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Heterobimetallic Pd–Sn Catalysis: A Suzuki, Tandem Ring-Closing Sequence toward Indeno[2,1-*b*]thiophenes and Indeno[2,1-*b*]indoles

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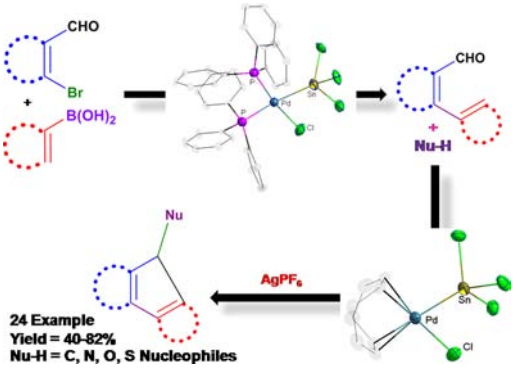
ABSTRACT



Indeno[2,1-*b*]thiophene and indeno[1,2-*b*]indole motifs have been obtained in moderate to good yields from easily available substituted boronic acids, 2-bromo aryl/vinyl aldehydes, and nucleophiles such as arenes/heteroarenes and others using a catalytic combination of bimetallic "Pd–Sn" and $AgPF_6$. This formal three-component coupling involves a Suzuki reaction followed by nucleophile assisted tandem ring closure. The sequential synthesis of substituted heterocycle-fused indenes, benzofluorene, and fluorenes was also accomplished.

Heterocycle-fused indenes and indenofluorenes have recently attracted attention in view of a number of promising factors. For example an indenofluorenyl core is an important building block for blue fluorescent organic light emitting diodes (OLEDs), organic field effect transistors, organic solar cells, and green phosphorescent OLEDs (PhOLEDs).[1] On the other hand indenothiophenes and indenoindoles constitute a very important class of heterocyclic ligands used for the design of organometallic catalysts.[2,3] Metallocene catalysts derived from these ligands show very high activity in the polymerization of olefins.[2,3] Also, the oligothiophene skeleton bearing terminal unsubstituted or substituted indeno[1,2-*b*]thiophene represents a promising class of organic materials for *p*-type organic semiconductors.[4] Additionally, 5,10-dihydroindeno-[l,2-*b*]indoles exhibit a wide range of biological activities and

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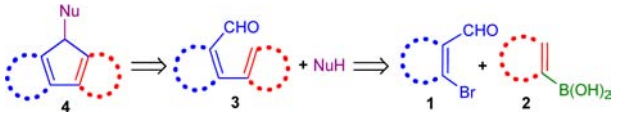
are potential nontoxic antioxidant, membrane stabilizing agents.[5] Few synthetic routes are available for indenothiophenes and indenoindoles.[2,4,6] To the best of our knowledge, there are only a few reports of indeno[1,2-*b*]thiophenes and indeno[1,2-*b*]indoles having varied substitution at the 8/10 positions.[2,4a,6c] This provides an opportunity to develop new and efficient methods for selective design of heterocycle-fused indenes. In this regard, a tandem catalysis approach appears to be synthetically attractive.[7]

Keeping this in view we wished to construct the indenothiophene/indenoindole core **4** from corresponding aldehyde **3** and nucleophiles (such as arene, heteroarene, 1,3-diketo, alcohol, amine, and thiol) *via* a tandem ring-closing route (Scheme 1). Precursor **3** could be synthesized in a straightforward manner by Suzuki coupling[8] between **1** and **2**. The Lewis acidic activation of aldehyde **3** accompanied by tandem ring closing would furnish **4**.

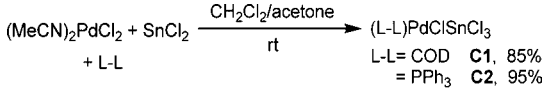
Scheme 1. Retrosynthesis



Our continuing effort to develop bimetallic catalysis for carbon−carbon and carbon−heteroatom bond formation[9] encouraged us to test the efficacy of a heterobimetallic 'Pd−Sn' catalyst in mediating both the Suzuki and ring-closing reactions. In view of the importance of ligands in catalysis,[10] we synthesized discrete heterobimetallic 'Pd−Sn' complexes with diene and phosphine ligands *via* the insertion reaction of $SnCl_2$ across $PdCl_2(MeCN)_2$ (Scheme 2).[11]

For the synthesis of arylaldehyde **3** *via* Suzuki coupling, the model reaction between 4-bromobenzaldehyde and phenylboronic acid was chosen. Based on TOF values

Scheme 2. Preparation of Pd−Sn Heterobimetallics



(for details please see Supporting Information), PdCl-$(PPh_3)_2SnCl_3$ **C2** was selected as the catalyst. The Suzuki coupling between various aryl and heteroaryl substituted boronic acids **2** with bromo derivatives **1** afforded the desired motif **3** in moderate to excellent yields (Figure 1; for details please see Supporting Information).

