Fuctionalization of Linear and Angular Phenothiazine and Phenoxazine Ring Systems via Pd(0)/XPhos Mediated Suzuki-Miyaura Cross-coupling Reactions

Efeturi A. Onoabedje,[a*] Uchechukwu C. Okoro,[a] David W. Knight,[b] and Amitabha Sarkar[c]

[a]Department of Pure and Industrial Chemistry, University of Nigeria, Nsukka, Nigeria
[b]School of Chemistry, Department of Organic Chemistry, Cardiff University, Wales, UK
[c]Department of Organic Chemistry, India Association for the Cultivation of Science, Kolkata 700032, India
*E-mail: efeturi.onoabedje@unn.edu.ng

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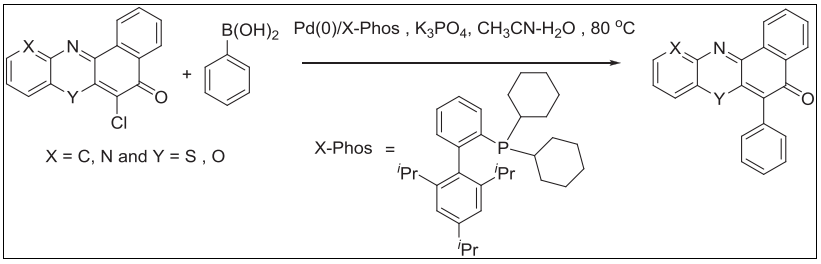

Chloro-substituted phenothiazines and phenoxazines were successfully derivatized with phenylboronic and styrylboronic acids using Suzuki–Miyaura cross-coupling reaction catalyzed by Pd(0)/XPhos for the first time in good yields. The protocol employed 4 mol% Pd and 7 mol% XPhos with K_3PO_4 in acetonitrile at 80°C. The reaction condition is compatible with carbonyl and unprotected N–H groups in substrates. Structural assignments were established by combined spectroscopic (UV, IR, ^1H, and ^{13}C NMR), MS, and elemental analytical data.

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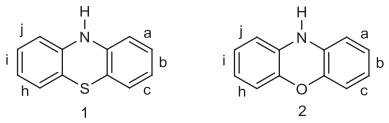
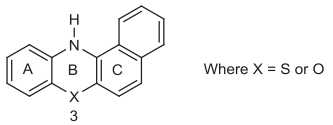
INTRODUCTION

The ever expanding therapeutic applications of phenothiazine **1** and phenoxazine **2** and their derivatives motivated the investigation of facile reaction protocols for functionalization of these compounds [1–5].



Phenothiazine and phenoxazine triheterocyclic provide the basic structures for various classes molecules of pharmacotherapeutic agents with a broad spectrum of biological activity [1,6]. Recent reviews and reports on the progress of biological activities of various synthesized phenothiazines revealed that they exhibit promising antibacterial and antifungal [7,8], anticancer [9,10], multidrug resistance reversal [10,11], anti-inflammatory [12,13], antiviral [3], antimalarial [3], analgesic [14], and other properties. Interestingly, most of the activities of phenothiazine are closely exhibited by phenoxazine and its derivatives. For example, novel water soluble 2-amino-4,4α,7-dimethyl-3*H*-phenoxazine was reported to possess antiproliferative, immunosuppressive, antibacterial, antiviral [15,16], and antimalarial effects. In addition, multidrug resistance modulator in cancer cell of phenoxazines has been reported in several papers [17,18]. Previously, phenothiazine group of drugs was known as antipsychotic drugs and phenothiazine derivatives, and in particular, chlorpromazine, promethazine, and diethazine were applied as tranquilizers, antihistamines, and for the treatment of Parkinson disease, respectively [19,20]. In addition to the physiological activities of phenothiazines and their derivatives, their reversible oxidative properties, which give rise to characteristic deep-colored radical cation absorption, made them attractive spectroscopic probes in molecular arrangements for photoinduced electron transfer studies and material scientific motifs [21,22]. Undoubtedly, the analogous phenoxazines also exhibit reversible oxidation characteristics. Reports disclosed that phenoxazine derivatives are widely applied as organic light-emitting diodes [23–26]. The earliest modification of the structure of the parent compounds **1** and **2** in which benzene rings are fused to the sides of ring A and/or C results in nonlinear phenothiazine and phenoxazine rings of which benzo[a]phenothiazine and benzo[a]phenoxazine **3** and their derivatives were the most popular ones [27–31].



Classical chemical methods have been employed in the syntheses of phenothiazine and phenoxazine derivatives. However, the application of transition metal-catalyses is largely unexplored in spite of its popularity in C–C bond formation in the recent time because of their mild reaction

