Article

A mild and metal-free protocol towards the synthesis of triarylmethanes by reactions of (hetero)arylboronic acids and ortho-hydroxyarylaldehydes

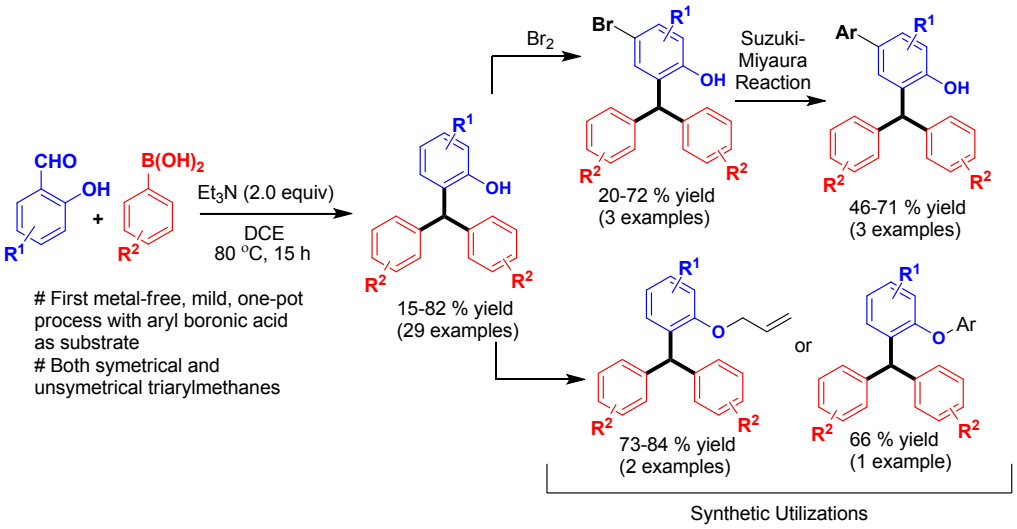
Irfana Jesin, A. Antony Haritha Mercy, Ravindra S., Ramesh Kataria, and Ganesh Chandra Nandi

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02807 • Publication Date (Web): 11 Jan 2020

A mild and metal-free protocol towards the synthesis of triarylmethanes by reactions of (hetero)arylboronic acids and *ortho*-hydroxyarylaldehydes

Irfana Jesin C. P.,[a] A. Antony Haritha Mercy,[a] Ravindra S.,[a] Ramesh Kataria,[b] Ganesh Chandra Nandi*[a]

[a]Department of Chemistry, National Institute of Technology-Tiruchirappalli-620015, Tamilnadu, India. E-mail: ganeshnandi@gmail.com; nandi@nitt.edu
[b]Department of Chemistry & Centre for Advanced Studies in Chemistry, Panjab University, Chandigarh-160014, India



ABSTRACT: Herein, we have reported a metal-free, mild and novel protocol for the synthesis of various triarylmethanes (TRAMs) in moderate to good yields *via* the reactions of aryl boronic acids and *ortho*-hydroxyarylaldehydes in the presence of stoichiometric amounts of Et_3N in dichloroethane at 80 °C. Additionally, the synthetic utilities of few synthesized TRAMs were proven by carrying out bromination on the –OH containing aryl part, and followed by functionalization of the bromine through a palladium-catalyzed Suzuki−Miyaura cross-coupling reaction with arylboronic acids in good yields. The –OH group was also alkylated and arylated through simple alkylation and Chan-Lam reaction respectively.

INTRODUCTION

Triarylmethane (TRAM) and its derivatives are highly captivating molecules in synthetic organic chemistry due to their structural and physical properties. Since the discovery of the triphenylmethyl radical by Gomberg in 1900s,[1] triaryl and tri-hetero arylmethanes have attracted much attention from organic chemists and many such compounds have found widespread

applications in synthetic, medicinal, and industrial chemistry. They are ubiquitous and found mainly in technologically and medicinally relevant molecules including as useful protective groups,[2] photochromic agents,[3] dyes,[4] and building blocks for dendrimers.[5] Additionally, ring hydroxylated TRAMs exhibit antioxidant, antitumor, antitubercular, antiviral, antifungal and anti-inflammatory activities (Figure 1).[6]

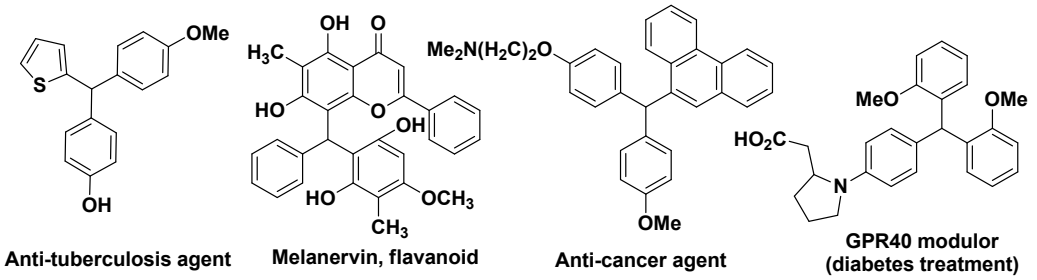
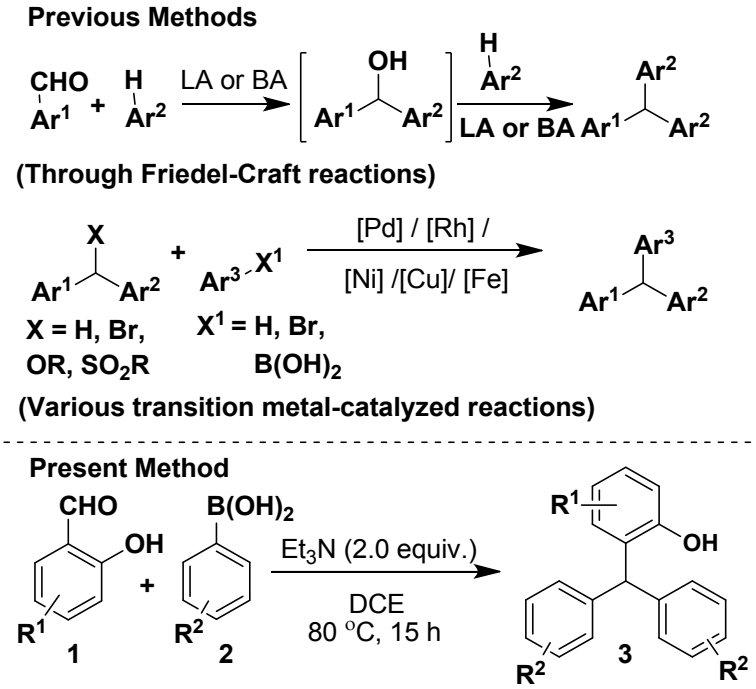


Figure 1. Representative examples of compounds containing hydroxylated TRAM skeleton.

The common methods for the synthesis of triaryl system is the biarylation of aldehydes through Friedel-Craft reaction conditions (with various types of Lewis and Bronsted acids as catalysts).[7] But the approach is limited to nucleophilic and electron rich arenes and often results in the formation of unwanted regioisomers. In order to overcome these shortcomings, a few transition metal catalyzed routes also have been developed.[8] The routes include the reactions between diarylmethane (or methanol or its derivatives) and suitably substituted arene nucleophile in the presence of various transition metal catalysts (Scheme 1). But these protocols require prefunctionaliztions to be a suitable coupling partner along with the use of expensive catalysts.

In the context of biological and synthetic importance of TRAMs and its derivatives, the demand for the development of environmentally benign and practical method for the synthesis of triarylmethanes is increasingly important in organic synthesis. Herein, we have reported a novel, metal-free and mild protocol for the synthesis of symmetrical and unsymmetrical TRAMs in moderate to good yields *via* the reactions of (hetero)aryl boronic acids and *ortho*-hydroxyarylaldehydes in the presence of stoichiometric amounts of triethylamines (Et_3N) in dichloroethane. To the best of our knowledge, it is the first report of metal-free synthesis of TRAMs with (hereto)arylboronic acid as a substrate. The *ortho*-OH group of arylaldehyde is the driving force for this reaction. The synthesized TRAMs were further structurally modified by carrying out bromination, followed by functionalization of the bromine through palladium-

catalyzed Suzuki−Miyaura cross-coupling reaction. The –OH group was also alkylated and arylated through simple alkylation and Chan-Lam reaction respectively



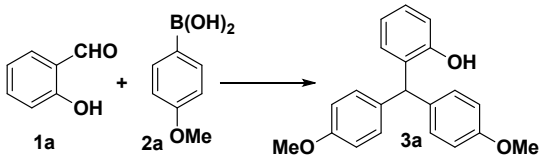
Scheme 1. Previous and present routes for the synthesis of TRAMs

RESULTS AND DISCUSSION

The optimization process was initiated with the reaction of salicylaldehyde (**1a**, 1.0 equiv) and 4-methoxyboronic acid (**2a**, 2.0 equiv) in the presence of stoichiometric amount of Et_3N as base in DCM at 40 °C for 15 h. Only 10% of corresponding TRAM (**3a**) was obtained (Table 1, entry 1). In order to increase the yield, the reaction was performed in a sealed tube at 80 °C, and interestingly, 64% of **3a** was formed (Table 1, entry 2). Replacement of DCM with DCE as solvent at 80 °C, delightedly increased the yield to 72% in 15 h (Table 1, entry 3). A further increase in temperature or time did not improve the product formation. Screening of other solvents such as; $CHCl_3$, Dioxane, MeOH, Toluene and H_2O (at 80 °C) were not successful as these provided poor or no yield (Table 1, entries 4-9). An attempt to perform the reaction under solvent-free conditions afforded 50% of product (Table 1, entry 10). After obtaining suitable solvent DCE (at 80 °C) for this transformation, we next examined the effect of other organic/inorganic bases (Table 1, entries 11-15), but our efforts were not productive. A control

experiment without base also failed to deliver the product (Table 1, entry 16). A control experiment with one equivalent of salicylaldehyde **1a** and arylboronic acid **2a** provided the desired product **3a**, but lots of aldehydes were remained unreacted as this reaction need 2.0 equiv of boronic acid and 1.0 equiv of aldehyde. On the basis of these investigations, best result was obtained when salicylaldehyde (**1a**, 1.0 equiv) was treated with 4-methoxyboronic acid (**2a,** 2.0 equiv) in the presence of stoichiometric amount of Et_3N (2.0 equiv) in DCE at 80 °C for 15 h (Table 1, entry 3).

