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Palladium-catalyzed Monoarylation of Arylhydrazines with Aryl Tosylates

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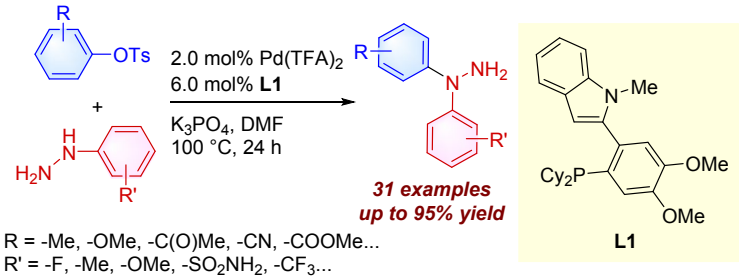
KEYWORDS: phosphine, palladium, phenylhydrazine, monoarylation, aryl tosylate



Abstract.

A palladium-catalyzed C–N bond coupling reaction between arylhydrazines and aryl tosylates for facile synthesis of unsymmetrical *N,N*-diarylhydrazines has been developed.

Employing the catalyst system of $Pd(TFA)_2$ associated with newly developed phosphine ligand **L1**, the monoarylation of arylhydrazine proceeds smoothly to afford desired products in good-to-excellent yields (up to 95%) with good functional group compatibility. This method provides an alternative synthetic pathway for accessing structurally diversified *N,N*-diarylhydrazines from simple and easily accessible coupling components.

Introduction

Arylhydrazines are resourceful building blocks in synthetic organic chemistry. They are widely used for assembling of a myriad of nitrogen-containing heterocycles, such as indole,[1] indazole,[2] carbazole,[3] and 1,2,4-benzotriazine derivatives[4] (Figure 1A). In particular, the unsymmetrical *N*,*N*-diarylhydrazines display distinctive physicochemical and biological properties that are favorable to medicinal chemistry (Figure 1B & C).[5] In addition to fruitful applications in pharmaceutical chemistry, hydrazine functional group also serves as an effective directing group in many aromatic C–H bond functionalizations (Figure 1D).[6] Given the versatility of arylhydrazine, there is a demand of exploring new synthetic method to allow easy manipulation of the substitution pattern of these important motifs.

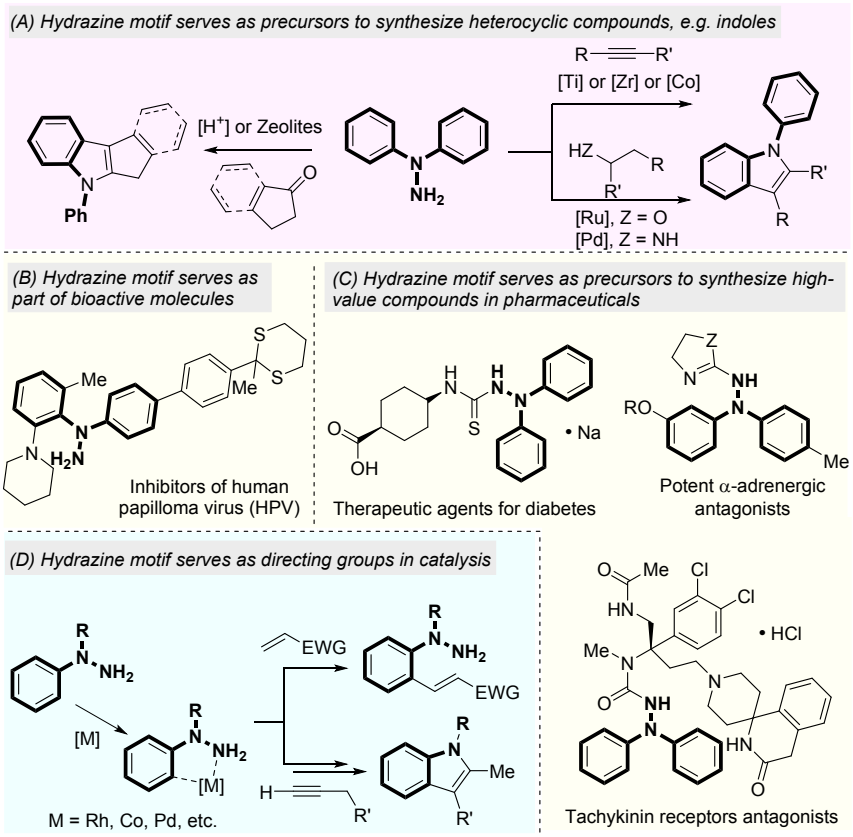


Figure 1. A brief glance of arylhydrazine scaffold in bioactive molecules and catalysis.

Traditional method for preparing *N*,*N*-diarylhydrazines is the Hofmann reaction of 1,1-diarylureas[7] and the oxidation of diaryl amines followed by reduction of the resulting aryl diazonium salts (Figure 2A).[8] Nevertheless, multistep synthetic pathway, harsh reaction conditions, narrow functional group compatibility, expensive starting materials, and low product yields may limit the attractiveness. In fact, modern catalysis has emerged as a powerful tool for constructing aromatic C–N bond.[9] This strategy demonstrates as a possible alternative of preparing *N*,*N*-diarylhydrazines.

