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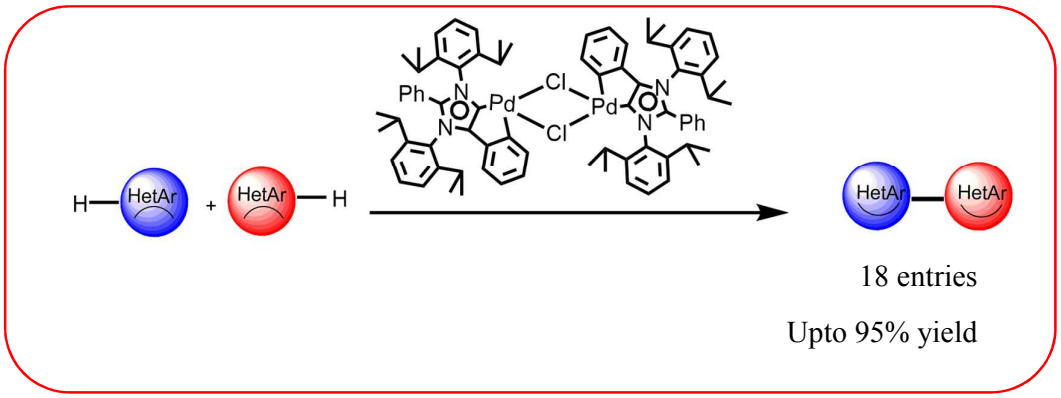
A Halobridged Abnormal NHC Palladium(II) Dimer for Catalytic Dehydrogenative Cross-Coupling Reactions of Heteroarenes

Sreejyothi P, ‡ Samaresh Chandra Sau, ‡ Pavan K. Vardhanapu and Swadhin K.Mandal*

Department of Chemical Sciences, Indian Institute of Science Education and Research, Kolkata, Mohanpur-741246, India. Email: swadhin.mandal@iiserkol.ac.in

TOC/Abstract Graphic:



Abstract

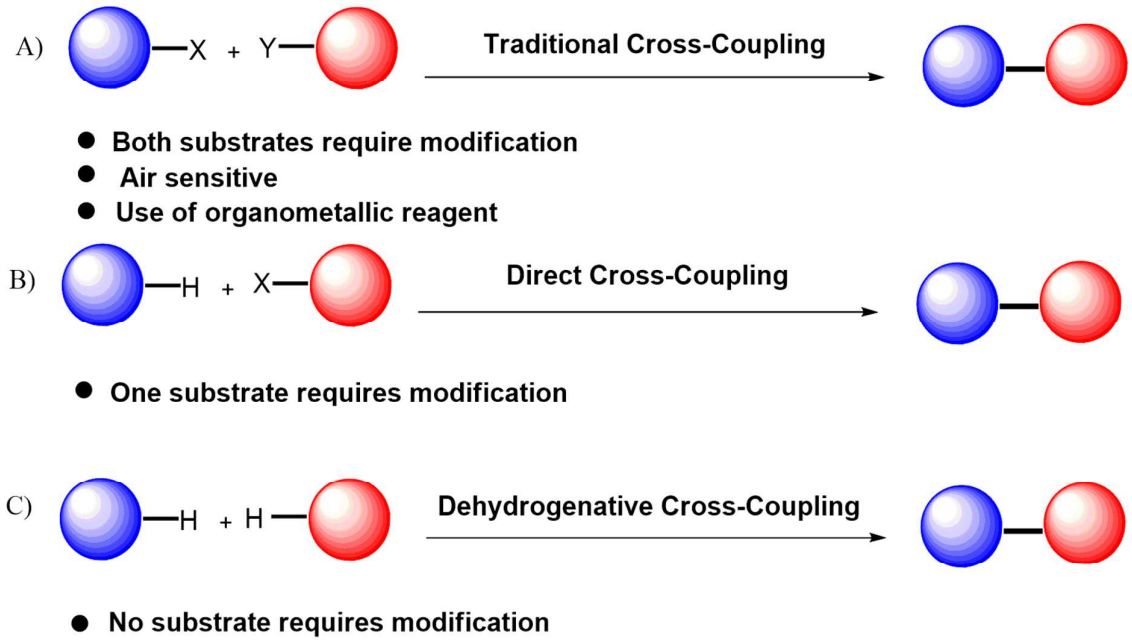
This work describes the dehydrogenative coupling of heteroarenes using a dimeric halo bridged palladium (II) catalyst bearing an abnormal NHC (*a*NHC) backbone. The catalyst can successfully activate the C–H bond of a wide range of heteroarenes, which include benzothiazole, benzoxazole, thiophene, furan, and N-methyl benzimidazole. Further, it exhibited good activity for heteroarenes bearing various functional groups such as CN, CHO, Me, OMe, OAc and Cl. Additionally, we isolated the active catalyst by performing stoichiometric reaction and characterized it as the acetato bridged dimer of (*a*NHC)PdOAc by single crystal X-ray study.

Keywords: abnormal N-heterocyclic carbene, dehydrogenative coupling, biheteroaryls, heterocoupling, dimeric palladium catalyst

Introduction:

Motifs bearing bonds between two heteroarenes are ubiquitously found in many natural products, pharmaceuticals, and electronic materials.[1] Development of new methods for the synthesis of heteroaryl scaffolds possesses significant importance. The traditional approach for the synthesis of biaryls has involved mainly the palladium-catalyzed cross-coupling reaction between two pre-activated substrates which include Heck, Suzuki–Miyaura, Negishi, Stille or Kumada coupling type reactions (Scheme 1A).[2,3,4] Owing to the requirement of pre-activated substrates for such traditional catalytic methods which involve several synthetic steps; development of an alternative pathway adopting atom as well as step economic process has been very much desired for long. The most obvious first step for such development towards this direction is the replacement of one pre-activated species with a simple arene or heteroarene. This process has been accomplished via C–H (bond) activation or C–H functionalization although the term direct arylation is generally a preferred one (Scheme 1B).[5] However, the most atom economic approach would involve replacement of both pre-activated substrates by simple arenes or heteroarenes. In fact, the coupling of two aryl C–H bonds to give the corresponding biaryl product would seem ideal (Scheme 1C). Nonetheless, given the strength of the C–H bond, such processes are often thermodynamically challenging.[6] Earlier, Fagnou,[7-8] Chang,[9] Buchwald,[10] Lu,[11] Sanford[12] and others[13-15] have made a significant breakthrough in the Pd(II)-catalyzed oxidative cross-coupling of unactivated heteroaryls with simple arenes. Nevertheless, the metal-catalyzed oxidative cross-coupling of two heteroaryl C-H bonds to form unsymmetrical biheteroaryl molecules remains a topic of significant challenge. Mori and co-workers reported the palladium-catalyzed, highly chemo and regioselective, dimerization of thiophenes to form bi-thiophenes for the first time for dehydrogenative cross coupling of heteroarenes.[16,17] Later on, Sanford,[18] You,[19]