Table 1. Reaction condition optimization for the synthesis of **3a**[a]



entry	solvent	base	yield (%)
1	DCM	NEt_3	10[b]
2	DCM	NEt_3	64
3	DCE	NEt_3	72
4	$CHCl_3$	NEt_3	55
5	1,4-Dioxane	NEt_3	20
6	1,4-Dioxane	NEt_3	35[c]
7	MeOH	NEt_3	NR
8	Toluene	NEt_3	30
9	H_2O	NEt_3	NR
10	No solvent	NEt_3	50
11	DCE	DBU	NR
12	DCE	*t*-BuOK	10
13	DCE	Cs_2CO_3	10
14	DCE	DIPEA	40
15	DCE	K_2CO_3	48
16	DCE	-	NR

[a]All reactions were carried out with 1.0 equiv of **1a**, 2.0 equiv of **2a**, 2.0 equiv of Et_3N in 1 mL of solvent at 80 °C for 15 h unless otherwise stated; [b] at 40 °C; [c] The reaction was continued for 24 h.

With the optimized reaction condition (Table 1, entry 3), we next explored the substrate scope for the formation of various TRAMs from different types of 2-hydroxyarylaldehydes **1** and (hetero)aryl boronic acids **2**. The results summarized in figure **2** show that all the reactions gave selective formation of TRAM derivatives. Various mono-/di- and tri-substituted aryl boronic acids afforded the corresponding TRAMs in moderate to good yields. Additionally, heterocyclic (2- or 3-thienyl, 2-benzothienyl, 2-furyl and 2-benzofuryl) boronic acids also tolerated well for this transformations and yielded the products (Figure 2, **3d**,**e**, **i-k, u-x**) in moderate yield. The bulky and fused (1-Naphthyl) boronic acid too delivered the desired product, albeit in less yields (**3m** and **3n**). Surprisingly, the reactions were effective only with electron rich arylboronic acids whereas electron deficient arylboronic acids were failed to deliver any product. 2-hydroxyarylaldehydes bearing electron donating/withdrawing substituents at different position also reacted smoothly with the boronic acids to afford the corresponding products in moderate to good yields. Our efforts to use simple arylaldehydes (without 2-hydroxy group) were not successful and it proved that the reaction conditions were specific for *o*-hydroxyaryl aldehydes (Ref. Scheme **3**). Furthermore, aromatic ketones (*o*-hydroxy acetophenone) and acids (salicylic acid) were too unreactive towards the product formation. In order to demonstrate the practical utility of this process, compound **3a** was synthesized in large scale with 1.5 g (9.82 mmol) of 4-methoxyphenylboronic acid and 600 mg (4.91 mmol) of salicylaldehyde and the 41% of **3a** was obtained. All the synthesized compounds were characterized by NMR (^{1}H, ^{13}C) and HR-mass spectrometry and the structure was unequivocally established by the X-ray single crystal diffraction analysis of one representative compound **3b** (See Supporting Information).

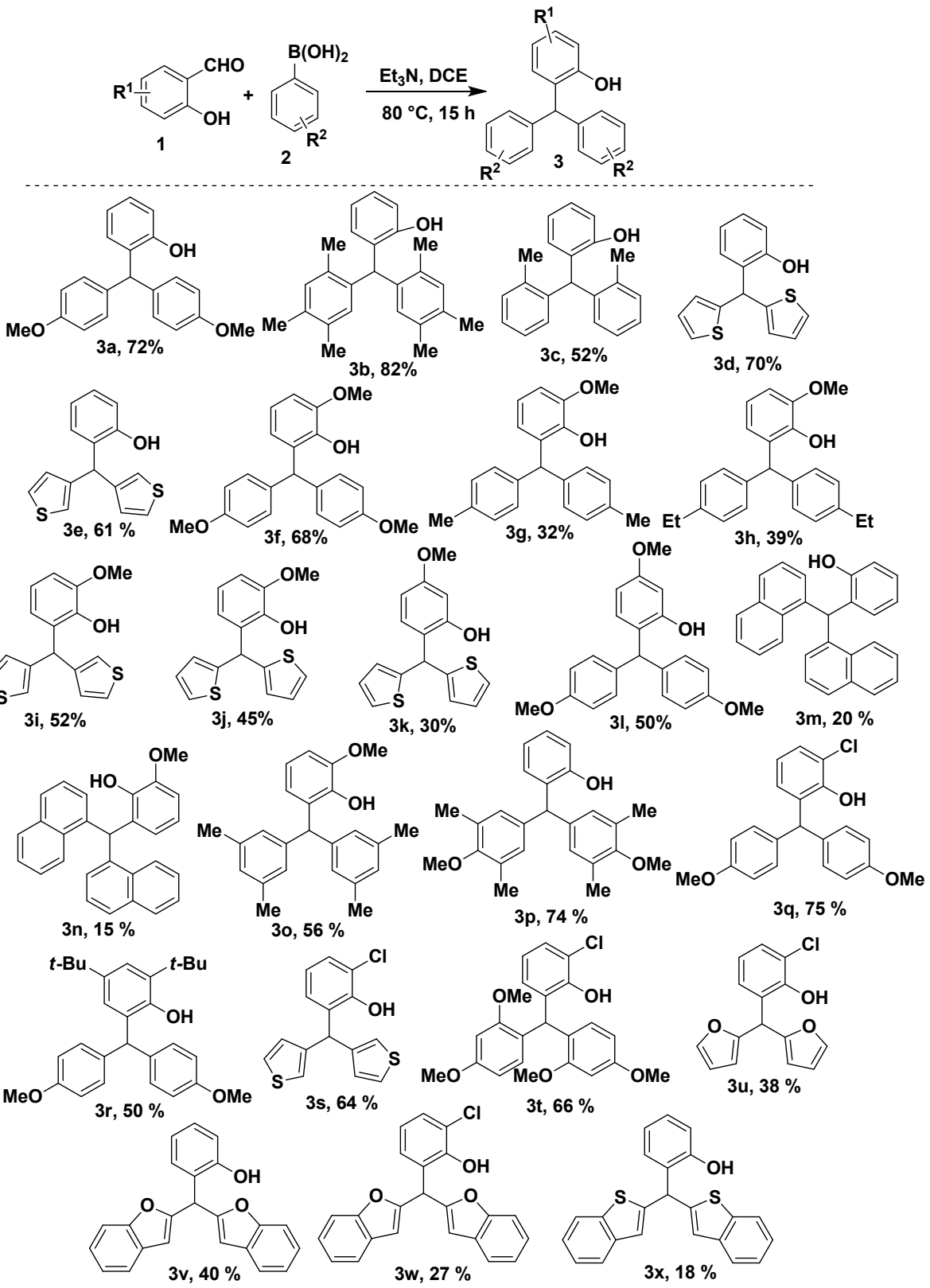
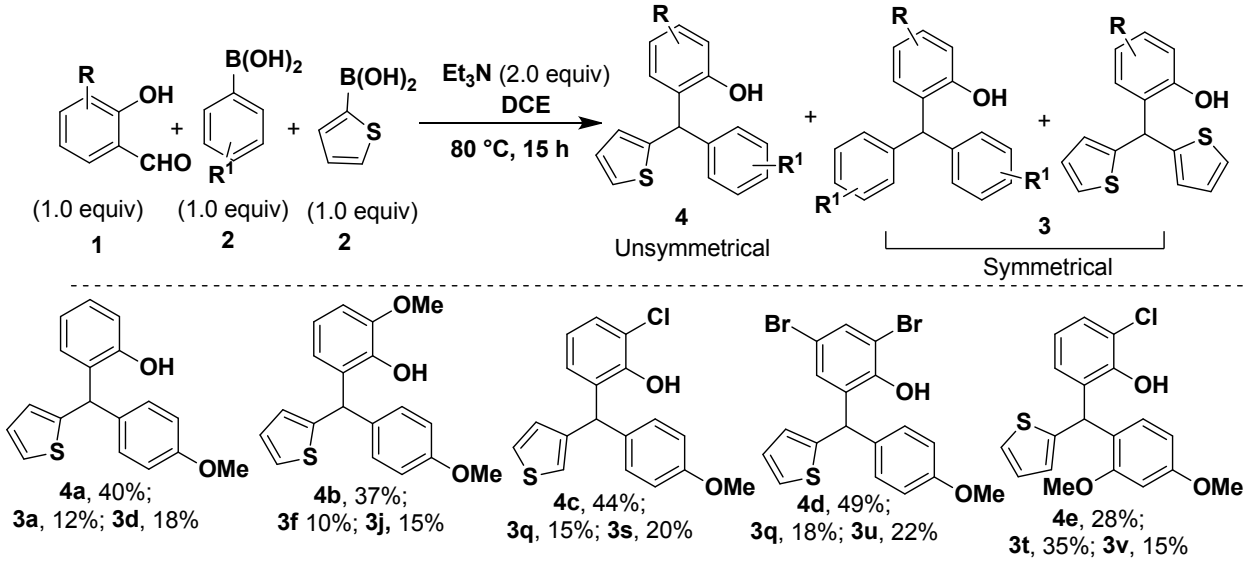


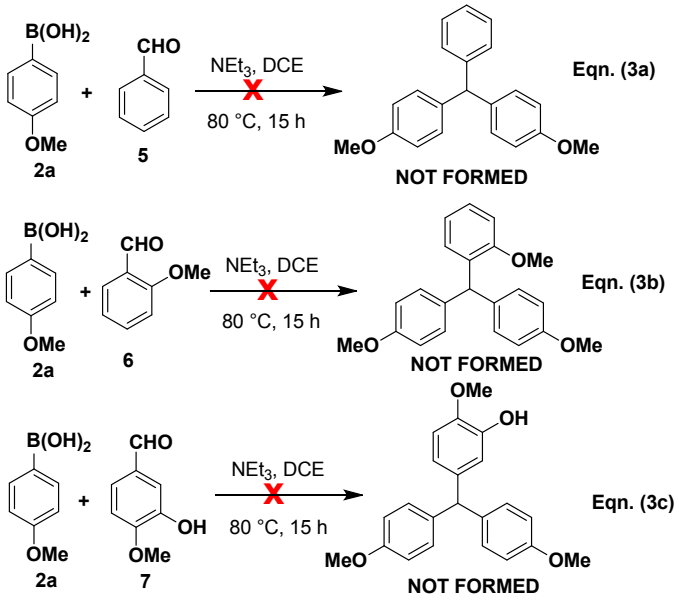
Figure 2. Substrate scope for reactions of arylboronic acids and 2-hydroxy arylaldehyde.