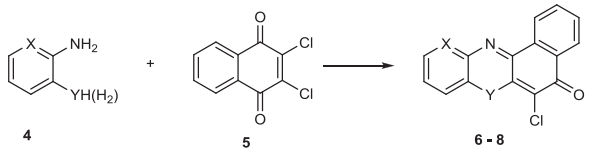
conditions. Moreover, the attention of the synthetic community has been drawn to the inclusion of chloroarenes and heterochloroarenes as coupling partners in palladium-catalyzed cross-coupling reactions because they are economically cheaper, easily available [32–34], and are pharmacophores in wide range of drugs [15,16,35]. To this end, several electron-rich and bulky ligands such as dialkylbiarylphosphines [36–38], *N*-heterocyclic carbenes [39–41], ferrocenyl dialkyl phosphene [42], and others have been developed to facilitate otherwise slow oxidative addition of aryl chlorides and to circumvent the potential binding of heterocyclic substrates to metal center in the catalyst. However, chlorophenothiazine and chlorophenoxazine that are relatively less expensive and easily available have rarely been used. Previously reported applications of Suzuki–Miyaura cross-coupling reactions involved the cross-coupling of organo boronic acid or its ester with aryl chlorides [43] or chloroquinolines [44]. Muller and coworkers described the functionalization of bromophenothiazines via Pd-catalyzed standard Suzuki coupling in several of their papers but not chlorophenothiazines [22,45–47]. Therefore, a convenient protocol for the transformation of chlorophenothiazines and chlorophenoxazines is described. To our knowledge, this is the first time this protocol is reported with these classes of substrates.

RESULTS AND DISCUSSION

The synthesis of the desired derivatives of phenothiazines and phenoxazines begins with synthesizing the pharmacologically relevant intermediates by employing the traditional anhydrous base catalyzed coupling reaction of 2,3-dichloro-1,4-naphthoquinone **5** with 2-aminothiophenol, 2-aminophenol, and 2-aminopyridinol (Scheme 1).

Inspired by Buchwald's earlier work [16,48–50] on application of dicyclohexylbiphenylphosphine-based catalytic system (such as XPhos) as a generic catalyst in Suzuki–Miyaura cross-coupling of (hetero)aryl substrates, the reaction protocol for derivatization of chlorophenothiazines/chlorophenoxazines was developed along the same line. $Pd(OAc)_2$ and XPhos (Pd/L = 1:2) was chosen as catalytic

Scheme 1. Synthesis of intermediates.

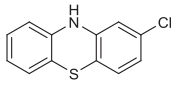
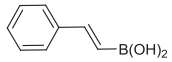
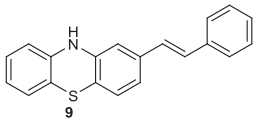
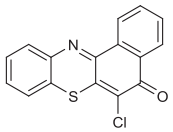
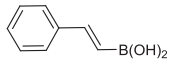
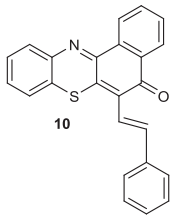
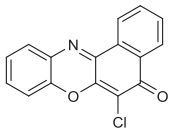
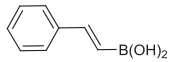
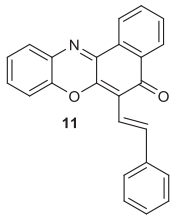
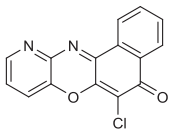
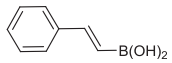
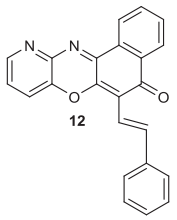
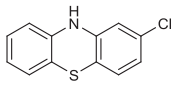
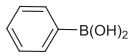
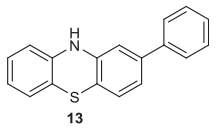
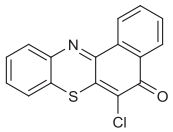
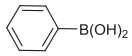
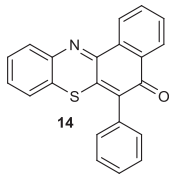
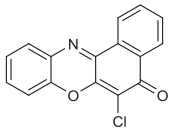
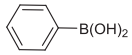
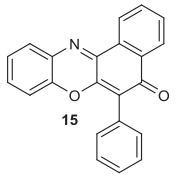