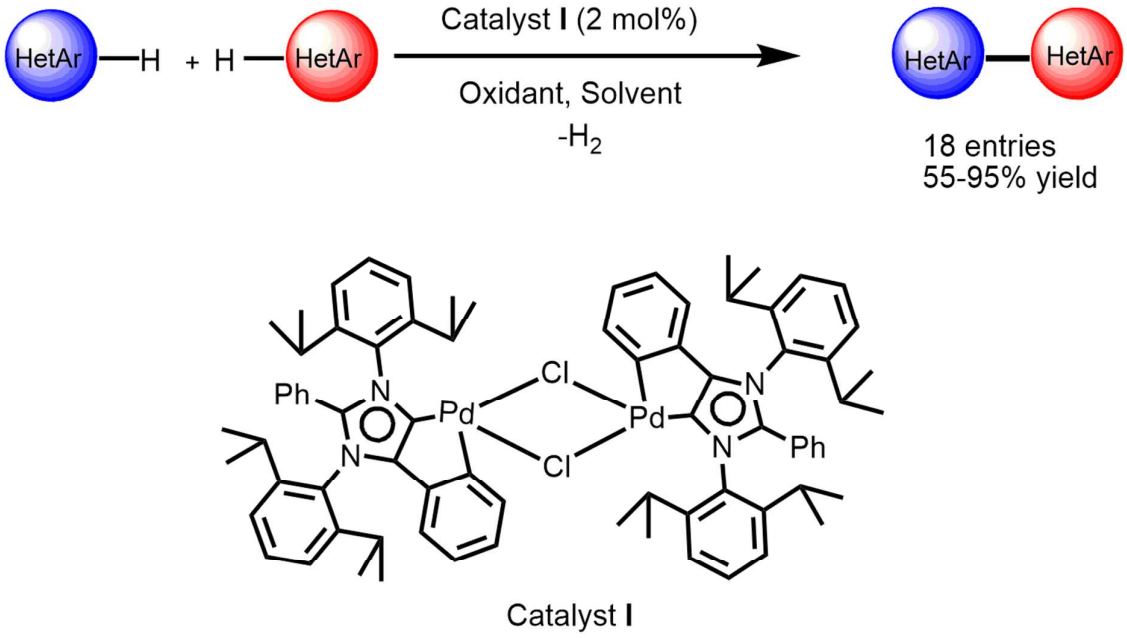
Dauglis,[20] Yamaguchi,[21] Zhang,[22] Wang[23] and other research groups[24-26] have further improved the strategies for dehydrogenative homocoupling of heteroarenes using Pd(II)/Cu(II) catalysts.



Scheme 1. General Schemes for Formation of Heterobiaryl Compounds: A) Traditional Cross-Coupling Reaction, B) Direct Cross-Coupling Reaction and C) Dehydrogenative Cross-Coupling Reaction

However, the dehydrogenative heterocoupling between two different heteroarenes remained mostly unaddressed until 2010. In 2010, Hu and You and coworkers demonstrated the Pd(II)-catalyzed C-H/C-H cross-coupling of various *N*-containing heteroarenes (e.g., azoles, and pyridine *N*-oxides) with five-membered heterocycles (e.g., thiophenes, and furans) using $Pd(OAc)_2$ and $Cu(OAc)_2$.[27] Later on, Ofial and co-workers demonstrated the dehydrogenative coupling between benzothiazoles and azoles to afford the unsymmetrical 2,2′-linkage between the same.[28] Following these work, You,[29-30]

Wang, [31] Yang[32] and others have made significant contributions in dehydrogenative cross-coupling of heteroarene partners.[33-45] It is to be noted that in all these reports, $Pd(OAc)_2$ was used as the catalyst in the presence of a sacrificial oxidant. There have been few studies on understanding of the mechanism of this fascinating reaction with the help of DFT studies[27] along with controlled experiments under stoichiometric conditions,[28,32,41] however, understanding the catalytic cycle by isolating the active catalyst and characterizing it by single crystal X-ray structure has been missing. In the current study, we examined the catalytic activity of a well-defined halobridged palladium (II) dimeric complex (Catalyst **I**)[46] bearing an abnormal N-heterocyclic carbene in the cross-coupling of two different heteroarenes. It may be noted that after the isolation of the first abnormal N-heterocyclic carbene by Bertrand and co-workers in 2010[47] we have developed this halobridged palladium (II) dimeric complex (Catalyst **I**)[46] for carrying Suzuki-Miyaura coupling of challenging aryl chloride substrates at ambient conditions. Later on, we applied this abnormal N-heterocyclic carbene for development of various



Scheme 2. Summary of Present Catalytic Method for Dehydrogenative Heterocoupling

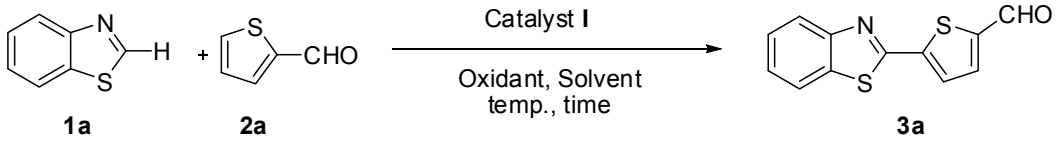
transition metal complexes for a range of catalytic transformations.[48-52] Herein we report that the well-defined halobridged *a*NHC dimer can catalyze dehydrogenative cross-coupling of two heteroarene partners under 2 mol% catalyst loading (Scheme 2). By performing stoichiometric reaction, an acetato bridged Pd(II)-*a*NHC dimer was isolated as the active catalyst and characterized by single crystal X-ray study and with the help of further control experiments, a plausible mechanism for the dehydrogenative cross-coupling reaction was proposed.

Results and discussion:

The chlorobridged *a*NHC-Pd dimer (Catalyst **I)** was prepared according to the previously reported method.[46] At first, a series of optimization reactions for cross-coupling between two heteroarenes was performed using benzothiazole (**1a**) and 2-formylthiophene (**2a**) as model substrates in presence of Catalyst **I** (Table 1). The conversion was monitored by ^{1}H NMR spectroscopy. To our delight, the reaction between one eqv. of benzothiazole with 4 eqv. 2-formylthiophene in DMSO at 110 ^{o}C resulted in a nearly quantitative conversion (by ^{1}H NMR spectroscopy) into the desired heterocoupled product **3a** which was isolated in 95% yield after the column chromatography (Table 1, entry 1). However, the use of 1 equiv. of **2a** instead of 4 equiv. led to decrease in the NMR conversion of **3a** (66%) and resulted in significant homocoupling of **1a.** It may be noted that earlier studies [27,32] also reported use of one coupling partner in excess in related dehydrogenative heterocoupling reactions. Further, the reaction was screened using various solvents. Among these solvents, DMSO turned out to be the best solvent (Table 1, entry 1) whereas other solvents such as DMF, DMAc and NMP resulted in 92%, 55% and 31% conversion, respectively (Table 1, entries 2-4). The reaction did not proceed in presence of THF (Table 1, entry 5). To study the effect of oxidant in the reaction, different oxidants were examined and AgOAc afforded the best conversion whereas

$AgNO_3$, Ag_2CO_3 and Ag_2O delivered 55%, 50% and 10%, respectively (Table 1, entries 6-8). Another control reaction was carried out by using $Cu(OAc)_2$ as an oxidant, which gave 99% NMR conversion (Table 1, entry 14). The conversion was reduced to 90% when the reaction was carried out at 100 ^oC keeping other conditions identical (Table 1, entry 9). The reaction did not proceed at all when it was carried out at 80 ^oC (Table 1, entry 10).

