Studies of palladium-catalyzed coupling reactions for preparation of hindered 3-arylpyrroles relevant to (–)-rhazinilam and its analogues

Léon Ghosez, Cécile Franc, Frédéric Denonne, Claire Cuisinier, and Roland Touillaux

Abstract: Suzuki cross-coupling reactions of 3-pyrroleboronic acid derivatives with haloaromatics and the reverse process i.e., the coupling of 3-iodo(bromo)pyrroles with arylboronic acids have been investigated as a potential key step in the synthesis of (–)-rhazinilam and analogues. It was found that 3-iodo-2-formyl-1-tosylpyrroles efficiently coupled with a variety of arylboronic acids in the presence of $PdCl_2$(dppf) as catalyst. This catalytic system is compatible with a broad spectrum of arylboronic acids — electron-rich, electron-poor, hindered, heterocyclic — which easily coupled with the pyrrole substrate.

Key words: 2-substituted-3-arylpyrroles, biaryls, coupling reactions, arylboronic acids, palladium coupling, catalysis.

Résumé : Nous avons étudié les réactions de couplage de Suzuki entre les acides 3-pyrroleboroniques et divers aromatiques halogénés ainsi que les réactions inverses de couplage entre les 3-iodo(bromo)- pyrroles avec des acides boroniques aromatiques. Cette réaction de couplage pourrait être une étape clé dans la synthèse du (–)-rhazinilame. Nous avons découvert que les 3-bromo- et 3-iodo-2-formyl-1-tosylpyrroles pouvaient être couplés efficacement avec un grand nombre d'acides boroniques en utilisant $PdCl_2$(dppf) comme catalyseur. Ce catalyseur permet d'introduire facilement une grande diversité d'acides arylboroniques (riches ou pauvres en électrons, encombrés ou hétérocycliques) en position 3 du pyrrole.

Mots clés : pyrroles 2-substitués-3-halogénés, biaryles, réactions de couplage, acides arylboroniques, couplage au palladium, catalyse.

Introduction

The pyrrole ring is common to many compounds which have found applications in the pharmaceutical field (1) and also in material sciences (see for example ref. 2). Not surprisingly, they have represented a continuous challenge for synthetic chemists (1, 3). In the context of a total synthesis of the alkaloid (–)-rhazinilam **1**, an inhibitor of microtubules disassembly (4) (Scheme 1), we became interested in the development of a convenient synthetic route towards 1,2-disubstituted-3-aryl pyrroles. Our goal was to develop a method applicable to the synthesis of the natural product and a large variety of simpler analogues **2**.

A literature survey indicated that efficient methods of synthesis of 1,2,3-trisubstituted pyrroles are not numerous (5). Most of them give rather low yields or lack generality. On the other hand, coupling reactions of aromatic compounds in the presence of Pd^0 or Ni^0 catalysts are nowadays part of the armamentarium of synthetic chemists (for a recent review see ref. 6). The palladium-catalyzed cross-coupling of arylboronic acids with aryl bromides or iodides was first described by Suzuki and co-workers (for recent reviews, see ref. 7). It has been shown to be applicable to the coupling of pyrrole derivatives with other aromatic compounds (8, 9). We selected a Suzuki coupling reaction of **3** with **4** as an attractive approach towards **2** since: (*i*) it is highly convergent; (*ii*) aryl- and heteroaryl halides as well as boron derivatives are easily available and readily undergo the cross-coupling reaction (see for example refs. 10, 11); (*iii*) the presence of a carbonyl or a carboxyl group at C-2 of the pyrrole should allow numerous transformations; (*iv*) a tosyl group on nitrogen should be a good model for a polymer-bound arylsulfonic group. An account of our first results was published in 1999 (12). Two more recent papers also report the

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This paper is dedicated to Professor Victor Snieckus in recognition of his important contribution to the development of organic synthesis.

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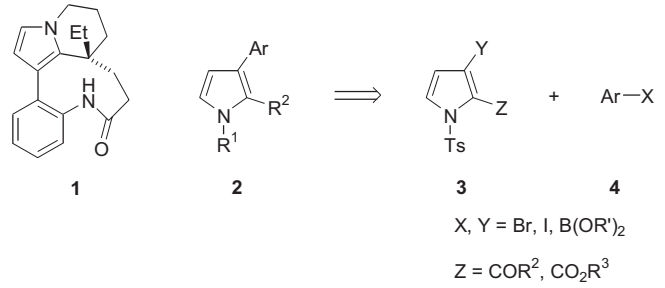
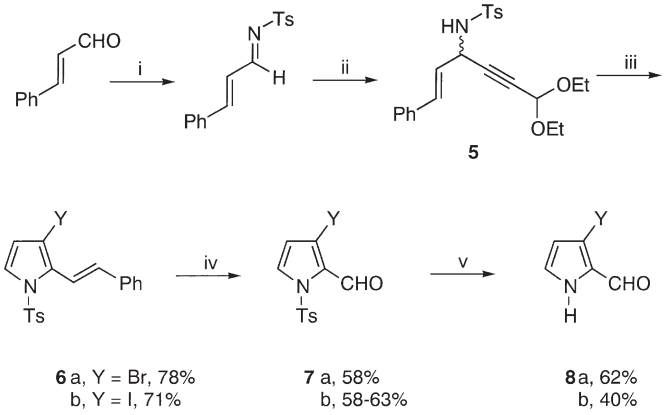
Scheme 1.



Scheme 2. Reagents and conditions: (*i*) $TsNH_2$, $BF_3{\cdot}OEt_2$, toluene, Δ; (*ii*) $HCCCH(OEt)_2$, *n*-BuLi, ether, –78°C then $ZnCl_2$ in ether, –78°C; (*iii*) 8.8 M HBr(aq) (9.5 equiv), 15 min, 80°C or 57% HI(aq) (7 equiv), 1 h, –10°C; (*iv*) $KMnO_4$ (3 equiv), H_2O–dioxane, 1 h, rt; (*v*) same as (*iv*) but at 90°C, yield from **5**.



use of a cross-coupling reaction involving substituted 3-iodopyrroles for the synthesis of analogues of (–)-rhazinilam (13). We now report the full details of our studies.

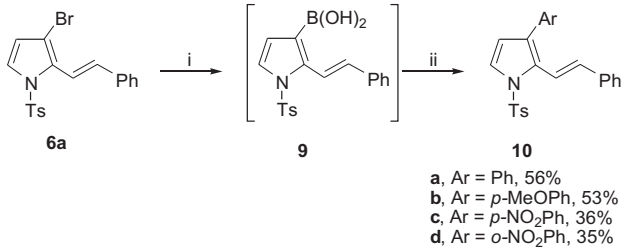
Synthesis of 1,2-disubstituted 3-halopyrroles

Our strategy required an easy access to 3-halopyrroles **3** (Y = Br, I) and the corresponding boronic acid (Y = $B(OH)_2$). We selected the efficient method described by Masquelin and Obrecht (3) using aldimines and acetylenic acetals or ketones as starting materials. Compound **5** was obtained in excellent yields as described (Scheme 2).

However, very low yields (<3%) of **6a** were obtained from the treatment of **5** with 2.4 M aq HBr as described by the authors. The use of a more concentrated HBr solution at 80°C for 15 min gave **6a** in 78% yield. Similarly, treatment of **5** with 57% aq HI gave a 71% yield of **6b** if the temperature was kept at –10°C to avoid degradation of the product under these strongly acidic conditions. This practical sequence has been applied to the preparation of up to 23 g of **6a** and 43 g of **6b**.

Pyrroles are extremely sensitive to oxidizing agents (1). However, the selective oxidation of the olefinic double bond of a 3-vinylpyrrole bearing an electron-withdrawing benzenesulfonyl group on nitrogen has been successfully performed with $NaIO_4$–OsO_4 cat (14). However, under these conditions, the oxidation of the styryl double bond of **6a**, **6b** took approximately 5 days. The oxidative cleavage with aq $KMnO_4$ was much faster. At room temperature, the products were the expected aldehydes **7a**, **7b**. At 90°C, hydrolytic cleavage of the tosyl group simultaneously occurred to yield **8a**, **8b**.

Scheme 3. Reagents and conditions: (*i*) *t*-BuLi in hexane, THF, –78°C then $B(OMe)_3$, –78°C then H_2O–MeOH, work-up; (*ii*) compound **9** (1.5 equiv), ArX (1 equiv), benzene–water–methanol (5:1.5:1), $Ba(OH)_2$ (1.5 equiv), $Pd(PPh_3)_4$ (5%), reflux.



Coupling reactions with 1-tosyl-2-styrylpyrrole boronic acid (9)

We first studied the synthesis of pyrroleboronic acid **9** and its coupling reaction with aryl iodides. Compound **9** was obtained from **6a** by a metal-bromide exchange with *t*-BuLi followed by treatment with trimethylborate and hydrolysis (Scheme 3).

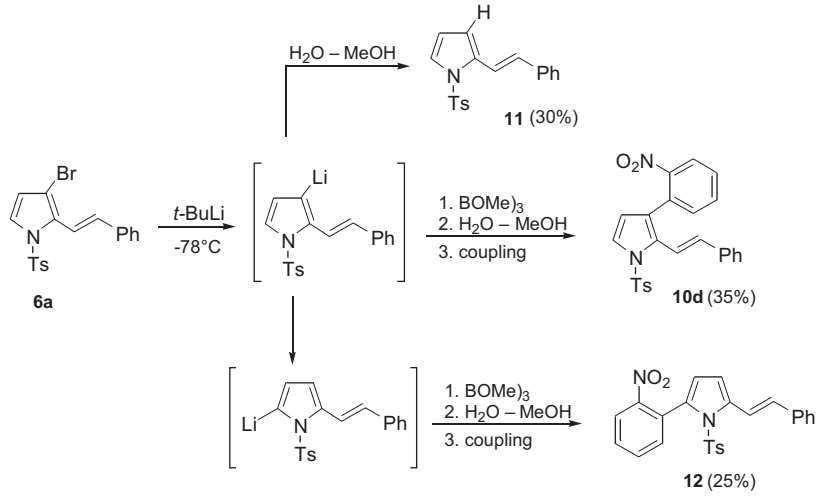
Compound **9** was used without purification. The coupling reactions were performed under the conditions described by Muchowski (8*a*) for related cases. Yields were moderate with phenyl iodide and *o*-iodoanisole. However the presence of an electron-withdrawing nitro group in *para* or *ortho* position of the iodide considerably lowered the yields. The coupling of **9** with *o*-iodonitrobenzene was of special interest in the context of the rhazinilam problem. Next to the expected coupling product **10d**, we found a reduction product **11** (30%) and, more surprisingly, a compound **12** (25%) resulting from a coupling at position 5 of pyrrole **9** (Scheme 4).

We were able to show that the reduction product was formed as a result of the incomplete conversion of the organolithium intermediate into the corresponding boronic acid. Product **12** could be the result of an isomerization of the 3-lithio compound to the thermodynamically more stable 5-lithio isomer. There was little hope to improve the yields of **10d** by bringing the temperature further down; this would probably slow down the isomerization of the organolithium compound but also increase the amount of reduction product. We thus decided to study the Suzuki coupling reactions between 3-bromo- or 3-iodo-pyrrole derivatives **6a**, **6b** and **7a**, **7b** with various arylboronic acids.

Study of the coupling conditions of 1,2-disubstituted-3-halopyrroles with arylboronic acids

We first examined the reaction of **6b** with the commercially available phenylboronic acid **13a**. We used $Ba(OH)_2$ (15) as base (Scheme 5, Table 1). In the presence of $Pd(PPh_3)_4$ as catalyst, no coupling product **10a** was obtained in solvent mixtures (entries 1 and 2) which had been successfully used in similar coupling reactions (6, 7).

Scheme 4.



Scheme 5.