	6	7	8
X	C	C	N
Y	S	O	O

system in combination with either of the bases, Na_2CO_3, K_2CO_3, or K_3PO_4, and aqueous polar solvents. The preliminary experiment was conducted by reacting 2-chloro-10*H*-phenothiazine with styryl boronic acid to afford 2-styryl-10*H*-phenothiazine **9**. This reaction employed $Pd(OAc)_2$ (2 mol%), XPhos (4 mol%) and K_3PO_4 (3 mM) in acetonitrile at 80°C. The formation of product was observed in trace amounts after an hour, which increase with time. However, after 8 h, there was no noticeable change in TLC even after the reaction was allowed to run overnight. The product was isolated with a yield of 53% after work-up by solvent extraction and purified by flash chromatography on silica gel using 5% EtOAc/95% pet ether as eluent. The spectral and elemental analysis data of the isolated product were in agreement with molecular formula $C_{20}H_{15}NS$ and assigned structure. While the ^{1}HNMR spectrum integrated accurately for 15 protons, the ^{13}C NMR spectrum displayed signals for all the carbon nuclei in the expected product. This was further confirmed by the mass spectrum that showed molecular ion peak at *m/z* of 301.10 [(8), M^+]. No product was formed when the reaction was run in the absence of the ligand, XPhos, even when reaction was conducted over a longer period (25 h). Similarly, the use of PPh_3 in place of XPhos gave no conversion after 8 h and a little amount of conversion (less than 10%) after 25 h, further confirming that the ligand played a crucial role in the cross-coupling reaction. Apart from the bulkiness that has been proven to aid in generation of monoligated complex ion, L_1Pd that was believed to undergo oxidative reaction more readily than $[PdL_2]$ complex [51–53], the strong σ electron donating character of XPhos appears to contribute to the ease with which 2-chloro-10*H*-phenothiazine was coupled to boronic acid. It was speculated that the electron richness of the ligand minimized the binding of the heteroatoms in the substrate to metal center thereby increasing the rate of the reaction as well as yields of expected product. Excess boronic acid was employed to compensate for the part that might be converted to side products such as homocoupled products as the catalyst is being reduced to its active Pd(0). The use of Na_2CO_3 in place of K_3PO_4 gave lower product yields (24%), while K_2CO_3 gave comparable yields with K_3PO_4 under these conditions. Furthermore, there was no significant difference in product yields when DMF/H_2O (2:1) and *n*-BuOH/H_2O (2:1) were used in place of CH_3CN/H_2O (2:1) under these conditions. Buchwald applied CH_3CN/H_2O (1.5:1) per millimoles of halide to achieve excellent yields of biaryls [16]. Moseley [54] observed that acetonitrile, ethanol, and THF in combination with water at 9:1, 4:1, and 1:1 ratios made little difference in the Suzuki–Miyaura cross-coupling reaction of (hetero) chloroaromatics with $Pd(dbpf)Cl_2$ as preformed catalyst. The reactions performed without solvent degassing did give comparable yield of products under these conditions. Although only $Pd(OAc)_2$ was applied as palladium source in

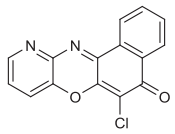
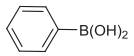
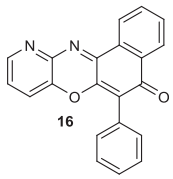
Table 1

Suzuki–Miyaura cross-coupling of chlorophenothiazines and phenoxazines.[a]

Entry	Aryl chloride	Boronic acid	Product	Reaction time (h)	Isolated % yield[b]
1			 **9**	6	67
2			 **10**	8	60
3			 **11**	8	51
4			 **12**	8	55
5			 **13**	6	71
6			 **14**	7	43
7			 **15**	7	54

(*Continued*)

Table 1
(*Continued*)

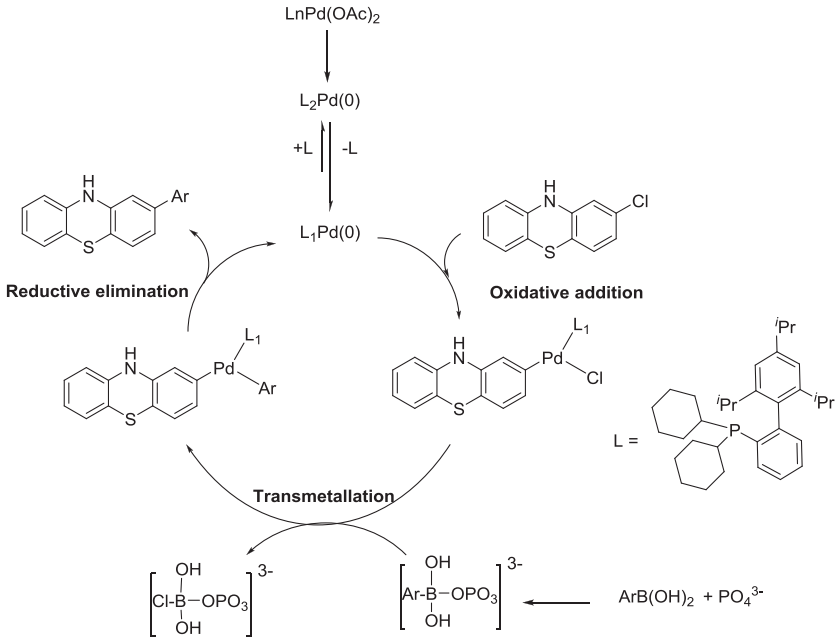
Entry	Aryl chloride	Boronic acid	Product	Reaction time (h)	Isolated % yield[b]
8			 **16**	8	44

[a]Reaction conditions: chlorophenothiazine/chlorophenoxazine (1 equiv.), boronic acid (1.2 .), K_3PO_4 (3 m*M*), CH_3CN–H_2O (2:1) (3 mL), $Pd(OAc)_2$ (4 mol%), XPhos (7 mol%).
[b]Isolated yield after purification by flash column chromatography.

this reaction, it is possible that other common palladium salts such as $PdCl_2$ and $Pd_2(dba)_3$ in conjunction with XPhos would effect similar transformation.

