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# Pt-catalyzed regio- and stereoselective pyridylthiolation of terminal alkynes

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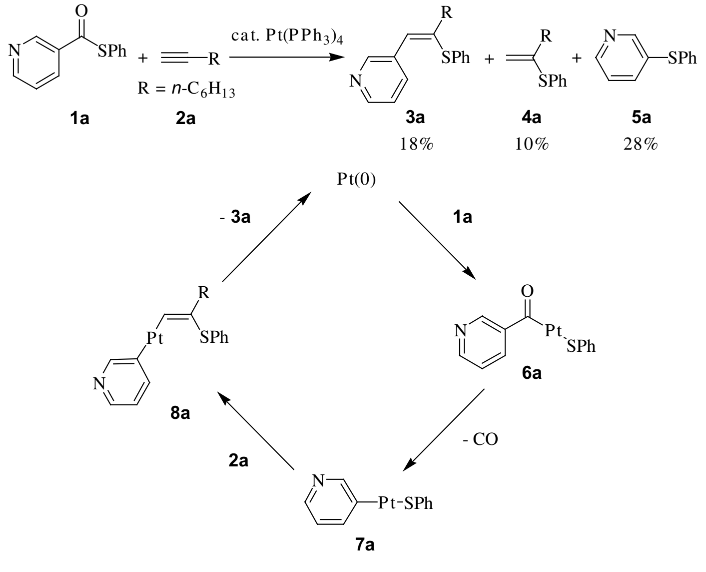
**Abstract**—Three-component cross-coupling reactions among 3-iodopyridynes, terminal alkynes and ArSK took place in the presence of Pt-catalyst to give pyridine derivatives with conjugated vinyl groups in moderate yields.

The reactions utilizing organic sulfur compounds as reactants of transition-metal catalyzed reactions are now ubiquitous, although a misconception that sulfur-containing compounds should poison the catalysts once had been prevailed among many chemists.[1] We have been interested in the reactivities of organic sulfur compounds as ligands of transition metals[2] and recently discovered one simple principle to simultaneously introduce carbon and sulfur functionalities into alkynes with the aid of the Pt-catalyst.[3] Herein described is an approach to synthesize functionalized pyridine derivatives by applying the carbothiolation prototype.

First, the reaction of (3-pyridyl)C(O)SPh (**1a**, 1.0 mmol) with 1-octyne (**2a**, 1.2 mmol) was attempted in toluene (0.5 mL) in the presence of $Pt(PPh_3)_4$ (0.05 mmol) to



**Scheme 1.** The route to Pt-catalyzed pyridylthiolation of **2a** by **1a** ($PPh_3$ on Pt omitted).

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*Keywords*: Alkyne; Carbothiolation; Platinum.

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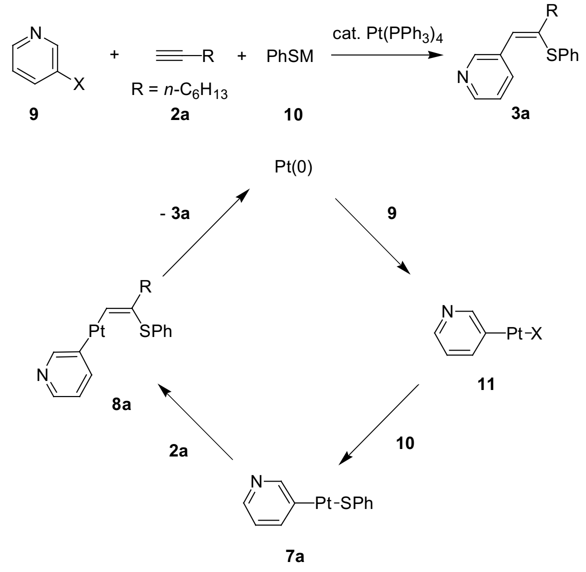
anticipate the formation of Z-(3-pyridyl)CH=C($n$-$C_6H_{13}$)-(SPh) (**3a**) through oxidative addition of thioester (**1a**) to Pt(0) to give (3-pyridyl)C(O)Pt(SPh) (**6a**), decarbonylation to afford 3-pyridyl-Pt-SPh (**7a**), insertion of 1-octyne (**2a**) into an S–Pt bond of **7a**[4] to yield vinylplatinum (**8a**) and following reductive elimination of **3a** with the regeneration of Pt(0) (Scheme 1). No starting thioester (**1a**) remained after 24h; however, contrary to the cases of arylthiolation[3b] and thienylthiolation,[3d] the yield of the anticipated **3a** was unsatisfactory (18%) and the formations of many by-products including $CH_2$=C(SPh)($n$-$C_6H_{13}$) (**4a**) (10%) and 3-pyridyl-SPh (**5a**) (28%) were also confirmed.