Inspired by the synthesis of symmetrical TRAMs **3**, we next turned our attention to the synthesis of unsymmetrical TRAMs **4** with the optimized reaction conditions. Hence, we treated various 2-hydroxyarylaldehyde with 4-methoxyphenyl boronic acid and 2-thienyl boronic acids (in 1:1:1 ratio). Delightfully, the corresponding unsymmetrical TRAMs (**4a**-e) were obtained in moderate yield along with the less amount of symmetrical products (Scheme **2**).



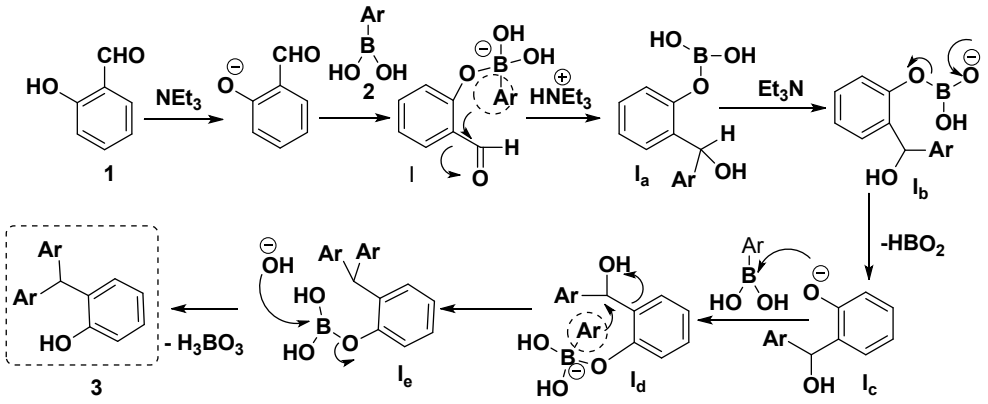
Scheme 2. Synthesis of unsymmetrical TRAMs

In order to comprehend the impact of –OH group in aryl aldehyde for the reaction, some control experiments were performed as mentioned in scheme **3**. Hence, 4-methoxy phenylboronic acid **2a** was treated with benzaldehyde (no *ortho*-OH group) under the optimized reaction condition, but it failed to furnish anticipated product (Scheme 3, eqn. 3a), which proves that –OH group must be present in arylaldehydes. Next, we took *ortho*-OMe substituted arylaldehyde (*ortho*-anisaldehyde) and treated it with 4-methoxy phenylboronic acid, however reaction did not proceed to afford the corresponding product (Scheme **3**, eqn. 3b). The result indicates that the free -OH group is necessary for the successful product formation. Thereafter, the unsuccessful reaction between the 4-methoxy phenylboronic acid and *meta*-OH substituted aryl aldehyde (3-Hydroxy-4-methoxybenzaldehyde) attested that the -OH group should be in -*ortho* position only (Scheme 3, eqn. 3c). These studies clearly indicate the significance of phenolic -OH at *ortho* position of aryl aldehydes.



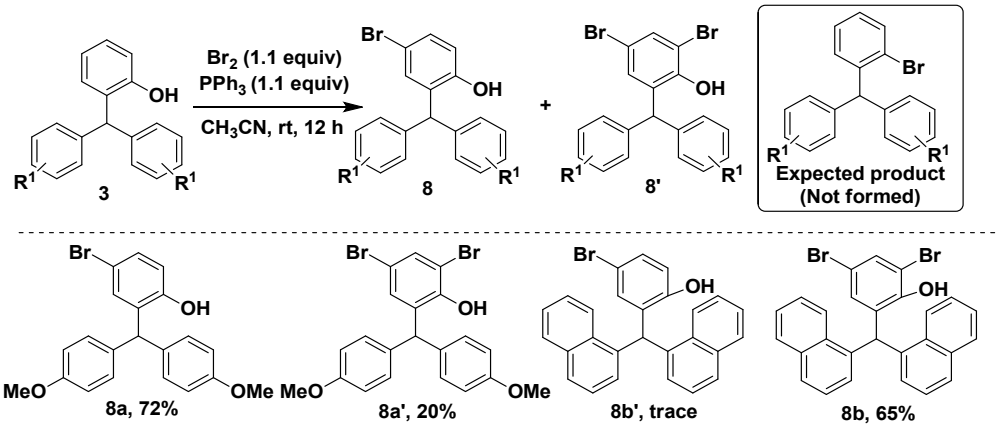
Scheme 3. Control experiments for investigating the importance of –OH in aldehyde

On the basis of the above-mentioned investigations, together with the related reports, a plausible reaction pathway for this reaction has been outlined in scheme **4**. The process started with the abstraction of phenolic proton of arylaldehyde by Et_3N to generate corresponding anion, followed by reaction with boronic acid **2** to obtain intermediate **I**, which underwent aryl group rearrangement (intramolecular)[9] followed by protonation to form intermediate $\mathbf{I_a}$. The intermediate $\mathbf{I_a}$ through abstraction of proton (by Et_3N) from –OH attached to boron (of $\mathbf{I_a}$), generated intermediate $\mathbf{I_b}$, which after elimination of oxo-borinic acid yielded phenoxide $\mathbf{I_c}$. Subsequent nucleophilic attack on another boronic acid by $\mathbf{I_c}$, followed by intramolecular rearrangement (of aryl group) and removal of boric acid furnished triarylmethane **3**. From the mechanism, it may be attributed that electron rich aryl part of boronic acid weakens the C(Ar)-B bond length (of intermediate **I**, $\mathbf{I_d}$) due to electronic repulsion of negatively charged boron and electron rich aryl group; thereby facilitated the intramolecular rearrangement (of Ar group). In contrary, the electron poor aryl part of boronic acid may strengthen the corresponding C(Ar)-B bond, hence no reaction occurs.



Scheme 4. Proposed mechanism for the synthesis of TRAM

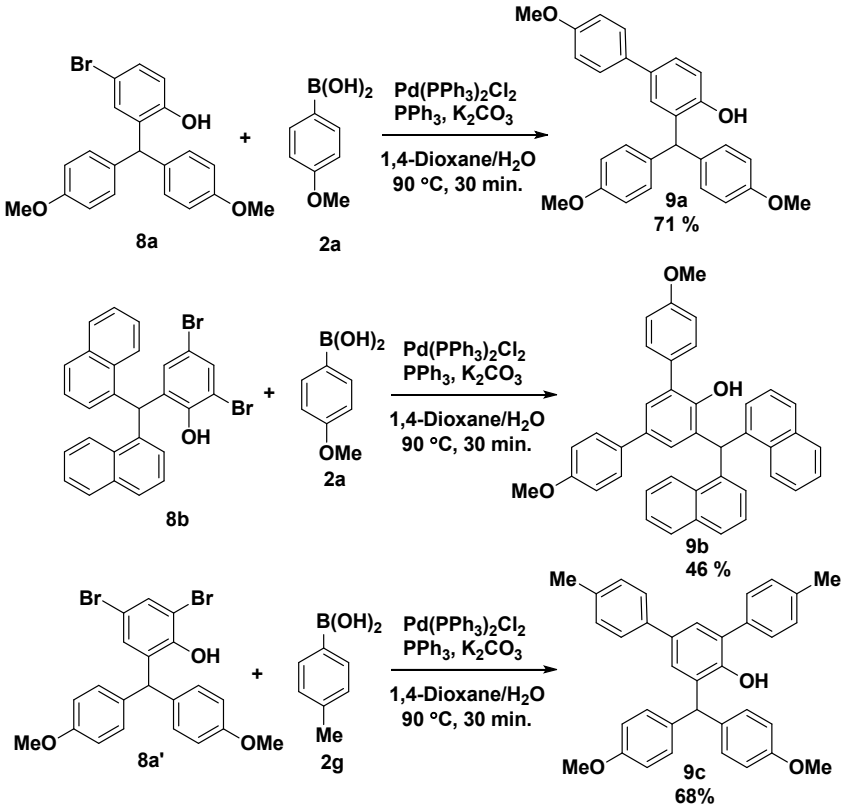
The presence of phenolic –OH group in synthesized triarylmethanes **3**, prompted us to consider the synthetic usefulness of these compounds. Consequently, compound **3a** was treated with Br_2/PPh_3 in acetonitrile in order to transform –OH to –Br. However, to our surprise, -OH was acted as a directing group and bromination took place on the aryl ring to give mono-/di-brominated products **8**/**8'** respectively (Scheme 5). Interestingly, TRAM obtained from 4-methoxyphenyl boronic acid yielded monobrominated product (**8a**) as major one, however, TRAM from 1-naphthylboronic acid delivered dibrominated product as major one under similar reaction conditions.