Encouraged by the results from cross-coupling of 2-chloro-10*H*-phenothiazine and styryl boronic acid to afford 2-styryl-10*H*-phenothiazine, the amount of the catalyst and ligand was doubled with a view to increasing the product yield, and 67% yield of coupled product was indeed obtained. Therefore, the catalyst-ligand load for the reaction was fixed at 4 mol% $Pd(OAc)_2$ and 7 mol% XPhos and reaction scope expanded to include the cross-coupling of 2-chloro-10*H*-phenothiazine with phenyl boronic acid to obtained 2-phenyl-10*H*-phenothiazine in isolated yield of 71% at a conversion of over 90%. Again the spectroscopic and elemental analysis data were in agreement with molecular structure and formula, $C_{18}H_{13}NS$. Without further reaction optimization, the procedure was applied in coupling other substrates to styrylboronic and phenylboronic acids, running the reaction for a maximum of 8 h. Table 1 gives the yields of product formations. Moderate to high yields were recorded for all reactions. The reaction of 2-chloro-10*H*-phenothiazine with styrylboronic and phenylboronic acids respectively gave higher yields than 6-chloro-*5H*-benzo[a]phenothiazin-5-one **6**, 6-chloro-*5H*-benzo[a]phenoxazin-5-one **7**, and 6-chloro-*5H*-naphtho [2,1-b]pyrido[2,3-e][1,4]oxazin-5-one **8** tetra cyclic substrates. It was presumed that the electron richness of the tetracyclic substrates and the steric hindrance provided by the ketonic groups that are *ortho* to the chloro substituents contributed to lower their yields. The molecular structures of the synthesized compounds were established on the basis of NMR, UV and mass spectroscopic, and microanalysis

Scheme 2. Mechanism for XPhos catalyzed Suzuki-Miyaura cross-coupling reactions of chlorophenothiazine/chlorophenoxazine.



data and were in agreement with the assigned molecular structures and formulas. The number of aromatic (and vinylic for **9**, **10**, **11**, and **12**) protons was nicely accounted for in the proton magnetic spectra of the compounds that were found at 8.88–6.56 ppm. The vinylic protons were highly deshielded by the pi electrons of the fused conjugated tetracyclic rings that their chemical shifts [55] shifted from their normal absorption range of 4.6–5.9 and merged with aromatic protons in such a way that they are not distinguishable. The deshielding effect of the vinylic protons were much pronounced in compounds **10**, **11**, and **12** because of additive deshielding effect generated by the carbonyl group *ortho* to the styryl moieties in the compounds. The carbon nuclei were similarly accurately represented in the carbon nuclear magnetic spectra for all compounds with the carbonyl carbon signals found in a far distance low field from the other sp2 hybridized carbon peaks. Although derivatives **9–12** were prepared as mixture of *E* and *Z* isomers, they were named as (*E*)-2-styryl-10*H*-phenothiazine, (*E*)-6-styryl-5*H*-benzo[a]phenothiazin-5-one, (*E*)-6-styryl-5*H*-benzo[a] phenoxazin-5-one, and (*E*)-6-styryl-5*H*-naphtho[2,1-b]pyrido [2,3-e][1,4]oxazin-5-one respectively as a result of greater stabilities of the *E* alkenes over the *Z* alkenes. The more stable *E* alkene gives the major product. The IR absorption maxima for carbonyl functional groups in synthesized compounds were supposed to be in the range of 1610–1640 cm^{-1} lower than the carbonyl frequency in 1,4-naphthoquinone because of ionic resonance effect [56]. Furthermore, the synthesized derivatives are highly colored with UV–visible absorption maxima range of 268–814 nm. The UV–visible spectra data disclosed bathochromic shifts except compound **9** as a result of increase in conjugation with compounds **10** and **11** exhibiting the highest shifts. It was speculated that the coplanarity of compounds **10–16** contributed to their red shifts as a result of extended pi conjugation. It had been reported that phenothiazine derivatives with extended pi-conjugated substituents often display intense luminescence upon UV–vis excitation with Stokes shifts that might be due to solvent relaxation and, in part, to geometry changes in excited state [21]. The favorable electronic properties of phenothiazine have led to their applications as electrophore probes in supramolecular assemblies for photoinduced electron transfer and sensor studies and as electron-donor components in material scientific investigations such as electrically conducting charge-transfer composites, polymers, Do–Acc arrangements, and also as chromophores in dye-sensitized photovoltaic cells [22]. Besides, the mass spectra data were in agreement with molecular structures and formulas of the synthesized derivatives. The mass spectra data were in agreement with molecular structures and formulas of the synthesized derivatives by furnishing their molecular ion peaks except for compound **13** that gave no meaningful data. However, results from elemental analysis of compound **13** were consistent with its molecular formula and assigned structure.

By using 2-chloro-10*H*-phenothiazine electrophilic substrate, we present a general mechanism for Suzuki–Miyaura cross-coupling of chlorophenothiazine/chlorophenoxazine (Scheme 2).

CONCLUSION

The catalyst system generated from palladium acetate and XPhos converted highly electron-rich and heterocyclic chlorophenothiazines and chlorophenoxazines in moderate to high yields to afford highly colored derivatives at relatively mild reaction temperatures. The reaction conditions tolerated both carbonyl functional groups and unprotected N–H moiety in substrates. Further research is in progress to optimize the reaction conditions and develop catalytic system to explore related cross-coupling protocols to diversify target molecular motifs.