To test the tandem ring-closing reaction of **3** in the presence of a nucleophile, the model reaction between 2-(thiophen-3-yl)benzaldehyde **3a** and 2-methylthiophene was studied, which gave rise to 8-(5-methylthiophen-2-yl)-8*H*-indeno[2,1-*b*]thiophene **4a** (Table 1).

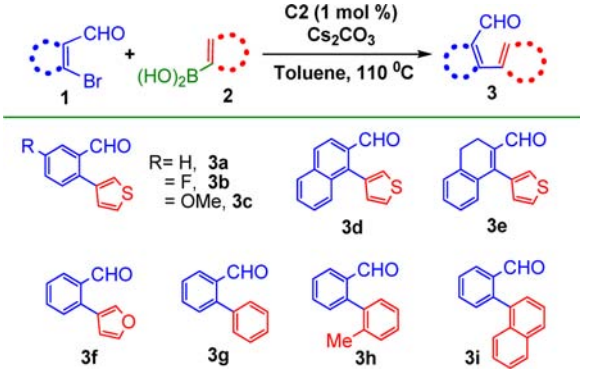
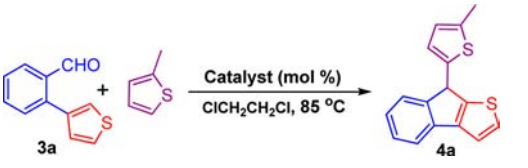


Figure 1. Construction of motif **3** via Suzuki coupling.

Table 1. Screening of Catalysts for Cyclization[a]



entry	catalyst (mol %)	additive (mol %)	time (h)	yield[b] (%)
1	$PdCl(COD)SnCl_3$ (10)	–	16	7
2	$PdCl(PPh_3)_2SnCl_3$ (05)	$AgPF_6$ (05)	10	0
3	**$PdCl(COD)SnCl_3$ (05)**	**$AgPF_6$ (05)**	**6**	**70**
4	$PdCl_2(COD)$ (05)	$AgPF_6$ (05)	12	0
5	$PdCl_2$ (05)	$AgPF_6$ (05)	12	0
6	$SnCl_2$ (10)	$AgPF_6$ (10)	12	0
7	–	$AgPF_6$ (10)	16	0

[a] A mixture of aldehyde (0.25 mmol), 2-methylthiophene (0.75 mmol), catalyst, and $AgPF_6$ in 2 mL of dry $ClCH_2CH_2Cl$ was stirred at 85 °C for an appropriate time. [b] ^1H NMR yield using triphenylmethane as an external standard.

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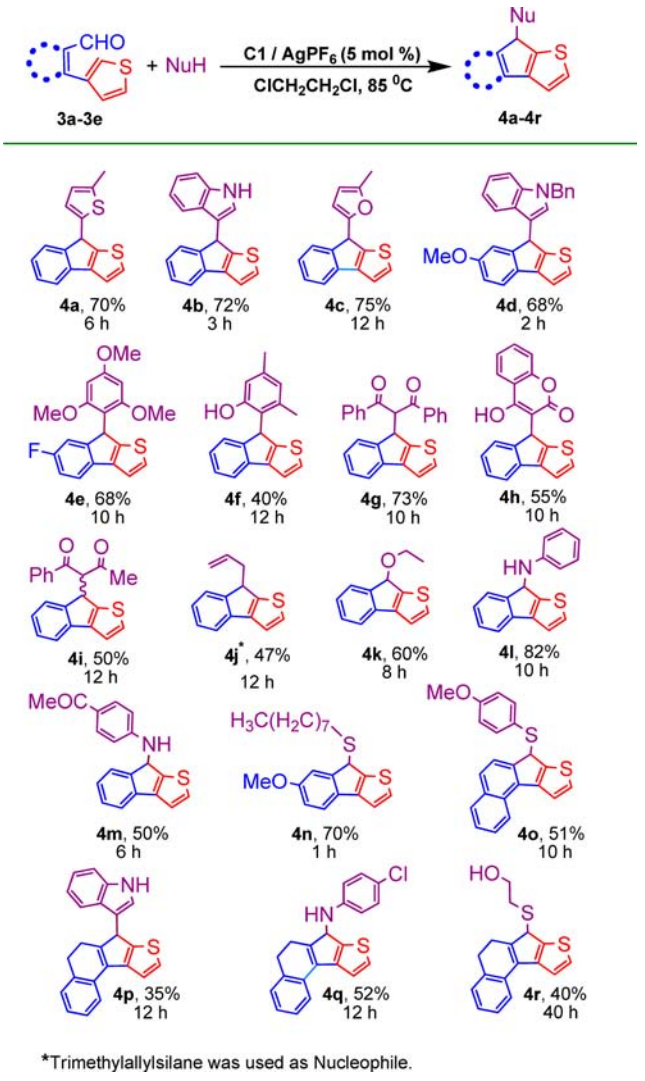

Figure 2. Substrate scope in nucleophile assisted tandem ring closing.