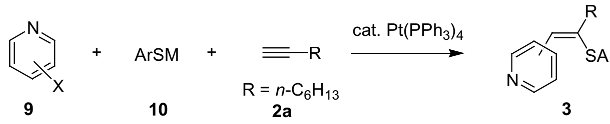
**Scheme 2.** The route to Pt-catalyzed pyridylthiolation of **2** by **9** and **10**.

On the other hand, the reaction using (2-pyridyl)-C(O)SPh (**1b**) was sluggish (36% conversion after 24h) to afford Z-(2-pyridyl)CH=C($n$-$C_6H_{13}$)(SPh) (**3b**) in 22% yield.

Thus, we next examined the syntheses of **3a** using the combination of reagents of 3-pyridyl-X (**9**; X = Cl, Br, and I) with PhSM (**10**; M = Li, Na, K, and Sn($n$-Bu)$_3$) as the sources of generation of 3-pyridyl-Pt-SPh (**7a**) through oxidative addition of 3-pyridyl-X (**9**) to Pt(0) to produce 3-pyridyl-Pt-X (**11**)[5] and following transmetallation with thiolate (**10**) (Scheme 2), instead of oxidative addition of thioester to Pt(0) and decarbonylation (Scheme 1).

Among examined (Table 1, entries 1–6), the combined use of 3-pyridyl-I (**9a**) and PhSK (**10c**) brought about the best result; **3a** was isolated in 78% yield together with 14% of 3-pyridyl-SPh (**5a**) and 8% of (Z,Z)-(3-pyridyl)($n$-$C_6H_{13}$)C=CHCH=C($n$-$C_6H_{13}$)(SPh) (**12a**) (entry 3).[6] The conversions were low in the cases of employing PhSLi (**10a**), 3-pyridyl-Br (**9b**), and 3-pyridyl-Cl (**9c**) (entries 1, 5, and 6), while fairly comparable yields of **3a** with that of using PhSK (**10c**) were resulted in when PhSNa (**10b**) and PhSSn($n$-Bu)$_3$ (**10d**) were exploited in the reactions with 3-pyridyl-I (**9a**) (entries 2 and 4). These results demonstrated that the efficiency of the pyridylthiolation could significantly depend on how intermediate 3-pyridyl-Pt-SPh (**7a**) was produced in situ. The Pt-catalyzed reaction of 3-pyridyl-I (**9a**) with PhSK (**10c**) in the absence of alkyne led to the formation of 3-

**Table 1.** Pt-catalyzed pyridylthiolation of **2a** by **9** and **10**[a]



| Entry | 9 | X | 10 | Ar | M | 3 | Yield of 3[b] |
|---|---|---|---|---|---|---|---|
| 1 | **9a** | 3-I | **10a** | Ph | Li | **3a** | 3[c] |
| 2 | **9a** | 3-I | **10b** | Ph | Na | **3a** | 72[d] |
| 3 | **9a** | 3-I | **10c** | Ph | K | **3a** | 78[e] |
| 4[f] | **9a** | 3-I | **10d** | Ph | Sn($n$-Bu)$_3$ | **3a** | 67 |
| 5 | **9b** | 3-Br | **10c** | Ph | K | **3a** | 5 |
| 6 | **9c** | 3-Cl | **10c** | Ph | K | **3a** | 0 |
| 7 | **9a** | 3-I | **10e** | $p$-$BrC_6H_4$ | K | **3c** | 65 |
| 8 | **9a** | 3-I | **10f** | $p$-$MeOC_6H_4$ | K | **3d** | 65 |
| 9 | **9d** | 2-I | **10c** | Ph | K | **3b** | 7[g] |
| 10[h] | **9d** | 2-I | **10c** | Ph | K | **3b** | 0[i] |

[a] Unless otherwise noted, **9** (1.0mmol), **10** (1.1mmol), **2a** (1.2mmol), Pt(PPh$_3$)$_4$ (0.05mmol), and toluene (0.5mL) under reflux for 24h.

[b] Isolated yield.

[c] Compounds **9a** (80% recovered), **4a** (54% based on **10a**), and (3-pyridyl)(R)C=CHCH=C(R)(SPh) (**12a**) (9% based on **9a**).

[d] Compound **9a** (11% recovered), **4a** (3%), and (**12a**) (3%).

[e] Compounds **5a** (14%) and **12a** (8%).

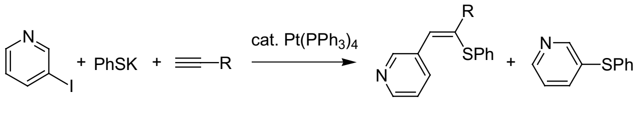
[f] Compounds **10d** (1.5mmol), Pt(PPh$_3$)$_4$ (0.10mmol) under reflux for 30h.