Table 1. Optimization of different reaction conditions for dehydrogenative cross-coupling of benzothiazole (**1a**) with 2-formylthiophene (**2a**).[a]



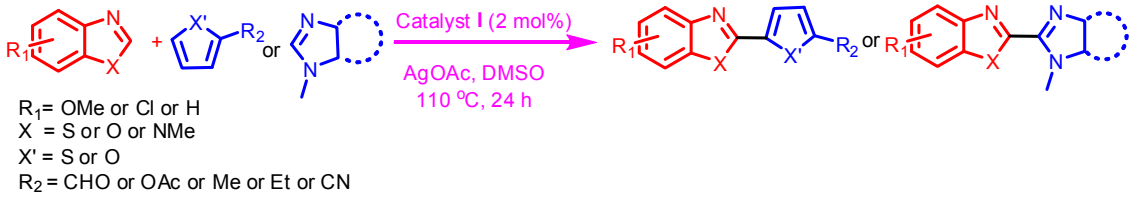
Entry	Solvent	Oxidant	Catalyst	Time (h)	Temperature (°C)	NMR Conversion (%)
1	**DMSO**	**AgOAc**	**Catalyst I**	**24**	**110**	>99 (95[b])
2	DMF	AgOAc	Catalyst **1**	24	110	92
3	DMAc	AgOAc	Catalyst **I**	24	110	55
4	NMP	AgOAc	Catalyst **I**	24	110	31
5	THF	AgOAc	Catalyst **I**	24	110	N.R
6	DMSO	$AgNO_3$	Catalyst **I**	24	110	55
7	DMSO	Ag_2CO_3	Catalyst **I**	24	110	50
8	DMSO	Ag_2O	Catalyst **I**	24	110	10
9	DMSO	AgOAc	Catalyst **I**	24	100	90

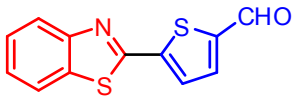
10	DMSO	AgOAc	Catalyst **I**	24	80	N.R
11	DMSO	AgOAc	-	24	80	N.R
12[c]	DMSO	AgOAc	Catalyst **I**	24	110	95
13	DMSO	AgOAc	**Ia**	24	110	90
14	DMSO	$Cu(OAc)_2$	Catalyst **I**	24	110	99

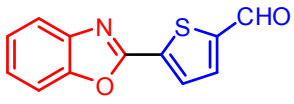
[a] **Reaction conditions**: Benzothiazole (0.366 mmol), 2-formylthiophene (1.464 mmol), Oxidant (0.732 mmol), Catalyst **I** (0.0073 mmol, 2 mol% catalyst loading) and solvent DMSO (3 mL). [b] Isolated yield. [c] 1 mol% catalyst loading. N.R stands for "No Reaction".

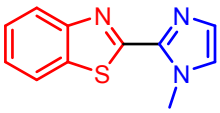
A control reaction when performed without using the Catalyst **I**, did not result in the formation of any desired product which establishes inevitable role of the catalyst in this reaction (Table 1, entry 11). Experiments performed at catalyst loading as low as 1 mol % yielded slightly less yet fairly good conversion (93%, Table 1, entry 12). For further substrate scope, the reaction conditions corresponding to entry 1 in Table 1 was followed. With the standardized conditions (entry 1, Table 1), we moved on to investigate further substrate scope for dehydrogenative cross-coupling of heteroarenes. A wide range of substrates was investigated and moderate to excellent yields (55-95%) were obtained. The present catalytic protocol was found suitable for coupling of benzothiazole, benzoxazole, N-methyl benzimidazole with different functionalized thiophenes, furfural, N-methyl imidazole. It is noteworthy that our reaction went smoothly and was able to tolerate a wide range of functional groups in thiophenes (Table 2, **3a**, **3i, 3l**, **3k**, **3p**). Moreover, imidazole and benzimidazole which are rather inactive than thiazoles based on

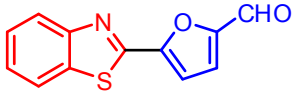
Table 2: Catalytic cross dehydrogenative heterocoupling of heteroarenes using Catalyst **I**[a]

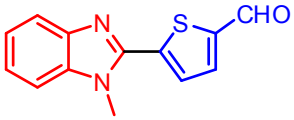


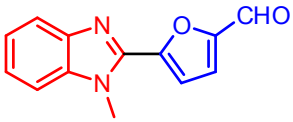

3a (95%)

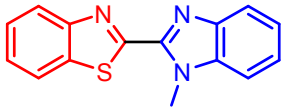

3b (82%)

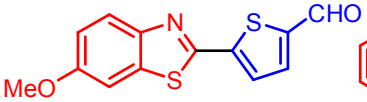

3c (68%)

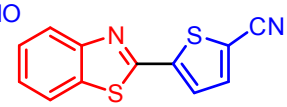

3d (88%)

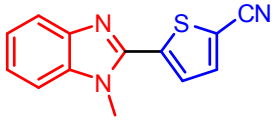

3e (55%)

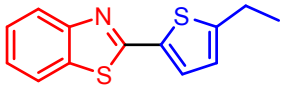

3f (58%)

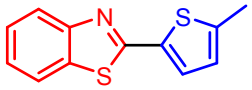

3g (77%)

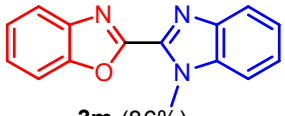

3h (92%)

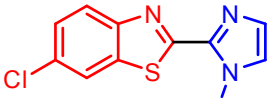

3i (76%)

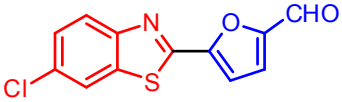

3j (84%)

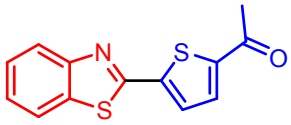

3k (59%)

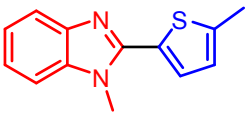

3l (80%)

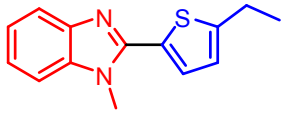

3m (86%)


3n (83%)


3o (60%)


3p (79%)


3q (73%)