Using PdCl(COD)$SnCl_3$ **C1** alone, we observed negligible formation of **4a** (entry 1, Table 1). Gratifingly, the reactivity of **C1** was dramatically enhanced in the presence of $AgPF_6$ (entry 3).[12] Individually $AgPF_6$ as well as $PdCl_2$(COD)/$AgPF_6$, $SnCl_2$/$AgPF_6$, $PdCl_2$/$AgPF_6$, and [$PdCl(PPh_3)_2SnCl_3$]/$AgPF_6$ were ineffective toward the cyclization of **3a**.

With the above results in hand, we have successfully tested the ring closing of **3a**−**3d** with various nucleophiles in the presence of the catalytic **C1**/$AgPF_6$ combination (Figure 2). In the case of heteroarenes (such as indole, thiophene, and furan derivatives) as a nucleophile, the desired cyclized products **4a**−**4d** were obtained in moderate to good yields (Figure 2). In our hands, only electron-rich arenes (such as 2,4,6-trimethoxybenzene and 3,5-dimethylphenol) were active, and the corresponding cyclized products **4e** and **4f** were obtained in 68% and 40% yield, respectively. Arenes such as anisole, toluene, and benzene were unreactive.[13] In addition to arenes and heteroarenes, substituted 1,3-dicarbonyls and organometallic nucleophiles such as allylsilane also promoted the desired ring-closing reaction leading to cyclized products **4g**−**4i** and **4j**. Using amine, thiol, and alcohol as nucleophiles, we could construct C−N, C−S, and C−O linkages at the 8-position of the indenothiophene moiety (as in **4l**, **4m**, **4n**, **4o**, and **4k**). Interestingly, both aliphatic and aromatic thiols were active as nucleophiles (products **4n** and **4o**). However, aliphatic amines and aromatic alcohols were unreactive. In the case of aromatic alcohols, C-alkylation was observed as in **4f**. α,β-Unsaturated aldehyde **3e** was less reactive due to a decreased electrophilicity at the carbonyl carbon, and tandem ring closing was successful in the presence of indole, amine, and thiol, albeit with a lower yield of the desired product (**4p**−**4r**). In the case of the bifunctional nucleophile 2-mercaptoethanol, only **4r** (from the −SH attack) was obtained.

As in the case of indenothiophene, the indenoindole ring was also successfully formed from *tert*-butyl 2-(2-formylphenyl)-1*H*-indole-1 carboxylate **3j**[14,15] with carbon and heteroatom nucleophiles in moderate to high yields (Figure 3), but allylsilanes and alcohols were unreactive. We failed to prepare the indeno[2,1-*b*]furan moiety from the corresponding 2-(furan-3-yl)benzaldehyde **3f** and 2-methyl thiophene under standard reaction conditions.

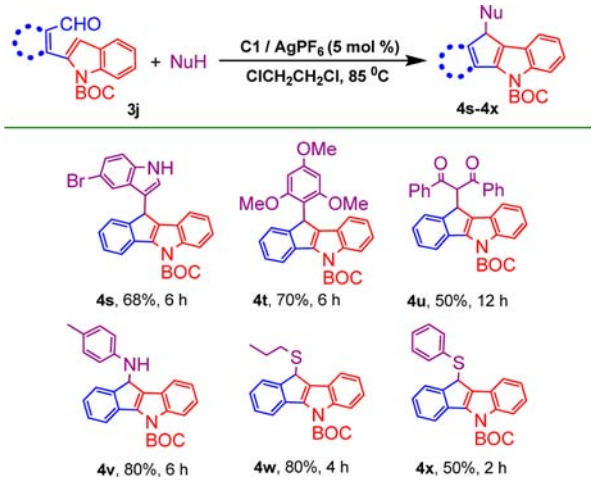

Figure 3. Various 10-substituted indeno[1,2-*b*]indoles.