EXPERIMENTAL

General information. Commercially available starting materials and reagents were purchased from Aldrich Chemical Company (UK) and were used without further purification. Unless otherwise stated, all compounds were synthesized and characterized in the School of Chemistry, Organic Chemistry Laboratory, Cardiff University, Wales, UK. Melting points were determined with a Fisher-Johns apparatus and are uncorrected. ^{1}H and ^{13}C NMR data were recorded with Brucker DPX 400 and 600 MHz spectrophotometer (UK) relative to TMS as internal standard. All and chemical shifts reported in parts per million (δ), and coupling constants (J) are reported in hertz. Multiplicity is indicated using the following abbreviations: br for broad, s for singlet, d for doublet, t for triplet, dd for doublet of doublets, and m for multiplet. The mass spectral data were obtained on a Varian 1200 Quadruple Mass and Micromass Quadro II spectrometers (UK). Elemental analysis was carried out with ThermoQuest FLASH series (CHNS) elemental analyzer (UK). UV–visible spectra were recorded on Cecil 7500 Aquarius 7000 series spectrometer at Chemistry Advance Laboratory, Sheda Science and Technology Complex Abuja, Nigeria, using matched 1 cm quartz cells and methanol as solvent. The absorption maxima are recorded in nanometer (nm), and figures in parenthesis are log of ε.

Synthesis of intermediates. ***6-Chloro-5H-benzo[a]phenothiazin-5-one, 6.*** To a suspension of 2-aminothiophenol (2.5 g, 20 m*M*) in (50 mL) chloroform was added Na_2CO_3 (2.12 g, 20 m*M*), the mixture heated to boiling temperature before adding 2,3-dichloro-1,4-napthoquinone (4.54 g, 20 m*M*), and entire mixture refluxed for 3 h while stirring with magnetic bar. The reaction mixture was cooled to room temperature, and solvent was distilled off in a vacuum. Water (25 mL) was added to the dark solid, stirred, and filtered to remove

inorganic salts and air-dried. The solid was recrystallized from benzene acetone after treatment with activated charcoals to obtain reddish-brown shiny solid. Yield = 5.01 g (84%), melting point: 220–222°C. δ_H (400 MHz $CDCl_3$): 8.87–8.84 (1H, m); 8.33–8.31 (1H, m); 7.97–7.94 (1H, m), 7.74–7.72 (2H, m); 7.54–7.42 (3H, m). δ_c (600 MHz $CDCl_3$): 173.85 (carbonyl carbon), 143.80, 138.41, 135.20, 134.10, 133.29, 132.00, 131.62, 130.21, 128.34, 126.53, 125.97, 125.33, 125.18, 123.55. UV–visible λ_{max} (MeOH): 381.5(7.06); 4.79 (7.21); 747.5 (6.97). IR (ν_{max} cm^{-1}): 1640, 1593, 1578, 1510, 1290, 1155, 1090, 905, 855, 828, 777, 721, 681, 644. *Anal.* Calcd. for $C_{16}H_8ClNOS$: C, 64.54; H, 2.71; Cl, 11.91; N, 4.70; S, 10.77. Found: C, 64.59; H, 2.77; Cl, 11.71; N, 4.49; S, 10.89.

6-Chloro-*5H-benzo[a]phenoxazin-5-one, 7*. A mixture of 2-aminophenol (2.18 g, 20 m*M*) and KOH (2.24 g, 20 m*M*) was stirred at room temperature for ½ h in methanol (100 mL) followed by addition of 2,3-dichloro-1,4-napthoquinone (4.54 g, 20 m*M*), and the entire reaction mixture stirred at room temperature for 6 h. The solvent was distilled off in a vacuum, water (50 mL) added to the yellowish-brown solid, stirred, and filtered, and solid further wash with 5% HCl (25 mL) and air-dried. The crude product was recrystallized from benzene toluene after treatment with activated charcoal to give yellow-orange-colored solid. Yield = 4.85 g (86%), melting point: 205–207°C. δ_H (400 MHz CDCl): 8.68–8.66 (1H, m); 8.31–8.29 (1H, m); 7.81–7.79 (1H, dd, J = 7.80); 7.76–7.68 (2H, m); 7.49–7.46 (1H, m); 7.41–7.33 (2H, m). δ_c (600 MHz $CDCl_3$): 177.46 (carbonyl carbon), 146 .89, 146.15, 143.80, 132.63, 132.41, 132.09, 131.85, 131.44, 130.27, 129.93, 126.63, 125.85, 124.94, 116.19. UV–visible λ_{max} (MeOH): 354.5 (7.88); 440 (7.54); 747 (7.01). IR (ν_{max} cm^{-1}): 1640, 1570, 1330, 1310, 1280, 1250, 1150, 1100, 1010, 920, 840, 780, 760, 690. *Anal.* Calcd for $C_{16}H_8ClNO_2$: C, 68.22; H, 2.86; Cl, 12.58; N, 4.97. Found: C, 68.31; H, 3.01; Cl, 12.75; N, 5.10.

