Synthesis of Benzofused O- and N-Heterocycles through Cascade Carbopalladation/Cross-Alkylation of Alkynes Involving the C–C Cleavage of Cyclobutanols

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ABSTRACT: We report a Pd-catalyzed route to heterocycles bearing a tetrasubstituted alkene fragment. Our approach merges the intramolecular carbopalladation of tethered alkynes with an alkylation step produced by the C–C cleavage of cyclobutanol derivatives. An alkenyl-Pd(II) intermediate has been isolated and characterized by X-ray diffraction studies. Interestingly, the nature of the tethering alkynyl chain influences the E/Z stereochemistry of the alkenyl fragment in the functionalized heterocycles.

INTRODUCTION

The development of Pd-catalyzed cascade reactions based on the carbopalladation of alkynes has become a direct entry to the synthesis of substituted alkenes.1−9 Such reactions have been performed in either intra- or intermolecular fashion, with the resulting alkynyl-Pd intermediate being coupled afterward with different species, such as boronic acids,10−12 organotin reagents,13−18 and C-,19 N-,20,21 and O-nucleophiles,22 among many others (Scheme 1).23−28 Parallel studies have demonstrated the ability of Pd to perform the opening of strained cycloalkanols through β-carbon elimination (β, Scheme 1).29,30 This process leads to a σ-alkyl-Pd(II) intermediate, which can evolve in different manners, depending on the substitution pattern of the cycloalkanol.31−37 For instance, they can participate in further intramolecular steps, or be cross-coupled with aryl-,38−42 alkynyl-,43,44 and alkynylhalides,45 or propargyl carbonates,46 among others.29,47,48 Therefore, cyclopropyl- or cyclobutyl alcohols can behave as alkylating reagents under the appropriate conditions.

The merging of both aspects of palladium chemistry (carbopalladation/alkylation via opening of cycloalkanols) has rarely been reported in the literature. Werz et al. disclosed an interesting cascade reaction relying on the formal anti-carbopalladation of an internal alkyne, evolving through further intramolecular trapping of the alkynyl-Pd(II) intermediate by a tethered cyclopropanol moiety (c, Scheme 1).49 Very recently, Murakami, Chen, and co-workers reported the synthesis of 2,3-dihydrobenzofurans through the use of alkynyl-tethered aryliodides and benzylocyclobutanols (d, Scheme 1).50,51

With these precedents in mind, and given our interest in the topics of Pd chemistry and the processes related to C–C cleavage,52−57 we aimed to extend the applicability of these types of cascades to the synthesis of heterocycles bearing an alkylated olefin moiety (Scheme 1).

RESULTS AND DISCUSSION

We studied the feasibility to perform the envisioned carbopalladation/alkylation cascade reaction employing the 2-bromoarylether 1a and the cyclobutanol derivative 2a (Table 1). Initial screening of experimental conditions revealed the formation of some amounts of the byproduct 4a, likely arising from the protodepalladation of the plausible alkenyl-Pd(II) intermediate generated upon the carbopalladation of the internal alkyne moiety. The use of 10 mol% of [Pd(dba)₂] along with 20 mol% of PPh₃ showed good selectivity to give the desired compound 3a in THF or toluene as solvents (entries 3 and 4, Table 1). Replacing PPh₃ by other ligands such as JohnPhos, PC₅, or Xantphos did not improve the yields of 3a (entries 5−7, Table 1). The increase of the amount of Cs₂CO₃ in the reaction mixture could not suppress the protodepalladation process leading to the byproduct 4a, and other organic bases like NEt₃ precluded the formation of 3a. We tested Pd sources like Pd(OAc)₂, [PdCl₂(PPh₃)₂], and [Pd(PPh₃)₄]. While the first two were not effective for this...
Scheme 1. Merger of Carbopalladation of Alkynes and C–C Cleavage of Cycloalkanols

Previous works
a) General functionalization of alkynes through carbopalladation (See, for example, Negishi, 1990; Takemoto, 2005; Latens, 2015)

b) Pd-catalyzed alkylation via C–C cleavage of strained cycloalkanols (Uemura and Nishimura, 1999; Martin and Ziad, 2012)
c) Intramolecular carbopalladation/cyclopropanol opening cascade (Werz et al, 2018)
d) Intramolecular carbopalladation/alkylation cascade of alkenes (Murakami, Liu et al., 2021; Chen, Zhang et al., 2021)

This work. Intramolecular carbopalladation/alkylation of alkynes

transformation, [Pd(PPh3)4] showed a comparable activity to [Pd(dba)2], reaching a 70% yield of the desired product.