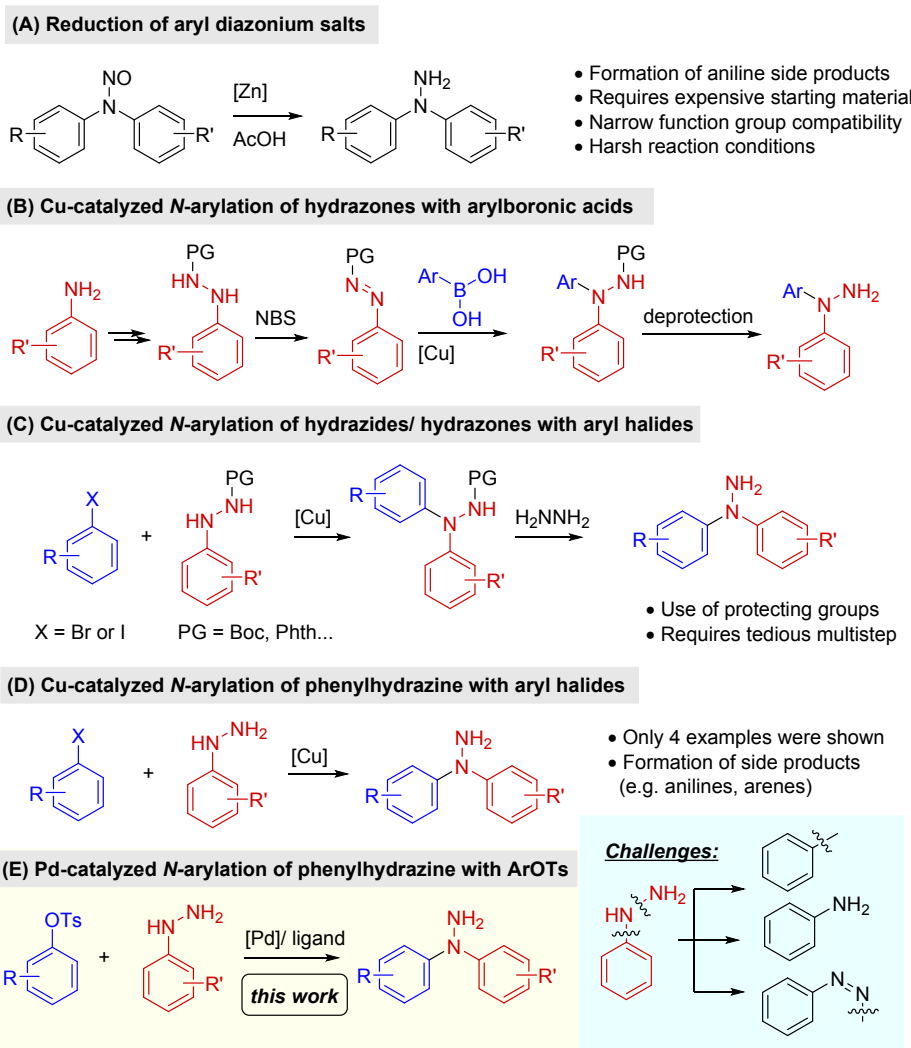


Figure 2. Selected synthetic methods of *N*,*N*-diarylhydrazines

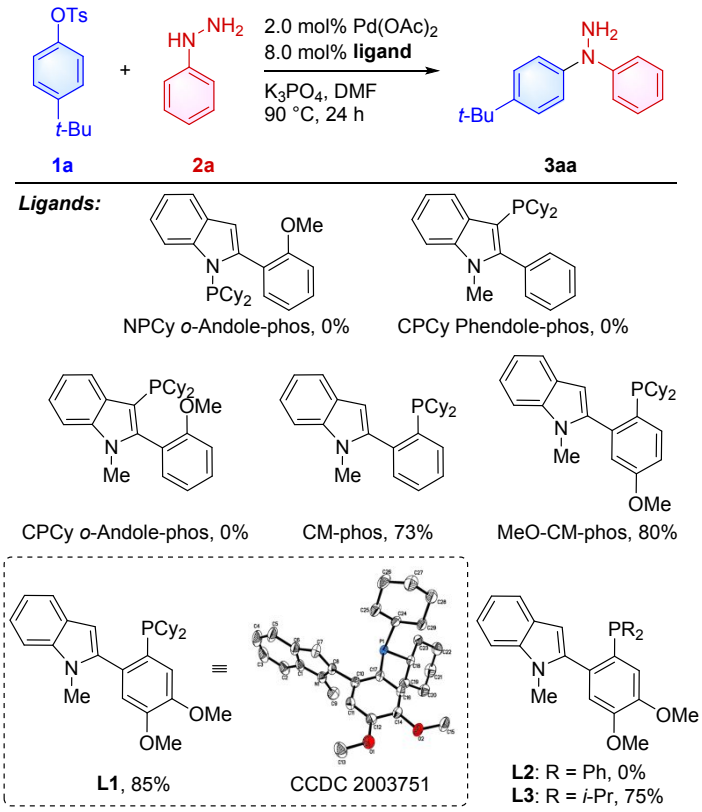
N-Arylation of amides/ hydrazides/ hydrazones under copper catalysis have been precedents.[10] Yet, tedious deprotection of Boc or Phth group was required to afford the

desirable *N*,*N*-diarylhydrazines (Figure 2B & C).[11] The reaction scheme of accessing substituted arylhydrazine without reciprocal protecting/deprotecting step remains sporadically studied. Perhaps this synthetic route suffers from the formation of byproducts such as arene and aniline, along with the desired products (i.e. Ar-NH-NH_2 serves as aryl and amine sources[12] and even as initiator of direct arylation[13]). In 2006, a streamlined copper-catalyzed *N*-arylation of phenylhydrazine with aryl iodides/bromides was reported (Figure 2D).[14] Four successful examples were shown and the reaction time was found to be 36 hours. In fact, it would be attractive to explore new method for facile and modular synthesis of unsymmetrically substituted *N*,*N*-diarylhydrazines. In continuing our relevant research works of investigating ligand system for tackling monoarylation of multi-arylation-possible substrates,[15] and C–N bond coupling reactions,[16] we herein report the first general examples of Pd-catalyzed monoarylation of arylhydrazine with aryl tosylates for affording *N*,*N*-diarylhydrazines.

Results and Discussion

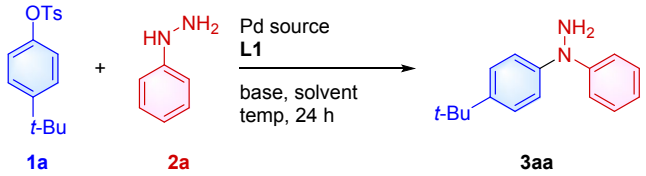
In order to probe the feasibility of the monoarylation of arylhydrazine, non-activated 4-*tert*-butylphenyl tosylate and phenylhydrazine were initially employed as benchmarking substrates. Poor conversions were observed with XPhos and SPhos whereas CataCXium PCy and Xantphos were found to be ineffective.[17] An array of our indolylphosphine ligands were tested for their efficacy in promoting this reaction (Scheme 1). Ligands having *N*-PCy_2 and C3(indole)-PCy_2 moieties, for instance, **NPCy-*o*-Andole-phos**, **CPCy-Phendole-phos** and **CPCy-*o*-Andole-phos** were found to be entirely ineffective. It is interesting to show that only the dialkylphosphino component located at the 2-arene position of ligands were able to catalyze this reaction. Among new ligands **L1**-**L3** surveyed, **L1** gave the best product yield. No reaction was observed when less electron-rich **L2** was used as the ligand. This result was possibly due to the incapability of facilitating oxidative cleavage of the C(Ar)−O bond of aryl tosylate. The ligand structure **L1** was unambiguously characterized by single crystal X-ray crystallographic analysis.

Scheme 1. An evaluation of our proprietary indolylphosphines and new ligands **L1-L3** in Pd-catalyzed monoarylation of phenylhydrazine[a]



[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), $Pd(OAc)_2$ (2.0 mol%), ligand (8.0 mol%; Pd/**L** = 1:4), K_3PO_4 (0.6 mmol) and DMF (1.5 mL) were stirred at 90 °C under nitrogen atmosphere for 24 h. GC yields using tetradecane as the internal standard were reported.

Table 1. Initial reaction conditions screening of Pd-catalyzed monoarylation of phenylhydrazine with **1a**[a]



entry	catalyst (mol%)	base	solvent	% yield[b]
1	$Pd(OAc)_2$ (2.0)	K_3PO_4	DMF	85
2	$Pd(OAc)_2$ (2.0)	K_2CO_3	DMF	70
3	$Pd(OAc)_2$ (2.0)	Cs_2CO_3	DMF	84
4	$Pd(OAc)_2$ (2.0)	$K_3PO_4 \cdot H_2O$	DMF	82
5[c]	$Pd(OAc)_2$ (2.0)	K_3PO_4	DMF	78

6[d]	$Pd(OAc)_2$ (2.0)	K_3PO_4	DMF	89
7[e]	$Pd(OAc)_2$ (2.0)	K_3PO_4	DMF	73
8	$Pd(OAc)_2$ (2.0)	K_3PO_4	*t*-BuOH	67
9	$Pd(OAc)_2$ (2.0)	K_3PO_4	DMA	82
10	$Pd(OAc)_2$ (2.0)	K_3PO_4	toluene	68
11	$Pd(OAc)_2$ (2.0)	K_3PO_4	DMA:DMF = 1:1	83
12	$PdCl_2(ACN)_2$ (2.0)	K_3PO_4	DMF	87
13	$PdCl_2(COD)$ (2.0)	K_3PO_4	DMF	92
14	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	95
15	$Pd_2(dba)_3$ (1.0)	K_3PO_4	DMF	87
16	$Pd(TFA)_2$ (1.0)	K_3PO_4	DMF	87
17[f]	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	40
18[g]	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	90
19[h]	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	97 (95)
20[i]	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	85
21[j]	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	73
22[k]	$Pd(TFA)_2$ (2.0)	K_3PO_4	DMF	80