6-Chloro-*5H-naphtho[2,1-b]pyrido[2,3-e][1,4]oxazin-5-one, 8*. By method similar to preparation of compound **7**, 6-chloro-*5H*-naphtho[2,1-b]pyrido[2,3-e][1,4]oxazin-5-one, **8** was prepared from 2-aminopyridin-3-ol (2.20 g, 20 m*M*), 2,3-dichloro-1,4-napthoquinone (4.54, 20 m*M*), KOH (2.24 g, 20 m*M*), and methanol (100 mL) as yellow-orange solid and recrystallized from acetone after treatment with activated carbon. Yield = 4.47 g (81%), melting point: 207–208°C. δ_H (400 MHz $CDCl_3$): 8.84–8.82 (1H, m); 8.62–8.61 (1H, dd, J = 8.61); 8.32–8.30 (1H, m); 7.79–7.76 (3H, m), 7.45–7.43 (1H, dd, J = 7.45). δ_c (600 MHz $CDCl_3$): 177.27 (carbonyl carbon), 150.23, 147.27, 146.09, 144.37, 140.68, 133.11, 132.93, 131.37, 129.83, 126.82, 126.21, 125.95, 124.59, 115.90. UV–visible λ_{max} (MeOH): 350.5 (7.38); 441.0 (7.47); 746 (7.03). IR (ν_{max} cm^{-1}): 1650, 1565, 1560, 1555, 1420, 1330, 1900, 1270, 1230, 1120, 1100, 1030, 920, 870, 810, 775, 710, 690. *Anal.* Calcd. for $C_{16}H_8ClNO_2$: C, 68.22; H, 2.86; Cl, 12.58; N, 4.97. Found: C, 68.39; H, 3.02; Cl, 12.77; N, 5.10.

The general procedure for Suzuki cross-coupling reactions. To an oven dried 10-mL round-bottom flask containing 2 mL of CH_3CN and 1 mL of water was charged with RX (1 m*M*), $RB(OH)_2$ (1.2 m*M*), and K_3PO_4 (588 mg, 3 m*M*), and the entire reaction mixture degassed for ½ h by gentle bubbling of nitrogen gas through the reaction vessel while stirring gently with magnetic bar. The reaction temperature was gradually increased to 40°C before Pd $(OAc)_2$ (8.92 mg, 4 mol%), XPhos (32.5 mg, 7 mol%) were added, and reaction vessel was immediately corked with rubber septum. The reaction left under the temperature of 30°C for 30 min before raising to 80°C. After 5–8 h, the reaction was cooled to room temperature, and solvent evaporated in a vacuum. This was followed by addition of 5 mL of water, and crude product extracted with dichloromethane (DCM) (10 mL × 4). The combined organic extracts were dried with $MgSO_4$, and crude product was purified by flash column chromatography on silica gel.

***(E)*-2-Styryl-10H-phenothiazine, 9*.** The general procedure was used to convert styryl boronic acid and 2-chloro-10*H*-phenothiazine to the title product in 6 h. Purification by flash chromatography (5% EtOAc/95% pet ether as the eluent) gave the analytically pure product as yellow solid, mp 168–169°C; % yields = 202 mg (67%). δ_H (400 MHz, $CDCl_3$): 7.85(1H, s, br, N–H proton); 7.43–7.37 (1H, m); 7.23–7.20 (1H, m); 7.13–7.11 (1H, m); 6.88–6.86 (1H, m); 6.90–6.76 (3H, m); 6.71–6.66 (3H, m), 6.61–6.56 (3H, m). δ_c (600 MHz, $CDCl_3$: 144.67, 142.38, 138.40, 133.69, 133.40, 130.24, 129.52, 129.31, 128.46, 128.39, 128.13, 127.32, 127.23, 123.38, 122.39, 118.03, 117.34, 115.69, 115.63, 115.03, 114.98. UV–visible λ_{max} (MeOH): 644.5 (6.87); 746 (7.03). MS (AP), *m/z* (% relative intensity): 59.05(17), 80.05(12), 100.07(100), 117.09(72), 118.10(6), 167.08(2), 198.05(2), 199.05(18), 200.06(4), 233.01(28), 234.02(16), 235.01(12), 236.01(5), 275.04(20), 301.10[(8),M^+], 302.11 [(20),M^++1]. *Anal.* Calcd. for $C_{20}H_{15}NS$: C, 79.70; H, 5.02; N, 4.65; S, 10.64. Found: C, 79.51; H, 5.17; N, 4.70; S, 10.58.

***(E)*-6-Styryl-5H-benzo[a]phenothiazin-5-one, 10*.** The general procedure was employed to convert styrylboronic acid and 6-chlorobenzo-5*H*-phenothia-5-one to the title product in 8 h. Purification by flash column chromatography with 10% EtOAc/90% pet ether as eluent gave analytically pure product as dark purple solid, mp 181–183°C. Yield = 181 mg (60%). δ_H (400 MHz, $CDCl_3$): 8.80–8.78 (1H, m); 8.28–8.26 (1H, m); 7.88–7.84 (2H, m); 7.69–7.65 (2H, m), 7.57–7.55 (2H, dd, J = 7.56); 7.43–7.39 (2H, m); 7.36–7.32 (3H, m), 7.27–7.24 (1H, t, J = 7.25); 7.07–7.03(1H, d, J = 7.05). δ_c (600 MHz, $CDCl_3$): 179.30 (carbonyl carbon, C=O), 145.28, 138.79, 138.44, 137.72, 134.25, 132.81, 132.52, 131.62, 131.22, 129.58, 128.75, 128.75, 128.47, 127.95, 127.07, 126.29, 125.46, 124.94, 123.43, 120.57.