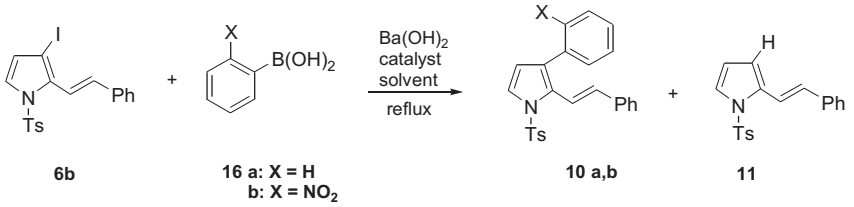


Table 1. Conditions for the cross-coupling of **6b** with phenyl- and *o*-nitrophenylboronic acids.

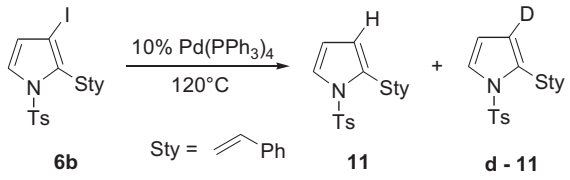
Entry	X	Catalyst	Solvent	*T* (°C)	Yield of **10** (%)	Yield of **11** (%)
1	H	5% $Pd(PPh_3)_4$	MeOH–C_6H_6–H_2O (1:3:2)	80	0	—
2	H	5% $Pd(PPh_3)_4$	DME–H_2O (2:1)	80	0	—
3	H	5% $Pd(PPh_3)_4$	DMF–H_2O (4:1)	80	86[a]	—
4	NO_2	10% $Pd(PPh_3)_4$	DMF–H_2O (4:1)	120	36[b]	64[b]
5	NO_2	10% $PdCl_2(PPh_3)_2$	DMF–H_2O (4:1)	120	50[b]	50[b]
6	NO_2	10% $PdCl_2$dppe	DMF–H_2O (4:1)	120	42[b]	58[b]
7	NO_2	10% $PdCl_2$dppf	DMF–H_2O (4:1)	120	80[a]	—
8	NO_2	10% $PdCl_2$dppf	DMF–H_2O (4:1)	120	73[a]	—

[a]Isolated pure coupling products.
[b]NMR yields.

Table 2. Hydrodeiodination of **6b**.

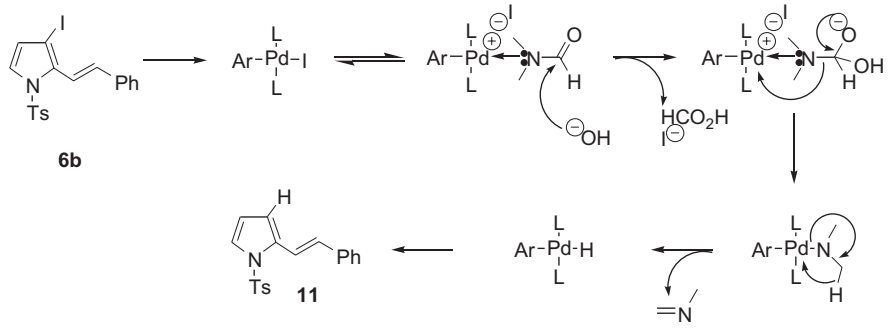
Entry	Base	Solvent	Product
1	None	DMF–H_2O (1:1)	**6b**
2	$Ba(OH)_2$	$MeCONMe_2$–H_2O (1:1)	**6b**
3	$Ba(OH)_2$	DMF–D_2O (1:1)	**11**
4	$Ba(OH)_2$	$DCONMe_2$–H_2O (1:1)	**11**
5	$Ba(OH)_2$	$DCON(CD_3)_2$–H_2O (1:1)	**d-1**

Scheme 6.

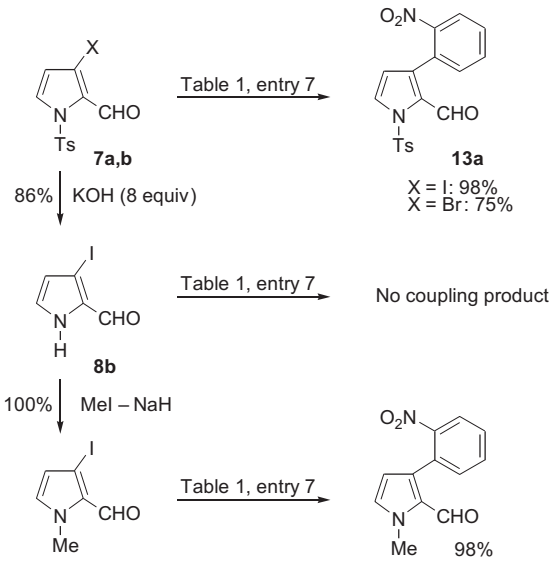


Running the coupling reaction in a more polar solvent (entry 3) led to a high yield of **10a**. The accelerating effect of a polar solvent such as DMF had been used before to effect Suzuki coupling reactions (15*b*, 15*e*) of bromo- and iodo-pyrroles (9*a*). However, when we applied these conditions to the coupling of **6b** with the electron-deficient and hindered *o*-nitrophenylboronic acid, we observed a dramatic decrease of the yield of coupling product **10b**, even at higher temperatures (entry 4). The presence of chloride ion (16) or the use of a bidentate phosphine (17) such as dppe (18) (entries 5 and 6) did not much improve the yield of coupling product **10b**. The major product **11** of the reaction resulted

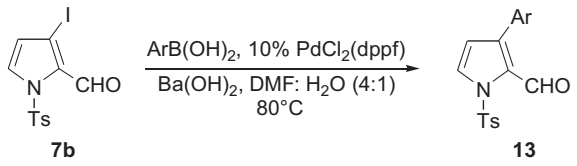
Scheme 7.



Scheme 8.



Scheme 9.



from the reductive cleavage of the carbon—iodine bond. We also observed variable amounts of nitrobenzene resulting from a base-catalyzed hydrolysis of *o*-nitrophenylboronic acid (19).

The use of 1,1′-bis(diphenylphosphino)ferrocene (dppf) bidentate ligand (20*a*, 20*b*; for a more recent example see ref. 20*c*) on palladium led to a significant increase of rate and yield (entries 7 and 8); the reaction was over in a few minutes even at 80°C and yields of coupling product **10b** were up to 80%. After completion of our work, Buchwald, Hermann, Fu and co-workers (21) reported new efficient catalysts for Suzuki cross-coupling reactions. However, no cross-coupling reactions involving a pyrrole derivative was described and we have not examined these new catalysts.

The palladium-catalyzed dehalogenation of aromatic compounds has been abundantly documented (review see ref. 22). Hydrodehalogenation products have sometimes been observed as by-products of Pd-catalyzed cross-coupling reactions (23). In these cases, water or tertiary amines have been assigned the role of hydride donors. In Table 2, we describe a study of the hydrodeiodination reaction of **6b** (Scheme 6).

It shows that: (*i*) no hydrodeiodination was observed in the absence of base or when DMF was replaced by *N*,*N*-dimethylacetamide (entries 1 and 2); (*ii*) no incorporation of deuterium was observed in the presence of D_2O or $Me_2NC(O)D$ (entries 3 and 4); (*iii*) incorporation of deuterium at C-3 of **11** occurred when the reaction was run in $(D_3C)_2NC(O)D$ (entry 5). These observations were rationalized by the mechanism outlined in Scheme 7.

We have successfully applied the conditions of Table 1, entry 7 to the coupling of 2-formyl-3-halo-1-tosylpyrroles **7a**, **7b** with *o*-nitrophenylboronic acid (Scheme 8). Under these conditions, $Ba(OH)_2$ did not add to the aldehyde function of **7a**, **7b** (NMR control) and was thus available for the coupling reaction.

As expected, the reaction of iodopyrrole was much faster than that of the corresponding bromide and gave a higher yield of **13a**. The coupling reaction could also be effected in very high yield on the *N*-methylated pyrrole but did not occur when nitrogen was unsubstituted.

Generalization of the coupling reaction

With these optimized conditions in hand, we carried out the cross-coupling reaction of **7b** with a wide variety of aryl and heteroarylboronic acids (Scheme 9, Table 3).

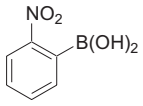
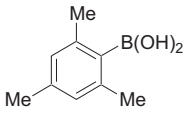
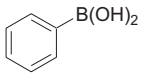
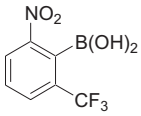
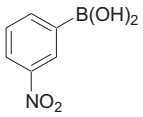
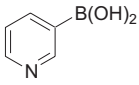
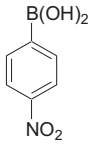
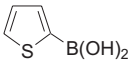
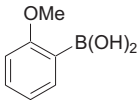
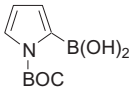
High yields of cross-coupled 1,2-disubstituted-3-arylpyrroles have been obtained. The reaction tolerates both electron-rich and electron-poor arylboronic acids. It could also be applied successfully to the coupling of **7b** with the sterically hindered mesitylboronic acid.

The electron-poor 2-nitro-6-(trifluoromethyl)phenylboronic acid **14** was prepared by nitration of 2-(trifluoromethyl)-phenylboronic acid (Scheme 10). The conditions described for the nitration of boric acid (28), gave no reaction and sulfuric acid had to be used to obtain **14** in a 42% yield, together with its isomer **15** (12%). However, 2-nitro-6-(trifluoromethyl)phenylboronic acid **14** gave no coupling product. Interestingly, the corresponding aniline **16** gave 3-tosyl-9-(trifluoromethyl)-3*H*-pyrrolo[2,3-*c*]-quinoline **17** in 26% yield (Scheme 10).

This illustrates a further application of this coupling reaction for the synthesis of pyrroles fused to other heterocycles. However, at this stage, we did not try to optimize the reaction.

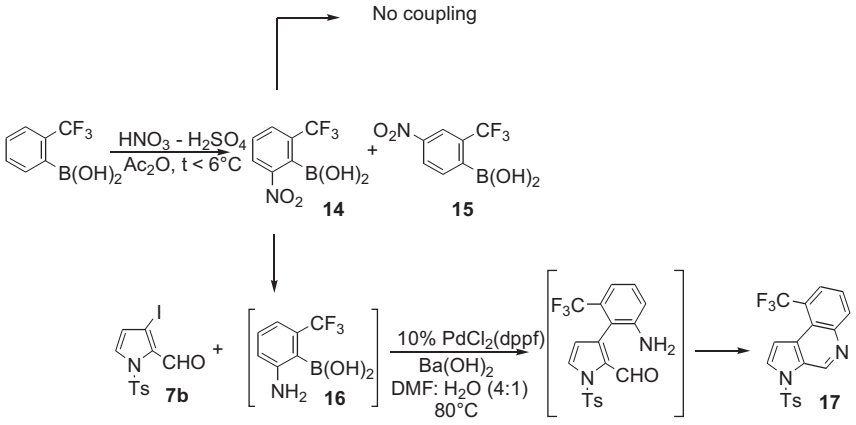
In conclusion, we have fulfilled our goal and developed a practical synthetic route towards 1,2-disubstituted-3-aryl-(heteroaryl)pyrroles. The method should offer the possibility of

Table 3. Cross-coupling reactions of iodopyrrole **7b** with aryl- and heteroarylboronic acids.

$ArB(OH)_2$	Ref.	Yield[a]	$ArB(OH)_2$	Ref.	Yield[a]
	(24)	98		(25)	61
	[b]	92			-
	[b]	88		[b]	66
	(24)	84		(26)	85
	[b]	88		(27)	77

[a]Yield of isolated pure products.
[b]Commercially available.