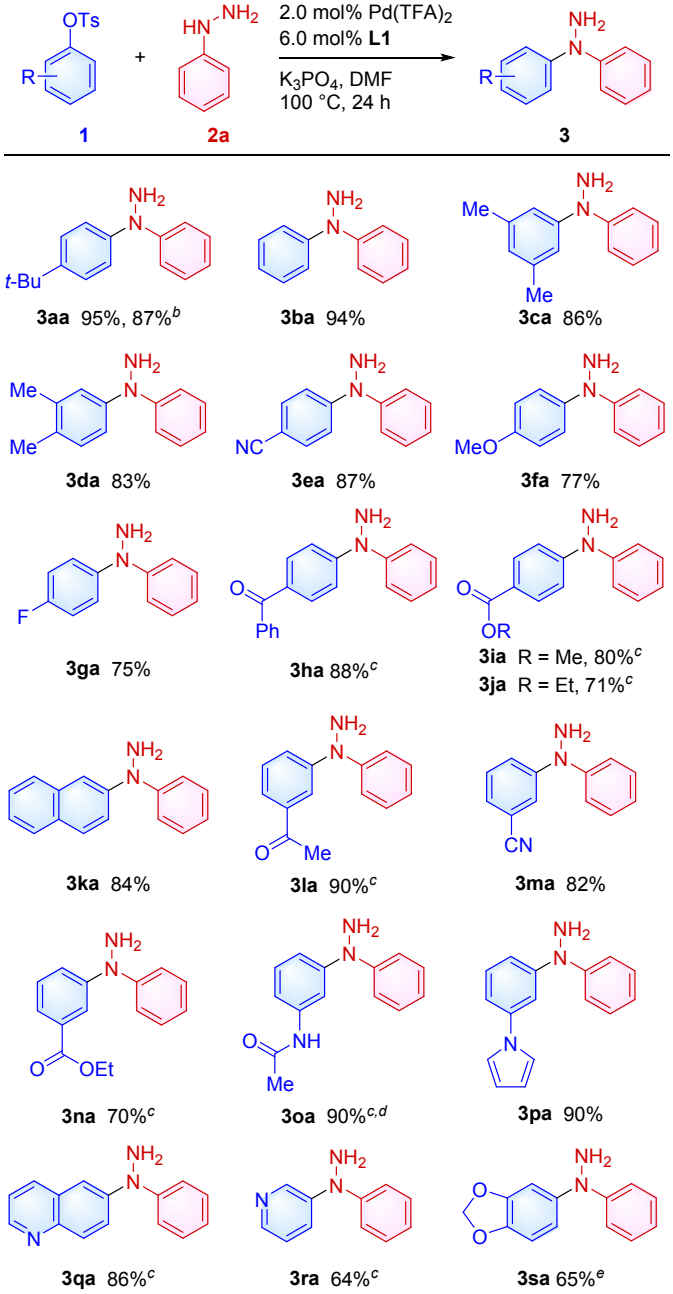
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (1.0 mmol), Pd source (as indicated), Pd/**L1** = 1:4, base (0.6 mmol), $PhB(OH)_2$ (0.01 mmol) and solvent (1.0 mL) were stirred at 90 °C under nitrogen for 24 h. [b]Yields were determined by GC-FID with tetradecane as the internal standard. Isolated yield was shown in parentheses. [c]1.5 equiv. of K_3PO_4 was used. [d]100 °C was used. [e]105 °C was used. [f]Pd/L = 1:1 was used. [g]Pd/L = 1:2 was used. [h]Pd/L = 1:3 was used. [i]3.0 equiv. of **2a** was used. [j]No $PhB(OH)_2$ was added. [k]Phenylhydrazine hydrochloride (2.0 equiv.) and K_3PO_4 (5.0 equiv.) were used instead of **2a**.

Having identified the effective ligand, we next put effort to investigate the best reaction parameters fit for the Pd/**L1** catalyst system (Table 1). Commonly used K_3PO_4, Cs_2CO_3 and $K_3PO_4 \cdot H_2O$ bases gave comparable results (entry 1 vs entries 3-4). Lowering the amount of K_3PO_4 gave a lower product yield (entry 1 vs entry 5). DMF provided a better result than *t*-BuOH and other common organic solvents (entry 1 vs entries 8-11). $Pd(TFA)_2$ metal source showed the best performance among others investigated (entry 1 vs entries 12-15).[18] Reducing the Pd catalyst loading to 1.0 mol% resulted a drop of product yield. (entry 14 vs entry 16). The best metal-to-ligand ratio was found to be 1:3 (entry 14 vs entries 17-19). Phenylhydrazine hydrochloride salt, a more

stable form of phenylhydrazine, was also tested as the coupling partner, yet a 75% yield was given (entry 14 vs entry 22).

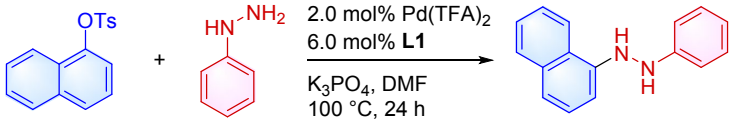
Encouraged by the optimized Pd/**L1** catalyst system, we then turned our attention to examine the substrate scope (Scheme 2). In general, the reaction proceeded smoothly with a broad spectrum of aryl tosylates. Electron-neutral (Scheme 2, products **3aa**-**3da**), -rich (Scheme 2, product **3fa**), and -deficient (Scheme 2, products **3ea**, **3ga**) aryl tosylates were well-tolerated. Particular functional groups, including methyl ester, nitrile, and enolizable keto moieties (Scheme 2, products **3ja, 3la**, and **3ma**, respectively) remained intact under these reaction conditions. When 3-acetamidophenyl tosylate (**1o**) was used as coupling partner, the *N*-arylation reaction occurred selectively at the hydrazine NH instead of the amido NH position (Scheme 2, product **3oa**). Heterocycles such as quinoline, pyrrole, and pyridine were all compatible under this catalyst system (Scheme 2, products **3pa**, **3qa**, and **3ra**, respectively). Sterically congested naphthalen-1-yl tosylate (**1t**) did not afford the targeted *N*,*N*-diarylhydrazine but **3ta** was resulted (Scheme 3). A similar example was demonstrated by Stradiotto in 2010 for the *N*-arylation of phenylhydrazine with aryl chloride using Pd/Mor-DalPhos catalyst system (in which *N*,*N'*-diarylhydrazines was formed).[19]

Scheme 2. Palladium-catalyzed monoarylation of phenylhydrazine with aryl tosylates[a]



[a]Reaction conditions: **1** (0.5 mmol), **2a** (2.5 mmol), $Pd(TFA)_2$ (2.0 mol%), **L1** (6.0 mol%; Pd/L = 1:3), K_3PO_4 (1.5 mmol), $PhB(OH)_2$ (0.02 mmol) and DMF (1.5 mL) were stirred at 100 °C under nitrogen for 24 h. Isolated yields were reported. Reaction times were not optimized for each substrate. [b]Isolated yields of gram-scale synthesis (10.0 mmol, 2.09 g). [c]1.0 mmol of **2a** was used. [d]No $PhB(OH)_2$ was added. [e]1.5 mmol% of **2a** was used.