UV–visible λ_{max} (MeOH): 267.5 (8.12); 286.0 (8.05); 330 (7.89); 495.5(7.88); 814 (6.89). MS (AP), *m/z* (% relative intensity): 124.07(45), 166.12(2), 231.11(2), 275.07(5), 348.09(7), 349.09 [(100), M^+], 350 [(10), M^+ +1]. *Anal*. Calcd. for $C_{24}H_{15}NOS$: C, 78.88; H, 4.14; N, 3.83; S, 8.77. Found: C, 78.91; H, 4.11; N, 4.02; S, 8.82.

(E)-6-Styryl-5H-benzo[a]phenoxazin-5-one, 11. General protocol was applied in the conversion of styrylboronic acid and 6-chlorobenzo-5*H*-phenoxazin-5-one to the title product in 8 h. Analytical pure product was obtained by flash column chromatography using 10% EtOAc/ 90% pet ether eluent as dark purple solid, mp: dec. above 185–187°C. Yields = 179 mg (51%). δ_H (400 MHz, $CDCl_3$): 8.60–8.58 (1H, m); 8.24–8.22 (1H, m); 8.04–8.00 (1H, d, *J* = 8.02); 7.74–7.63 (3H, m); 7.56–7.48 (3H, m); 7.44–7.38(3H, m); 7.34–7.22(3H, m). δ_c (600 MHz, $CDCl_3$): 182.88 (carbonyl carbon, C=O), 147.13, 146.62, 144.21, 138.45, 136.34, 133.12, 131.99, 131.72, 131.19, 130.97, 129.66, 128.10, 126.96, 126.37, 125.42, 124.47, 117.73, 115.79, 114.98. UV–visible λ_{max} (MeOH): 287.5(7.81); 313.0 (8.01); 491.0 (7.43); 643.5(7.01); 737 (6.98); 809 (7.10). MS (AP), *m/z* (% relative intensity): 74.06(3), 90.01(9), 92.01(5), 116.06(5), 322.12(1), 343.90(4), 350.11[(100), M^+-1], 351.11[(30), M^+-2]. *Anal*. Calcd. for $C_{24}H_{15}NO_2$: C, 82.51; H, 4.33; N, 4.01. Found: C, 82.21; H, 4.53; N, 4.21.

(E)-6-Styryl-5H-naphtho[2,1-b]pyrido[2,3-e][1,4]oxazin-5-one, 12. General protocol was applied in the conversion of styrylboronic acid and 6-chlorobenzo-5*H*-naphtho[2,1-b]pyrido[2,3-e]oxazin-5-one to the title product in 8 h. Purification by flash column chromatography (40% EtOAc/ 60% pet ether eluent) gave the analytical pure product as dark purple solid, mp: dec above 170°C. Yields = 228 mg (65%). δ_H (400 MHz, $CDCl_3$): 8.75–8.73 (1H, dd, *J* = 8.74); 8.53–8.51 (1H, dd, *J* = 8.52); 8.25–8.22 (1H, dd, *J* = 8.24); 8.05–8.01 (1H, d, *J* = 8.03); 7.71–7.65(3H, m); 7.55–7.53 (2H, d, *J* = 7.54); 7.44–7.40 (1H, d, *J* = 7.42); 7.37–7.30 (3H, m); 7.26–7.24(1H, m). δ_c (600 MHz, $CDCl_3$): 182.85 (carbonyl carbon, C=O), 151.41, 146.71, 145.58, 145.03, 138.07, 137.73, 132.72, 132.49, 131.93, 128.75, 128.50, 127.07, 126.52, 125.56, 125.47, 124.05, 117.25. UV–visible λ_{max} (MeOH): 306.0 (8.99); 450.0 (7.65); 749.5 (6.87). MS (AP), *m/z* (% relative intensity): 75.04(3), 90.01(36), 92.01(12), 116.07(6), 126.03(1), 279.09(1), 338.34(3), 351.11[(100), M^+-1], 352.11[(25), M^+-2]. *Anal*. Calcd. for $C_{23}H_{14}N_2O_2$: C, 78.84; H, 4.03; N, 8.00. Found: C, 79.02; H, 4.15; N, 8.14.

2-Phenyl-10H-phenothiazine, 13. General protocol was applied in the conversion of phenylboronic acid and 2-chloro-10*H*-phenothiazine to obtain the title product in 6 h. Analytical pure product was obtained as yellow solid by flash column chromatography (5% EtOAc/95% pet ether eluent), mp: 146–147°C; % yields = 195 mg (71%). δ_H (400 MHz, $CDCl_3$): 7.85 (1H, br, s, N–H proton), 7.44–7.42 (2H, d, *J* = 7.43), 7.31–7.27 (2H, m); 7.22–7.18 (1H, m); 6.96–6.94 (1H, dd, *J* = 6.95); 6.89–6.81 (4H, m); 6.68–6.60 (2H, m). δ_c (600 MHz, $CDCl_3$): 143.72, 143.13, 141.39, 141.22, 129.68, 128.36, 128.27, 127.54, 127.29, 127.21, 122.97, 121.45, 118.27, 117.75, 115.51, 113.79. UV–visible λ_{max} (MeOH): 504.5(7.21); 324.5(8.15). *Anal*. Calcd. for $C_{18}H_{13}NS$: C, 78.51; H, 4.76; N, 5.09; S, 11.64. Found: C, 78.38; H, 4.88; N, 5.20; S, 11.52.