Scheme 10.



building libraries of a wide variety of 2-substituted-3-arylpyrroles or polycyclic heteroaromatics derived therefrom using a polystyrene-bound 2-formyl-3-iodo-1-sulfonylpyrrole. Further applications of these findings to the total synthesis of (–)-rhazinilam and analogues will be reported in due course.

Experimental

General

Melting points were taken on Buchi Melting Point B-545 or on a Microthermal 8103 apparatus. NMR experiments

were performed on GEMINI-200, GEMINI-300, and Brucker AM-500 spectrometers. Internal standards were TMS (^{1}H NMR) and $CDCl_3$ (77.23 ppm, ^{13}C NMR). IR spectra were recorded on PerkinElmer 681 and Bio-Rad FTS 135 spectrometers (polystyrene ref. 1601 cm^{-1}). Mass spectra were recorded on Varian MAT-44 or FINNIGAN-MAT TSQ-70 spectrometers (electronic impact 70 eV or chemical ionization 100 eV with 2 μbar isobutane as the ionizing gas).

Tetrakis(triphenylphosphine)palladium (29) and dichloro-(diphenylphosphinoferrocene)palladium (30), *o*-nitrophenylboronic and *p*-nitrophenylboronic acids were prepared as described in the literature (28). Unless otherwise noted, the other boronic acids used were purchased from commercial sources. THF and toluene were distilled from sodium-benzophenone. Organic phases were dried over magnesium sulphate. Solvents were degassed by bubbling argon for at least 15 min. Chromatographic separations were performed with silica gel purchased from Merck (thickness 40–63 μm)

*3-Bromo-2-styryl-1-tosylpyrrole (**6a**) (RN: 168030-84-0)*

To a solution of *(E)-N*-(4,4′-diethoxy-1-styrylbut-2-ynyl)-4-toluenesulfonamide (3) (18 g, 45 mmol) in toluene (100 mL) was added bromohydric acid (48% aqueous, 48 mL, 425 mmol). The reaction mixture was stirred for 10 min at 80°C and then allowed to cool to room temperature. It was poured into ice and ether, sodium hydroxide (14.4 g, 360 mmol) was then added, and the pH adjusted to 7 with 1 N aqueous sodium hydroxide. The aqueous phase was extracted with ether, the organic layers were washed with brine, dried and concentrated in vacuo. Purification by flash chromatography on silica gel (10% diethyl ether in petroleum ether) Yield of **4**: 14.1 g, 78%, pale yellow solid (mp 97°C). R_f = 0.38 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z* (IE, 70 eV): 403 (100, $[M + 2]^{\bullet+}$), 401 (80, $M^{\bullet+}$), 249 (18, $[M + 2\text{-Tos} + H]^{\bullet+}$), 247 (20, $[M\text{-Tos} + H]^{\bullet+}$), 168 (48), 167 (97, (249 and 247 -Br)$^{\bullet+}$), 166 (14), 139 (14). IR: 3149–3025, 1596, 1469, 1371, 1145–1089, 1028, 965. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.67 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.49 (d, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.38 (t, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.36 (d, ^3J = 16.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 7.33 (d, ^3J = 3.4 Hz, 1H, $NCHCH$), 7.35–7.22 (m, 1H, $CHC(CHCH)_2CH$), 7.23 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.20 (d, ^3J = 16.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 6.35 (d, ^3J = 3.4 Hz, 1H, $NCHCH$), 2.36 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 145.33 ($NSO_2C(CHCH)_2CCH_3$), 136.81 ($CHC(CHCH)_2CH$), 135.27 ($NSO_2C(CHCH)_2CCH_3$), 133.81 ($CHC(CHCH)_2CH$), 129.19 (NCC), 129.85 ($NSO_2C(CHCH)_2CCH_3$), 128.65 ($CHCHC(CHCH)_2CH$), 128.05 ($CHCHC(CHCH)_2CH$), 127.13 ($NSO_2C(CHCH)_2CCH_3$), 126.47 ($CHCHC(CHCH)_2CH$), 122.32 ($NCHCH$), 116.15 ($NCHCH$), 115.18 ($CHCHC(CHCH)_2CH$), 102.13 (NCC), 21.48 (CH_3).

*3-Iodo-2-styryl-1-tosylpyrrole (**6b**) (RN: 233770-17-7)*

To a solution of *(E)-N*-(4,4′-diethoxy-1-styrylbut-2-ynyl)-4-toluenesulfonamide **5** (3) (25 g, 61 mmol) in toluene (200 mL) at –10°C was added iodohydric acid (57% aqueous, 57 mL, 424 mmol). The mixture was stirred for 1 h at room temperature then poured into ice and ether. Sodium hydroxide (13.3 g, 333 mmol) was then added and the pH adjusted to 7 with 1 N aqueous sodium hydroxide. The aqueous phase was extracted with ether, the combined organic layers washed with brine, dried and concentrated in vacuo. Purification by flash chromatography on silica gel (10% diethyl ether in petroleum ether) Yield of **4**: 19 g, 71%, pale solid (mp 119°C). R_f = 0.7 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 449 (100, $M^{\bullet+}$), 335 (18), 279 (18), 167 (33). HRMS calcd. for $C_{19}H_{16}INO_2S$: 448.9946; found: 448.9950. IR: 1369, 1175, 670. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.65 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.49 (d, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.39 (t, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.34 (d, ^3J = 3.4 Hz, 1H, $NCHCH$), 7.31 (m, 1H, $CHC(CHCH)_2CH$), 7.29 (d, ^3J = 16.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 7.21 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.12 (d, ^3J = 16.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 6.43 (d, ^3J = 3.4 Hz, 1H, $NCHCH$), 2.37 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 500 MHz) δ: 145.30 ($NSO_2C(CHCH)_2CCH_3$), 136.53 ($CHC(CHCH)_2CH$), 135.21 ($NSO_2C(CHCH)_2CCH_3$), 134.74 ($CHC(CHCH)_2CH$), 132.11 (NCC), 129.80 ($NSO_2C(CHCH)_2CCH_3$), 128.67 ($CHCHC(CHCH)_2CH$), 128.15 ($CHCHC(CHCH)_2CH$), 127.21 ($NSO_2C(CHCH)_2CCH_3$), 126.50 ($CHCHC(CHCH)_2CH$), 123.71 ($NCHCH$), 120.64 ($NCHCH$), 116.24 ($CHCHC(CHCH)_2CH$), 69.16 (NCC), 21.51 (CH_3).

*2-Formyl-3-bromo-1-tosylpyrrole (**7a**)*

To a solution of **6a** (0.1 g, 0.25 mmol) in dioxane (3 mL) was added potassium permanganate (0.2 g, 0.75 mmol) and water (1 mL). The mixture was stirred at room temperature for 1 h then treated with saturated aqueous sodium thiosulfate (1 mL), then with 1 N HCl until the mixture was discoloured. The aqueous phase was extracted with ethyl acetate, the combined organic layers were washed with brine, dried and concentrated in vacuo. Purification by flash chromatography on silica gel (20% diethyl ether in petroleum ether). Yield of **7a**: 52 mg, 58%, pale yellow solid (mp 70°C). R_f = 0.54 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 329 (15, $[M + 2]^{\bullet+}$), 327 (16, $M^{\bullet+}$), 265 (26, $[M + 2\text{-}SO_2]^+$), 263 (26, $[M - SO_2]^+$), 174 (24, $[M + 2\text{-}C_7H_7SO_2]^+$), 172 (23, $[M - C_7H_7SO_2]^+$), 155 (84, $[C_7H_7SO_2]^+$), 91 (100, $[C_7H_7]^+$). IR: 1677, 1373, 1175. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.84 (s, 1H, CHO), 7.87 (d, ^3J = 8.4 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.70 (d, ^3J = 3.3 Hz, 1H, $NCHCH$), 7.33 (d, ^3J = 8.4 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.48 (d, ^3J = 3.3 Hz, 1H, $NCHCH$), 2.43 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 176.89 (CHO), 145.46 ($NSO_2C(CHCH)_2CCH_3$), 133.79 ($NSO_2C(CHCH)_2CCH_3$), 129.24 ($NSO_2C(CHCH)_2CCH_3$), 128.52 (NCH), 127.53 ($NSO_2C(CHCH)_2CCH_3$), 127.33 ($NCCHO$), 115.11 (CBr), 114.84 ($NCHCH$), 20.97 (CH_3). Anal. calcd. for $C_{12}H_{10}BrNO_3S$: C 43.92, H 3.07, N 4.27; found: C 43.80, H 2.78, N 4.15.

*2-Formyl-3-iodo-1-tosylpyrrole (**7b**) (RN: 233770-15-5)*

To a solution of **6b** (17 g, 37.8 mmol) in dioxane (300 mL) was added potassium permanganate (17.9 g, 113.4 mmol) and water (150 mL). The mixture was stirred at room temperature for 1 h, then treated with a saturated aqueous sodium thiosulfate (100 mL) and with 1 N HCl until the mixture was discoloured. The mixture was stirred overnight. The pale yellow precipitate was filtered, dissolved in ethyl acetate, washed with brine, dried and concentrated in vacuo.

Purification by recrystallization from cyclohexane and ether. Yield of **7b**: 8.3 g, 58%, pale yellow solid (mp 104°C). R_f = 0.50 (30% diethyl ether in petroleum ether). MS (EI) *m/z* (70eV): 375 (46, M^+), 311 (44), 220 (34), 155 (72), 91 (100). IR: 3140, 1682, 1429, 1317, 1175, 668. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.79 (s, 1H, C*H*O), 7.84 (d, ^3J = 8.3 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.66 (d, ^3J = 3.3 Hz, 1H, NC*H*CH), 7.33 (d, ^3J = 8.3 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.60 (d, ^3J = 3.3 Hz, 1H, NCHC*H*), 2.42 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 178.7 (*C*HO), 145.89 ($NSO_2C(CHCH)_2CCH_3$), 134.45 ($NSO_2C(CHCH)_2CCH_3$), 130.00 (N*C*H), 129.76 ($NSO_2C(CHCH)_2CCH_3$), 129.38 (N*C*CHO), 127.84 ($NSO_2C(CHCH)_2CCH_3$), 120.58 (NCH*C*H), 82.17 (*C*I), 21.51 (CH_3). Anal. calcd. for $C_{12}H_{10}INO_3S$: C 38.42, H 2.69, N 3.73; found: C 38.32, H 2.49, N 3.62.

*3-Bromo-2-formylpyrrole (**8a**)*

To a solution of **6a** (0.50 g, 1.24 mmol) in dioxane (10 mL) was added potassium permanganate (0.59 g, 3.73 mmol) and water (3 mL). The mixture was refluxed overnight then allowed to cool to room temperature and filtered on a Celite® pad. The organic layer was washed with sodium thiosulfate, brine, dried and concentrated in vacuo. Purification by flash chromatography on silica gel (30% diethyl ether in petroleum ether). Yield of **8a**: 134 mg, 62%, white solid (mp 118°C). R_f = 0.40 (40% diethyl ether in petroleum ether). MS (EI) *m/z* (70 eV): 175 (94, $[M + 2]^{\bullet+}$), 173 (100, $M^{\bullet+}$), 146 (20, $[M + 2\text{-}COH]^+$), 144 (20, $[M - COH]^+$). IR: 3238, 1635. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.82 (br s, 1H, N*H*), 9.59 (s, 1H, C*H*O), 7.07 (ddd, ^3J = 3.2 Hz, ^3J = 2.6 Hz, ^5J = 1.1 Hz, 1H, NC*H*CH), 6.39 (dd, ^3J = 2.6 Hz, ^4J = 2.4 Hz, 1H, NCHC*H*). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.47 (*C*HO), 129.0 (N*C*CHO), 125.77 (N*C*H), 114.24 (NCH*C*H), 109.34 (*C*Br). Anal. calcd. for C_5H_4BrNO: C 34.51, H 2.32, N 8.05; found: C 34.79, H 2.04, N 7.78.