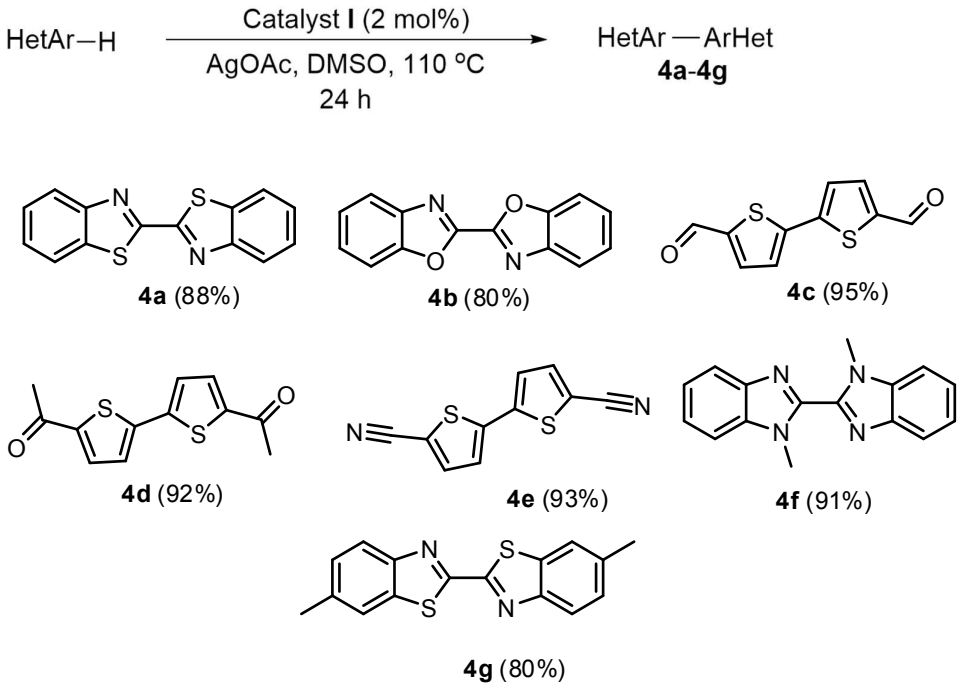

3r[b] (68%)

[a] **Reaction conditions**: Benzothiazole/benzoxazole/N-methylbenzimidazole (0.366 mmol), thiophene/furfural/N-methylimidazole (1.464 mmol), AgOAc (0.732 mmol),

Catalyst **I** (0.0073 mmol) and solvent DMSO (3 mL), 24 h, 110 °C. [b] NMR conversion. Isolated yields are given in the parentheses.

their pK_a values[4] and would often require harsh conditions for C2-H activation have also shown good to excellent activity (55-86%) with our conditions (Table 2, **3c**, **3e**, **3f**, **3g**, **3j**, **3m**, **3n**, **3q, 3r**). Benzothiazole showed more activity (95%, Table 2, **3a**) towards formylated thiophene coupling partner whereas with formylated furan coupling partner delivered relatively less yield (88%, Table 2, **3d**). Substituted benzothiazole coupling partners also displayed good reactivity ranging from 60-92% (Table 2, **3h**, **3n**, **3o**).

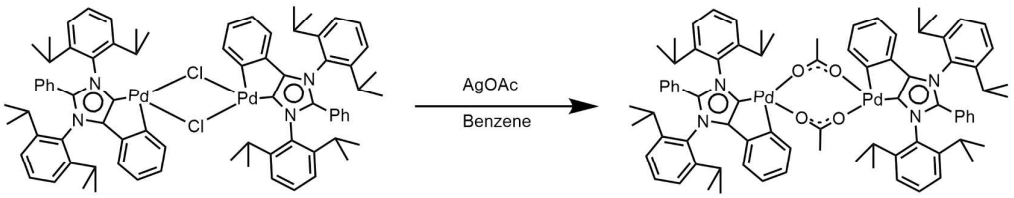
Table 3. Catalytic cross dehydrogenative homocoupling with a variety of heteroarenes using Catalyst **I**[a]



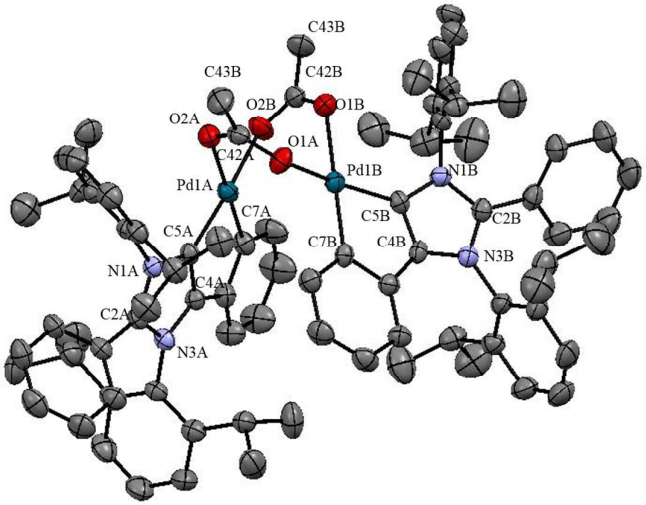
Reaction conditions: Heteroarene (0.366 mmol), AgOAc (0.732 mmol), Catalyst **1** (0.0073 mmol) and solvent DMSO (3 mL), 24 h, 110 °C. Isolated yield is given in the parentheses.

During the course of reaction, we have observed formation of homocoupling product in varied yield as a side product along with formation of the desired heterocoupled product. This obsevation further made us curious to check the homocoupling reactions using the optimized conditions. We noticed under such conditions, dehydrogenative homocoupling of heteroarenes also proceeded smoothly. As shown in Table 3, the reaction progressed well with a various heteroarenes such as benzothiazole, benzoxazole, N-methyl benzimidazole, furan as well as thiophene and delivered yield in the range of 80-95%. The substrates with two heteroatoms displayed comparable activity (82-91%, Table 3, **4a**, **4b**, **4f** and **4g**) to those with a single heteroatom (92-95%, Table 3, **4c**, **4d** and **4e**). The substituted benzothiazoles showed less reactivity (80%, Table 3, **4g**) in comparison with naked benzothiazole (88%, Table 3, **4a**). Further, this catalyst exhibited high functional group tolerance as it activated a wide range of substrates with different functional groups, which include CN, CHO, Me and OAc. Further, we moved to check the reaction mechanism for this dehydrogenative coupling reactions. In order to investigate the mechanism of the dehyrogenative cross-coupling reaction, several stoichiometric experiments were conducted. A stoichiometric reaction was carried out between Catalyst **I** and AgOAc under nitrogen atmosphere (Scheme 3). NMR spectroscopic studies of the reaction mixture indicated appearance of a new peak in ^{1}H and ^{13}C NMR spectra at 1.95 and 183.2 ppm, respectively. This observation suggests the replacement of the chloride bridge with the acetate group. Delightfully, we were able to generate suitable single crystals from the reaction mixture for X-ray analysis in hexane/benzene 2:1 mixture, which unambiguously established the molecular structure of an acetato bridged Pd(*a*NHC) dimer (**Ia**). This obsevation is reminiscent of the anion metathesis reaction of chloride with a trifluoroacetate anion for a previously reported chloro bridged palladium *a*NHC dimer.[51] In complex **Ia**, the palladium center exhibited a