Scheme 5. Bromination of TRAM 3

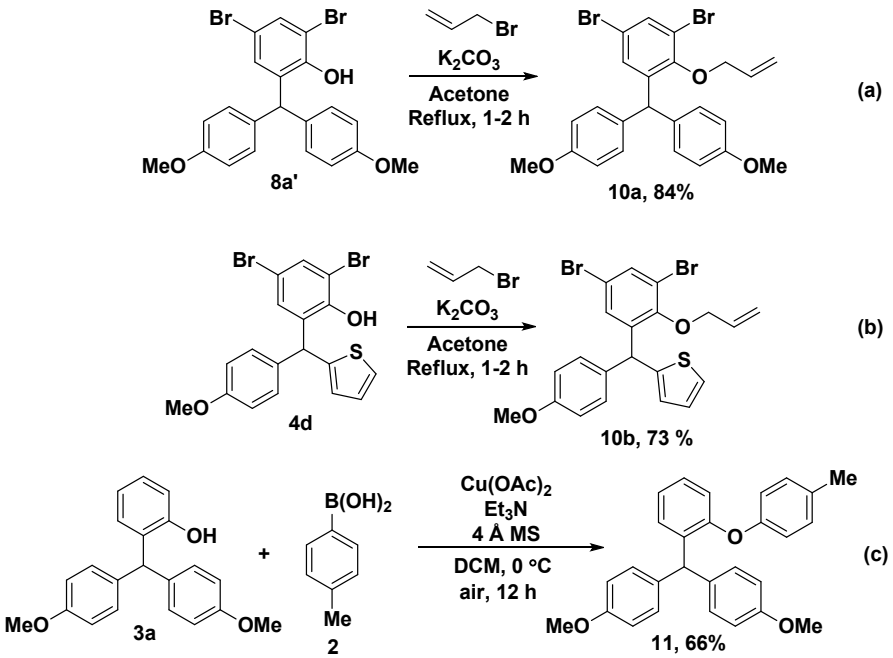
In order to find out the synthetic importance of **8**, The –Br functionality of **8** was further used in Suzuki− Miyaura cross-coupling reaction[10] with 4-methoxyphenylboronic acid **2a** in the presence of $Pd(PPh_3)_2Cl_2$ (catalyst), PPh_3 (ligand), K_2CO_3 (base) in 1,4-dioxane/H_2O (solvent) at

90 °C to furnish corresponding "difficult to access" mono- or di- arylated product **9** (Scheme 6) in moderate to good yields in very short time (30 mins). These successful attempts proved that dendrimer like architectures also could be synthesized by using suitable substrates.



Scheme 6. Suzuki-Miyaura coupling of brominated triarylmethanes

With the intention of increasing the synthetic usefulness of the synthesised triarylmethanes, the –OH groups were further alkylated and arylated through simple alkylation and Chan-Lam reaction (Scheme **7**). *O*-Alkylated/arylated TRAM scaffolds are present in a number of pharmaceutically relevant compounds and natural products (Figure **1**). The *O*-allylated symmetrical and unsymmetrical TRAMs were synthesised by using allyl bromide (as reagent), K_2CO_3 (base) in acetone (solvent) at 60 °C in very good yields (Scheme **7**, eqn. a and b). Similarly the *O*-arylated TRAM was obtained via a copper catalysed Chan-Lam coupling process[11] with arylboronic acids in good yields (66%) (Scheme **7**, eqn. c).[11]



Scheme 7. *O* - Alkylation and arylation of TRAM

CONCLUSIONS

In conclusion, electronically and structurally diverse TRAMs were prepared in moderate to good yields through simple, mild, metal-free reactions of arylboronic acids and *ortho*-hydroxyarylaldehydes. Notably, it is the first metal-free report, where aryl boronic acid has been used as substrate, Noteworthy is the fact that the TRAMs that possess thienyl groups, which are difficult to install using typical Friedel–Crafts reaction conditions, were readily prepared through this strategy. With the prevalence of the tertiary benzylic centre moiety in bioactive molecules and materials, we demonstrated the synthetic utility of the methodology for synthesizing complex derivatives of TRAMs by performing O-alkylation/arylation and the concise synthesis of bromine derivative of TRAM, which was further used effectively in Suzuki-Miyaura cross coupling reaction to deliver the coupling product.

EXPERIMENTAL SECTION

General

The starting material 2-hydroxyarylaldehyde, arylboronic acids and bases were purchased from various suppliers and used as received. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded

on NMR spectrophotometer operating at 500 MHz and 126 MHz respectively. $CDCl_3$ were used as solvent to record NMR spectra. Mass spectra were recorded using ion trap and Q-TOF mass analyser. Melting points were uncorrected.

General procedure for the synthesis of symmetrical and unsymmetrical[a] triarylmethanes (3a-x and 4a-e)

To a 1.0 mL dichloroethane solution of 2-hydroxyarylaldehyde (**1)** (20 mg, 0.1638 mmol) and arylboronic acid (49.7 mg, 0.327 mmol) in a 15 mL Schlenk tube, Et_3N (45.6 µL, 0.327 mmol) was added, and the reaction mixture was heated and stirred at 80 °C (oil bath) for the required period of time. After completion, the reaction mixture was diluted with water, and extracted with DCM (2 X 10 mL). The combined organic layer was then washed with brine, dried and purified through column chromatography with 3-7 % of EtOAc in hexane as eluent.

[a]For the synthesis of unsymmetrical triarylmethanes, two different arylboronic acids were used in equal ratio.

Large scale synthesis of 2-(Bis(4-methoxyphenyl)methyl)phenol (3a)

To a 20.0 mL dichloroethane solution of 4-methoxyphenylboronic acid (**2a**) (1.5g, 9.82 mmol) and salicylaldehyde (**1a**) (600 mg 4.91 mmol) in a 50 mL RB flask, Et_3N (1.37mL, 9.82 mmol) was added, and the reaction mixture was heated and stirred at 80 °C (oil bath) for 15 h. After completion, the reaction mixture was diluted with water, and extracted with DCM (4 X 50 mL). The combined organic layer was then washed with brine, dried and purified through column chromatography with 7 % of EtOAc in hexane as eluent. Product **3a** was isolated in 41 % (650 mg) yield.

General procedure for the synthesis of bromine derivative (8/8') of triarylmethanes

To a cold suspension of (1.1 equiv) of PPh_3 (18 mg, 0.0687 mmol) in 1 mL acetonitrile, Br_2 (3.5 µL, 1.1 equiv)was added dropwise with continuous stirring for 1.5 h. After 30 minutes of stirring at 0 °C, a solution of TRAM (**3)** (20 mg, 0.0625 mmol) in acetonitrile was added dropwise to the PPh_3-Br_2 mixture, and the reaction mixture was warmed and stirred at room temperature for 12 h. After completion of the reaction the solvent was evaporated and washed with satd. $NaHCO_3$ solution (3 X 10 mL), and extracted with DCM (3 X 10 mL). The organic layer was then washed with water, dried and purified

through column chromatography with 2-7 % of EtOAc/hexane as eluent to yield brominated TRAM **8/8'**.

General procedure for Suzuki-Miyaura coupling reaction of brominated TRAM for the synthesis of compound 9a-c

A mixture of brominated TRAM **(8)** (20 mg, 0.0501 mmol), arylboronic acid (11.42 mg, 0.0751 mmol), K_2CO_3 (20.7 mg, 0.15 mmol), PPh_3 (1.31 mg, 10 mol %), in 1,4-dioxane (1.5 mL) and distilled water (0.5 mL) was degassed with a stream of argon passing through the solution for 15 min. Thereafter, $Pd(PPh_3)_2Cl_2$ (1.75 mg, 5 mol %) was added, and the reaction mixture was stirred under an argon atmosphere for 30 min at 90 °C. After completion, the reaction mixture was cooled, diluted with water (15 mL) and extracted with DCM (3 X 20 mL). The collected organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with 7-10 % of EtOAc/Hexane as eluent to give product **9**.

General procedure for *O*-allylation of TRAM (10a-b)

To a stirring solution of TRAM (**3**) (33 mg, 0.0690 mmol) in acetone (1.5 mL), 1.0 equiv of allyl bromide (8.3 mg, 0.069 mmol) and 1.1 equiv of K_2CO_3 (10.5 mg, 0.0759 mmol) were added and refluxed. Stirring continued for 1-2 hrs, after completion of reaction (checked by TLC), allow the reaction mixture to cool, then solvent was evaporated. The reaction mixture was then washed with water, and extracted with ethyl ether (3 X 10 mL). The organic layer was further washed with water, dried and purified through column chromatography with 2-3 % of EtOAc in hexane as eluent to give product **10**.

General procedure for O-arylation of TRAM (11)

To a solution of TRAM (**3a)** (20 mg, 0.0624 mmol) and phenylboronic acid (**2**) (17 mg, 0.125 mmol) in anhydrous DCM (1 mL) were added powdered activated 4 Å molecular sieves (100 mg), catalyst $Cu(OAc)_2$ (11.3 mg, 0.062 mmol) and Et_3N (43.5 µL, 0.311 mmol). The mixture was cooled to 0 °C and stirred for 12 hours under air atmosphere. The reaction was quenched with an excess of *n*-hexane and precipitated catalyst and molecular sieves were separated by filtration. The filtrate was evaporated under vacuum and the residue was purified by column chromatography with 1-2 % of EtOAc in hexane as eluent to afford pure product (**11**).

Characterization data of the isolated compounds

2-(Bis(4-methoxyphenyl)methyl)phenol (3a): Off white solid. Yield: 72% (38 mg from 0.1638 mmol of corresponding aldehyde), mp 112-113 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (t, J = 7.5 Hz, 1H), 7.04 (d, J = 8.5 Hz, 4H), 6.84-6.78 (m, 7H), 5.60 (s, 1H), 4.77 (s, 1H), 3.78 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.4, 153.6, 134.8, 130.9, 130.4, 130.3, 127.9, 120.8, 116.2, 114.1, 55.4, 49.5. IR (KBr): 3390, 3033, 2998, 2932, 2834, 2058, 1500, 813, 755, 621 cm^1. HRMS (ESI-TOF) m/z: [M-H]$^-$ calcd for $C_{21}H_{19}O_3$ 319.1340; found 319.1339.