Scheme 3. Palladium-catalyzed *N*-arylation of steric hindered **1t** with **2a**[a]



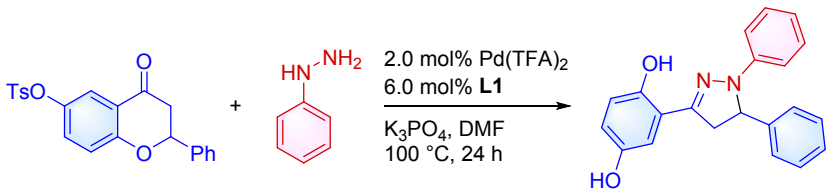
1t **2a** **3ta** 77%

see SI for X-ray structure

[a]Reaction conditions: **1t** (0.5 mmol), **2a** (1.0 mmol), $Pd(TFA)_2$ (2.0 mol%), **L1** (6.0 mol%), K_3PO_4 (1.5 mmol), $PhB(OH)_2$ (0.02 mmol) and DMF (1.5 mL) were stirred at 100 °C under nitrogen for 24 h. Isolated yield.

When 4-oxo-2-phenylchroman-6-yl tosylate (**1u**) was used as the coupling partner, an unexpected side product **3ua** was generated in 89% yield (Scheme 4). It is believed that **1u** underwent condensation to give flavanone hydrazone, followed by alkali hydrolysis and cyclization to afford the pyrazoline **3ua**. This transformation was confirmed to proceed in the absence of palladium complex. The structure of **3ua** was confirmed by X-ray crystallography (see Supporting Information for detail).

Scheme 4. Formation of pyrazoline by reaction of **1u** with **2a**[a]



1u **2a** **3ua** 89%

see SI for X-ray structure

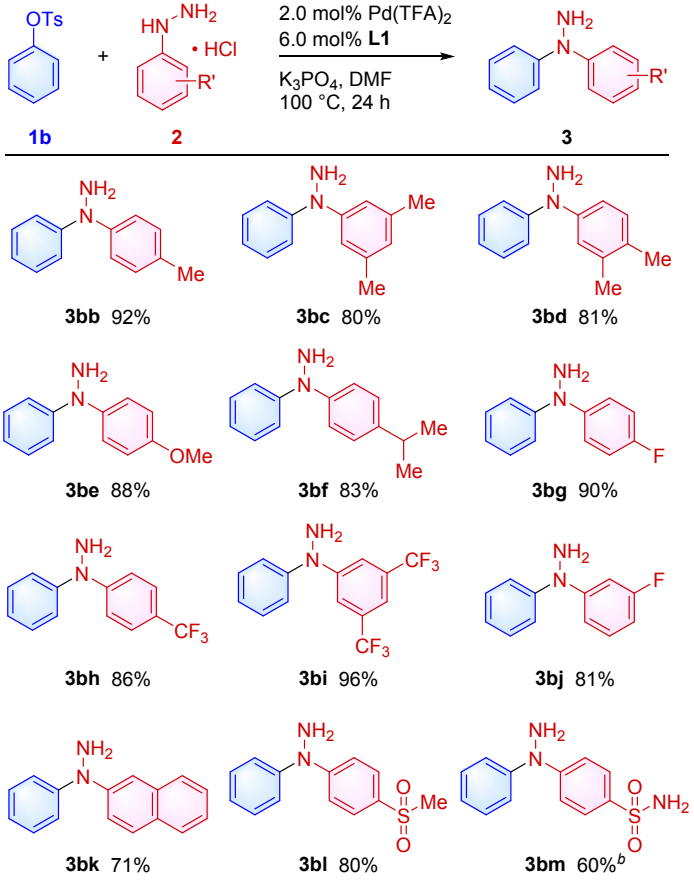
reaction conditions differ from the above	yield of **3ua**
w/o $Pd(TFA)_2$	88%
w/o $Pd(TFA)_2$ and **L1**	87%

[a]Reaction conditions: **1u** (0.5 mmol), **2a** (1.0 mmol), $Pd(TFA)_2$ (2.0 mol%), **L1** (6.0 mol%), K_3PO_4 (1.5 mmol), $PhB(OH)_2$ (0.02 mmol) and DMF (1.5 mL) were stirred at 100 °C under nitrogen for 24 h. Isolated yield.

The scope of the monoarylation reaction with respect to other substituted arylhydrazines was next investigated and the results are compiled in Scheme 5. Arylhydrazines with different substitution patterns, in terms of electronic properties and

substitution positions on the arene ring, were tested. In general, the corresponding *N,N*-diarylhydrazines were furnished in good-to-excellent yields. It should be noted that 4-hydrazineylbenzenesulfonamide hydrochloride (**2m**) having three different NH groups, was found to be a feasible substrate to afford the desired product **3bm.**

Scheme 5. Palladium-catalyzed monoarylation of arylhydrazine hydrochloride **2** with aryl tosylate **1b**[a]



[a]Reaction conditions: **1b** (0.5 mmol), **2** (1.0 mmol), $Pd(TFA)_2$ (2.0 mol%), **L1** (6.0 mol%; Pd/L = 1:3), K_3PO_4 (2.5 mmol), $PhB(OH)_2$ (0.02 mmol) and DMF (1.5 mL) were stirred at 100 °C under nitrogen for 24 h. Isolated yields were reported. Reaction times were not optimized for each substrate. [b]1.5 mmol of K_3PO_4 was used.

In conclusion, we have developed an efficient Pd/**L1** catalyst system for the first general monoarylation of arylhydrazine with aryl tosylates. The structure of **L1** was

unambiguously characterized and its efficacy was found more successful than the corresponding CM-phos and MeO-CM-phos in dealing with this arylation process. The newly reported Pd/**L1** system exhibited good functional group compatibility (e.g. methyl ester, NH amido, enolizable keto, and heterocycles etc.) and offered good-to-excellent product yields (up to 95%). This method provides an alternative synthetic pathway for preparing structurally diverse *N,N*-diarylhydrazines from simple and readily accessible coupling partners. We believe this newly developed palladium catalyst system will be useful in other C–N coupling processes in relevance.

Experimental Section

General Information. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. All Pd-catalyzed cross-coupling reactions were performed in Rotaflo®(England) re-sealable screw-cap Schlenk tube (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bar (4 mm × 10 mm). Toluene were freshly distilled over sodium under nitrogen.[20] *N*,*N*-Dimethylformamide (DMF) was distilled from calcium hydride under reduced pressure. Dichloromethane was freshly distilled over calcium hydride under nitrogen atmosphere. *t*-BuOH was first distilled over sodium and stored with calcium hydride under nitrogen. A new bottle of *n*-butyllithium was used (note: since the concentration of *n*-BuLi from old bottles may vary, a titration is highly recommended prior to use). Ligand **NPCy *o*-Andole-phos**,[21] **CPCy Phendole-phos**,[22] **CPCy *o*-Andole-phos**,[23] **CM-phos**[24] and **MeO-CM-phos**[25] were developed by Kwong and prepared according to literatures.[26] Thin layer chromatography was performed on precoated silica gel 60 F_{254} plates. Silica gel (230-400 mesh) was used for column chromatography. ^{1}H NMR spectra were recorded on a 500 MHz spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with TMS (δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a 126 MHz spectrometer and the spectra were

referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a ESI- Q Exactive Focus Orbitrap mass spectrometer which the ionization method is electrospray ionization (ESI). GC-MS analysis was conducted on a GCD system. Products described in GC yield were obtained on the basis of authentic samples/ *n*-tetradecane calibration standard from GC-FID system.

