *Nippon Kagaku Kaishi* **1978**, 775.
3. (a) Roth, B.; Aig, E.; Rauckman, B. S.; Strelitz, J. Z.; Phillips, A. P. *J. Med. Chem.* **1981**, *24*, 933; (b) Matsumoto, T.; Singh, I. P.; Etoh, H.; Tanaka, H. *Chem. Lett.* **2001**, 210; (c) Katritzky, A. R.; Tao, H.; Jiang, R.; Suzuki, K.; Kirichenko, K. *J. Org. Chem.* **2007**, *72*, 407.
4. (a) Nay, B.; Collet, M.; Lebon, M.; Cheze, C.; Vercauteren, J. *Tetrahedron Lett.* **2002**, *43*, 2675; (b) Cottineau, B.; Chenault, J.; Guillaumet, G. *Tetrahedron Lett.* **2006**, *47*, 817.
5. (a) Butsugan, Y.; Nagai, K.; Nagaya, F.; Tabuchi, H.; Yamada, K.; Araki, S. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1707; (b) Bergh, A.; Leffler, H.; Sundin, A.; Nilsson, U. J.; Kann, N. *Tetrahedron* **2006**, *62*, 8309; (c) Li, C.; Wang, J. *J. Org. Chem.* **2007**, *72*, 7431.
6. (a) Shi, Z.; He, C. *J. Org. Chem.* **2004**, *69*, 3669; (b) Roelens, F.; Huvaere, K.; Dhooge, W.; Cleemput, M. V.; Comhaire, F.; Keukeleire, D. D. *Eur. J. Med. Chem.* **2005**, *40*, 1042; (c) Roelens, F.; Heldring, N.; Dhooge, W.; Bengtsson, M.; Comhaire, F.; Gustafsson, J. A.; Treuter, E.; Keukeleire, D. D. *J. Med. Chem.* **2006**, *49*, 7357.
7. (a) Miyai, T.; Onishi, Y.; Baba, A. *Tetrahedron Lett.* **1998**, *39*, 6291; (b) Dube, D.; Scholte, A. A. *Tetrahedron Lett.* **1999**, *40*, 2295; (c) Miyai, T.; Onishi, Y.; Baba, A. *Tetrahedron* **1999**, *55*, 1017; (d) Augustine, J. K.; Naik, Y. A.; Mandal, A. B.; Alagarsamy, P.; Akabote, V. *Synlett* **2008**, 2429.
8. (a) Chandrasekhar, S.; Chandrasekhar, G.; Vijeender, K.; Reddy, M. S. *Tetrahedron Lett.* **2006**, *47*, 3475; (b) Chandrasekhar, S.; Chandrashekar, G.; Reddy, M. S.; Srihari, P. *Org. Biomol. Chem.* **2006**, *4*, 1650; (c) Chandrasekhar, S.; Chandrashekar, G.; Babu, B. N.; Vijeender, K.; Reddy, K. V. *Tetrahedron Lett.* **2004**, *45*, 5497; (d) Chandrasekhar, S.; Reddy, C. R.; Babu, B. N. *J. Org. Chem.* **2002**, *67*, 9080. and references cited therein.
9. (a) Gevorgyan, V.; Rubin, M.; Benson, S.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **2000**, *65*, 6179; (b) Parks, D. J.; Piers, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 9440; (c) Gevorgyan, V.; Rubin, M.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **2001**, *66*, 1672; (d) Parks, D. J.; Blackwell, J. M.; Piers, W. E. *J. Org. Chem.* **2000**, *65*, 3090; (e) Dierker, G.; Ugolotti, J.; Kehr, G.; Froehlich, R.; Erker, G. *Adv. Synth. Cat.* **2009**, *351*, 1080; (f) Chojnowski, J.; Rubinsztajn, S.; Cella, J. A.; Fortuniak, W.; Cypryk, M.; Kurjata, J.; Kazmierski, K. *Organometallics* **2005**, *24*, 6077.