2-(Bis(2,4,5-trimethylphenyl)methyl)phenol (3b): White solid. Yield: 82% (46 mg from 0.1638 mmol of corresponding aldehyde), mp 90-92 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (td, J = 7.5, 1.5 Hz, 1H), 6.95 (s, 2H), 6.83-6.79 (m, 2H), 6.66 (d, J = 7.5 Hz, 1H), 6.55 (s, 2H), 5.66 (s, 1H), 4.62 (s, 1H), 2.21 (s, 6H), 2.11 (s, 6H), 2.10 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.7, 137.4, 134.7, 133.9, 133.9, 132.0, 130.2, 130.0, 129.8, 127.6, 120.8, 116.0, 44.0, 19.5, 19.3, 18.9. IR (KBr): 3866, 3006, 2966, 2916, 2862, 1592, 1500, 887, 753 cm^{-1}. HRMS (ESI-TOF) m/z: [M+Na]$^+$ calcd for $C_{25}H_{28}ONa$ 367.2032; found 367.2001.

2-(Di-*o*-tolylmethyl)phenol (3c): White solid. Yield: 52% (26 mg from 0.1638 mmol of corresponding aldehyde), mp 105-106 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18-7.14 (m, 5H), 7.13-7.09 (m, 2H), 6.85-6.80 (m, 4H), 6.67 (d, J = 7.5 Hz, 1H), 5.87 (s, 1H), 2.19 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.6, 140.4, 137.0, 130.7, 130.4, 129.4, 128.9, 127.9, 126.8, 126.1, 121.0, 116, 44.4, 19.6. HRMS (ESI-TOF) m/z: [M-H]$^-$ calcd for $C_{21}H_{19}O$ 287.1441; found 287.1443.

2-(Di(thiophen-2-yl)methyl)phenol (3d): Brown sticky liquid. Yield: 70% (31 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (d, J = 5.0 Hz, 2H), 7.17 – 7.12 (m, 2H), 6.95 (t, J = 4.0 Hz, 2H), 6.90 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 3.5 Hz, 2H), 6.79 (d, J = 8.0 Hz, 1H), 6.17 (s, 1H), 4.92 (brs, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.0, 146.6, 130.4, 129.5, 128.7, 126.8, 126.3, 124.9, 121.2, 116.3, 41.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{15}H_{13}OS_2$ 273.0402; found 273.0419.

2-(Di(thiophen-3-yl)methyl)phenol (3e): Brown sticky liquid. Yield: 61% (27 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.29 (m, 2H), 7.15 (td, J = 7.0, 8.0 Hz, 1H), 6.96-6.93 (m, 3H), 6.89-6.86 (m, 3H), 6.81 (dd, J = 8.0, 1.0 Hz, 1H), 5.75 (s,

1H), 4.92 (brs, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 153.5, 143.5, 129.9, 129.8, 128.6, 128.3, 126.2, 122.6, 121.1, 116.5, 42.6. IR (KBr): 3505, 3102, 2924, 1592, 1485, 1454 , 837, 755, 588 cm[1]. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{13}OS_2$ 273.0402; found 273.0431.

2-(Bis(4-methoxyphenyl)methyl)-6-methoxyphenol (3f): Yellow solid. Yield: 68% (39 mg from 0.1638 mmol of corresponding aldehyde), mp 112-115 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.03 (d, J = 8.5 Hz, 4H), 6.81 (d, J = 8.5 Hz, 4H), 6.81-6.74 (m, 2H), 6.48 (t, J = 4.5 Hz,1H), 5.79 (s, 1H), 5.72 (s, 1H), 3.86 (s, 3H), 3.77 (s, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 158.0, 146.5, 143.3, 136.1, 130.6, 130.3, 122 .5, 119.2, 113.7, 108.8, 56.1, 55.3, 48.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{23}O_4$ 351.1591; found 351.1571.

2-(Di-*p*-tolylmethyl)-6-methoxyphenol (3g): White solid. Yield: 32% (17 mg from 0.1638 mmol of corresponding aldehyde), mp 108-110 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.09 (d, J = 7.5 Hz, 4H), 7.04 (d, J = 8.0 Hz, 4H), 6.78-6.76 (m, 2H), 6.53-6.50 (m, 1H), 5.85 (s, 1H), 5.75 (s, 1H), 3.87 (s, 3H), 2.33 (s, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.4, 143.3, 140.7, 135.7, 130.4, 129.3, 129.0, 122.6, 119.1, 108.7, 56.1, 49.0, 21.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{23}O_2$ 319.1693; found 319.1710.

2-(Bis(4-ethylphenyl)methyl)-6-methoxyphenol (3h): White solid. Yield: 39% (22 mg from 0.1638 mmol of corresponding aldehyde), mp 88-90 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.09 (d, J = 8.0 Hz, 4H), 7.03 (d, J = 8.0 Hz, 4H), 6.75 (m, 2H), 6.51 (t, J = 4.5 Hz 1H), 5.84 (s, 1H), 5.71 (s, 1H), 3.85 (s, 3H), 2.60 (q, J = 7.5 Hz, 4H), 1.21 (t, J = 7.5 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 145.3, 142.3, 140.8, 139.9, 129.4, 128.2, 126.6, 121.6, 117.9, 107.6, 54.9, 47.9, 27.4, 14.4. HRMS (ESI-TOF) m/z: $[M - H]^-$calcd for $C_{24}H_{25}O_2$ 345.1860; found 345.1863.

2-(Di(thiophen-3-yl)methyl)-6-methoxyphenol (3i): Brown sticky liquid. Yield: 52% (26 mg from 0.1638 mmol of corresponding aldehyde). ^1H NMR (500 MHz, $CDCl_3$): δ 7.25-7.23 (m, 2H), 6.92 (dd, J = 5.0, 1.5 Hz, 2H), 6.83-6.82 (m, 2H), 6.78-6.75 (m, 2H), 6.61 (dd, J = 6.5, 3.0 Hz, 1H), 5.92 (s, 1H), 5.75 (brs, 1H), 3.88 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 145.3, 143.3, 142.0, 128.6, 127.6, 124.2, 121.1, 120.6, 118.3, 107.8, 55.0, 39.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{15}O_2S_2$ 303.0508; found 303.0519.

2-(Di(thiophen-2-yl)methyl)-6-methoxyphenol (3j): Brown solid. Yield: 45% (22 mg from 0.1638 mmol of corresponding aldehyde), mp 85-87 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, J = 5.0 Hz, 2H), 6.94-6.92 (m, 2H), 6.85-6.79 (m, 5H), 6.31 (s, 1H), 5.81 (s, 1H), 3.88 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.3, 145.3, 141.7, 128.6, 125.4, 124.9, 123.3, 120.2,

118.4, 108.3, 55.0, 38.8. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{15}O_2S_2$ 303.0508; found 303.0513.

2-(Di(thiophen-2-yl)methyl)-5-methoxyphenol (3k): Brown solid. Yield: 30% (15 mg from 0.1638 mmol of corresponding aldehyde), mp 88-89 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (d, J = 5.0 Hz, 2H), 7.01 (d, J = 8.5 Hz, 1H), 6.95-6.94 (m, 2H), 6.86-6.85 (m, 2H), 6.47 (d, J = 8.5 Hz, 1H), 6.40 (s, 1H), 6.06 (s, 1H), 4.90 (s, 1H), 3.76 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 160.0, 154.0, 147.0, 130.2, 126.8, 126.2, 125.0, 122.9, 106.3, 102.4, 55.4, 40.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{16}H_{15}O_2S_2$ 303.0508; found 303.0525.

4-Methoxy-2-(bis(4-methoxyphenyl)methyl)phenol (3l): Yellow solid. Yield: 50% (29 mg from 0.1638 mmol of corresponding aldehyde), mp 113-115 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.04 (d, J = 8.0 Hz, 4H), 6.84 (d, J = 8.5 Hz, 4H), 6.66 (d, J = 8.5 Hz, 1H), 6.41-6.34 (m, 2H), 5.50 (s, 1H), 4.84 (brs, 1H), 3.78 (s, 6H), 3.75 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.6, 158.4, 154.4, 134.9, 130.9, 130.3, 123.2, 114.1, 106.0, 102.3, 55.4, 55.3, 49.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{23}O_4$ 351.1591; found 351.1609.

2-(Di(naphthalen-1-yl)methyl)phenol (3m): Brown solid. Yield: 20% (12 mg from 0.1638 mmol of corresponding aldehyde), mp 119-120 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H), 7.47-7.44 (m, 2H), 7.39-7.36 (m, 2H), 7.32 (t, J = 7.0 Hz, 2H), 7.17-7.14 (m, , 2H), 6.98 (d, J = 7.5 Hz, 2H), 6.87 (dd, J = 8.0, 1.0 Hz, 1H), 6.79 – 6.73 (m, 2H), 4.81 (brs, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.2, 138.8, 134.3, 131.9, 131.1, 129.9, 128.9, 128.1, 127.8, 127.3, 126.5, 125.7, 125.5, 124.2, 121.2, 116.1, 43.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{21}O$ 361.1587; found 361.1568.

2-(Di(naphthalen-1-yl)methyl)-6-methoxyphenol (3n): Brown solid. Yield: 15% (10 mg from 0.1638 mmol of corresponding aldehyde), mp 194-196 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.43-7.40 (m, 2H), 7.37-7.34 (m, 2H), 7.30-7.27 (m, 3H), 6.97 (d, J = 7.5 Hz, 2H), 6.77 (dd, J = 8.0, 1.0 Hz, 1H), 6.67 (t, J = 8.0 Hz, 1H), 6.42 (dd, J = 8.0, 1.5 Hz, 1H), 5.82 (s, 1H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 146.6, 143.1, 139.7, 134.2, 132.1, 129.3, 128.8, 127.4, 127.2, 126.4, 125.6, 125.4, 124.4, 123.3, 119.3, 109.1, 56.2, 42.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{23}O_2$ 391.1693; found 391.1718.

2-(Bis(3,5-dimethylphenyl)methyl)-6-methoxyphenol (3o): Off white solid. Yield: 56% (31 mg from 0.1638 mmol of corresponding aldehyde), mp 91-94 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ

6.84 (s, 2H), 6.77 – 6.74 (m, 6H), 6.52 – 6.49 (m, 1H), 5.76 (s, 1H), 5.73 (s, 1H), 3.88 (s, 3H), 2.25 (s, 12H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 146.4, 143.5, 143.3, 137.6, 130.2, 128.0, 127.3, 122.8, 119.1, 108.7, 56.1, 49.6, 21.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{27}O_2$ 347.2006; found 347.1992.