[g] (2-Pyridyl)SPh (**5b**) (91%).

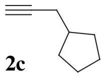
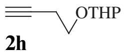
[h] Without Pt(PPh$_3$)$_4$.

[i] Compounds **9d** (9% recovered), **5b** (91%).

**Table 2.** Examples of Pt-catalyzed pyridylthiolation of **2** with **9a** and **10c**[a]



**9a** **10c** **2** **3** **5a**

| Entry | **2** | Yield (%) of **3**[b] | | Yield (%) of **5a**[b] |
|---|---|---|---|---|
| 1 | $\equiv$–$C_8H_{17}$-*n*<br>**2b** | **3e** | 77 | 16 |
| 2 | <br>**2c** | **3f** | 72 | 16 |
| 3[c] | $\equiv$–Ph<br>**2d** | **3g** | 23 | 56 |
| 4 | $\equiv$–$C_6H_4$-*p*-OMe<br>**2e** | **3h** | 44 | 53 |
| 5[d] | $\equiv$–$(CH_2)_3CN$<br>**2f** | **3i** | 34 | 27 |
| 6[e] | $\equiv$–$(CH_2)_4OH$<br>**2g** | **3j** | 50 | 22 |
| 7 | <br>**2h** | **3k** | 50 | 21 |
| 8 | $H_7C_3$–$\equiv$–$C_3H_7$<br>**2i** | **3l** | ND | 8 |
| 9 | $\equiv$–$CH_2Br$<br>**2j** | **3m** | ND | ND |

[a] Compounds **9a** (1.0 mmol), **10c** (1.1 mmol), **2** (1.2 mmol), $Pt(PPh_3)_4$ (0.05 mmol), and toluene (0.5 mL) under reflux for 24 h.

[b] Isolated yield.

[c] 30 h.

[d] Compounds **10c** (1.5 mmol), **2a** (1.5 mmol), and $Pt(PPh_3)_4$ (0.10 mmol).

[e] $Pt(PPh_3)_4$ (0.10 mmol).

pyridyl-SPh (**5a**) (14%) with the recovery of 3-pyridyl-I (**9a**) (77%), while no reaction proceeded when the solution of 3-pyridyl-I (**9a**) and PhSK (**10c**) was just refluxed without catalyst, proving that Pt-complex also catalyzed the production of 3-pyridyl-SPh (**5a**). The reactions using *p*-$BrC_6H_4SK$ (**10e**) and *p*-$MeOC_6H_4SK$ (**10f**) also afforded the desired pyridylthiolation products **3c** and **3d** in moderate yields (entries 7 and 8). However, due to the high susceptibility of 2-iodopyridine (**9d**) to nucleophilic substitution by PhSK (**10c**) even in the absence of catalyst (entry 10), the yield of **3b** was not improved by this combination of reagents (entry 9). When the reaction of 1-octyne (**2a**) with 3-pyridyl-I (**9a**) and PhSK (**10c**) was conducted in the presence of $Pd(PPh_3)_4$ instead of $Pt(PPh_3)_4$, a mixture of **3a** (5%), 3-pyridyl-SPh (**5a**) (40%) and (*Z*,*Z*)-(3-pyridyl)(*n*-$C_6H_{13}$)C=CHCH=C(*n*-$C_6H_{13}$)(SPh) (**12a**) (2%) was produced. Both $Pt(norbornene)_3$ and $Pt(norbornene)_3/P(n\text{-}Bu)_3$ were ineffective as catalysts for the formation of **3a**.

The scope and limitations of the present Pt-catalyzed pyridylthiolation of alkynes were summarized in Table 2. The reaction using the aliphatic alkynes **2b** and **2c** gave the pyridylthiolation products **3e** and **3f** in modest yields (entries 1 and 2). The ratios of **3** and **5** were significantly dependent on the nature of alkynes. Although predominant amounts of 3-pyridyl-SPh (**5a**) were produced when phenylacetylene (**2d**) and its derivative (**2e**) were used, highly conjugated pyridine derivatives **3g** and **3h** were synthesized by simple procedures, respectively (entries 3 and 4). The reaction of 5-hexynenitrile (**2f**) gave the corresponding adduct **3i** in 34% yield together with many by-products (entry 5). The protection of hydroxyl group hardly influenced the result of the reaction (entries 6 and 7). Neither internal alkyne (**2i**) nor propargyl bromide (**2j**) was active for the present transformation (entries 8 and 9).

In conclusion, this paper provides a convenient method for the synthesis of pyridine derivatives with 3-vinyl functionality. Further study is now continued to unveil the versatility of Pt-catalyzed carbothiolation chemistry.

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