(12) While mechanistic details are awaited, $AgPF_6$ could be ascribed as a halogen abstractor leading to a more reactive cationic bimetallic 'Pd−Sn' species. For catalysis via a dual combination of a transition metal precursor and $AgPF_6$, please see: (a) Corma, A.; García, H.; Leyva, A. *J. Organomet. Chem.* **2005**, *690*, 3529. (b) Fuente-Hernandez, A.; Costes, P.; Kalck, P.; Ruiz-García, J. A.; Jáuregui-Haza, U.; Urrutigoïty, M.; Dechy-Cabaret, O. *Catal. Commun.* **2010**, *12*, 142. (c) Werner, H.; Münch, G.; Laubender, M. *Inorg. Chim. Acta* **2005**, *358*, 1510.

(13) Others and our group have recently addressed the issue of nucleophilicity of arenes and heteroarenes in organic reactions. Please see: (a) Galabov, B.; Ilieva, S.; Koleva, G.; Allen, W. D.; Schaefer, H. F.; Schleyer, P. R. *WIREs Comput. Mol. Sci.* **2012**, doi:10.1002/wcms.1112. (b) Pratihar, S.; Roy, S. *J. Org. Chem.* **2010**, *75*, 4957.

(14) With 1-(*tert*-butoxycarbonyl)-1*H*-inden-2-ylboronic acid and 2-bromobenzaldehyde, a deboronation product was obtained as the major product instead of the desired *tert*-butyl 2-(2-formylphenyl)-1*H*-indole-1-carboxylate **3j** by using **C2**.

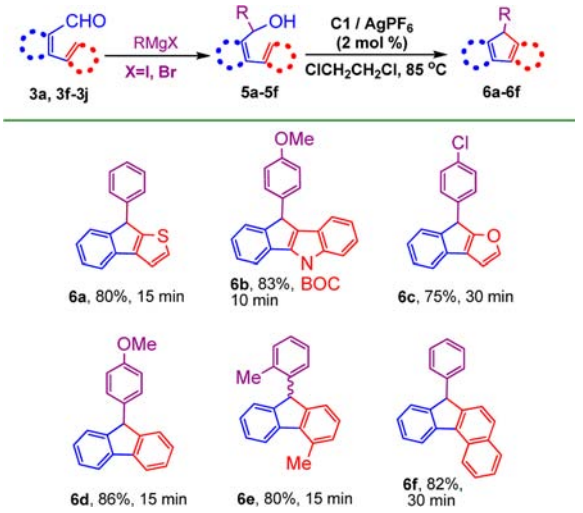

Figure 4. Stepwise route to heterocycle-fused indenes, fluorenes, and benzofluorene.

As indicated earlier, during the course of our investigation, we observed that less reactive arenes (such as anisole, toluene, benzene) were inactive toward cyclization of **3a** and **3j**. Interestingly, heteroarene substituted biaryl alcohols **5a**–**5c** efficiently cyclized into the corresponding hetero indeno core **6a**–**6c** in the presence of **C1**/$AgPF_6$ (Figure 4). Similarly, biaryl alcohols **5d**–**5f** were used to prepare fluorene **6d** and **6e** and benzo[*c*]fluorene **6f**.

The structures of **4o** and **6b** were established by X-ray crystallographic analysis (Figure 5).

(15) $Pd(PPh_3)_4$ was used to prepare **3j** following the method as noted in reference: Lötter, A. N. C.; Pathak, R.; Sello, T. S.; Fernandes, M. A.; Otterlo, W. A. L. V.; Koning, C. B. D. *Tetrahedron* **2007**, *63*, 2263.

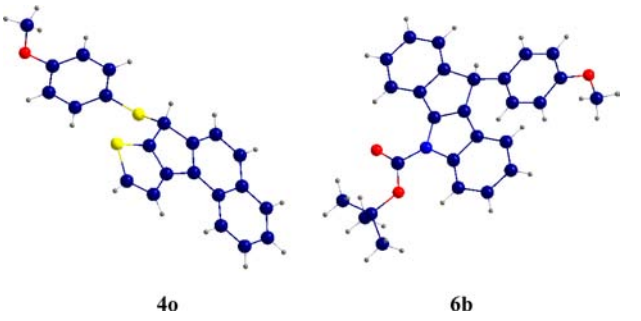

Figure 5. Crystal structure of **4o** and **6b**, DIAMOND plot with 30% probability thermal ellipsoids.

In conclusion, we have presented a synthetically attractive approach employing a Pd–Sn hetereobimetallic catalyst for a direct Suzuki coupling and tandem ring-closing sequence for the synthesis of indenothiophenes and indenoindoles having varied substitution at the 8/10 positions. Other heterocycle-fused indenes, fluorenes, and benzofluorene were also made via a stepwise route.

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Supporting Information Available. Experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.