A)

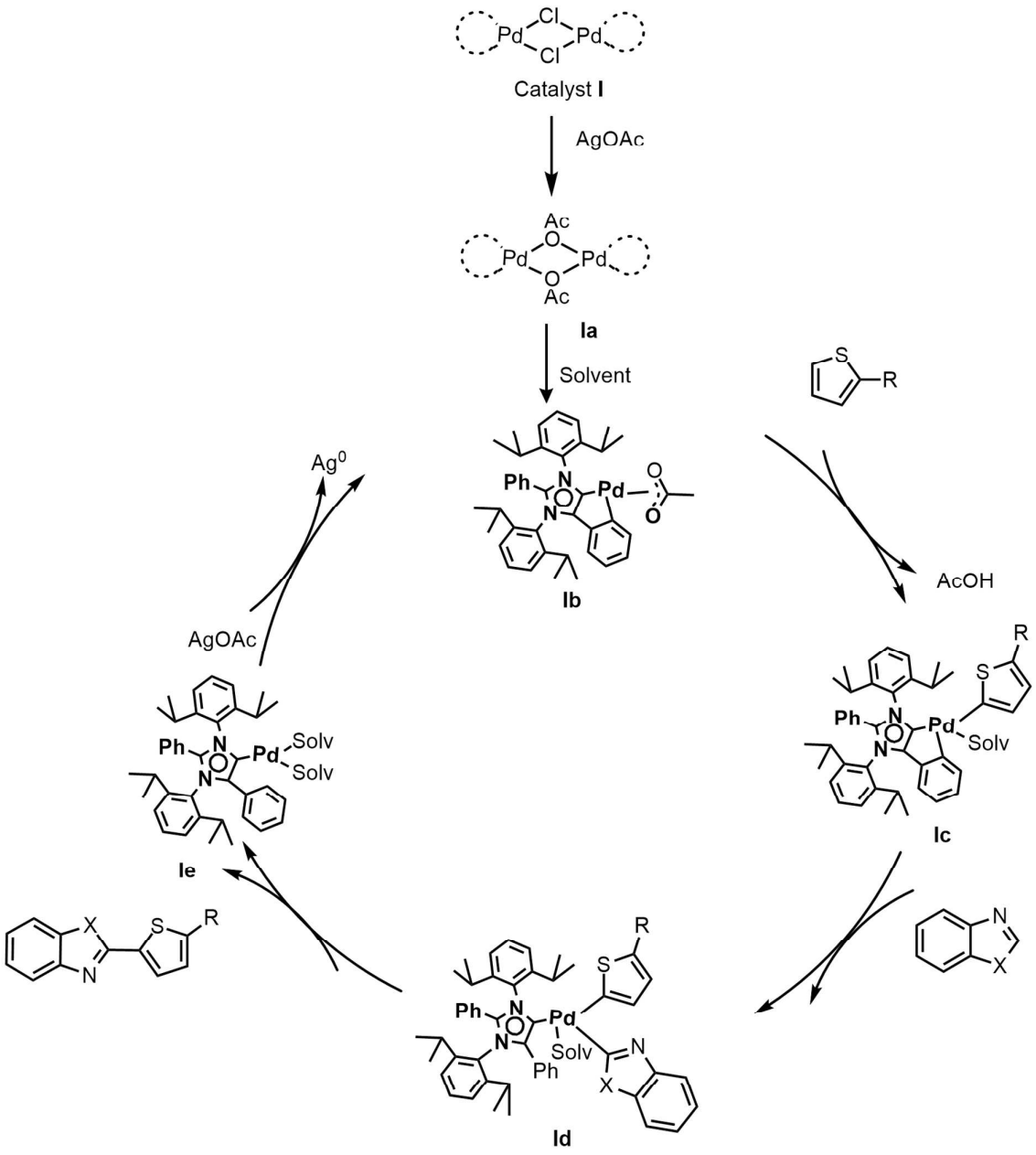


B)



Scheme 3. A) Reaction of the Chloro Bridged Palladium Dimer with AgOAc Leads to the Formation of an Acetato Bridged Dimeric Complex **Ia**. B) Perspective ORTEP View of the Molecular Structure of **Ia**. Thermal Ellipsoids are Drawn with 50% Probability. The Lattice Held Benzene and Hexane as Well as Hydrogen Atoms have been Omitted for the Sake of Clarity. Selected Bond Lengths (Å) and Bond Angles (deg): Pd(1A)-O(2A), 2.148(3); Pd(1A)-O(2B), 2.129(3); Pd(1A)-C(5A), 1.962(4); Pd(1A)-C(7A) 1.980(5); Pd(1A)-Pd(1B), 2.9618(5); C(5A)-Pd(1A)-C(7A), 79.63(18); C(5A)-Pd(1A)-O(2A), 98.08(16); C(5A)-Pd(1A)-O(2B), 162.54(16)

distorted square planar geometry. The Pd1A-O2B bond distance in **Ia** was measured as 2.148 Å. The palladium-C(carbene) bond exhibited a bond distance of 1.962 Å (Pd1A-C5A) whereas, Pd1A-C7A (ortho-metalated) showed a bond distance of 1.980 Å. These distances were consistent with previously reported similar ortho-metalated Pd dimers of



Scheme 4. Plausible Mechanistic Cycle for the Dehydrogenative Cross-Coupling of Heteroarenes

abnormal NHC.[46, 51] Next, the complex **Ia** was used as the catalyst for the dehydrogenative cross-coupling reaction following the same catalytic conditions and it yielded the desired product in excellent yield (90%, Table 1, entry 13). This result confirmed that the isolated acetato bridged dinuclear palladium complex **Ia** is an active

catalyst for the reaction. Next, another stoichiometric reaction was performed by taking **Ia**, AgOAc, and benzothiazole (**1a**) at 100 °C in DMSO-d_6 for 24 h which resulted in the missing of C2-H peak of **1a** as monitored by ^{1}H NMR spectroscopy (see SI, Figure S53). This clearly indicates the C2-H abstraction of the substrate takes place during the catalytic activation process.