Preparation of 2-(2-(dicyclohexylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1*H*-indole (L1)

1-(2-Bromo-4,5-dimethoxyphenyl)ethan-1-one.[27] An oven-dried 250-mL single-neck round-bottom flask equipped with a Teflon-coated magnetic stir bar was charged with 4,5-dimethoxyacetophenone (9.01 g, 50.0 mmol) and *N*-bromosuccinimide (9.79 g, 55.0 mmol) in $[bmim]PF_6$ (100.0 mL). The solution was placed in preheated oil bath (27 °C) overnight. After completion of the reaction, as indicated by TLC and GC-MS, the reaction mixture was washed with diethyl ether several times. The organic layer was concentrated under rotary evaporation. The crude product was purified by flash column chromatography on silica gel to afford 1-(2-bromo-4,5-dimethoxyphenyl)ethan-1-one. Off white powder, 64% yield (8.45 g). Hexane: Ethyl acetate = 4:1, R_f = 0.33. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (s, 1H), 7.03 (s, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 2.66 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 199.5, 151.6, 148.1, 132.7, 116.4, 112.6, 111.8, 56.3, 56.1, 30.4.

2-(2-Bromo-4,5-dimethoxyphenyl)-1H-indole.[28] An oven-dried 250-mL single-neck round-bottom flask equipped with a Teflon-coated magnetic stir bar was charged with 1-(2-bromo-4,5-dimethoxyphenyl)ethan-1-one (7.77 g, 30.0 mmol) and phenylhydrazine(3.6 mL, 36.0 mmol) *via* syringe. Phosphoric acid (15.0 mL) was added slowly and the reaction mixture was stirred for 30 min. Polyphosphoric acid (50.0 g) was added to the reaction mixture slowly with continuous stirring, and then placed in a preheated oil bath (85 °C) for 15 min. The bath temperature was raised to 105 °C and the reaction mixture was heated for 40 min. After completion of the reaction, the resulting mixture was then poured into ice water and extracted with water and dichloromethane for

several times. The organic layer was separated and the aqueous layer was washed with dichloromethane. The combined organic layer was concentrated under rotary evaporation. The crude product was purified by flash column chromatography on silica gel to afford 2-(2-bromo-4,5-dimethoxyphenyl)-1*H*-indole ligand precursor. Pale yellow powder, 75% yield (7.47 g). Hexane: Ethyl acetate = 4:1, R_f = 0.26. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.61 (s, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 8.0 H, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.12 (s, 1H), 7.07 (s, 1H), 6.74 (m, 1H), 3.92 (s, 3H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.3, 148.4, 136.5, 136.1, 128.2, 125.7, 122.4, 120.6, 120.1, 116.3, 113.8, 111.6, 110.9, 102.8, 56.2, 56.1.

N-Methyl-2-(2'-bromo-4',5'-dimethoxyphenyl)indole. An oven-dried 250-mL three-neck round-bottom flask was equipped with a Teflon-coated magnetic stir bar, and charged with sodium hydride (60 % dispersion in mineral oil, washed with anhydrous hexane before use) (0.96 g of NaH in oil, 24.0 mmol). The necks were fitted with pressure-equalizing dropping funnel and charged with 2-(2-bromo-4,5-dimethoxyphenyl)-1*H*-indole (6.64 g, 20.0 mmol), rubber septum and nitrogen stopcock inlet. The flask was evacuated and backfilled with nitrogen three times. Anhydrous tetrahydrofuran (5.0 mL) was added to the reaction flask *via* syringe to form a suspension of sodium hydride. The suspension was cooled to 0 °C in ice-water bath. The solution of 2-(2-bromo-4,5-dimethoxyphenyl)-1*H*-indole was added dropwise *via* dropping funnel to the reaction mixture. Upon completion of addition, the reaction mixture was allowed to reach room temperature and stirred for 30 min. Dimethyl sulfate (1.9 mL, 20.6 mmol) was added and the mixture was stirred for overnight. After completion of the reaction, methanol was added to quench the reaction and the mixture was extracted with water and ethyl acetate. The combined organic layer was concentrated and purified by column chromatography to afford *N*-methyl-2-(2'-bromo-4',5'-dimethoxyphenyl)indole ligand precursor. Pale yellow solid, 91% yield (6.30 g), m.p. = 50.3-53.5 °C. Hexane: Ethyl acetate = 4:1, Rf = 0.46. 1H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 8.0 H, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.25-7.22 (m, 2H), 6.99 (s, 1H), 6.59 (s, 1H), 3.97 (s, 3H), 3.90 (s, 3H), 3.64 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 149.6, 147.7, 139.4, 136.8, 127.3, 125.8, 121.4, 120.3, 119.5, 115.2, 115.0, 114.9, 109.3, 101.6, 55.9, 55.8, 30.3; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}BrNO_2$ 346.0437; Found 346.0434.

*2-(2-(Dicyclohexylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1H-indole (**L1**)*. *N*-Methyl-2-(2'-bromo-4',5'-methoxyphenyl)indole (3.46 g, 10.0 mmol) was dissolved in freshly distilled THF (25.0 mL) at room temperature under nitrogen atmosphere. The solution was cooled to -78 °C in dry ice/acetone bath. Titrated *n*-BuLi (11.0 mmol) was added dropwise with a syringe. After the reaction mixture was stirred for 30 min, chlorodicyclohexylphosphine (2.64 mL, 12 mmol) in THF was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure. The product was recrystallized by methanol to afford 2-(2-(dicyclohexylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1*H*-indole (**L1**). Off-white solid, 54% yield (2.50 g), m.p. = 164.0-164.8 °C. Hexane: Ethyl acetate = 4:1, R_f = 0.64. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.07 (s, 1H), 6.85 (d, *J* = 3.0 Hz, 1H), 6.37 (s, 1H), 3.99 (s, 3H), 3.86 (s, 3H), 3.50 (s, 3H), 1.72–1.63 (m, 11H), 1.28–1.07 (m, 11H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 148.9, 148.4, 141.2 (overlapped), 136.6, 134.3, 134.1, 128.3, 128.1, 127.6, 121.1, 120.2, 119.4, 114.6, 114.5, 109.5, 103.2, 103.1, 56.1, 55.8, 35.4, 33.4, 30.8, 30.7, 30.0, 27.3, 26.4. ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ −10.43. HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{39}NO_2P$ 464.2712, Found 464.2707.

Preparation of 2-(2-(diphenylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1*H*-indole (L2)

N-Methyl-2-(2′-bromo-4′,5′-dimethoxyphenyl)indole (0.69 g, 2.0 mmol) was dissolved in freshly distilled THF (10.0 mL) at room temperature under nitrogen atmosphere. The solution was cooled to −78 °C in dry ice/acetone bath. Titrated *n*-BuLi (2.2 mmol) was added dropwise with a syringe. After the reaction mixture was stirred for 30 min, chlorodiphenylphosphine (0.43 mL, 2.4 mmol) in THF was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure. The product was recrystallized by methanol to afford 2-(2-(diphenylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1*H*-indole (**L2**). Off-white solid, 49% yield (0.45 g), m.p. = 166.9-168.3 °C, Hexane: Ethyl acetate = 4:1, R_f = 0.54. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.5 Hz, 1H), 7.31-7.29 (m, 7H), 7.23-7.21 (m, 5H), 7.09

(t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 3.5 Hz, 1H), 6.61 (d, *J* = 2.5 Hz, 1H), 6.21 (s, 1H), 3.88 (s, 3H), 3.62 (s, 3H), 3.48 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 149.0, 148.9, 139.3, 139.2, 137.9, 137.8, 136.8, 133.4, 133.3, 131.8, 131.5, 130.2, 130.1, 128.3, 128.2 , 128.1, 127.3, 121.2, 120.3, 119.3, 116.0, 114.1 (overlapped), 109.2, 103.6, 103.5, 55.8, 55.5, 30.4 (overlapped); $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$): δ −13.22. HRMS(ESI) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{27}NO_2P$ 452.1173; Found 452.1173.