*3-Iodo-2-formylpyrrole (**8b**) (RN: 40566-07-2)*

To a solution of **6a** (0.1g, 0.22 mmol) in dioxane (2 mL) was added potassium permanganate (0.1g, 0.66 mmol) and water (0.6 mL). The mixture was refluxed overnight then allowed to cool to room temperature and filtered on a Celite® pad. The organic layer was then washed with sodium thiosulfate, brine, dried and concentrated in vacuo. Purification by flash chromatography on silica gel (30% diethyl ether in petroleum ether). Yield of **8b**: 20 mg, 40%, white solid (decomposed at 128°C). R_f = 0.57 (50% diethyl ether in petroleum ether). MS (EI) *m/z* (70 eV): 221 (100, $M^{\bullet+}$), 220 (100, $[M - H]^+$), 192 (16, $[M - COH]^+$). IR: 3255, 1635, 1340, 758, 737. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 9.90 (br s, 1H, N*H*), 9.45 (s, 1H, C*H*O), 7.12–7.05 (m, 1H, NC*H*CH), 6.53 (t, ^3J = ^4J = 2.55 Hz, 1H, NCHC*H*). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 180.00 (*C*HO), 130.78 (*C*CHO), 126.98 (N*C*H), 119.21 (NCH*C*H), 77.23 (*C*I).

*2-Styryl-1-tosylpyrrole boronic acid (**9**)*

To a solution of 3-bromo-2-styryl-1-tosylpyrrole **6a** in dry THF (12 mL) at –78°C was added *t*-BuLi (1.7 M in pentane, 3.3 mL, 5.3 mmol). The mixture was stirred for 25 min and turned brown. A solution of trimethyl borate (2.8 mL, 25 mmol) in THF (50 mL) at –78°C was then added via cannula. The reaction mixture turned orange. After 45 min, the reaction was quenched by adding 0.5 mL of methanol and 0.5 mL of water. The solution was poured into water (20 mL), the aqueous phase extracted with diethyl ether. The combined organic phases were washed with brine, dried and concentrated in vacuo. The crude product was used in the coupling reaction without further purification.

Coupling reactions

Method A refers to the coupling reaction of 2-styryl-1-tosylpyrrole boronic acid **9** with iodoaryls: A mixture of aryliodide (1 equiv), crude boronic acid **9** (1.5 equiv, 0.16 M), barium hydroxide octahydrate (1.5 equiv), and tetrakis(triphenylphosphine)palladium (0.05 equiv) in a degassed mixture of water, methanol, and benzene (3:2:10) was refluxed for 16 h. It was then concentrated and the crude material was dissolved in ethyl acetate and filtered on a Celite® pad to remove metallic palladium. The filtrate was then dried and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Method B refers to the coupling reaction of 3-iodo-2-styryl-1-tosylpyrrole **6b** with an arylboronic acid: A mixture of 3-iodo-2-styryl-1-tosylpyrrole **6b** (1 equiv, 0.044 M), boronic acid (1.5 equiv), barium hydroxide octahydrate (1.5 equiv), and catalyst (0.05 or 0.1 equiv) in a degassed mixture of DMF and water (4:1) was placed in a bath which had been preheated to 120°C. After 20 min, it was cooled to room temperature and diluted with ethyl acetate and water. After filtration on a Celite® pad, the solution was washed with water, brine, dried and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Method C refers to the coupling reaction of 2-formyl-3-iodo-1-tosylpyrrole **7b** with an arylboronic acid: A mixture of 2-formyl-3-iodopyrrole (1 equiv, 0.044 M), aryl boronic acid (1.5 equiv), barium hydroxide octahydrate (1.5 equiv) and dichloro(diphenylphosphinoferrocene)palladium(II) (0.1 equiv) in a degassed mixture of DMF and water (4:1) was placed in a bath which had been preheated to 80°C. After 5 min, it was cooled to room temperature and diluted with ethyl acetate and water. After filtration on a Celite® pad, the solution was washed with water, brine, dried and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

*3-Phenyl-2-styryl-1-tosylpyrrole (**10a**)*

Method A: 1.36 g (3.71 mmol) of the crude boronic acid **9**, 0.5 g (2.47 mmol) of iodobenzene, 1.17 g (3.71 mmol) of barium hydroxide octahydrate, 57 mg (0.05 mmol) of tetrakis(triphenylphosphine)palladium. Eluent: 10% of diethyl ether in petroleum ether. Yield of **10a**: (560 mg, 56%).

Method B: 0.3 mg (0.7 mmol) of the 3-iodo-2-styryl-1-tosylpyrrole **6b**, 0.5 mg (1 mmol) of phenylboronic acid, 0.17 mg (1 mmol) of barium hydroxide octahydrate, and 38 mg (0.03 mmol) of tetrakis(triphenylphosphine)palladium. Eluent: 10% diethyl ether in petroleum ether. Yield of **10a**: 240 mg, 90%, white solid (mp 140°C). R_f = 0.74 (30% diethyl ether in petroleum ether). MS (CI) *m/z*: 400 (100, $[M + 1]^+$), 247 (46, $[400 - SO_2C_6H_4CH_3]^{\bullet+}$), 157 (16, $[SO_2C_6H_5CH_3 + 2H]^+$). HRMS calcd. for $C_{25}H_{22}NO_2S$: 400.1371; found: 400.1351. IR: 3148–2869, 1369, 1175, 1136. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.68 (d, ^3J = 8.4 Hz, 2H,

$NSO_2C(CHCH)_2CCH_3$), 7.41 (d, ^3J = 3.4 Hz, 1H, NC*H*CH), 7.41–7.38 (m, 2H), 7.38 (d, ^3J = 16.5 Hz, 1H, C*H*CHC(CHCH)$_2$CH), 7.32–7.28 (m, 4H), 7.25–7.19 (m, 4H), 7.20 (d, ^3J = 8.4 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.38 (d, ^3J = 16.5 Hz, 1H, CHC*H*C(CHCH)$_2$CH), 6.36 (d, ^3J = 3.4 Hz, 1H, NCHC*H*), 2.35 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 144.86 ($NSO_2C(CHCH)_2CCH_3$), 137.03 (CHC(CHCH)$_2$CH), 135.88 ($NSO_2C(CHCH)_2CCH_3$), 135.35 (CC(CHCH)$_2$CH), 133.99 (CHC(CHCH)$_2$CH), 129.68 ($NSO_2C(CHCH)_2CCH_3$), 128.58 (CC(CHCH)$_2$CH), 128.54 (CHC(CHCH)$_2$CH), 128.47 (NCC), 128.41 (CC(CHCH)$_2$CH), 127.68 (CHC(CHCH)$_2$CH), 127.20 ($NSO_2C(CHCH)_2CCH_3$), 127.17 (NCC), 126.76 (CC(CHCH)$_2$CH), 126.18 (CHCHC(CHCH)$_2$CH), 122.57 (NCHCH), 116.35 (CHCHC(CHCH)$_2$CH), 113.45 (NCHCH), 21.48 (CH_3).

*3-(*o*-Methoxyphenyl)-2-styryl-1-tosylpyrrole (**10b**)*

Method A: 1.36 g (3.71 mmol) of the crude boronic acid **9**, 0.58 g (2.47 mmol) of *o*-iodomethoxybenzene, 1.17 g (3.71 mmol) of barium hydroxide octahydrate, 57 mg (0.05 mmol) of tetrakis(triphenylphosphine)palladium. Eluent: 10% diethyl ether in petroleum ether. Yield of **10c**: 0.56 g, 53%, yellow solid (mp 147°C). R_f = 0.56 (30% diethyl ether in petroleum ether). MS (CI) *m*/*z*: 430 (57, $[M + 1]^+$), 275 (100, $[M + 1\text{-}C_7H_7SO_2]^{\bullet+}$). HRMS calcd. for $C_{26}H_{24}NO_3S$: 430.1476; found: 430.1459. IR: 1594, 1496, 1369, 1178, 1137, 671. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.71 (d, ^3J = 8.2 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.47 (d, ^3J = 16.5 Hz, 1H, CHCHC(CHCH)$_2$CH), 7.41 (d, ^3J = 3.4 Hz, 1H, NCHCH), 7.30–7.20 (m, 7H, CHC(CHCH)$_2$CH and $NSO_2C(CHCH)_2CCH_3$), 6.91 (dt, ^3J = 8.2 Hz, ^4J = 1.2 Hz, 1H, $CH_3OCCCHCH$), 6.90 (d, ^3J = 8.2 Hz, 1H, CH_3OCCH), 6.85 (m, 2H, $CH_3OCCHCHCH$), 6.37 (d, ^3J = 3.4 Hz, 1H, NCHCH), 6.25 (d, ^3J = 16.5 Hz, 1H, CHCHC(CHCH)$_2$CH), 3.02 (s, 3H, CH_3), 2.35 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 156.60 (CH_3OC), 144.69 ($NSO_2C(CHCH)_2C$), 137.37 (CHCHC(CHCH)$_2$C), 136.05 (NSO_2C), 131.97 (CHCHC(CHCH)$_2$CH), 131.29 (CH_3OCCCH), 129.65 ($NSO_2C(CHCH)_2C$), 129.33 (NCC), 128.57 (CHCHC-(CHCH)$_2$CH), 128.42 (CHCHC(CHCH)$_2$CH), 127.35 ($CH_3OCCHCH$), 127.06 ($NSO_2C(CHCH)_2C$), 126.05 (CHCHC(CHCH)$_2$CH), 124.67 (NCC), 124.30 (CH_3OCC), 122.04 (NCHCH), 120.54 ($CH_3OCCCHCH$), 116.92 (CHCHC(CHCH)$_2$CH), 115.40 (NCHCH), 111.17 (CH_3OCCH), 55.38 (CH_3O), 21.45 (CH_3).

*3-(*p*-Nitrophenyl)-2-styryl-1-tosylpyrrole (**10c**)*

Method A: 1.36 g (3.71 mmol) of crude boronic acid **9**, 0.62 g (2.47 mmol) of *p*-iodonitrobenzene, 1.17 g (3.71 mmol) of barium hydroxide octahydrate, 57 mg (0.05 mmol) of tetrakis(triphenylphosphine)palladium. Eluent: 20% diethyl ether in petroleum ether. Yield of **10c**: 400 mg, 36%, yellow solid (mp 141°C). R_f = 0.36 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 444 (100, $M^{\bullet+}$), 289 (69, $[M - C_7H_7SO_2]^+$), 243 (85, $[289 - NO_2]^{\bullet+}$), 241 (62). IR: 3052–2850, 1598, 1516, 1374, 1342, 1178, 1139, 670. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 8.14 (d, ^3J = 9.0 Hz, 2H, $NO_2CCHCHC$), 7.65 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.58 (d, ^3J = 8.9 Hz, 2H, $NO_2CCHCHC$), 7.46 (d, ^3J = 3.4 Hz, 1H, NCHCH), 7.39 (d, ^3J = 16.5 Hz, 1H, CHCHC(CHCH)$_2$CH), 7.34–7.22 (m, 7H, CHC(CHCH)$_2$CH and $NSO_2C(CHCH)_2CCH_3$), 6.40 (d, ^3J = 3.4 Hz, 1H, NCHCH), 6.30 (d, ^3J = 16.5 Hz, 1H, CHCHC(CHCH)$_2$CH), 2.36 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 146.02 (CNO_2), 144.96 ($NSO_2C(CHCH)_2C$), 142.12 ($NO_2CCHCHC$), 135.98 (NSO_2C), 135.73 (CHCHC(CHCH)$_2$CH), 135.23 (CHCHC-(CHCH)$_2$C), 129.47 ($NO_2C(CHCH)_2C$), 128.77 (NSO_2C-(CHCH)$_2$C), 128.41 (CHCHC(CHCH)$_2$CH), 128.40 (NO_2C-(CHCH)$_2$C), 128.05 (CHCHC(CHCH)$_2$CH), 127.97 (NCC), 127.07 ($NSO_2C(CHCH)_2C$), 126.00 (CHCHC-(CHCH)$_2$CH), 125.99 ($NO_2C(CHCH)_2C$), 125.31 (NCC), 123.45 (NCHCH), 115.46 (CHCHC(CHCH)$_2$CH), 113.04 (NCHCH). Anal. calcd. for $C_{25}H_{20}N_2O_4S$: C 67.55, H 4.54, N 6.30; found: C 67.82, H 4.40, N 6.09.