10. (a) Reddy, C. R.; Vijeender, K.; Parida, B. B.; Madhavi, P. P.; Chandrasekhar, S. *Tetrahedron Lett.* **2007**, *48*, 2765; (b) Chandrasekhar, S.; Debjit, B.; Reddy, C. R. *Synthesis* **2007**, 1509.
11. These results indicate that the electron-rich arene will first undergo Friedel–Crafts alkylation with aldehyde followed by nucleophilic addition of hydride or with arene based on their reactivity.
12. The importance of triarylmethanes, see: (a) Mibu, N.; Sumoto, K. *Chem. Pharm. Bull.* **2000**, *48*, 1810; (b) Nair, V.; Thomas, S.; Mathew, S. C.; Abhilash, K. G. *Tetrahedron* **2006**, *62*, 6731.
13. Earlier methods for the preparation of triarylmethanes, see: (a) Roomi, M.; MacDonald, S. *Can. J. Chem* **1970**, *48*, 139; (b) Banerji, J.; Chatterjee, A.; Manna, S.; Pascard, C.; Prange, T.; Shoolery, J. *Heterocycles* **1981**, *15*, 325; (c) Chen, D.; Yu, L.; Wang, P. G. *Tetrahedron Lett.* **1996**, *37*, 4467; (d) Babu, G.; Sridhar, N.; Perumal, P. T. *Synth. Commun.* **2000**, *30*, 1609; (e) Yadav, J. S.; Reddy, B. V. S.; Murthy, C. V. S. R.; Kumar, G. M.; Madan, C. *Synthesis* **2001**, 783; (f) Yadav, J. S.; Reddy, B. V. S.; Satheesh, G. *Tetrahedron Lett.* **2004**, *45*, 3673; (g) Sharma, G. V. M.; Reddy, J. J.; Lakshmi, P. S.; Krishna, P. R. *Tetrahedron Lett.* **2004**, *45*, 7729. and references cited therein.
14. Recent methods for the preparation of triarylmethanes, see: (a) Nair, V.; Abhilash, K. G.; Vidya, N. *Org. Lett.* **2005**, *7*, 5857; (b) Nair, V.; Abhilash, K. G.; Vidya, N. *Synthesis* **2006**, 3647; (c) Roy, S.; Roy, U. K.; Choudhury, J.; Poddar, S. *J. Org. Chem.* **2007**, *72*, 3100; (d) Kodomari, M.; Nagamatsu, M.; Akaike, M.; Aoyama, T. *Tetrahedron Lett.* **2008**, *49*, 2537.
15. *Spectral data of new compounds*: (**3e**): mp 95.7–96.5 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.78 (dd, $J$ = 1.32, 8.12 Hz, 1H), 7.35 (dt, $J$ = 1.3, 7.5 Hz, 1H), 7.25–7.13 (m, 2H), 6.13 (s, 2H), 4.22 (s, 2H), 3.81 (s, 3H), 3.73 (s, 6H); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 160.2 (2C), 158.8, 149.9, 136.7, 132.2, 130.6, 126.0, 123.7, 108.1, 90.3 (2C), 55.5 (2C), 55.3, 24.2; HRMS (ESI) calcd for $C_{16}H_{17}NO_5Na$: 326.1015 M+Na$^+$, found: 326.1004 M+Na$^+$; IR (KBr): $\nu_{max}$ 2924, 2853, 1606, 1520, 1462, 1352, 1211, 1150 cm$^{-1}$; (**3f**): mp 162.4–163.6 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 6.99 (q, $J$ = 5.6, 8.3 Hz, 1H), 6.82 (t, $J$ = 8.7 Hz, 1H), 6.17 (s, 1H), 6.1 (s, 3H), 3.78 (s, 4H), 3.51 (s, 7H); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 161.9, 159.6, 159.1, 158.8, 141.1, 129.0, 