Preparation of 2-(2-(diisopropylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1*H*-indole (L3)

N-Methyl-2-(2′-bromo-4′,5′-dimethoxyphenyl)indole (0.69 g, 2.0 mmol) was dissolved in freshly distilled THF (10 mL) at room temperature under nitrogen atmosphere. The solution was cooled to −78 °C in dry ice/acetone bath. Titrated *n*-BuLi (2.2 mmol) was added dropwise with a syringe. After the reaction mixture was stirred for 30 min, chlorodiisopropylphosphine (0.38 mL, 2.4 mmol) in THF was added. The reaction was allowed to warm to room temperature and stirred overnight. The solvent was removed under reduced pressure. The product was recrystallized by methanol and *n*-hexane to afford 2-(2-(diisopropylphosphino)-4,5-dimethoxyphenyl)-1-methyl-1*H*-indole (**L3**). Off-white solid, 55% yield (0.42 g), m.p. = 112.3-114.8 °C, *n*-Hexane: Ethyl acetate = 4:1, R_f = 0.74. ^1H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.11 (s, 1H), 6.90 (d, *J* = 3.0 Hz, 1H), 6.42 (s, 1H), 4.00 (s, 3H), 3.89 (s, 3H), 3.55 (s, 3H), 2.21 (bs, 1H), 1.90 (bs, 1H), 1.01 (s, 12H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 148.9, 148.4, 141.0 (overlapped), 136.5, 134.0, 133.8, 128.5, 128.3, 127.5, 121.0, 120.1, 119.3, 114.5 (overlapped), 114.3, 114.2, 109.3, 103.1 (overlapped), 55.9, 55.7, 30.6 (overlapped), 25.6, 23.2, 20.1, 18.3; $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$): δ −2.01. HRMS(ESI) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{31}NO_2P$ 384.2086 found 384.2086.

General Procedures for Ligand and Reaction Condition Screenings

Pd source (indicated in Table 1) and ligand (indicated in Table 1) were loaded into Schlenk tube with a Teflon-coated magnetic stirrer bar (4.5 mm x 12 mm). The tube was evacuated and backfilled with nitrogen (3 cycles). Precomplexation was applied by

adding freshly distilled DCM (1.0 mL) and Et_3N (0.05 mL) into the tube. The solution was stirred and warmed using oil bath (~50°C) for about 1 min until the solvent started boiling. After cooling down, the solvent in tube was removed under high vacuum. 4-*tert*-Butylphenyl tosylate (**1a**) (60.8 mg, 0.2 mmol), phenylboronic acid (1.2 mg, 0.01 mmol) and base (indicated in Table 1) were loaded into the Schlenk tube which was again evacuated and re-filled with nitrogen for three times. Phenylhydrazine (**2a**) (the equivalence was indicated in Table 1 with respect to **1a**) and the solvent (0.6 mL) were added while the mixture was being stirred at room temperature for ~10 min. The Schlenk tube was then placed in a preheated oil bath (temperature indicated in Table 1) for 24 hours. The reaction tube was allowed to reach room temperature. Water, ethyl acetate and *n*-tetradecane (52 μL, internal standard) were added to the mixture. The organic layer was subjected to GC analysis. The GC yield was previously calibrated by authentic sample/ *n*-tetradecane calibration curve.

General Procedures for monoarylation of Substituted Phenylhydrazines with Aryl Tosylates

$Pd(TFA)_2$ (3.3 mg, 0.01 mmol), **L1** (13.8 mg, 0.03 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The tube was evacuated and flushed with nitrogen for three cycles. Precomplexation was applied by adding freshly distilled DCM (1.0 mL) and Et_3N (0.10 mL) into the tube. The solution was stirred and warmed using oil bath (~50 °C) for about 1 min until the solvent started boiling. After cooling down, the solvent in tube was removed under high vacuum. Aryl tosylates (0.5 mmol), $PhB(OH)_2$ (1.4 mg, 0.02 mmol), and K_3PO_4 (0.318 g, 1.5 mmol) were loaded to the Schlenk tube which was again evacuated and re-filled with nitrogen for three times. DMF (1.5 mL) was then added while the mixture was being continuously stirred at room temperature for ~5 min. Phenylhydrazine derivatives (1.0-2.5 mmol, indicated in Scheme's footnote) was added *via* syringe. The tube was then placed into a preheated oil bath (100 °C) and stirred for 24 hours. After completion of reaction, the reaction tube was allowed to cool to room temperature and quenched with water and diluted with ethyl acetate. The organic layer was separated and the aqueous layer was washed with ethyl acetate. The filtrate

was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

1-(4-(*tert*-Butyl)phenyl)-1-phenylhydrazine (Scheme 1 and 2, Product 3aa)

Yield: 95% (114 mg for 0.5 mmol scale) and 87% (2.09 g for 10 mmol scale). Off white solid, m.p. = 69.3-65.4 °C. R_f = 0.63 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.0 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 8.0 Hz, 4H), 6.96 (t, *J* = 7.5 Hz, 1H), 4.14 (s, 2H), 1.36 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 149.3, 146.6, 145.4, 128.8, 125.9, 120.9, 120.1, 118.1, 34.2, 31.3; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{21}N_2$ 241.1699; Found 241.1698.

***N,N*-Diphenylhydrazine (Scheme 2, Product 3ba)**[8d]

Yield: 94% (86 mg). Light yellow oil. R_f = 0.57 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.5 Hz, 4H), 7.29 (d, *J* = 8.0 Hz, 4H), 7.06 (t, *J* = 7.0 Hz, 2H), 4.18 (s, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 149.0, 128.9, 121.8, 119.3.

1-(3,5-Dimethylphenyl)-1-phenylhydrazine (Scheme 2, Product 3ca; Scheme 4, Product 3bc)

Yield: 86% (91 mg for product **3ca**) and 80% (85 mg for product **3bc**). Light yellow oil. R_f = 0.63 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.86 (s, 2H), 6.68 (s, 1H), 4.13 (s, 2H), 2.29 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 149.3, 149.2, 138.7, 128.9, 124.1, 121.3, 119.0, 117.7, 21.4; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{17}N_2$ 213.1386; Found 213.1385.

1-(3,4-Dimethylphenyl)-1-phenylhydrazine (Scheme 2, Product 3da; Scheme 4, Product 3bd)

Yield: 83% (88 mg for product **3da**) and 81% (86 mg for product **3bd**). Light yellow oil. R_f = 0.60 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.08 (s, 1H), 7.02-7.01 (m, 1H), 6.94 (t, *J* = 7.0 Hz, 1H), 4.12 (s, 2H), 2.28 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ

149.7, 147.1, 137.4, 131.3, 130.2, 128.7, 122.6, 120.5, 118.7, 117.6, 19.9, 19.0; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{17}N_2$ 213.1386; Found 213.1385.