Reaction of 2-styryl-1-tosylpyrrole boronic acid and o-*iodonitrobenzene (method A)*

1.36 g (3.71 mmol) of crude boronic acid **9**, 0.62 g (2.47 mmol) of *o*-iodonitrobenzene, 1.17 g (3.71 mmol) of barium hydroxide octahydrate, 57 mg (0.05 mmol) of tetrakis(triphenylphosphine)palladium. Eluent: 10–30% diethyl ether in petroleum ether. Yield of **11** : 359 mg, 30%; **10d**: 385 mg, 35%; and **12**: 275 mg, 25%. R_f = 0.26 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 444 (100, M^+), 240 (48), 230 (42). HRMS calcd. for $C_{25}H_{20}N_2O_4S$: 444.1143; found: 444.1149. IR: 3160–2853, 1528, 1370–1348, 1172. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 8.09 (dd, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1H, $NO_2CCHCHCH$), 7.67 (d, 2H, ^3J = 7.2 Hz, CHC(CHCH)$_2$CH), 7.60 (dt, ^3J = 7.9 Hz, ^4J = 1.4 Hz, 1H, $NO_2CCHCHCH$), 7.55 (dt, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, $NO_2CCHCHCH$), 7.50 (d, ^3J = 16.5 Hz, 1H, CHCHC(CHCH)$_2$CH), 7.39 (d, ^3J = 8.0 Hz, 2H, NSO_2C-(CHCH)$_2$CCH$_3$), 7.42–7.37 (m, 2H, CHC(CHCH)$_2$CH), 7.35 (dd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, NO_2CCCH), 7.30–7.26 (m, 1H, CHC(CHCH)$_2$CH), 7.14 (d, ^3J = 8.0 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.57 (d, ^3J = 3.4 Hz, 1H, NCCH), 6.52 (d, ^3J = 16.5 Hz, 1H, CHCHC(CHCH)$_2$CH), 6.24 (d, ^3J = 3.4 Hz, 1H, NC(CHCHPh)CH), 2.33 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 149.06 (CNO_2), 144.86 ($NSO_2C(CHCH)_2CCH_3$), 137.47 (CHC(CHCH)$_2$CH), 136.94 ($NCCCNO_2$), 135.83 ($NSO_2C(CHCH)_2CCH_3$), 133.22 ($CHCCNO_2$), 132.58 (NCCHCHPh), 131.79 ($CHCHCCNO_2$), 130.42 (CHC(CHCH)$_2$CH), 129.51 ($CCNO_2$), 129.42 ($NSO_2C(CHCH)_2CCH_3$), 129.08 (NO_2CCHCH), 128.67 (CHCHC(CHCH)$_2$CH), 127.82 (CHCHC(CHCH)$_2$CH), 126.94 ($NSO_2C(CHCH)_2CCH_3$), 126.55 (CHCHC(CHCH)$_2$CH), 124.16 (NO_2CCH), 118.49 (CHCHC(CHCH)$_2$CH), 116.64 (NC(CHCHPh)CH), 111.99 (NCCH), 21.60 (CH_3).

*3-(*o*-Nitrophenyl)-2-styryl-1-tosylpyrrole (**10d**)*

Method B: 90 mg (0.2 mmol) of the 3-iodo-2-styryl-1-tosylpyrrole **6b**, 50 mg (0.3 mmol) of *o*-nitrophenylboronic acid, 95 mg (0.3 mmol) of barium hydroxide octahydrate, and 15 mg (0.02 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 20% diethyl ether in petroleum ether. Yield of **10d**: 71 mg, 80%, yellow solid (mp 104°C). R_f = 0.33 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 444 (100, M^+), 289 (16, $[M - C_7H_7SO_2]^{\bullet+}$), 255 (18), 242 (19). HRMS calcd. for $C_{25}H_{20}N_2O_4S$: 444.1143; found: 444.1131. IR: 3162–2859, 1526, 1370, 1190–1089. ^{1}H NMR

($CDCl_3$, 500 MHz) δ: 7.87 (dd, ^3J = 8.0 Hz, ^4J = 1.3 Hz, 1H, $NO_2CCHCHCH$), 7.63 (d, ^3J = 8.0 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.50 (dt, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, $NO_2CHCHCH$), 7.41 (dt, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, $NO_2CHCHCH$), 7.41 (d, ^3J = 3.4 Hz, 1H, NCHCH), 7.37 (dd, ^3J = 7.9 Hz, ^4J = 1.3 Hz, 1H, NO_2CCCH), 7.30 (d, ^3J = 16.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 7.28–7.20 (m, 3H, $CHC(CHCH)_2CH$), 7.22 (d, ^3J = 8.0 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.16–7.14 (m, 2H, $CHC(CHCH)_2CH$), 6.24 (d, ^3J = 3.4 Hz, 1H, NCHCH), 6.02 (d, ^3J = 16.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 2.35 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 149.48 (CNO_2), 145.07 ($NSO_2C(CHCH)_2CCH_3$), 136.62 ($CHC(CHCH)_2CH$), 135.77 ($NSO_2C(CHCH)_2CCH_3$), 134.00 ($CHC(CHCH)_2CH$), 132.64 ($CHCCNO_2$), 132.60 ($CHCHCHCCNO_2$), 130.36 ($CCNO_2$), 129.80 ($NSO_2C(CHCH)_2CCH_3$), 129.75 (NCC), 128.47 ($CHCHC(CHCH)_2CH$), 128.17 (NO_2CCHCH), 127.90 ($CHCHC(CHCH)_2CH$), 126.87 ($NSO_2C(CHCH)_2CCH_3$), 126.23 ($CHCHC(CHCH)_2CH$), 124.2 (NO_2CCCH), 123.30 (NCC), 122.93 (NCHCH), 115.85 ($CHCHC(CHCH)_2CH$), 113.82 (NCHCH), 21.60 (CH_3).

*2-Styryl-1-tosylpyrrole (**11**) and 3-[^{2}H]-2-styryl-1-tosylpyrrole (**d-11**)*

To 3-iodo-2-styryl-1-tosylpyrrole **6b** (100 mg, 0.22 mmol), barium hydroxide octahydrate (1.5 equiv), and catalyst (0.05 or 0.1 equiv), a degassed mixture of DMF (8 mL) and water (2 mL) was added. The mixture was then placed in a bath preheated to 120°C. After 20 min, it was cooled to room temperature and diluted with ethyl acetate and water. After filtration on a Celite® pad (washed with ethyl acetate), the solution was washed with water, brine, and dried. Purification by flash chromatography on silica gel (20% diethyl ether in petroleum ether). Yield of **11**: 57 mg, 79%, colourless oil. R_f = 0.38 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 323 (100, M^+), 168 (54, $[M - C_7H_7SO_2]^+$). HRMS calcd. for $C_{19}H_{17}NO_2S$: 323.0980; found: 323.0979. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.68 (d, ^3J = 8.5 Hz, 2H, $(NSO_2C(CHCH)_2CCH_3$), 7.55 (d, ^3J = 15.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 7.45 (d, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.35 (dd (t), ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.33 (dd, ^3J = 3.4 Hz, ^4J = 1.6 Hz, 1H, NCHCH), 7.30–7.26 (m, 1H, $CHC(CHCH)_2CH$), 7.23 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.78 (d, ^3J = 15.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 6.52 (dd, ^3J = 3.4 Hz, ^4J = 1.6 Hz, 1H, NCCH), 6.27 (t, ^3J = 3.4 Hz, 1H, NCHCH), 2.35 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 144.85 ($NSO_2C(CHCH)_2CCH_3$), 136.94 ($CHC(CHCH)_2CH$), 135.93 ($NSO_2C(CHCH)_2CCH_3$), 129.80 ($NSO_2C(CHCH)_2CCH_3$), 129.56 ($CHC(CHCH)_2CH$), 128.60 ($CHCHC(CHCH)_2CH$), 128.20 (NCCH), 127.63 ($CHCHC(CHCH)_2CH$), 126.77 ($NSO_2C(CHCH)_2CCH_3$), 126.33 ($CHCHC(CHCH)_2CH$), 123.23 (NCHCH), 116.79 ($CHCHC(CHCH)_2CH$), 112.46 (NCHCH), 111.56 (NCCH), 21.47 (CH_3).

When using deuterated DMF-d_7, **d-11** was obtained. R_f = 0.38 (30% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 324 (38, M^+), 169 (100, $[M - C_7H_7SO_2]^{\bullet+}$), 168 (58, [M-D + H-$C_7H_7SO_2]^+$), 91 (24, $[C_7H_7]^+$), 44 (64). HRMS calcd. for $C_{19}H_{16}DNO_2S$: 324.1042; found: 324.1048. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 7.68 (d, ^3J = 8.5 Hz, 2H, $(NSO_2C(CHCH)_2CCH_3$), 7.55 (d, ^3J = 15.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 7.45 (d, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.35 (t, ^3J = 8.3 Hz, 2H, $CHC(CHCH)_2CH$), 7.33 (d, ^3J = 3.4 Hz, 1H, NCHCH), 7.27–7.25 (m, 1H, $CHC(CHCH)_2CH$), 7.23 (d, ^3J = 8.5 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.78 (d, ^3J = 15.5 Hz, 1H, $CHCHC(CHCH)_2CH$), 6.27 (d, ^3J = 3.4 Hz, 1H, NCHCH), 2.35 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 144.85 ($NSO_2C(CHCH)_2CCH_3$), 136.94 ($CHC(CHCH)_2CH$), 135.93 ($NSO_2C(CHCH)_2CCH_3$), 133.84 (NCCH), 127.63 ($CHCHC(CHCH)_2CH$), 129.80 ($NSO_2C(CHCH)_2CCH_3$), 129.56 ($CHC(CHCH)_2CH$), 128.60 ($CHCHC(CHCH)_2CH$), 126.77 ($NSO_2C(CHCH)_2CCH_3$), 126.33 ($CHCHC(CHCH)_2CH$), 123.23 (NCHCH), 116.79 ($CHCHC(CHCH)_2CH$), 112.38 (NCHCH), 111.34 (t, NCCD), 21.47 (CH_3).