Additionally, we checked relative reactivity of two coupling partners **1a** and **2a** separately in homocoupling reaction, over a duration of 1h which in turn showed that 2-formylthiophene (**2a**) is more reactive than the corresponding benzothiazole (**1a**) (see SI, Figures S54-55). Homocoupling of **1a** in 1h shows only 10% NMR conversion, whereas **2a** exhibited 28% NMR conversion for homocoupling reaction. Previously, Hu, You and coworkers by DFT calculation also proposed that among the two heteroarene partners namely thiophene and N-methylbenzimidazole, the abstraction of C2 proton in thiophene is relatively faster than that of the other partner which prompted them to propose thiophene activation as the first step in their catalytic cycle.[27] Based on the above observations, a plausible catalytic cycle is proposed for the dehydrogenative cross-coupling of heteroarenes in Scheme 4. In this proposed scheme, we considered that the catalysis is initiated by the conversion of Catalyst **I** to **Ia** in presence of AgOAc, which may be termed as catalyst activation step. The complex **Ia** was isolated in analytically pure form and was well characterized by X-ray crystallography and NMR spectroscopy. In presence of a coordinating solvent such as DMSO, **Ia** can be converted into a mononuclear Pd complex **Ib**. Such dissociation of NHC containing Pd dimer into a monomeric complex is well-documented in the literature by Herrmann and co-workers.[53] The mononuclear complex **Ib** subsequently undergoes a rapid palladation of the heteroarene (with more reactive heteroarene) by the formation of heteroarylpadallium(II) intermediate **Ic** with release of an acetic acid molecule. It may be noted that earlier

studies also suggested the formation of a HetAr–PdL_n intermediate as the key step in the initiation of the catalytic cycle.[27-28] This intermediate further promotes the second C-H activation of another heteroarene partner during which cleavage of ortho C-H activated Pd-carbene bond can takes place to make sure the Pd oxidation state remains in the most favored bivalent state leading to the formation of a bisheteroaryl Pd intermediate (**Id**). Such a cleavage of Pd-C(orthometalated) bond in *a*NHC-Pd dimeric complex has been reported in earlier study.[51] However, at this point, we cannot discard the possibility of complete decoordination of Pd center by cleavage of the other Pd-NHC bond as observed in recent studies.[54] Finally, the bisheteroaryl Pd intermediate (**1d**) upon reductive elimination leads to formation of the cross-coupled product and Pd(0) species (**Ie**), which on oxidation by AgOAc regenerates the catalytically active species **1b**.

Conclusion:

In summary, it may be concluded that our catalytic conditions can successfully lead to hetero dehydrogenative cross-coupling for a wide range of heteroarenes such as benzothiazole, benzoxazole, N-methyl benzimidazole, N-methyl imidazole, different substituted thiophenes, and furfural with good to excellent yield. Additionally, this catalyst exhibited high functional group tolerance as it activated a wide range of substrates with different functional groups. The use of a well-defined catalyst enabled us to understand the mechanistic details by performing a series of control reaction. Additionally, we have been able to trap a catalytically active acetato bridged Pd(II) organometallic dimer and characterized by single crystal X-ray study.

Experimental Section:

General Consideration:

Catalyst synthesis was performed in oven dried glasswares (130 °C) under dry and oxygen free atmosphere (nitrogen) using standard Schlenk line technique. The solvents were dried using Na/benzophenone mixture or CaH_2 prior to use. All chemicals were purchased from Sigma-Aldrich, Alfa Aesar, Merck or Spectrochem and used as received. Thin-layer chromatography (TLC) was performed on a Merck 60 F254 silica gel plate (0.25 mm thickness). Column chromatography was performed on a Merck 60 silica gel (100−200 mesh). The ^{1}H and ^{13}C NMR spectra were recorded on 400 and 500 MHz spectrometers in $CDCl_3$ with residual undeuterated solvent ($CDCl_3$, 7.26/77.0) as an internal standard. Chemical shifts (δ) and J values are given in ppm, and Hz, respectively. All chemical shift values were reported in ppm using tetramethylsilane as a reference. Chemical shifts (δ) downfield from the reference standard were assigned positive values. Catalyst **I** was synthesized using the experimental procedure reported in literature.[46]

General procedure for catalytic dehydrogenative heterocoupling of heteroarenes: 10 mg (2 mol %) Catalyst **I**, heteroarene (for example **1a,** 0.36 mmol), AgOAc (0.73 mmol), heteroarene (for example, **2a**, 1.46 mmol) and 3 mL of dry DMSO were taken in a 5 mL pressure tube. The catalytic reactions were performed at 110 ^{o}C in closed condition using metal clip for 24 h. After completion, the reaction mixture was diluted with ethylacetate and then transferred into a separating funnel. The organic layer was dried using Na_2SO_4 and evaporated under reduced pressure and the residue was then purified through a short column chromatography (silica gel 100-200 mesh) using appropriate ratio of hexane and ethyl acetate to provide pure products.

General procedure for catalytic dehydrogenative homocoupling of heteroarenes: General procedure for catalytic dehydrogenative homocoupling of heteroarenes: 10 mg (2 mol %) Catalyst **I**, heteroarene (for example **1a**,0.36 mmol), AgOAc (0.73 mmol) and 3 mL of dry DMSO were taken in a 5 mL pressure tube. The catalytic reactions were performed at 110 ^{o}C in closed condition using metal clip for 24 h. After completion, the reaction mixture was diluted with ethylacetate and then transferred into a separating funnel. The organic layer was dried using Na_2SO_4 and evaporated under reduced pressure and the residue was then purified through a short column chromatography (silica gel 100-200 mesh) using appropriate ratio of hexane and ethyl acetate to provide pure products.

Synthesis and characterization data of Ia: Under nitrogen atmosphere, a 50 mL Schlenk flask was charged with 100 mg (0.07 mmol) of Catalyst **I** and 20 mg (0.12 mmol) of AgOAc in benzene (10 mL) and allowed to stir for 12 h at room temperature. Reaction mixture was filtered and the solvent was evaporated under reduced pressure. X ray quality crystals were grown in benzene/hexane mixture (2:1 v/v) at room temperature. The resulting solid was washed with hexane (3 × 1 mL) and dried under reduced pressure to afford **Ia** as yellow crystals: Yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): 7.57 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.36 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.76 (t, *J* = 8.0 Hz, 2H), 6.63 (t, *J* = 8.0 Hz, 2H), 5.68 (d, *J* = 8.0 Hz, 1H), 2.91-2.84 (m, 2H), 2.74-2.69 (m, 2H), 1.93 (s, 3H), 1.51 (d, *J* = 8.0 Hz, 6H), 1.07 (d, *J* = 8.0 Hz, 6H). 1.02 (d, *J* = 8.0 Hz, 6H), 0.97 (d, *J* = 8.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): 183.3, 152.1, 150.1, 145.2, 145.1, 144.3, 139.6, 138.7, 133.6, 132.2, 131.3, 130.6, 130.5, 130.0, 128.5, 128.3, 125.1, 124.9, 124.4, 123.6, 123.2, 119.2, 29.0, 28.9, 25.3, 24.9, 24.4, 22.9, 22.6. Anal. Calcd for $C_{91}H_{105}N_4O_4Pd_2$: C, 71.36; H, 6.91; N, 3.66; Found: C, 70.85; H, 6.71; N, 3.61. The calculated molecular formula was

determined from crystallographically determined asymmetric unit which contained lattice held benzene molecule and half molecule of hexane (used as solvents for crystallization).