4-(1-Phenylhydrazinyl)benzonitrile (Scheme 2, Product 3ea)

Yield: 87% (91 mg). Off white solid. R_f = 0.26 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, *J* = 8.0 Hz, 4H), 7.30 (d, *J* = 7.5 Hz, 2H), 7.25-7.22 (m, 1H), 7.12 (d, *J* = 8.5 Hz, 2H), 4.21 (s, 2H); ^{13}C NMR{^{1}H} (126 MHz, $CDCl_3$) δ 152.4, 146.7, 133.0, 129.9, 126.0, 124.1, 120.1, 114.5, 100.5; HRMS(ESI) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{12}N_3$ 210.1025; Found 210.1025.

1-(4-Methoxyphenyl)-1-phenylhydrazine (Scheme 2, Product 3fa; Scheme 4, Product 3be)[29]

Yield: 77% (82 mg for product **3fa**); 88% (94 mg for product **3be**). Off white solid. R_f = 0.49 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 - 7.19 (m, 4H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.85 (t, *J* = 7.5 Hz, 1H), 4.09 (s, 2H), 3.82 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.5, 150.4, 142.7, 128.8, 124.7, 119.7, 115.9, 114.7, 55.5.

1-(4-Fluorophenyl)-1-phenylhydrazine (Scheme 2, Product 3ga; Scheme 4, Product 3bg)[1e]

Yield: 75% (76 mg for product **3ga**); 90% (91 mg for product **3bg**). Light yellow oil. R_f = 0.53 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 7.5 Hz, 2H), 7.22-7.20 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.01 (t, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 4.13 (s, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 158.7 (d, J_F = 0.24 Hz), 149.6, 145.3 (d, J_F = 0.003 Hz), 129.0, 122.6 (d, J_F = 0.008 Hz, 2C), 121.2, 117.8, 115.7 (d, J_F = 0.02 Hz, 2C); ^{19}F{^{1}H} NMR (470 MHz, $CDCl_3$) δ -120.3.

Phenyl (4-(1-phenylhydrazinyl)phenyl)methanone (Scheme 2, Product 3ha)

Yield: 88% (127 mg). Light yellow solid, m.p. = 89.3-90.8 °C. R_f = 0.74 (Ethyl acetate: Hexane = 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.0 Hz, 4H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.46 -7.38 (m, 2H), 7.34 (d, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 2H), 7.15 (d, *J* = 8.0

Hz, 3H), 4.27 (s, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 195.2, 152.7, 147.0, 138.7, 132.0, 131.4, 129.6, 129.5, 127.9 (overlapped), 125.2, 123.6, 113.9; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{17}N_2O$ 289.1335; Found 289.1331.

Methyl 4-(1-phenylhydrazinyl)benzoate (Scheme 2, Product 3ia)

Yield: 80% (97 mg). Light yellow oil. R_f = 0.29 (Ethyl acetate: Hexane = 1:4). ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.5 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 7.5 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 2H), 4.22 (s, 2H), 3.86 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.1, 152.8, 147.4, 130.8, 129.6, 125.1, 123.5, 120.5, 114.4, 51.7; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O_2$ 243.1128; Found 243.1126.

Ethyl 4-(1-phenylhydrazineyl)benzoate (Scheme 2, Product 3ja)[30]

Yield: 71% (91 mg). Light yellow oil. R_f = 0.33 (Ethyl acetate: Hexane = 1:4). ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 4.34-4.30 (q, *J* = 7.0 Hz, 2H), 4.22 (s, 2H), 1.36 (t, *J* =7.0 Hz, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.5, 152.6, 147.3, 130.7, 129.4, 124.8, 123.2, 120.8, 114.3, 60.3, 14.3.

1-(2-Naphthalenyl)-1-phenylhydrazine (Scheme 2, Product 3ka; Scheme 4, Product 3bk)[7b]

Yield: 84% (98 mg for product **3ra**); 71% (83 mg for product **3bk**). Light yellow oil. R_f = 0.51 (Ethyl acetate: Hexane = 1:4). ^1H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.5 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 2H), 7.60 (s, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.44 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.41-7.36 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 4.25 (s, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 149.0, 146.5, 134.2, 129.4, 129.0, 128.4, 127.4, 126.8, 126.2, 123.9, 122.3, 120.6, 120.0, 113.8.

1-(3-(1-Phenylhydrazinyl)phenyl)ethan-1-one (Scheme 2, Product 3la)

Yield: 90% (102 mg). Light yellow oil. R_f = 0.23 (Ethyl acetate: Hexane = 1:4). ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.34-7.30 (q, *J* = 8.0 Hz, 3H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 4.20 (s, 2H),

2.57 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.3, 149.4, 148.6, 138.0, 129.4, 129.0, 123.3, 122.6, 121.0, 120.8, 117.2, 26.8; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{15}N_2O$ 227.1178; Found 227.1177.

3-(1-Phenylhydrazinyl)benzonitrile (Scheme 2, Product 3ma)[31]

Yield: 82% (86 mg). Light yellow oil. R_f = 0.34 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.24 (d, *J* = 7.0 Hz, 3H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 4.15 (s, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 149.7, 147.7, 129.8, 129.5, 125.0, 123.0, 122.6, 120.4, 119.3, 119.2, 112.6.

Ethyl 3-(1-phenylhydrazineyl)benzoate (Scheme 2, Product 3na)

Yield: 70% (90 mg). Light yellow oil. R_f = 0.39 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91(s, 1H), 7.61(d, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.34-7.28 (m, 3H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 4.38-4.33 (q, *J* = 7.5 Hz, 2H), 4.20 (s, 2H), 1.37 (t, *J* = 7.5 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 166.6, 149.1, 148.6, 131.3, 129.2, 128.7, 122.8, 122.6, 122.1, 120.3, 119.0, 60.9, 14.2; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{17}N_2O_2$ 257.1284; Found 257.1282.

***N*-(3-(1-Phenylhydrazinyl)phenyl)acetamide (Scheme 2, Product 3oa)**

Yield: 90% (108 mg). Off white solid, m.p. = 98.5-101.7 °C. R_f = 0.51 (Ethyl acetate: Hexane = 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.37 (s, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.0 Hz, 1H), 4.12 (s, 2H), 2.11 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 168.7, 149.6, 148.6, 138.6, 129.1, 129.0, 122.5, 120.3, 114.3, 112.9, 110.0, 24.3; HRMS (ESI) *m/z* $[M + Na]^+$ Calcd for $C_{14}H_{15}N_3ONa$ 264.1107; Found 264.1105.

1-(3-(1-Phenylhydrazinyl)phenyl)-1H-pyrrole (Scheme 2, Product 3pa)

Yield: 90% (112 mg). Off white solid, m.p. = 91.1-92.5 °C. R_f = 0.46 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, *J* = 7.5 Hz, 2H), 7.32-7.28 (m, 4H), 7.12-7.09 (m, 3H), 7.06 (d, *J* = 8.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.36 (s, 2H), 4.19 (s, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 150.2, 148.5, 141.3, 129.7, 129.3, 123.3, 121.1, 119.3,

114.8, 112.8, 110.0, 109.9; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{16}N_3$ 250.1339; Found 250.1336.

6-(1-Phenylhydrazinyl)quinoline (Scheme 2, Product 3qa)

Yield: 86% (101 mg). Light yellow solid, m.p. = 96.7-98.5 °C. R_f = 0.37 (Ethyl acetate: Hexane = 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (dd, *J* = 4.0, 1.0 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.61 (dd, *J* = 9.5, 2.5 Hz, 1H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.32-7.30 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H), 4.29 (s, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.6, 147.9, 147.1, 144.5, 134.7, 129.7, 129.4, 129.3, 123.7, 123.3, 121.5, 121.4, 111.4; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{14}N_3$ 236.1182; Found 236.1180.