6-Phenyl-5H-benzo[a]phenothiazin-5-one, 14. The general procedure was employed in conversion of phenylboronic acid and 6-chloro-5*H*-benzo[a]phenothiazin-5-one to provide the title product in 7 h. Purification by flash chromatography (10% EtOAc/90% pet ether eluent) gave analytical pure product as reddish solid, mp: dec above 180°C. Yield = 146 mg (43%). δ_H (400 MHz, $CDCl_3$): 8.85 (1H, d, *J* = 8.87); 8.30–8.27 (1H, dd, 8.28), 7.88–7.86 (1H, d, *J* = 7.87); 7.75–7.62 (3H, m); 7.51–7.36 (4H, m); 7.29–7.22 (3H, m). δ_c (600 MHz, $CDCl_3$): 178. 66 (carbonyl carbon, C=O), 144.80, 138 .32, 135.87, 134.62, 134.56, 132.85, 132 .31, 131. 92, 131.59, 131 .31, 129. 75, 129.50, 129.27, 129. 21, 128.76, 127.65, 126.12, 125.54, 124.84, 123.83, 115.27. UV–visible λ_{max} (MeOH): 368.5 (7.46); 482.0 (7.45); 748.5 (7.07). MS (AP), *m/z* (% relative intensity): 74.06(1), 90.01(7), 92.10(4), 116.07(2), 252.05(1), 298.01(1), 338.35(1), 340.08[(100), M^+-1], 341.08[(29), M^+-2]. *Anal*. Calcd. for $C_{22}H_{13}NOS$: C, 77.85; H, 3.86; N, 4.13; S, 9.45. Found: C, 78.02; H, 4.01; N, 4.24; S, 9.56.

6-Phenyl-5H-benzo[a]phenoxazin-5-one, 15. The general procedure was used to convert phenylboronic acid and 6-chloro-5*H*-benzo[a]phenoxazin-5-one to provide the title product in 7 h. Purification by flash column chromatography (10% EtOAc/ 90% pet ether eluent) supplied the analytical pure product as orange solid, mp: dec above 219°C. Yields = 174 mg (54%). δ_H (400 MHz, $CDCl_3$): 8.69–8.67 (1H, d, *J* = 8.68); 8.28–8.27 (1H, d, *J* = 8.27); 7.74–7.67 (3H, dd, *J* = 7.71); 7.45–7.43 (4H, d, *J* = 7.44); 7.35–7.33 (2H, d, *J* = 7.37); 7.08–7.06 (1H, d, *J* = 7.07). δ_c (600 MHz, $CDCl_3$): 182.37 (carbonyl carbon, C=O), 147.39, 146.83, 144.11, 132.84, 132.03, 131.98, 131.83, 131.24, 131.04, 130.91, 130.68, 129.58, 128.07, 127.97, 126.49, 125.14, 124.51, 119.38, 116.01. UV–visible λ_{max} (MeOH): 309.0 (8.87); 445.0 (8.96); 749 (6.60). MS (AP), *m/z* (% relative intensity): 74.06(2), 90.01(3), 115.09(3), 282.05(3), 324.12[(100), M^+-1], 325.13 [(25), M^+-2]. *Anal*. Calcd. for $C_{22}H_{13}NO_2$: C, 81.72; H, 4.05; N, 4.33. Found: C, 81.91; H, 4.16; N, 4.21.

6-Phenyl-5H-naptho[2,1-b]pyrido[2,3-e][1,4]oxazin-5-one, 16. The general procedure was used to convert phenylboronic acid and 6-chloro-5*H*- naphtho[2,1-b]pyrido[2,3-e][1,4] oxazin-5-one to the title product in 8 h. Analytical pure product was obtain by flash column chromatography (40% EtOAc/60% pet ether eluent) as red solid, mp: dec. above 238°C. Yield = 143 mg (44%). δ_H (400 MHz, $CDCl_3$): 8.88–8.85 (1H, m); 8.53–8.51 (1H, dd, *J* = 8.52); 8.31–8.29 (1H, m); 7.78–7.75 (2H, m); 7.47–7.44 (5H, m); 7.40–7.37 (1H, m), 7.32–7.29 (1H, dd, *J* = 7.31). δ_c (600 MHz, $CDCl_3$): 182.41 (carbonyl carbon, C=O), 151.75, 146.43, 145.95, 144.64, 140.91, 135.60, 132.94,

132.56, 131.91, 130.66, 130.55, 130.30, 129.56, 128.48, 128.33, 128.09, 127.56, 127.27, 126.65, 125.77, 125.57, 124.44, 120.63, 115.45. UV–visible λ_{max} (MeOH): 266.0 (8.96); 275.5 (8.83), 360.0 (8.63); 446.0 (8.15); 753.0 (6.55). MS(EI), *m/z* (% relative intensity): 65.0315(1), 83.9524(65), 104.0420(1), 162.0445(5), 189.0697(3), 214.0643(5), 240.0855(5), 266.0854(8), 295.0894(20), 312.1321(10), 323[(100), M^+ +1]. *Anal*. Calcd. for $C_{21}H_{12}N_2O_2$: C, 77.77; H, 3.73; N, 8.64. Found: C, 77.52; H, 3.85; N, 8.74.

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