*2-Formyl-3-(*o*-nitrophenyl)-1-tosylpyrrole (**13a**) (RN: 233770-18-8)*

Method C: 120 mg (0.32 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 80 mg (0.48 mmol) of *o*-nitrophenylboronic acid, 150 mg (0.48 mmol) of barium hydroxide octahydrate, 23 mg (0.032 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% diethyl ether in petroleum ether. Yield of **13a**: 120 mg, 98%, pale yellow solid (mp 143°C). R_f = 0.29 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 369 (8, M^+), 341 (42, $[M - CO]^+$), 324 (38, $[M - NO_2]^+$), 215 (100, $[M - C_7H_7SO_2]^+$), 187 (50, $[215 - CO]^+$), 155 (47, $[C_7H_7SO_2]^+$), 91 (88, $[C_7H_7]^+$). IR: 3074, 1678, 1536, 1269, 740. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.88 (s, 1H, CHO), 8.04 (dd, ^3J = 8.1 Hz, ^4J = 1.5 Hz, 1H, $CHCNO_2$), 7.79 (d, ^3J = 8.1 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.67 (d, ^3J = 3.3 Hz, 1H, NCHCH), 7.59 (td, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, $NO_2CCHCHCH$), 7.52 (td, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, NO_2CCHCH), 7.35 (d, ^3J = 8.1 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.33 (dd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, 1H, NO_2CCCH), 6.39 (d, ^3J = 3.3 Hz, 1H, NCHCH), 2.43 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.9 (CHO), 148.98 (CNO_2), 145.98 ($NSO_2C(CHCH)_2CCH_3$), 135.42 ($NSO_2C(CHCH)_2CCH_3$), 135.26 (NCCHO), 132.44 ($NO_2CCHCHCH$), 132.25 (NO_2CCCH), 130.15 ($NSO_2C(CHCH)_2CCH_3$), 129.2 (NO_2CCHCH), 128.48 (NO_2CC), 128.34 (NCC), 128.34 (NCH), 127.24 ($NSO_2C(CHCH)_2CCH_3$), 124.39 ($CHCNO_2$), 113.85 (NCHCH), 21.59 (CH_3). Anal. calcd. for $C_{18}H_{14}N_2O_5S$: C 58.37, H 3.81, N 7.56; found: C 58.23, H 3.56, N 7.37.

*2-Formyl-3-phenyl-1-tosylpyrrole (**13b**)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 73 mg (0.6 mmol) of phenylboronic acid, 189 mg (0.6 mmol) of barium hydroxide octahydrate, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% diethyl ether in petroleum ether. Yield of **13b**: 120 mg, 92%, white solid (mp 175°C). R_f = 0.37 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 325 (78, $M^{\bullet+}$), 260 (45, $[M - SO_2]^+$), 170 (100, $[M - C_7H_7SO_2]^+$), 169 (75), 155 (38, $[C_7H_7SO_2]^+$), 115 (41), 91 (53, $[C_7H_7]^+$). HRMS calcd. for $C_{18}H_{15}NO_3S$: 325.0772; found: 325.0765. IR: 1675, 1374, 1174. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.62 (s, 1H, CO*H*), 7.94 (d, ^3J = 8.8 Hz, 2H, $(NSO_2C(CHCH)_2CCH_3$), 7.84 (d, ^3J = 3.4 Hz, 1H, NCHCH), 7.40 (s, 5H), 7.34 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$),

6.49 (d, ^3J = 3.4 Hz, 1H, NCHC*H*), 2.43 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.22 (*C*HO), 145.36 (NSO_2C-$(CHCH)_2CCH_3$), 143.46 (N*C*CHO), 135.11 (NSO_2C-$(CHCH)_2CCH_3$), 132.27 (NCC*C*$(CHCH)_2CH$), 129.54 ($NSO_2C(CHCH)_2CCH_3$), 129.54 (N*C*HCH), 129.47 (NCCC-$(CHCH)_2C$), 128.63 (NCCC$(CHCH)_2CH$), 128.44 (NCCC-$(CHCH)_2CH$), 128.34 ($NSO_2C(CHCH)_2CCH_3$), 127.98 (NC*C*C$(CHCH)_2CH$), 112.80 (NCH*C*H), 21.61 (*C*H_3).

*2-Formyl-3-(*m-*nitrophenyl)-1-tosylpyrrole (**13c**) (RN: 233770-24-6)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 102 mg (0.6 mmol) of *m*-nitrophenylboronic acid, 189 mg (0.6 mmol) of octahydrate barium hydroxide, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% diethyl ether in petroleum ether. Yield of **13c**:130 mg, 88%, pale yellow solid (mp 142°C). R_f = 036 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 370 (51, $M^{\bullet+}$), 306 (67, $[215 + 91]^{\bullet+}$), 215 (63, $[M - C_7H_7SO_2]^+$), 214 (61, $[215 - H]^{\bullet+}$), 155 (100, $[C_7H_7SO_2]^+$), 91 (92, $[C_7H_7]^+$). IR: 1676, 1526, 1348, 1175, 669. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.87 (s, 1H, C*H*O), 8.25 (dd, ^4J = 2.3 Hz, ^4J = 1.7 Hz, 1H, CC*H*CNO$_2$), 8.20 (dd, ^3J = 8.3 Hz, ^4J = 2.3 Hz, 1H, CCHCNO$_2$C*H*), 7.87 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.77 (d, ^3J = 3.4 Hz, 1H, NC*H*CH), 7.74 (ddd, ^3J = 7.7 Hz, ^4J = 1.7 Hz, ^4J = 1.1 Hz, 1H, C*H*CCHCNO$_2$), 7.55 (t, ^3J = 7.7 Hz, 2H, C*H*CHCCHCNO$_2$), 7.34 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.50 (d, ^3J = 3.3 Hz, 1H, NCHC*H*), 2.42 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.33 (*C*HO), 147.98 (*C*NO$_2$), 146.01 ($NSO_2C(CHCH)_2CCH_3$), 138.42 (N*C*CHO), 135.33 (*C*HCCHCNO$_2$), 135.01 (*C*CHNO$_2$), 134.76 (NSO_2C-$(CHCH)_2CCH_3$), 129.97 ($NSO_2C(CHCH)_2CCH_3$), 129.15 (N*C*H), 129.05 (C*H*CHCCHNO$_2$), 127.97 (NC*C*), 127.83 ($NSO_2C(CHCH)_2CCH_3$), 124.16 (CCHNO$_2$), 123.17 (CCHCNO$_2$*C*H), 113.24 (NCH*C*H), 21.58 (*C*H_3). Anal. calcd. for $C_{18}H_{14}N_2O_5S$: C 58.37, H 3.81, N 7.56; found: C 58.46, H 3.72, N 7.33.

*2-Formyl-3-(*p-*nitrophenyl)-1-tosylpyrrole (**13d**) (RN: 233770-26-8)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 102 mg (0.6 mmol) of *p*-nitrophenylboronic acid, 189 mg (0.6 mmol) of barium hydroxide octahydrate, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% diethyl ether in petroleum ether. Yield of **13d**: 124 mg, 84%, pale yellow solid (mp 167°C). R_f = 0.38 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 370 (56, $M^{\bullet+}$), 306 (67, $[215 + 91]^{\bullet+}$), 294 (49), 226 (57), 215 (49, $[M - C_7H_7SO_2]^+$), 214 (43, $[215 - H]^{\bullet+}$), 155 (88, $[C_7H_7SO_2]^+$), 91 (86, $[C_7H_7]^+$), 44 (100). IR: 1677, 1517, 1345, 1137, 669. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.88 (s, 1H, C*H*O), 8.25 (d, ^3J = 8.8 Hz, 2H, NO$_2$CC*H*), 7.90 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.80 (d, ^3J = 3.3 Hz, 1H, NC*H*CH), 7.59 (d, ^3J = 8.8 Hz, 2H, NO$_2$CCHC*H*), 7.37 (d, ^3J = 8.8 Hz, 2H, NSO_2C-$(CHCH)_2CCH_3$), 6.51 (d, ^3J = 3.3 Hz, 1H,NCHC*H*), 2.45 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.36 (*C*HO), 147.67 (*C*NO$_2$), 146.07 ($NSO_2C(CHCH)_2CCH_3$), 139.16 (N*C*CHO), 138.69 (NO$_2$CCHCH*C*), 134.81 (NSO_2C-$(CHCH)_2CCH_3$), 130.29 (NO$_2$CCH*C*H), 129.96 (NSO_2C-$(CHCH)_2CCH_3$), 129.14 (N*C*H), 128.08 (NC*C*), 128.01 ($NSO_2C(CHCH)_2CCH_3$), 123.46 (NO$_2$C*C*H), 113.14 (NCH*C*H), 21.65 (*C*H_3). Anal. calcd. for $C_{18}H_{14}N_2O_5S$: C 58.37, H 3.81, N 7.56; found: C 58.30, H 3.66, N 7.48.

*2-Formyl-3-(*o-*methoxyphenyl)-1-tosylpyrrole (**13e**) (RN: 233770-28-0)*

Method C: 250 mg (0.7 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 151 mg (1 mmol) of o-methoxyphenylboronic acid, 315 mg (1 mmol) of barium hydroxide octahydrate, 48 mg (0.07 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% diethyl ether in petroleum ether. Yield of **13e**: 210 mg, 89%, white solid (mp 131°C). R_f = 0.31 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 355 (30, $M^{\bullet+}$), 324 (100, $[355 - OMe-H]^+$), 201 (44, $[M - C_7H_7SO_2]^+$), 185 (45), 170 (57, $[201 - OMe]^+$), 152 (49), 134 (30), 91 (45, $[C_7H_7]^+$). IR: 1676, 1174, 672. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.48 (s, 1H, C*H*O), 7.96 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.82 (d, ^3J = 3.3 Hz, 1H, NC*H*), 7.36–7.33 (m, 3H, CH$_3$OCCHC*H* and NSO_2C-$(CHCH)_2CCH_3$), 7.21 (d, ^3J = 8.2 Hz, 1H, CH$_3$OCCC*H*), 6.97–6.95 (m, 2H,CH$_3$OCC*H*CHC*H*), 6.49 (d, ^3J = 3.3 Hz, 1H, NCHC*H*), 3.23 (s, 3H, OCH_3), 2.41 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.32 (*C*HO), 156.62 (CH$_3$O*C*), 145.08 ($NSO_2C(CHCH)_2CCH_3$), 139.37 (N*C*CHO), 136.02 (NSO_2C), 131.75 (CH$_3$OCC*C*H), 130.08 (CH$_3$OCCH*C*H), 129.37 ($NSO_2C(CHCH)_2CCH_3$), 128.98 (N*C*H), 128.43 (NC*C*), 128.28 ($NSO_2C(CHCH)_2CCH_3$), 120.32 (CH$_3$OCCCH*C*H), 113.89 (NCH*C*H), 110.93 (CH$_3$OC*C*H), 55.36 (*C*H$_3$O), 21.50 (*C*H_3). Anal. calcd. for $C_{19}H_{17}NO_4S$: C 64.21, H 4.82, N 3.94; found: C 63.91, H 4.69, N 3.97.

*2-Formyl-3-mesityl-1-tosylpyrrole (**13f**) (RN: 233770-32-6)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 98 mg (0.6 mmol) of mesitylboronic acid (26), 189 mg (0.6 mmol) of barium hydroxide octahydrate, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 20% diethyl ether in petroleum ether. Yield of **13f**: 90 mg, 61%, white solid (mp 141°C). R_f = 0.57 (40% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 367 (83, M^+), 212 (43, $[M - C_7H_7SO_2]^+$), 184 (100 $[212 - CO]^+$), 168 (32, $[184 - CH_3\text{-}H]^+$), 155 (32, $[C_7H_7SO_2]^+$), 91 (33, $[C_7H_7]^+$). IR: 1679, 1370, 1175. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.32 (s, 1H, C*H*O), 7.87 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.85 (d, ^3J = 3.3 Hz, 1H, NC*H*), 7.33 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.89 (s, 2H, CH$_3$C(C*H*CCH$_3$)$_2$C), 6.26 (d, ^3J = 3.3 Hz, 1H, NCHC*H*), 2.43 (s, 3H, CH_3), 1.94 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 177.87 (*C*HO), 145.34 (NSO_2C-$(CHCH)_2CCH_3$), 142.1 (N*C*CHO), 137.84 (CH$_3$*C*-(CHCCH$_3$)$_2$C), 136.41 (CH$_3$C(CH*C*CH$_3$)$_2$C), 135.19 ($NSO_2C(CHCH)_2CCH_3$), 129.97 (N*C*H), 129.57 (NSO_2C-$(CHCH)_2CCH_3$), 128.74 (CH$_3$C(CHCCH$_3$)$_2$*C*), 128.40 (NC*C*), 128.03 (CH$_3$C(*C*HCCH$_3$)$_2$C), 127.80 (NSO_2C-$(CHCH)_2CCH_3$), 113.81 (NCH*C*H), 21.58 (*C*H$_3$), 20.38 (CH$_3$). Anal. calcd. for $C_{21}H_{21}NO_3S$: C 68.64, H 5.76, N 3.81; found: C 68.52, H 5.79, N 3.76.