3-(1-Phenylhydrazinyl)pyridine (Scheme 2, Product 3ra)[32]

Yield: 64% (59 mg). Light yellow oil. R_f = 0.25 (Ethyl acetate: Hexane = 1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.15 (d, *J* = 4.5 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.15 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 4.19 (s, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 148.1, 145.2, 141.8, 140.3, 129.5, 124.4, 123.6, 123.2, 120.7.

1-(Benzo[*d*][1,3]dioxol-5-yl)-1-phenylhydrazine (Scheme 2, Product 3sa)

Yield: 61% (74 mg). Light yellow oil. R_f = 0.51 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.5 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 2H), 6.72 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.96 (s, 2H), 4.08 (s, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 150.1, 148.1, 144.1, 144.1, 128.8, 120.2, 116.6, 115.8, 108.3, 104.6, 101.2; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{13}N_2O_2$ 229.0972; Found 229.0971.

1-(Naphthalen-1-yl)-2-phenylhydrazine (Scheme 3, Product 3ta)[33]

Yield: 77% (90 mg). Off white solid. R_f = 0.61 (Ethyl acetate: Hexane = 1:3). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.5 Hz, 2H), 7.53-7.48 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.03 (d, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 2H), 6.87 (t, *J* = 7.0 Hz, 1H), 6.31 (s, 1H), 5.68 (s, 1H); ^{13}C{^{1}H} NMR (126 MHz,

$CDCl_3$) δ 148.5, 143.1, 134.2, 129.4, 128.8, 126.5, 125.9, 125.2, 122.2, 120.1, 119.9, 119.6, 112.5, 106.2.

2-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)benzene-1,4-diol (Scheme 4, Product 3ua)

Yield: 89% (147 mg). Off white solid, m.p. = 129.8-133.2 °C. R_f= 0.65 (1:1 Ethyl acetate: *n*-Hexane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.45 (s, 1H), 7.36-7.33 (m, 2H), 7.30-7.27 (m, 3H), 7.19 (t, *J* = 7.5 Hz, 2H), 6.93 (t, *J* = 8.5 Hz, 3H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.57 (d, *J* = 2.5 Hz, 1H), 5.17 (dd, *J* = 7.5, 12.5 Hz, 1H), 4.92 (s, 1H), 3.81 (m, 1H), 3.13 (dd, *J* = 7.5, 17.5 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.1, 149.0, 148.1, 143.8, 141.7, 129.3, 129.1, 127.9, 125.9, 120.0, 117.7, 117.1, 116.5, 113.3, 113.2, 63.3, 43.8; HRMS(ESI) *m/z*: [M + H]$^+$ Calcd for $C_{21}H_{19}N_2O_2$ 331.1441; Found 331.1438.

1-(4-Methylphenyl)-1-phenylhydrazine (Scheme 4, Product 3bb)[29]

Yield: 92% (91 mg). Light orange oil. R_f = 0.57 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.28 (m, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.18 (s, 3H), 6.96 (t, *J* = 7.5 Hz, 1H), 4.15 (s, 2H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 149.6, 146.8, 132.4, 129.7, 128.8, 121.0, 120.7, 117.8, 20.7.

1-(4-Isopropylphenyl)-1-phenylhydrazine (Scheme 4, Product 3bf)

Yield: 83% (94 mg). Light yellow oil. R_f = 0.63 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.5 Hz, 2H), 7.20 (s, 6H), 6.95 (t, *J* = 7.5 Hz, 1H), 4.14 (s, 2H), 2.95-2.90 (m, 1H), 1.29 (d, *J* = 7.0 Hz, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 149.4, 147.0, 143.3, 128.8, 127.0, 121.8, 121.7, 117.9, 33.4, 24.0; HRMS (ESI) *m/z*: [M + H]$^+$: Calcd for $C_{15}H_{19}N_2$ 227.1543; Found 227.1542.

1-Phenyl-1-(4-(trifluoromethyl)phenyl)hydrazine (Scheme 4, Product 3bh)

Yield: 86% (108 mg). Light yellow oil. R_f = 0.51 (Ethyl acetate: Hexane = 1:4). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 7.0 Hz, 1H), 4.19 (s, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 151.8, 147.8, 129.6, 126.1 (q, J_F = 0.004 Hz, 1C), 124.8, 123.6, 123.0,

121.2 (q, J_F = 0.03 Hz, 1C), 115.4; $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$) δ -61.3; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{12}F_3N_2$ 253.0947; Found 253.0946.

1-(3,5-Bis(trifluoromethyl)phenyl)-1-phenylhydrazine (Scheme 4, Product 3bi)

Yield: 96% (153 mg). Light yellow oil. R_f = 0.55 (Ethyl acetate: Hexane = 1:4). ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 2H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 10.0 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 4.22 (s, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 150.3, 147.2, 132.0 (q, J_F = 0.02 Hz, 2C), 130.1, 126.8, 125.9, 123.3 (q, J_F = 0.27 Hz, 2C), 115.0 (q, J_F = 0.003 Hz, 2C), 112.2 (q, J_F = 0.04 Hz, 2C); $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$) δ -63.0; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{11}F_6N_2$ 321.0821; Found 321.0822.

1-(3-Fluorophenyl)-1-phenylhydrazine (Scheme 4, Product 3bj)[34]

Yield: 81% (82 mg). Light yellow oil. R_f = 0.57 (Ethyl acetate: Hexane = 1:4). ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 7.5 Hz, 2H), 7.17 (q, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.94-6.89 (m, 2H), 6.59 (t, *J* = 8.0 Hz, 1H), 4.16 (s, 2H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 163.4 (d, J_F = 0.24 Hz, 1C), 151.1(d, J_F = 0.01 Hz, 1C), 148.4, 129.9 (d, J_F = 0.01 Hz, 1C), 129.4, 123.8, 121.8, 112.6 (d, J_F = 0.003 Hz, 1C), 107.0 (d, J_F = 0.009 Hz, 1C), 104.3 (d, J_F = 0.03 Hz, 1C); $^{19}F\{^1H\}$ NMR (470 MHz, $CDCl_3$) δ -112.4.

1-(4-(Methylsulfonyl)phenyl)-1-phenylhydrazine (Scheme 4, Product 3bl)

Yield: 80% (105 mg). Off white solid, m.p. = 126.0-128.7 °C. R_f = 0.63 (Ethyl acetate: Hexane = 1:1). ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 8.5 Hz, 2H), 4.26 (s, 2H), 2.98 (s, 3H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 153.3, 146.8, 129.8, 128.9, 128.5, 126.0, 124.2, 114.1, 44.8; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{14}SN_2O_2Na$ 285.0668; Found 285.0665.

4-(1-Phenylhydrazineyl)benzenesulfonamide (Scheme 4, Product 3bm)

Yield: 60% (79 mg). White solid, m.p. = 144.1-146.0 °C. R_f = 0.30 (Ethyl acetate: Hexane = 1:1). ^1H NMR (500 MHz, DMSO-D_6) δ 7.59-7.58 (m, 2H), 7.39-7.35 (m, 4H), 7.18-7.16

(m, 2H), 7.13-7.09 (m, 1H), 7.07 (s, 2H), 5.21 (s, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-D_6) δ 152.2, 147.8, 133.5, 129.6, 127.2, 124.4, 123.2, 114.8; HRMS(ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{12}H_{13}N_3SO_2Na$ 286.0620; Found 286.0618.

Supporting Information Available: Copies of ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and ^{19}F NMR spectra, as well as X-ray crystallographic data of **L1**, product **3aa**, **3ta** and **3ua.** This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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