Spectral Data of the Compounds:

1) *5-(benzothiazol-2-yl)thiophene-2-carbaldehyde (**3a**)*:[32] yellow solid, yield 83 mg, 95%; purified by column chromatography using 5% EtOAc in hexane;^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) 9.97 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 4.0 Hz, 1H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.55-7.52 (m, 1H), 7.46-7.42 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 182.7, 159.9, 153.7, 145.6, 145.3, 136.1, 135.3, 128.4, 126.9, 126.3, 123.7, 121.8.
2) *2-(5-formylthiophen-2-yl)-benzoxazole (**3b**)*:[27] brown solid, yield 68 mg, 53%; purified by column chromatography using 5% EtOAc in hexane. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 10.00 (s, 1H), 7.97 (d, *J* = 3.8 Hz, 1H), 7.83 (d, *J* = 3.8 Hz, 1H), 7.80-7.78 (m, 1H), 7.61-7.59 (m, 1H), 7.42 -7.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 182.8, 157.4, 150.8, 146.2, 141.8, 137.9, 136.1, 130.0, 126.3, 125.4, 120.5, 111.0.
3) *2-(1-methyl-1H-imidazol-2-yl)benzothiazole (**3c**)*:[28] yellow solid, yield 53 mg, 68%; purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.03 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.51-7.47 (m, 1H), 7.43-7.41 (m, 1H), 7.24 (s, 1H), 7.09 (s, 1H), 4.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 158.3, 153.9, 140.3, 135.0, 128.6,126.4, 125.8, 125.0, 123.4, 121.7, 36.0.
4) *5-(benzothiazol-2-yl)furan-2-carbaldehyde (**3d**)*:[32] brown solid, yield 73 mg, 88%; purified by column chromatography using 10% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.77 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.58-7.54 (m, 1H), 7.49-7.45 (m, 1H), 7.40 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 177.9, 155.9, 153.7, 153.3, 152.8, 135.0, 126.9, 126.3, 123.7, 121.8, 121.5, 112.7.
5) *1-methyl-2-(5-formylthiophen-2-yl)-benzimidazole (**3e**)*:[27] yellow solid, yield 48 mg, 55%; purified by column chromatography using 10% EtOAc in hexane;^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) 9.99 (s, 1H), 7.86-7.84 (m, 2H), 7.81-7.80 (m 1H), 7.43-7.33 (m, 3H), 4.06 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm)

182.3, 146.1, 145.2, 142.4, 141.7, 136.6, 136.0, 129.1, 124.2, 123.5, 120.1, 109.8, 32.2.

6) *1-methyl-2-(5-formylfuran-2-yl)-benzimidazole (**3f**)*[27] yellow solid, yield 48 mg, 58%; purified by column chromatography using 10% EtOAc in hexane; ^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) 9.78 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.44–7.32 (m, 5H), 4.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 177.3, 152.8, 150.9, 143.0, 142.8, 136.0, 124.2, 123.2, 122.5, 120.1, 114.3, 109.8, 32.2.

7) *2-(1-methyl-1H-benzoimidazol-2-yl)benzothiazole (**3g**)*:[41] pale yellow solid, yield 74 mg, 88 %; purified by column chromatography using 5% EtOAc in hexane;^{1}H NMR (400MHz, $CDCl_3$): δ (ppm) 8.13 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.56-7.34 (m, 5H), 4.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm); 159.8, 154.0, 145.1, 142.7, 137.1, 135.3, 126.4, 126.1, 124.5, 123.8. 123.3, 121.7, 120.5, 110.4, 29.7.

8) *5-(6-methoxybenzothiazol-2-yl)thiophene-2-carbaldehyde (**3h**):* yellow solid, yield 92 mg, 92 %; purified by column chromatography using 5% EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.96 (s, 1H), 7.98-7.95 (m, 1H), 7.77-7.76 (m, 1H), 7.65-7.64 (m, 1H), 7.34-7.33 (m, 1H), 7.14-7.12 (m, 1H), 3.91 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 183.1, 159.0, 157.4, 147.9, 144.8, 137.0, 136.2, 127.6, 126.6, 124.1, 116.4, 104.0, 58.1. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{10}NO_2S_2$ 276.0153; Found 276.0147.

9) *5-(benzothiazol-2-yl)thiophene-2-carbonitrile (**3i**):*[32] yellow solid, yield 67 mg, 76%; purified by column chromatography using 15% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.07 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.64 – 7.63 (m, 1H), 7.59-7.58 (m, 1H), 7.56-7.52 (m, 1H), 7.47-7.43 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 158.6, 153.4, 143.9, 137.8, 135.1, 127.5, 127.0, 126.3, 123.7, 121.7, 113.7, 112.0.

10) *5-(1-methyl-1H-benzoimidazol-2-yl)thiophene-2-carbonitrile (**3j**):* yellow solid, yield 73 mg, 84%; purified by column chromatography using 10 % EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.80 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 4.0 Hz, 1H), 7.50 (d, *J* = 4.0 Hz, 1H), 7.37-7.32 (m, 4H), 3.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 145.2, 142.6, 139.7, 137.7, 136.6, 126.8, 124.1, 123.3, 120.2, 113.6, 117.7, 109.7, 31.7. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{13}H_{10}N_3S$ 240.0595; Found 240.0570.

11) *2-(5-ethylthiophen-2-yl)benzothiazole (**3k**):*[32] yellow oil, yield 53 mg, 59%; purified by column chromatography using 10% EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.00 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.49–7.45 (m, 2H), 7.36-7.34 (m, 1H), 6.83-6.82 (m, 1H), 2.90 (q, *J* = 8.0 Hz, 2H), 1.36 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 161.7, 153.7, 152.3, 134.4, 128.7, 126.2, 124.9, 124.6, 122.7, 121.3, 24.1, 16.0.

12) *2-(5-methylthiophen-2-yl)benzothiazole (**3l**):*[32] yellow oil, yield 67 mg, 80 %; purified by column chromatography using 10% EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.99 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz. 1H), 7.47-7.43 (m, 2H), 7.35-7.32 (m, 1H), 6.80-6.79 (m, 1H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 161.6, 153.6, 144.8, 134.9, 134.5, 128.8, 126.4, 126.3, 124.9, 122.7, 121.4, 15.7.

13) *2-(1-methyl-1H-benzo[d]imidazol-2-yl)benzooxazole (**3m**):* brown solid, yield 78 mg, 86%; purified by column chromatography using 10 % EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94-7.92 (m, 1H), 7.87-7.85 (m, 1H), 7.73-7.70 (m, 1H), 7.51-7.39 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): 155.2, 150.1, 142.7, 141.5, 139.7, 136.3, 126.6, 125.1, 125.0, 123.6, 121.2, 120.6, 111.3, 110.1, 32.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{11}N_3ONa$ 272.0800; Found 272.0769.

14) *6-chloro-2-(1-methyl-1H-imidazol-2-yl)benzothiazole (**3n**):* brown solid, yield 75 mg, 83%; purified by column chromatography using 10 % EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.92-7.89 (m, 2H), 7.45-7.42 (m, 1H), 7.19 (m, 1H), 7.07 (m, 1H), 4.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 160.0, 152.6, 140.2, 136.0, 131.4, 129.9, 127.0, 125.3, 123.9, 121.2, 35.6. HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_9ClN_3S$ 250.0206; Found 250.0200.