*2-Formyl-3-(3-pyridyl)-1-tosylpyrrole (**13g**)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, crude 3-pyridylboronic acid (28) from diethyl-3-pyridylborane (588 mg, 4 mmol), 189 mg (0.6 mmol) of barium hydroxide octahydrate, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% ethyl acetate in dichloromethane. Yield of **13g**: 128 mg, 77%, pale yellow oil. R_f = 0.49 (50% ethyl acetate in dichloromethane). MS (EI) *m/z*: 326 (100, $M^{\bullet+}$), 262 (27), 261 (28), 171 (35, $[M - SO_2C_7H_7)^+]$, 170 (29), 155 (44, $[SO_2C_7H_7]^+$), 91 (66, C_7H_7). HRMS calcd. for $C_{17}H_{14}N_2O_3S$: 326.0725; found: 326.0711. IR: 1675, 1377, 1175. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.82 (s, 1H, CO*H*), 8.66 (s, 1H, CC*H*N), 8.62 (d, ^3J = 4.8 Hz, 1H, (NC*H*CHCH), 7.91 (d, ^3J = 8.2 Hz, 2H, ($NSO_2C(CHCH)_2CCH_3$), 7.82 (d, ^3J = 3.1 Hz, 1H, NC*H*CH), 7.79 (d, ^3J = 3.1 Hz, 1H, (NCHCHC*H*), 7.39–7.26 (m, 3H, NCHC*H*CH and $NSO_2C(CHCH)_2CCH_3$), 6.51 (d, ^3J = 3.2 Hz, 1H, NCHC*H*), 2.44 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 177.80 (*C*HO), 149.30 (C*C*HN), 149.1 (N*C*HCHCH), 145.48 ($NSO_2C(CHCH)_2CCH_3$), 137.57 ($NSO_2C(CHCH)_2CCH_3$), 136.37 (*C*HCCHN), 134.59 (N*C*CHO), 129.51 (NSO_2C-$(CHCH)_2CCH_3$), 128.92 (N*C*HCH), 128.21 (*C*CHN), 127.87 (NC*C*), 127.64 ($NSO_2C(CHCH)_2CCH_3$), 122.64 (*C*HCHN), 112.75 (NCH*C*H), 21.26 (CH_3).

*2-Formyl-3-thiophenyl-1-tosylpyrrole (**13h**) (RN: 233770-30-4)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 77 mg (0.6 mmol) of 2-thiophenylboronic acid, 189 mg (0.6 mmol) of octahydrate barium hydroxide, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% diethyl ether in petroleum ether. Yield of **13h**: 113 mg, 85%, white solid (mp 146°C). R_f = 0.34 (40% diethyl ether in petroleum ether). MS (EI) *m/z*: 331 (72, M^+), 176 (100, $[M - C_7H_7SO_2]^+$). IR: 1670, 1374, 1174. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.99 (s, 1H, CO*H*), 7.87 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.75 (d, ^3J = 3.4 Hz, 1H, NC*H*CH), 7.44 (dd, ^3J = 3.6 Hz, ^4J = 1.1 Hz, 1H, SCC*H*), 7.39 (dd, ^3J = 5.1 Hz, ^4J = 1.1 Hz, 1H, SC*H*CH), 7.33 (d, ^3J = 8.8 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.08 (dd, ^3J = 5.1 Hz, ^4J = 3.6 Hz, 1H, SCHC*H*), 6.58 (d, ^3J = 3.4 Hz, 1H, NCHC*H*), 2.42 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 178.37 (*C*HO), 145.61 ($NSO_2C(CHCH)_2$-CCH_3), 135.01($NSO_2C(CHCH)_2CCH_3$), 134.42 (N*C*CHO), 133.61 (S*C*CH), 129.77 ($NSO_2C(CHCH)_2CCH_3$), 129.38 (N*C*HCH), 129.04 (SC*C*H), 127.94 ($NSO_2C(CHCH)_2CCH_3$), 127.67 (S*C*HCH), 127.48 (NC*C*), 112.92 (NCH*C*H), 21.61 (CH_3). Anal. calcd. for $C_{16}H_{13}NO_3S_2$: C, 57.98, H 3.95, N 4.23; found: C 58.09, H 4.07, N 4.13.

*2-Formyl-3-(1-*tert*-butoxycarbonyl)-pyrrole-1-tosylpyrrole (**13i**)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 127 mg (0.6 mmol) of 1-*tert*-butoxycarbonylpyrrol-2-ylboronic acid (31), 189 mg (0.6 mmol) of barium hydroxide octahydrate, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 20% diethyl ether in petroleum ether. Yield of **13i**: 128 mg, 77%, pale yellow oil. R_f = 0.59 (40% diethyl ether in petroleum ether). MS (EI) *m/z*: 414 (71, M^+), 314 (100), 159 (96). HRMS calcd. for $C_{21}H_{22}N_2O_5S$: 414.1249; found: 414.1241. IR: 1700, 1700, 1371, 1316, 1174. ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 9.64 (s, 1H, CO*H*), 7.91 (d, ^3J = 8.4 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 7.71 (d, ^3J = 3.4 Hz, 1H, NC*H*CH), 7.38 (dd, ^3J = 3.3 Hz, ^4J = 1.8 Hz, 1H, NCHC*H*CH), 7.33 (d, ^3J = 8.4 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 6.40 (d, ^3J = 3.4 Hz, 1H, NCHC*H*), 6.22–6.18 (m, 2H, NCC*H* and NCHC*H*), 2.42 (s, 3H, CH_3), 1.37 (s, 9H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 178.13 (*C*HO), 148.55 (O*C*ON), 145.41 ($NSO_2C(CHCH)_2CCH_3$), 135.14 ($NSO_2C(CHCH)_2CCH_3$), 134.18 (N*C*CHO), 129.58 ($NSO_2C(CHCH)_2CCH_3$), 129.35 (N*C*CH), 128.17 ($NSO_2C(CHCH)_2CCH_3$), 128.08 (N*C*HCH), 124.11 (NC*C*), 123.53 (*C*HNC), 117.68 (NC*C*H), 114.25 (NCH*C*H), 110.55 (NCH*C*HCH), 84 ($C(CH_3)_3$), 27.49 ($C(CH_3)_3$), 21.57 (CH_3).

*2-Nitro-6-trifluoromethylboronic acid (**14**) and 4-nitro-6-trifluoromethylboronic acid (**15**)*

To a solution of nitric acid (90% aqueous, 2.25 mL, 48 mmol) and sulfuric acid (6.8 mL, 128 mmol) and a few urea crystals at 0°C, a solution of 2-(trifluoromethyl)phenylboronic acid (3.2 g, 16 mmol) in acetic anhydride (42 mL) was slowly added through an addition funnel. During the addition, the temperature was kept under 5°C. After the addition, the mixture was stirred for 4 h at 0°C and overnight at room temperature. It was then poured onto ice (500 mL) and sodium hydroxide was added until the pH reached a value between 3 and 5. The aqueous phase was then extracted with diethyl ether. The organic layer was washed with brine, dried and concentrated in vacuo. The purification by reverse-phase MPLC yielded 2-nitro-6-trifluoromethylboronic acid (**14**) (1.6 g, 42%) as a white solid (mp 154°C) and 4-nitro-2-trifluoromethylboronic acid (**15**) (0.46 g, 12%) as a white solid (mp 141°C).

***(14)**:* r.t. = 11.9 min (col. MATREX 4 RP 18 15 μ; eluent: CH_3CN–H_2O, 35:65; flow 0.5 mL min^{-1}; UV detector 254 nm, 25°C). MS (EI) *m/z*: 235 (3, $M^{\bullet+}$), 191 (100, $[M - B(OH)_2 + H]^{\bullet+}$), 171 (88, $[M - NO_2\text{-}F]^+$). HRMS calcd. for $C_7H_5BF_3NO_4$: 235.0263; found: 235.0266. IR: 3591 and 3385, 1543, 1387–1292 (B—OH), 1134. ^{1}H NMR (DMSO-d_6, 500 MHz) δ: 8.46 (d, ^3J = 7.6 Hz, 1H, C*H*CNO_2), 8.28 (s, 2H, $B(OH)_2$), 8.14 (d, ^3J = 7.6 Hz, 1H, C*H*CF_3), 7.81 (t, ^3J = 7.6 Hz, 1H, CHC*H*CH). ^{13}C NMR (DMSO-d_6, 75 MHz) δ: 150.47 (*C*NO_2), 133.5–132 (m, C-B), 131.77 (CH*C*HCH), 130.02 (*C*HCCF_3), 125.32 (*C*CF_3), 126.56 (*C*HCNO_2), 120.92 (*C*F_3).

***(15)**:* r.t. = 19.2 min (col. MATREX 4 RP 18 15 μ; eluent: CH_3CN–H_2O 35:65; flow 0.5 mL min^{-1}; UV detector 254 nm, 25°C). MS (EI) *m/z*: 235 (100, $M^{\bullet+}$), 189 (24, $[M - NO_2]^+$), 171 (55, $[189 - F]^+$), 125 (39, $[189 - B(OH)_2\text{-}F]^+$), 75 (25, $[M - CF_3\text{-}NO_2\text{-}B(OH)_2]^{\bullet+}$). HRMS calcd. for $C_7H_5BF_3NO_4$: 235.0263; found: 235.0257. IR: 3470–3359, 1530, 1409–1321 (B—OH), 1287, 1128. ^{1}H NMR (DMSO-d_6, 75 MHz) δ: 8.71 (s, 2H, $B(OH)_2$), 8.42 (d, ^3J = 9.2 Hz, 1H, C*H*CNO_2), 8.14 (s, 1H, NO_2C*H*CF_3), 7.83 (d, ^3J = 9.2 Hz, 1H, C*H*$CB(OH)_2$). ^{13}C NMR (DMSO-d_6, 50 MHz) δ: 146.80 (NO_2C), 134.11 (NO_2CCHCH), 132.5–130.85 (m, *C*-B), 126.28 (*C*CF_3), 125.94 (NO_2CCH*C*H), 121.35 (*C*F_3), 119.85 (NO_2C*C*HCF_3).

*2-Amino-6-trifluoromethylboronic acid (**16**)*

Palladium (10% on activated carbon, 38 mg) was added to a solution of *o*-nitro-*o*′-trifluoromethylboronic acid (**14**) in ethanol (10 mL). The resulting suspension was then stirred under hydrogen (2 bar) overnight, filtered on a Celite® pad and concentrated in vacuo. Owing to its unstability, the product was used in the coupling reaction without further purification.