128.9, 113.9, 113.6, 113.3, 91.7 (2C), 56.0 (2C), 55.0, 36.4; HRMS (ESI) calcd for $C_{16}H_{16}O_3F$: 275.1095 M−H$^-$, found: 275.1083 M−H$^-$; IR (neat): $\nu_{max}$ 2935, 2838, 1596, 1460, 1223, 1120 cm$^{-1}$; (**3g**): mp 121.8–122.9 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.07 (t, $J$ = 7.8 Hz, 1H), 6.81 (d, $J$ = 7.5 Hz, 1H), 6.66 (s, 1H), 6.58 (dd, $J$ = 2.4, 8.1 Hz, 1H), 6.14 (s, 2H), 3.88 (s, 2H), 3.8 (s, 3H), 3.7 (s, 6H); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 159.6 (2C), 158.8, 155.2, 144.1, 128.9, 120.9, 115.3, 112.1, 109.8, 90.6 (2C), 55.7 (2C), 55.3, 28.1; HRMS (ESI) calcd for $C_{16}H_{19}O_4$: 275.1296 M+H$^+$, found: 275.1283 M+H$^+$; IR (neat): $\nu_{max}$ 3392, 2928, 2841, 1605, 1458, 1201, 1117 cm$^{-1}$; (**3h**): mp 126.8–127.8 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 6.66 (d, $J$ = 8.7 Hz, 1H), 6.51 (dd, $J$ = 3.1, 8.7 Hz, 1H), 6.15 (d, $J$ = 3.0 Hz, 1H), 6.09 (s, 2H), 3.83 (s, 3H), 3.80 (s, 3H), 3.78 (s, 2H), 3.73 (s, 6H), 3.60 (s, 3H); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 159.8 (2C), 159.3, 153.4, 151.8, 131.6, 115.1, 110.6, 109.3, 108.2, 90.58 (2C), 56.1 (2C), 55.7, 55.4, 55.2, 22.2; HRMS (ESI) calcd for $C_{18}H_{22}O_5Na$: 341.1375 M+Na$^+$, found: 341.1364 M+Na$^+$; IR (neat): $\nu_{max}$ 2925, 2834, 1603, 1461, 1202, 1118 cm$^{-1}$; (**3i**): mp 95.7–96.7 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.11–6.76 (m, 8H), 6.16 (s, 2H), 3.98 (s, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 3.71 (s, 6H); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 159.7 (2C), 159.2, 155.3, 155.0, 151.7, 132.9, 129.0, 126.3, 122.9, 119.2 (2C), 118.1, 114.5 (2C), 108.7, 90.5 (2C), 55.6 (2C), 55.3 (2C), 22.1; HRMS (ESI) calcd for $C_{23}H_{25}O_5$: 381.1715 M+H$^+$, found: 381.1701 M+H$^+$; IR (KBr): $\nu_{max}$ 2925, 2837, 1602, 1502, 1452, 1211, 1118 cm$^{-1}$; (**3j**): $[\alpha]_D^{27}$ −29.6 (*c* 0.8, $CHCl_3$);

$^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.44–7.27 (m, 5H), 6.12 (s, 2H), 5.92 (d, $J$ = 3.9 Hz, 1H), 4.64 (s, 1H), 4.56 (d, $J$ = 3.9 Hz, 1H), 4.54–4.42 (m, 2H), 3.8 (s, 3H), 3.72 (s, 7H), 3.17–3.02 (m, 2H), 1.44 (s, 3H), 1.29 (s, 3H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 159.6 (2C), 159.2, 138.1, 128.2 (2C), 127.5 (2C), 127.3, 111.1, 107.3, 104.6, 90.6 (2C), 82.4, 82.3, 79.8, 71.7,55.5 (2C), 55.2, 26.7, 26.3, 21.3; HRMS (ESI) calcd for $C_{24}H_{30}O_7Na$: 453.1879 M+Na$^+$, found: 453.1889 M+Na$^+$; IR (neat): $\nu_{max}$ 2932, 2841, 1603, 1458, 1207, 1134, 1076 cm$^{-1}$; (**3k**): mp 184.2–186.3 $^0$C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.41–7.24 (m, 5H), 6.56–6.50 (m, 2H), 4.55 (s, 2H), 4.51 (s, 2H), 3.81–3.67 (m, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 160.8 (2C), 140.7, 138.1, 128.3, 128.2, 127.8, 127.6, 126.8, 105.4, 100.3, 99.6, 72.0, 55.3 (2C), 29.6; HRMS (ESI) calcd for $C_{16}H_{19}O_3$: 259.1329 [M+H]$^+$, found: 259.1327 [M+H]$^+$; IR (neat): $\nu_{max}$ 3449, 2924, 2851, 1601, 1460, 1355, 1202, 1153, 1061, 753 cm$^{-1}$; (**3l**): mp 208.9–210.3 °C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.45–7.24 (m, 15H), 6.65–6.60 (m, 2H), 5.04 (s, 4H), 4.53 (s, 2H), 4.50 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 160.8 (2C), 140.7 (2C), 138.1 (2C), 128.3 (3C), 128.2 (2C), 127.8 (4C),127.6 (2C), 126.8, 100.3, 99.6 (2C), 72.0 (2C), 55.3, 29.6; MA (APCI): $m/z$ 411 [M+H]$^+$; IR (neat): $\nu_{max}$ 3450, 2922, 2853, 1600, 1453, 1376, 1217, 1155, 1056, 770 cm$^{-1}$; (**4c**): mp 170–172 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 6.72–6.59 (m, 2H), 6.12–6.08 (m, 5H), 3.79 (s, 6H), 3.55 (s, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 159.5, 152.0, 151.8, 148.7, 148.6, 142.5, 112.1, 111.5, 111.2, 91.4, 55.8, 55.1, 36.4; HRMS (ESI) calcd for $C_{25}H_{26}F_3O_6$: 479.1676 [M+H]$^+$, found: 479.1675 [M+H]$^+$; IR (KBr): $\nu_{max}$ 2934, 2838, 1593, 1225, 1124 cm$^{-1}$; (**4d**): mp 188–189 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.15–7.05 (m, 2H), 6.65 (d, $J$ = 8.8 Hz, 1H), 6.33 (s, 1H), 6.13 (s, 1H), 6.10 (s, 4H), 3.77 (s, 6H), 3.57 (s, 12H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 159.6, 159.3, 154.7, 132.8, 129.1, 117.3, 111.4, 91.7, 56.0, 55.1, 34.0; HRMS (ESI): calcd for $C_{25}H_{27}BrO_7$: 519.3817; found: 521.098 [M+2]; IR (KBr): $\nu_{max}$ 2925, 2843, 1596, 1461, 1117 cm$^{-1}$; (**4e**): $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.97 (s, 2H), 7.44–7.29 (m, $J$ = 4H), 7.28–7.13 (m, $J$ = 2H), 7.11–6.88 (m, $J$ = 4H), 6.67 (s, 2H), 5.82 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 136.6, 126.5, 123.5, 122.2, 119.5, 119.52, 118.1, 112.6, 112.3, 111.2, 39.5; MS (ESI): $m/z$ 376.3; IR (KBr): $\nu_{max}$ 3415, 1627, 1523, 1342, 1093, 750 cm$^{-1}$; (**4f**): $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.24 (dd, $J$ = 2.4, 8.4 Hz, 1H), 7.19 (d, $J$ = 8.4 Hz, 1H), 6.69 (d, $J$ = 8.4 Hz,1H), 5.93 (dd, $J$ = 3.0, 14.5 Hz, 4H), 5.57 (br s, 1H), 5.52 (s, 1H), 2.25 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 152.7, 152.0, 150.6, 132.4, 131.2, 128.0, 118.2, 112.8, 108.7, 106.2, 77.4, 76.9, 76.5, 39.8, 13.6; MS (ESI): $m/z$ 347.4; IR (KBr): $\nu_{max}$ 3503, 2921, 2853, 1487, 1216, 782 cm$^{-1}$.