2-(Bis(4-methoxy-3,5-dimethylphenyl)methyl)phenol (3p): Yellow solid. Yield: 74% (46 mg from 0.1638 mmol of corresponding aldehyde), mp 100-101 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.15 (td, J = 7.5, 1.5 Hz, 1H), 6.86 (td, J = 8.0, 1.5 Hz, 1H), 6.83-6.80 (m, 2H), 6.77 (s, 4H), 5.47 (s, 1H), 4.96 (s, 1H), 3.72 (s, 6H), 2.23 (s, 12H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 155.8, 153.7, 137.6, 131.0, 130.8, 130.5, 129.7, 127.9, 120.7, 116.4, 59.8, 50.3, 16.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{29}O_3$ 377.2111; found 377.2132.

2-(Bis(4-methoxyphenyl)methyl)-6-chlorophenol (3q): White solid. Yield: 75% (44 mg from 0.1638 mmol of corresponding aldehyde), mp 126-128 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20 (dd, J = 7.5, 2.0 Hz, 1H), 7.01 (d, J = 8.5 Hz, 4H), 6.83 (d, J = 9.0 Hz, 4H), 6.78-6.75 (m, 2H), 5.77 (s, 1H), 5.64 (s, 1H), 3.78 (s, 6H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 158.1, 149.0, 135.2, 132.7, 130.3, 129.2, 127.0, 120.6, 120.1, 113.8, 55.3, 48.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{20}ClO_3$ 355.1095; found 355.1100.

2-(Bis(4-methoxyphenyl)methyl)-4,6-di-tert-butylphenol (3r): Colourless sticky liquid. Yield: 50% (35 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14 (d, J = 2.0 Hz, 1H), 6.98 (d, J = 8.5 Hz, 4H), 6.77 (d, J = 8.5 Hz, 4H), 6.54 (d, J = 2.0 Hz, 1H), 5.39 (s, 1H), 4.56 (s, 1H), 3.71 (s, 6H), 1.30 (s, 9H), 1.09 (s, 9H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 158.5, 150.2, 142.0, 136.2, 134.5, 130.4, 128.6, 125.1, 122.4, 114.2, 55.4, 50.7, 34.9, 34.4, 31.7, 30.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{29}H_{37}O_3$ 433.2737; found 433.2705.

2-Chloro-6-(di(thiophen-3-yl)methyl)phenol (3s): Pale yellowish sticky liquid. Yield: 64% (33 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (dd, J = 5.0, 3.0 Hz, 2H), 7.22 (dd, J = 8.0, 1.5 Hz, 1H), 6.91 (dd, J = 5.0, 1.5 Hz, 2H), 6.89 (dd, J = 8.0, 1.5 Hz, 1H), 6.83 – 6.82 (m, 2H), 6.81-6.79 (m, 1H), 5.91 (s, 1H), 5.67 (s, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 159.8, 148.7, 143.6, 131.6, 128.4, 128.3, 127.2, 125.6, 122.3, 120.8, 41.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{12}ClOS_2$ 307.0013; found 307.0030.

2-(Bis(2,4-dimethoxyphenyl)methyl)-6-chlorophenol (3t): White solid. Yield: 66% (45 mg from 0.1638 mmol of corresponding aldehyde), mp 128-130 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (dd, J = 8.0, 1.5 Hz, 1H), 6.69-6.67 (m, 4H), 6.47 (d, J = 2.5 Hz, 2H), 6.37 (dd, J = 8.5, 2.5 Hz, 2H), 6.20 (s, 1H), 5.60 (s, 1H), 3.78 (s, 6H), 3.70 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.5, 158.1, 149.1, 132.6, 130.0, 128.3, 126.7, 123.6, 120.2, 119.9, 103.6, 98.9, 55.8, 55.3, 36.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{24}ClO_5$ 415.1307; found 415.1301.

2-Chloro-6-(di(furan-2-yl)methyl)phenol (3u): Brown sticky liquid. Yield: 38% (17 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, J = 1.0 Hz, 2H), 7.26 – 7.23 (m, 1H), 7.02 (dd, J = 7.5, 1.0 Hz, 1H), 6.84 (t, J = 8.0 Hz, 1H), 6.33 (dd, J = 3.0, 2.0 Hz, 2H), 6.05 (d, J = 3.2 Hz, 2H), 5.91 (s, 1H), 5.77 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.5, 148.8, 142.2, 128.4, 127.9, 127.3, 121.1, 120.2, 110.4, 107.8, 38.4 HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{12}ClO_3$ 275.0469; found 275.0467.

2-(Di(benzofuran-2-yl)methyl)phenol (3v): Off White solid. Yield: 40% (23 mg from 0.1638 mmol of corresponding aldehyde), mp 118-119 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (d, J = 7.0 Hz, 2H), 7.43 (d, J = 8.5 Hz, 2H), 7.24 – 7.19 (m, 7H), 6.91 (td, J = 7.5, 1.0 Hz, 1H), 6.81 (dd, J = 8.0, 1.0 Hz, 1H), 6.49 (s, 2H), 6.10 (s, 1H), 5.36 (s, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.3, 155.2, 153.3, 130.0, 129.1, 128.4, 124.7, 124.1, 122.9, 121.3, 120.9, 116.2, 111.3, 105.34, 39.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{17}O_3$ 341.1172; found 341.1163.

2-Chloro-6-(di(benzofuran-2-yl)methyl)phenol (3w): Pale yellowish sticky liquid. Yield: 27% (17 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (dd, J = 7.5, 1.0 Hz, 2H), 7.44 (dd, J = 8.0, 1.0 Hz, 2H), 7.31 – 7.15 (m, 6H), 6.86 (t, J = 7.5 Hz, 1H), 6.50 (t, J = 1.0 Hz, 2H), 6.18 (s, 1H), 5.83 (s, 1H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 156.0, 155.2, 149.1, 128.6, 128.4, 128.4, 126.0, 124.1, 122.9, 121.2, 120.9, 120.3, 111.3, 105.4, 39.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{16}ClO_3$ 375.0782; found 375.0780.

2-(Bis(benzo[b]thiophen-2-yl)methyl)phenol (3x): Yellow sticky liquid. Yield: 18% (11 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, J = 7.5 Hz, 2H), 7.66 (d, J = 7.5 Hz, 2H), 7.33 – 7.26 (m, 5H), 7.21 (td, J = 8.0, 1.5 Hz, 1H), 7.11 (s, 2H), 6.94 (td, J = 7.5, 1.0 Hz, 1H), 6.82 (dd, J = 8.0, 1.0 Hz, 1H), 6.31 (s, 1H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 153.0, 146.7, 140.0, 139.6, 129.8, 129.1, 129.0, 124.4, 124.3, 123.4, 123.3,

122.4, 121.3, 116.1, 42.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{17}OS_2$ 373.0715; found 373.0703.

2-((4-Methoxyphenyl)(thiophen-2-yl)methyl)phenol (4a): Brown sticky liquid. Yield: 40% (19 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21 (dd, J = 5.0, 1.0 Hz, 1H), 7.15-7.12 (m, 3H), 6.97-6.93 (m, 2H), 6.88-6.84 (m, 3H), 6.78 (dd, J = 8.0, 1.0 Hz, 1H), 6.71 (d, J = 3.5 Hz, 1H), 5.86 (s, 1H), 4.84 (s, 1H), 3.78 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.7, 153.3, 147.3, 134.7, 130.7, 129.9, 128.3, 126.8, 126.5, 124.9, 121.0, 116.3, 114.9, 114.1, 55.4, 45.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{17}O_2S$ 297.0944; found 297.0948.

2-Methoxy-6-((4-methoxyphenyl)(thiophen-2-yl)methyl)phenol (4b): Dark brown sticky liquid. Yield: 37% (20 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (dd, J = 5.0, 1.0 Hz, 1H), 7.15 (d, J = 9.0 Hz, 2H), 6.93-6.91 (m, 1H), 6.82 (d, J = 9.0 Hz, 2H), 6.78-6.77 (m, 2H), 6.70-6.66 (m, 2H), 6.02 (s, 1H), 5.76 (s, 1H), 3.87 (s, 3H), 3.77 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 157.1, 147.1, 145.2, 141.9, 134.5, 129.0, 128.7, 125.4, 125.0, 123.1, 120.6, 118.2, 112.6, 107.9, 54.9, 54.2, 42.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{19}O_3S$ 327.1049; found 327.1051.

2-Chloro-6-((4-methoxyphenyl)(thiophen-3-yl)methyl)phenol (4c): White solid. Yield: 44% (24 mg from 0.1638 mmol of corresponding aldehyde), mp 98-100 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (dd, J = 5.0, 3.0 Hz, 1H), 7.21 (dd, J = 8.0, 2.0 Hz, 1H), 7.08 (d, J = 8.5 Hz, 2H), 6.87 – 6.83 (m, 4H), 6.79 (t, J = 7.5 Hz, 1H), 6.72 – 6.71 (m, 1H), 5.81 (s, 1H), 5.65 (s, 1H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.3, 148.9, 144.3, 134.9, 132.2, 129.9, 128.8, 128.7, 127.1, 125.7, 122.7, 120.7, 120.1, 113.8, 55.3, 45.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{16}ClO_2S$ 331.0554; found 331.0541.

2,4-Dibromo-6-((4-methoxyphenyl)(thiophen-2-yl)methyl)phenol (4d): Yellow sticky liquid. Yield: 49% (36 mg from 0.1638 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43 (d, J = 2.5 Hz, 1H), 7.15 (dd, J = 5.0, 1.0 Hz, 1H), 7.04 (d, J = 8.5 Hz, 2H), 7.00 (d, J = 2.5 Hz, 1H), 6.87 (dd, J = 5.0, 3.5 Hz, 1H), 6.80 – 6.77 (m, 2H), 6.60 (dt, J = 2.5, 1.0 Hz, 1H), 5.88 (s, 1H), 5.57 (s, 1H), 3.72 (s, 3H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.6, 149.0, 146.4, 134.0, 133.9, 132.5, 132.1, 129.8, 126.8, 126.6, 124.9, 114.0, 112.6, 111.2, 55.3, 45.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{15}Br_2O_2S$ 452.9154; found 452.9170.