*3-Tosyl-9-(trifluoromethyl)-3*H*-pyrrolo[2,3-*c*]-quinoline (**17**)*

Method C: 150 mg (0.4 mmol) of the 3-iodo-2-formyl-1-tosylpyrrole **7b**, 120 mg (0.6 mmol) of the crude *o*-amino-*o*′-trifluoromethylboronic acid (**16**), 189 mg (0.6 mmol) of barium hydroxide octahydrate, 30 mg (0.04 mmol) of dichloro(diphenylphosphinoferrocene)palladium(II). Eluent: 30% ethyl acetate in petroleum ether. Yield of **17**: 40 mg, 26%, pale yellow solid (mp 163°C). R_f = 0.5 (70% diethyl ether in petroleum ether). MS (EI) *m*/*z*: 390 (100, $M^{\bullet+}$), 235 (15, $[M - C_7H_7SO_2]^+$), 155 (29, $[C_7H_7SO_2]^+$), 91 (21, $[C_7H_7]^+$) HRMS calcd. for $C_{19}H_{13}F_3N_2O_2S$: 390.0649; found: 390.0654. IR: no carbonyl signal. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.70 (s, 1H, C*H*N), 8.40 (d, ^3J = 8.0 Hz, 1H, C*H*CCCF$_3$), 8.02 (d, ^3J = 8.0 Hz, 1H, C*H*CCF$_3$), 7.86 (d, ^3J = 3.7 Hz, 1H, NC*H*CH), 7.85 (d, ^3J = 8.5 Hz, 1H, $NSO_2C(CHCH)_2CCH_3$), 7.69 (t, ^3J = 8.0 Hz, 1H, CHCHCCF$_3$), 7.45–7.43 (m, 1H, NCHC*H*), 7.26 (d, ^3J = 8.6 Hz, 2H, $NSO_2C(CHCH)_2CCH_3$), 2.34 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 145.94 ($NSO_2C(CHCH)_2CCH_3$), 144.74 (*C*NCH), 138.73 (CN*C*H), 135.26 (*C*HCNCCCF$_3$), 134.72 ($NSO_2C(CHCH)_2CCH_3$), 130.22 ($NSO_2C(CHCH)_2CCH_3$), 128.90 (N*C*C), 128.03 (N*C*H), 126.96 ($NSO_2C(CHCH)_2CCH_3$), 126.03 (*C*HCCF$_3$), 125.83 (NCCH*C*HCHCCF$_3$), 21.51 (*C*H$_3$).

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References

1. R.J. Sundberg. Pyrroles and their benzo derivatives. *In* Comprehensive heterocyclic chemistry. Vol. 4. *Edited by* A.R. Katritzky and C.W. Rees. Pergamon Press, Oxford. 1984. Part 3. pp. 246–254.
2. R.E. Niziurski-Mann and M.P. Cava. Heterocycles, **34**, 2003 (1992).
3. T. Masquelin and D. Obrecht. Synthesis, 276 (1995), and refs. cited therein.
4. (*a*) A. Banerji, P.L. Pajumder, and A. Chaterjee. Phytochemistry, **9**, 1491 (1970); (*b*) D.J. Abraham, R.D. Rosenstein, R.L. Lyon, and H.H.S. Fong. Tetrahedron Lett. **10**, 909 (1972); (*c*) K.T. De Silva, A.H. Ratcliffe, G.F. Smith, and G.N. Smith. Tetrahedron Lett. **10**, 913 (1972); (*d*) B. David, T. Sévenet, M. Morgat, D. Guénard, A. Moisand, Y. Tollon, and M. Wright. Cell Motil. Cytoskeleton, **28**, 317 (1994); (*e*) B. David, T. Sévenet, O. Thoison, K. Awong, M. Païs, M. Wright, and D. Guénard. Bioorg. Med. Chem. Lett. **7**, 2155 (1997); (*f*) C. Pascal, J. Dubois, D. Guénard, L. Tchertanov, S. Thoret, and F. Guéritte. Tetrahedron, **54**, 14737 (1998).
5. (*a*) K. Tanaka, K. Karigone, and S. Umio. Chem. Pharm. Bull. **17**, 611 (1969); (*b*) G.C. Spence, E.C. Taylor, and O. Büchardt. Chem. Rev. **70**, 231 (1970); (*c*) A.H. Ratcliffe, G.F. Smith, and G.N. Smith. Tetrahedron Lett. **52**, 5179 (1973); (*d*) F. Bellamy, P. Martz, and J. Streith. Heterocycles, **3**, 395 (1975); (*e*) H. Horikawa, T. Iwasaki, K. Matsumoto, and M. Miyoshi. J. Org. Chem. **43**, 335 (1978); (*f*) D.J. Arnold, L. Burgess-Dean, J.Hubbard, and M.A. Rahman. Aust. J. Chem. **47**, 969 (1994); (*g*) J.T. Gupton, S.A. Petrich, L.L. Smith, M.A. Bruce, P. Vu, K.X. Du, and E.E. Dueno. Tetrahedron, **52**, 6879 (1996).
6. S.P. Stanforth. Tetrahedron, **54**, 263 (1998).
7. N. Miyaura and A. Suzuki. Chem. Rev. **95**, 2457 (1995); A. Suzuki. J. Organomet. Chem. **576**, 147 (1999).
8. (*a*) J.M. Muchowski. J. Org. Chem. **57**, 1653 (1992); (*b*) G.G Grieb and D.M. Ketcha. Synth. Commun. **25**, 2195 (1995); (*c*) R. D'Alessio and A. Rossi. Synlett, 513 (1996); (*d*) D. Bolton, I. Boyfield, M.C. Coldwell, M.S. Hadley, A. Johns, C.N. Johnson, R.E. Markwell, D.J. Nash, G.I. Riley, E.E. Scott, S.A. Smith, G. Stemp, H.J. Wadsworth, and E.A. Watts. Bioorg. Med. Chem. Lett. **7**, 327 (1997); (*e*) C.N. Johnson, G. Stemp, N. Arnaud, S.C. Stephen, and T. Gallagher. Synlett, 1025 (1998); (*f*) T. Murashima, D. Shiya, K. Nishi, H. Uno, and N. Quo. J. Chem. Soc. Perkin Trans. 1, **16**, 2671 (2000).
9. (*a*) C.K. Chang, and N. Bag. J. Org. Chem. **60**, 7030 (1995); (*b*) J. Cossy and D. Belotti. J. Org. Chem. **62**, 7900 (1997); (*c*) M.G. Banwell, B.L. Flynn, E. Harmel, and D.C.R. Hockless. J. Chem. Soc. Chem. Commun. 207 (1997); (*d*) H.W. Chan, P.C. Chan, J.H. Lin, and H.N.C. Wong. J. Chem. Soc. Chem. Commun. 1515 (1997); (*e*) A. Fürstner, J. Grabowski, and C.W. Lehmann. J. Org. Chem. **64**, 8275 (1999); (*f*) T. Murashima, D. Shiya, K. Nishi, H. Uno, and N. Ono. J. Chem. Soc. Perkin Trans. 1, **16**, 2671 (2000); (*g*) J.H. Liu, Q.-C. Yang, T.C.W. Mak, and H.N.C. Wong. J. Org. Chem. **65**, 3587 (2000).
10. (*a*) F.R. Bean and J.R. Johnson. J. Am. Chem. Soc. **54**, 4415 (1932); (*b*) H.L. Mutreities. *In* The chemistry of boron and its compounds. Wiley, New York. 1967; (*b*) S. Murahashi, M. Yamamura, K. Yanagisawa, N. Mita, and K. Kondo. J. Org. Chem. **44**, 2408 (1979); (*c*) M.J. Sharp and V. Snieckus. Tetrahedron Lett. **26**, 5997 (1985); (*d*) N. Miyaura, T. Ishiyama, H. Sazaki, M. Ishikawa, M. Satoh, and A. Suzuki. J. Am. Chem. Soc. **111**, 314 (1989); (*e*) M.P. Groziak, A.D. Ganguly, and P.D. Robinson. J. Am. Chem. Soc. **116**, 7597 (1994).
11. V. Snieckus. Chem. Rev. **90**, 879 (1990).
12. C. Franc, F. Denonne, C. Cuisinier, and L. Ghosez. Tetrahedron Lett. **40**, 4555 (1999).
13. (*a*) M. Banwell, A. Edwards, J. Smith, E. Hamel, and P. Verdier-Pinard. J. Chem. Soc. Perkin Trans. 1, 1497 (2000); (*b*) C. Dupond, D. Guénard, C. Thal, S. Thoret, and F. Guéritte. Tetrahedron Lett. **41**, 5853 (2000).
14. D. Xiao and D.M. Ketcha. Org. Prep. Proced. Int. **4**, 503 (1995).
15. (*a*) T. Watanabe, N. Miyaura, and A. Suzuki. Synlett, 207 (1992); (*b*) A. Suzuki. Pure Appl. Chem. **66**, 213 (1994); (*c*) J.M. Fu, M.J. Sharp, and V. Snieckus. Can. J. Chem. **72**, 227 (1994); (*d*) A. James and V. Snieckus. Tetrahedron Lett. **38**, 8142 (1997); (*e*) J.C. Anderson, H. Namli, and C.A. Roberts. Tetrahedron, **53**, 15123 (1997).
16. C. Amatore, A. Tatand, and A. Suarez. J. Am. Chem. Soc. **115**, 9531 (1993).

17. G.W. Parshall and S.D. Ittel. Homogeneous catalysis. Wiley, New York. 1992.
18. J. Chatt, F.A. Hart, and H.R. Watson. J. Chem. Soc. 2537 (1962).
19. S. Gronowitz, A.B. Hörnfeldt, and Y. Yang. Chem. Scr. **28**, 281 (1988).
20. (*a*) T. Oh-e, N. Miyaura, and A. Suzuki. J. Org. Chem. **58**, 2201 (1993); (*b*) N.A. Bumaym, A.F. Nikitina, and I.P. Beletskaya. Russ. J. Org. Chem. **30**, 1619 (1994); (*c*) S. Mohri, M. Stefnovic, and V. Snieckus. J. Org. Chem. **62**, 7072 (1997).
21. (*a*) J.P. Wolfe, R.A. Singer, B.H. Yang, and S.L. Buchwald. J. Am. Chem. Soc. **121**, 9550 (1999); (*b*) V.P.W. Böhm, T. Weskamp, C.W.K. Gstöttmayr, and W.A. Hermann. Angew. Chem. Int. Ed. **39**, 1602 (2000); (*c*) A.F. Littke, C. Dai, and G.C. Fu. J. Am. Chem. Soc. **122**, 4020 (2000).
22. J. Tsuji. Palladium reagents and catalysis. John Wiley and Sons, New York. 1995. p. 249.
23. (*a*) F.R.S. Clark, R.O.C. Norman, and B.C. Thomas J. Chem. Soc. Perkin Trans. 1, 121 (1975); (*b*) W. Cabri and S. Penco. J. Org. Chem. **56**, 5796 (1991); (*c*) N.M. Ali, A. McKillop, M.B. Mitchell, R.A. Rebelo, and P.J. Wallbank. Tetrahedron, **48**, 8117 (1992); (*d*) S. Wiegand and H.J. Schäfer. Tetrahedron, **18**, 5341 (1995); (*e*) J.S. Mahenty, D. Mahnya, and N.G. Kundu. J. Chem. Soc. Perkin Trans. 1, 2577 (1997).
24. M.P. Groziak, A.D. Ganguly, and P.D. Robinson. J. Am. Chem. Soc. **116**, 7597 (1994). The separation of the *o*- (r.t. = 3.56 min) and *p*- (r.t. = 6.71 min) isomers was performed by HPLC (col. KROMASIL 10 μ, 4.6 × 250 mm, eluent: CH_3CN–H_2O 50:50, flow 0.5 ml min^{-1}. UV detector 254 mm, 25°C).
25. M.F. Hawthorne. J. Org. Chem. **23**, 1579 (1958).
26. M. Terashima, H. Kakim, M. Isihikura, and K. Kamata. Chem. Pharm. Bull. **31**, 4573 (1983).
27. S. Martina, V. Enkelmann, G. Wegner, and A.D. Schlater. Synthesis, 613 (1991).
28. W. Seaman and J.R. Johnson. J. Am. Chem. Soc. **53**, 71 (1931)
29. D.R. Coulson. Inorg. Synth. **13**, 121 (1972).
30. T. Hayashi, M. Konishi, and M. Kumada. Tetrahedron Lett. **20**, 1871 (1979).
31. L. Grehn and U. Ragnarsson. Angew. Chem. Int. Ed. Engl. **23**, 296 (1984).