15) *5-(6-chlorobenzothiazol-2-yl)furan-2-carbaldehyde (**3o**):*[55] yellow solid, yield 57 mg, 60 %; purified by column chromatography using 10 % EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.80 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.94-7.93 (m, 1H), 7.52-7.49 (m, 1H), 7.40-7.39 (m, 1H), 7.36-7.35 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$):177.9, 156.4, 153.4, 152.4, 152.3, 136.1, 132.3, 127.9, 124.4, 121.6, 121.5, 112.9. The compound was purified by column chromatography on silica gel with hexane and ethyl acetate mixture (95:05 v/v) as eluent.

16) *1-(5-(benzothiazol-2-yl)thiophen-2-yl)ethanone (**3p**)*:[32] yellow solid, yield 74 mg, 79 %; purified by column chromatography using 10% EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.07 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.70-7.69 (m, 1H),7.60-7.65 (m. 1H), 7.54-7.49 (m, 1H), 7.45-7.40 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): 190.1, 160.6, 154.3, 146.7, 144.3, 135.5, 132.1, 129.2, 127.2, 125.9, 123.1, 120.9, 27.0.

17) *1-methyl-2-(5-methylthiophen-2-yl)-1H-benzoimidazole (**3q**)*:[56] yellow oil, yield 70 mg, 73 %; purified by column chromatography using 10% EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.78-7.76 (m, 1H), 7.37-7.35 (m, 1H), 7.32-7.31 (m, 1H), 7.27-7.25 (m, 2H), 6.83 (m, 1H), 3.92 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 148.0, 143.5, 142.6, 136.4, 129.9, 128.2, 126.1, 122.7, 122.5, 119.5, 109.2, 31.6, 15.3.

18) *2-(5-ethylthiophen-2-yl)-1-methyl-1H-benzoimidazole(**3r**)*:[32] brown oil, yield 60 mg, 68 %, purified by column chromatography using 10% EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.79-7.77 (m, 1H), 7.39 (d, 3.8 Hz, 1H), 7.35-7.33 (m, 1H), 7.32-7.26 (m, 2H), 6.88 (d, 3.1 Hz, 1H), 3.96 (s, 3H), 2.93 (q, 8.0 Hz, 2H), 1.37 (t, 8.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 151.3, 148.3, 143.0, 137.0, 129.8, 128.1, 124.4, 122.7, 122.5, 119.7, 109.5, 32.0, 23.6, 15.9.

19) *2,2'-bibenzothiazole (**4a**)*:[21] colourless solid, yield 42 mg, 88%; purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.17 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.59-7.48 (m, 4H), ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 161.6, 153.4, 135.6, 126.9, 126.3, 124.1, 122.0.

20) *2,2'-bibenzoxazole (**4b**)*:[21] colourless solid, yield 34 mg, 80%; purified by column chromatography using 5 % EtOAc in hexane;^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.93 (d, *J* = 8.0 Hz, 2H), 7. 73 (d, *J* = 8.0 Hz, 2H), 7.53-7.46 (m, 4H), ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 151.9, 151.1, 141.2, 127.6, 125.9, 121.6, 111.5.

21) *2,2'-bithiophene-5,5'-dicarbaldehyde (**4c**)*:[16] yellow solid, yield 38 mg, 95 %; purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.92 (s, 2H), 7.72 (d, *J* = 4.0 Hz, 2H), 7.43 (d, *J* = 4.0 Hz, 2H), ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 182.4, 144.9, 144.0, 136.9, 126.5.

22) *1,1'-(2,2'-bithiophene-5,5'-diyl)diethanone (**4d**)*:[16] yellow solid, yield 41.4 mg, 92 %; purified by column chromatography using 5% EtOAc in hexane; ^{1}H NMR (400

MHz, $CDCl_3$): δ (ppm) 7.62 (d, J = 4.0 Hz, 2H), 7.30 (d, J = 4.0 Hz, 2H), 2.57 (s, 6H), ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 190.4, 144.3, 144.0, 133.2, 125.9, 26.9.

23) *2,2'-bithiophene-5,5'-dicarbonitrile (**4e**):*[57] yellow solid, yield 23 mg, 93 %; purified by column chromatography using 5% EtOAc in hexane; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.58 (d, *J* = 4.0 Hz 2H), 7.25 (d, *J* = 4.0 Hz, 2H), ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 141.6, 138.6, 126.0, 113.3, 110.1.

24) *1,1'-dimethyl-1H,1'H-2,2'-bibenzoimidazole (**4f**):* colourless solid, yield 43 mg, 91%; purified by column chromatography using 5% EtOAc in hexane; [21] ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.88 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.41-7.36 (m, 4H), 4.33 (s, 6H), ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 143.1, 142.5, 136.2, 124.1, 123.0, 120.3, 110.2, 32.3.

25) *6,6'-dimethyl-2,2'-bibenzothiazole (**4g**):*[42] colourless solid, yield 42 mg, 80%; purified by column chromatography using 15% EtOAc in hexane; ^1H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.01 (d, *J* = 8.0 Hz, 2H), 7.76 (s, 2H), 7.37-7.34 (m, 2H), 2.53 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 160.7, 151.7, 137.2, 136.0, 128.6, 123.3, 121.3, 22.1.

X-ray crystallographic details:

Suitable single crystal of compound **Ia** was selected and intensity data were collected on a SuperNova, Dual, Cu at zero, Eos diffractometer. The crystal was kept at 100.00(10) K during data collection. Using Olex2[58] the structure was solved with the Superflip[59] structure solution program using Charge Flipping and refined with the ShelXL[60] refinement package using Least Squares minimization.

Crystal data for **Ia:** $C_{91}H_{105}N_4O_4Pd_2$, M_r = 1531.59, monoclinic space group $P2_1/n$, a = 15.9861(5) Å, b = 22.1765(7) Å, c = 22.9883(8) Å, α = 90°, γ = 90°, β = 98.546(3)°, *V* = 8059.2(5) $Å^3$, Z = 35, calculated density 1.264 g cm^{-3}, μ(Mo Kα) = 0. 0.71073 mm^{-1}, = 100 K, 2θ range for data collection 4.972-65.63°, 95711 reflections measured, R1 = 0.0891 (I > 2σ(I)), wR2 = 0.2303 (all data). Crystallographic data for the structural analysis of **Ia** have been deposited at the Cambridge Crystallographic Data Centre

(CCDC) as file no: 1838603. This data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

ASSOCIATED CONTENT

The Supporting Information is available free charge on the ACS Publications website, at DOI:…..

X ray data for compound **Ia** (CIF)

X ray structure and spectroscopic data for all compounds (PDF)

AUTHOR INFORMATION

Corresponding Authors

***Email:** *swadhin.mandal@iiserkol.ac.in*

Author Contribution

‡ These authors contributed equally to this work. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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