2-Chloro-6-((2,4-dimethoxyphenyl)(thiophen-2-yl)methyl)phenol (4e): Off white solid. Yield: 28% (16 mg from 0.1638 mmol of corresponding aldehyde), mp 88-90 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21 (dd, J = 8.0, 1.5 Hz, 1H), 7.18 (dd, J = 5.0, 1.0 Hz, 1H), 6.93 (dd, J = 5.0, 3.5 Hz, 1H), 6.88 (d, J = 8.5 Hz, 2H), 6.78 (t, J = 8.0 Hz, 1H), 6.65 (dt, J = 2.0, 1.0 Hz, 1H), 6.47 (d, J = 2.5 Hz, 1H), 6.41 (dd, J = 8.5, 2.5 Hz, 1H), 6.27 (s, 1H), 5.74 (s, 1H), 3.79 (s, 3H), 3.75 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.9, 157.7, 148.9, 147.1, 132.1, 129.8, 128.2, 127.3, 126.6, 126.2, 124.2, 123.8, 120.5, 120.1, 103.9, 98.8, 55.8, 55.4, 38.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{18}ClO_3S$ 361.0660; found 361.0671.

2-(Bis(4-methoxyphenyl)methyl)-4-bromophenol (8a): White solid. Yield: 72% (18 mg from 0.0625 mmol of corresponding starting material), mp 135-138 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (dd, J = 8.5, 2.5 Hz, 1H), 7.02 (d, J = 8.5 Hz, 4H), 6.89 (d, J = 2.5 Hz, 1H), 6.85 (d, J = 9.0 Hz, 4H), 6.69 (d, J = 8.5 Hz, 1H), 5.52 (s, 1H), 4.78 (brs, 1H), 3.79 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.5, 152.7, 133.7, 133.2, 132.8, 130.7, 130.2, 118.0, 114.2, 113.1, 55.3, 49.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{20}BrO_3$ 399.0590; found 399.0608.

2-(Bis(4-methoxyphenyl)methyl)-4,6-dibromophenol (8a)': White solid. Yield: 20% (6 mg from 0.0625 mmol of corresponding starting material), mp 137-139 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (d, J = 2.5 Hz, 1H), 6.99 (d, J = 8.5 Hz, 4H), 6.89 (d, J = 2.5 Hz, 1H), 6.84 (d, J = 8.5 Hz, 4H), 5.71 (s, 1H), 5.56 (s, 1H), 3.79 (s, 6H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 158.3, 149.2, 134.4, 134.3, 132.6, 132.1, 130.1, 113.9, 112.5, 111.1, 55.2, 49.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{19}Br_2O_3$ 476.9695; found 476. 9672.

2,4-Dibromo-6-(di(naphthalen-1-yl)methyl)phenol (8b): Off white solid. Yield: 65% (19 mg from 0.0555 mmol of corresponding starting material), mp 200-202 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90-7.88 (m, 4H), 7.78 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 2.5 Hz, 1H), 7.46-7.45 (m, 2H), 7.41-7.39 (m, 2H), 7.34-7.31 (m, 2H), 7.24 (s, 1H), 6.94 (d, J = 7.0 Hz, 2H), 6.84 (d, J = 2.5 Hz, 1H), (Labile –OH peak is not visible). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.0, 138.0, 134.2, 133.2, 132.6, 131.7, 131.0, 129.0, 128.0, 127.1, 126.6, 125.8, 125.4, 123.8, 112.8, 111.3, 43.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{19}Br_2O$ 518.9777; found 518.9801.

3-(Bis(4-methoxyphenyl)methyl)-4'-methoxy-[1,1'-biphenyl]-4-ol (9a): White solid. Yield: 71% (15 mg from 0.0501 mmol of corresponding starting material), mp 170-172 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.32 (m, 3H), 7.09-7.08 (m, 4H), 7.00 (d, J = 2.0 Hz, 1H), 6.89 (d, J = 8.5 Hz, 2H), 6.87-6.84 (m, 5H), 5.63 (s, 1H), 4.76 (s, 1H), 3.81 (s, 3H), 3.79 (s, 6H). ^{13}C{^{1}H}

NMR (126 MHz, $CDCl_3$): δ 158.7, 158.4, 152.8, 134.6, 133.7, 133.6, 131.1, 130.4, 128.7, 127.8, 126.2, 116.7, 114.2, 114.1, 55.4, 55.3, 49.8. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{28}H_{26}O_4Na$ 449.1723; found 449.1702.

5'-(Di(naphthalen-1-yl)methyl)-4,4''-dimethoxy-[1,1':3',1''-terphenyl]-4'-ol (9b): Off white solid. Yield: 46% (12 mg from 0.0456 mmol of corresponding starting material), mp 110-113 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, J = 8.5 Hz, 2H), 7.87 (d, J = 7.5 Hz, 2H), 7.76 (d, J = 8.0 Hz, 2H), 7.46-7.43 (m, 4H), 7.40-7.37 (m, 2H), 7.35 (s, 1H), 7.34-7.32 (m, 3H), 7.23 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 7.0 Hz, 2H), 7.01 (d, J = 8.5, 2H), 6.99 (d, J = 2.5 Hz, 1H), 6.82 (d, J = 9.0 Hz, 2H), 5.39 (s, 1H), 3.85 (s, 3H), 3.76 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 159.5, 158.7, 149.1, 139.4, 134.2, 133.5, 132.8, 132.0, 130.6, 130.3, 129.4, 128.9, 128.5, 128.3, 127.7, 127.6, 127.3, 127.0, 126.4, 125.6, 125.5, 124.2, 114.9, 114.1, 55.5, 55.4, 42.9. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{41}H_{32}O_3Na$ 595.2244; found 595.2222.

5'-(Bis(4-methoxyphenyl)methyl)-4,4''-dimethyl-[1,1':3',1''-terphenyl]-4'-ol (9c): White solid. Yield: 68% (14 mg from 0.0418 mmol of corresponding starting material), mp 125-127 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 7.37 (d, J = 8.0 Hz, 2H), 7.34-7.31 (m, 3H), 7.27-7.25 (m, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 9.0 Hz, 4H), 7.04 (d, J = 2.0 Hz, 1H), 6.83 (d, J = 8.5 Hz, 4H), 5.81 (s, 1H), 5.30 (s, 1H), 3.78 (s, 6H), 2.39 (s, 3H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 158.2, 149.7, 138.2, 137.8, 136.4, 135.7, 134.3, 133.2, 131.7, 130.4, 130.0, 129.5, 129.2, 128.6, 128.3, 127.0, 126.7, 113.9, 55.3, 49.2, 21.3, 21.1. HRMS (ESI-TOF) m/z: $[M - H]^-$ calcd for $C_{35}H_{31}O_3$ 499.2279; found 499.2279.

4,4'-((2-(Allyloxy)-3,5-dibromophenyl)methylene)bis(methoxybenzene) (10a): Colourless sticky liquid. Yield: 84% (30 mg from 0.0690 mmol of corresponding aldehyde). ^1H NMR (500 MHz, $CDCl_3$): δ 7.58 (d, J = 2.5 Hz, 1H), 6.97 (d, J = 8.5 Hz, 5H), 6.83 (d, J = 8.5 Hz, 4H), 5.98-5.92 (m, 1H), 5.85 (s, 1H), 5.29-5.20 (m, 2H), 4.08 (dt, J = 6.0, 1.5 Hz, 2H), 3.79 (s, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 158.3, 153.2, 142.3, 135.0, 134.0, 133.0, 132.8, 130.3, 118.6, 118.4, 117.2, 113.96, 74.1, 55.3, 48.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{21}Br_2O_3$ 517.0008; found 517.0031.

2-((2-(Allyloxy)-3,5-dibromophenyl)(4-methoxyphenyl)methyl)thiophene (10b): Colourless sticky liquid. Yield: 73% (12 mg from 0.0330 mmol of corresponding aldehyde). ^1H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, J = 2.0 Hz, 1H), 7.15 (dd, J = 5.0, 1.0 Hz, 1H), 7.08 (d, J = 2.5 Hz, 1H), 7.00 (d, J = 8.5 Hz, 2H), 6.86 (dd, J = 5.0, 3.5 Hz, 1H), 6.77 (d, J = 8.5 Hz, 2H), 6.57 (dt, J =

3.5, 1.0 Hz, 1H), 5.98 (s, 1H), 5.96-5.88 (m, 1H), 5.26-5.16 (m, 2H), 4.15-4.04 (m, 2H), 3.72 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 158.6, 152.9, 147.0, 141.6, 134.6, 134.4, 132.9, 132.2, 129.8, 126.8, 126.7, 125.0, 118.5, 117.3, 114.0, 74.3, 55.3, 44.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{19}Br_2O_2S$ 492.9467; found 492.9473.

4,4'-((2-(*p*-Tolyloxy)phenyl)methylene)bis(methoxybenzene) (11): Colourless sticky liquid. Yield: 66% (17 mg from 0.0624 mmol of corresponding aldehyde). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.07 (t, J = 7.5 Hz, 1H), 6.97-6.92 (m, 8H), 6.76-6.71 (m, 5H), 6.61 (d, J = 8.0 Hz, 2H), 5.71 (s, 1H), 3.70 (s, 6H), 2.21 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$): δ 157.9, 155.5, 155.0, 136.2, 135.9, 132.3, 130.6, 130.3, 130.1, 127.6, 123.3, 119.0, 118.2, 113.6, 55.3, 48.3, 20.7. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{28}H_{27}O_3$ 411.1955; found 411.1961.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Crystallographic data for **3b**, and copies of the ^{1}H and ^{13}C NMR spectra.

ACKNOWLEDGMENT

The authors are thankful to the editor and reviewers for their constructive comments and suggestions. The authors are grateful to DST-SERB (Early Career Research Award), DST-INSPIRE Faculty Scheme, and DST-FIST program (Dept. of Chemistry, NIT-Trichy) for research grant and fellowship. RK thanks to DST, GOI for financial support in the form of PURSE Grant (II) and FIST (II) for Single crystal facility at Department of Chemistry, Panjab University, Chandigarh.

REFERENCES

(1) (a) Gomberg, M. An instance of trivalent carbon: Triphenylmethyl. *J. Am. Chem. Soc.* **1900**, 22, 757. DOI: 10.1021/ja02049a006. (b) Gomberg, M. On trivalent carbon. *J. Am. Chem. Soc.* **1901**, *23*, 496. DOI: 10.1021/ja02033a015. (c) Gomberg, M. On trivalent carbon. *J. Am. Chem. Soc.* **1902**, *24*, 597. DOI: 10.1021/ja02021a001.

(2) (a) Kocienski, P. J. in Protective Groups, 3rd ed., Georg Thieme, Stuttgart, **2003**. (b) Greene, T. W.; Wuts, P. G. M. in Protetive Groups in Organic Synthesis, 3rd ed., Wiley, New York, **1999.**

(3) Irie, M. Light-induced reversible pH change. *J. Am. Chem. Soc.* **1983**, *105*, 2078. DOI: 10.1021/ja00345a075.

(4) (a) Baptista, M. S.; Indig, G. L. Effect of BSA Binding on Photophysical and Photochemical Properties of Triarylmethane Dyes. *J. Phys. Chem. B*. **1998**, *102*, 4678. DOI: 10.1021/jp981185n. (b) Muthyala, R.; Katritzky, A. R.; Lan, X. A synthetic study on the preparation of triarylmethanes. *Dyes Pigm*. **1994**, *25*, 303. DOI: 10.1016/0143-7208(94)87017-9.

(5) (a) Sanguinet, L.; Twieg, R. I.; Wiggers, G.; Mao, G.; Singer, K. D.; Petschek, R. G. Synthesis and spectral characterization of bisnaphthylmethyl and trinaphthylmethyl cations. *Tetrahedron Lett*. **2005**, *46*, 5121. DOI: 10.1016/j.tetlet.2005.05.138. (b) Das, S. K.; Shagufta, Panda, G. An easy access to unsymmetric trisubstituted methane derivatives (TRSMs). *Tetrahedron Lett.* **2005,** *46*, 3097. DOI: 10.1016/j.tetlet.2005.03.001. (c) Rudzevich, Y.; Rudzevich, V.; Schollmeyer, D.; Thondorf, I.; Bo1hmer, V. Hydrogen Bonded Dimers of Triurea Derivatives of Triphenylmethanes. *Org. Lett.* **2005,** *7*, 613. DOI: 10.1021/ol0476265. (d) Rudzevich**,** V.; Schollmeyer**,** D.; Braekers**,** D.; Desreux**,** J. F.; Diss, R.; Wipff**,** G.; Böhmer, V. Carbamoylmethylphosphinoxide Derivatives Based on the Triphenylmethane Skeleton. Synthesis and Extraction Properties. *J. Org. Chem.* **2005,** *70*, 6027. DOI: 10.1021/jo050717a.

(6) (a) Mibu, M.; Yokomizo, K.; Uyeda M.; Sumoto, K. Synthesis and Antiviral Activities of Some 4,4'- and 2,2'- Dihydroxytriphenylmethanes. *Chem. Pharm. Bull.* **2005**, *53*, 1171. (b) Seligmann, O.; Wagner, H. Structure determination of melanervin, the first naturally occurring flavonoid of the triphenylmethane family. *Tetrahedron*. **1981,** *37*, 2601. DOI: 10.1016/S0040-4020(01)98963-X. (c) Maloy, K. P.; Gautam, P. V.; Manju, Y. K.; Sudhir, S. Thiophene containing triarylmethanes as antitubercular agents. *Bioorg. Med. Chem. Lett*. **2008**, *18*. 289. DOI: 10.1016/j.bmcl.2007.10.083.

(7) (a) Barbero, M.; Cadamuro, S.; Dughera, S.; Rucci, M.; Spano, G.; Venturello, P. Solvent-free Brønsted acid catalysed alkylation of arenes and heteroarenes with benzylic alcohols. *Tetrahedron.*, **2014**, *70*, 1818. DOI: 10.1016/j.tet.2014.01.011. (b) Wilsdorf, M.; Leichnitz, D.; Reissig, H.-U. Trifluoromethanesulfonic Acid Catalyzed Friedel–Crafts Alkylations of 1,2,4-Trimethoxybenzene with Aldehydes or Benzylic Alcohols. *Org. Lett*. **2013**, *15*, 2494. DOI: 10.1021/ol400972m. (c) Alonso, I.; Esquivias, J.; Arrayás, R. G.; Carretero, J. C. Understanding the Behavior of *N*-Tosyl and *N*-2-Pyridylsulfonyl Imines in Cu^{II}-Catalyzed Aza-Friedel−Crafts Reactions. *J. Org. Chem.* **2008,** *73*, 6401. DOI: 10.1021/jo800986g. (d) Liu, C.-R.; Li, M.-B.;

Yang, C.-F.; Tian, S.-K. Catalytic selective bis-arylation of imines with anisole, phenol, thioanisole and analogues. *Chem. Commun*. **2008**, 1249. DOI: 10.1039/B800066B. (e) Esquivias, J.; Arrayás, R. G.; Carretero, J. C. A copper(II) catalyzed aza-Friedel-Crafts reaction of *N*-(2-pyridyl)sulfonyl aldimines: synthesis of unsymmetrical diaryl amines and triaryl methanes. *Angew. Chem., Int. Ed*. **2006**, *45*, 629. DOI: 10.1002/anie.200503305. (f) Nair, V.; Vidya, N.; Abhilash, K. G. Efficient Condensation Reactions of Electron-Rich Arenes with Aldehydes and Enals Promoted by Gold(III) Chloride: Practical Synthesis of Triaryl- and Triheteroarylmethanes and Related Compound. *Synthesis* **2006**, *21*, 3647. DOI: 10.1055/s-2006-950209 (g) Nair, V.; Abhilash, K. G.; Vidya, N. Practical Synthesis of Triaryl- and Triheteroarylmethanes by Reaction of Aldehydes and Activated Arenes Promoted by Gold(III) Chloride**.** *Org. Lett*. **2005**, *26*, 5857. DOI: 10.1021/ol052423h. (h) Miao, M.; Yin, W.; Wang, L.; Chen, Z.; Xu, J.; Ren, H. Transition-Metal-Free Arylation and Alkylation of Diarylmethyl *p*-Tolyl Sulfones with Zinc Reagents. *J. Org. Chem.* **2018,** *83*, 10602. DOI: 10.1021/acs.joc.8b01428. (i) Gomes**,** R. F. A.; Coelho, J. A. S.; Frade**,** R. F. M.; Trindade, A. F.; Afonso, C. A. M. Synthesis of Symmetric Bis(*N*-alkylaniline)triarylmethanes via Friedel–Crafts-Catalyzed Reaction between Secondary Anilines and Aldehydes. *J. Org. Chem.* **2015,** *80*, 10404. DOI: 10.1021/acs.joc.5b01875. (j) Wang**,** A.; Xing**,** P.; Zheng**,** X.; Cao**,** H.; Yang, G.; Zheng, X. Deep eutectic solvent catalyzed Friedel–Crafts alkylation of electron-rich arenes with aldehydes. *RSC Adv.***, 2015, *5*,** 59022. DOI: 10.1039/C5RA08950F. (k) Zhang, Z.; Wang, H.; Qiu, N.; Kong, Y.; Zeng, W.; Zhang, Y.; Zhao J. Synthesis of Triarylmethanes via Palladium-Catalyzed Suzuki Coupling of Trimethylammonium Salts and Arylboronic Acids. *J. Org. Chem.* **2018**, *83*, 15, 8710. DOI: 10.1021/acs.joc.8b00965. (l) Mondal S.; Panda G. Synthetic methodologies of achiral diarylmethanols, diaryl and triarylmethanes (TRAMs) and medicinal properties of diaryl and triarylmethanes-an overview. *RSC Adv.,* **2014**, *4*, 28317. DOI: 10.1039/c4ra01341g. (m) Kshatriya, R.; Jejurkar, V. P.; Saha S. Advances In The Catalytic Synthesis Of Triarylmethanes (TRAMs). *Eur. J. Org. Chem.* **2019**, 3818. DOI: 10.1002/ejoc.201900465.

(8) Nambo, M.; Grudden, C. M. Recent Advances in the Synthesis of Triarylmethanes by Transition Metal Catalysis. *ACS Catal.* **2015,** *5*, 4734. DOI: 10.1021/acscatal.5b00909.

(9) (a) Cui, C.-X.; Li, H.; Yang, X.-J.; Yang, J.; Li,X.-Q. One-Pot Synthesis of Functionalized 2,5-Dihydrofurans via an Amine-Promoted Petasis Borono_Mannich Reaction. *Org. Lett.*, **2013**, *15*, 5944. DOI: 10.1021/ol402782f. (b) Wang, Q.; Finn, M. G. 2H-Chromenes from

Salicylaldehydes by a Catalytic Petasis Reaction. *Org. Lett*., **2000**, *2*, 4063. DOI: 10.1021/ol006710r.

(10) Potopnyk, M. A.; Volyniuk, D.; Luboradzki, R.; Ceborska,M.; Hladka, I.; Danyliv, Y.; Grazulevicius J. V. Application of the Suzuki−Miyaura Reaction for the Post functionalization of the Benzo[4,5]thiazolo[3,2-c][1,3,5,2]oxadiazaborinine Core: An Approach toward Fluorescent Dyes. *J. Org. Chem.* **2019**, *84*, 5614. DOI: 10.1021/acs.joc.9b00566.

(11) Cermák, J. K.; Církva, V. Copper-mediated synthesis of mono- and dichlorinated diaryl ethers. *Tetrahedron Lett*. **2014**, *55*, 4185. DOI: 10.1016/j.tetlet.2014.06.035.