With the optimized conditions in hand, we proceeded to study the scope and limitations of the reaction. Several aspects were assessed: the presence of electron-donating/withdrawing groups in the haloaryl moiety, the nature and length of the chain tethering the internal alkyne, and the use of different substituted cyclobutanols.

The reactions of haloaryl ethers bearing alkyl, methoxy, fluoro, or trifluoromethyl substituents with the 3,3-substituted cyclobutanol 2a afforded good yields of the expected dihydrobenzofuran derivatives 3b–3e (Scheme 2). The pyridine derivative 1g gave rise to the heterocycle 3f, albeit in moderate yield, perhaps due to competing coordination of the pyridine moiety to Pd(II). C3-unsubstituted cyclobutanol derivatives 2 were also productive in the cascade reaction, giving the functionalized dihydrobenzofuran derivatives 3g–j in comparable yields to those obtained with 2a (Scheme 2); therefore, the possible byproduct formation arising from β-H elimination processes seem to be overridden. The cyclobutanol derivative bearing a mesityl group in α-position led to mixtures where the desired compound 3k could not be identified. The compound 3l could be isolated in 44% yield from the reaction carried out employing the tertiary cyclobutanol bearing an i-Pr group.

Table 1. Optimization of the Carbopalladation/Alkylation Cascade

| entry | Pd source (10 mol %) | ligand (20 mol %) | solvent | yield 3a |
|-------|---------------------|------------------|---------|---------|
| 1     | [Pd(dba)2] | PPh3 | 1,2-DCE | traces |
| 2     | [Pd(dba)2] | PPh3 | 1,4- dioxane | traces |
| 3     | [Pd(dba)2] | PPh3 | THF | 62 |
| 4     | [Pd(dba)2] | PPh3 | toluene | 68 |
| 5     | [Pd(dba)2] | JohnPhos | toluene | – |
| 6     | [Pd(dba)2] | PCy3 | toluene | 60 |
| 7     | [Pd(dba)2] | Xantphos | toluene | 32 |
| 8     | [Pd(OAc)2] | PPh3 | toluene | traces |
| 9     | [PdCl2(PPh3)2] | – | toluene | traces |
| 10    | [Pd(PPh3)4] | – | toluene | 70 (67) |

"The reactions were carried out using 0.14 mmol of 1-bromo-2-((3-phenylprop-2-yn-1-yl)oxy)benzene (1a), 1.2 equiv of 3-methyl-1,3-diphenylcyclobutan-1-ol (2a), and 1.2 equiv of Cs2CO3 in 4 mL of dry solvent, under nitrogen atmosphere at 100 °C, in a Carius tube for 16 h. NMR yields using trimethylbenzene-1,3,5-tricarboxylate as standard. †Isolated yield.

Finally, the cross-coupling reactions of 2b and Me- or TMS-substituted alkynyl substrates were tested. We observed that among such substrates, only the silylated alkyne was competent to deliver the desired product 3m in 56% yield (Scheme 2). Possibly, the substrate leading to 3n could experience a β-H elimination upon the carbopalladation step to render an allenyl moiety, as described in other Pd-catalyzed reactions dealing with alkyl-substituted alkynes.58,59

In order to assess the stereochimerism of the exocyclic double bond present in the dihydrobenzofuran cores, a NOESY NMR experiment was carried out for compound 3d. The NOE contacts between the methylene group CH2c and –H atoms from the Ph ring, as well as the Ha of the heterocycle with the CH2b group of the aliphatic chain, pointed out the Z-stereochemistry for these compounds (Scheme 3).

As a general feature of compounds 3a–3m, we observed their relative sensitivity to chromatography purification in either silica gel or alumina. The decomposition of the compounds could be mimicked by using silica gel previously deactivated with Et3N, and EtOAc mixtures as eluents. Solutions of these compounds in CDCl3 also evolved different 1H NMR yields using trimethylbenzene-1,3,5-tricarboxylate as standard.† Isolated yield.
the formation of the corresponding coupling product $3s$ as the main component, which could be isolated in 58% yield (Scheme 5). Similarly, the oxindole derivatives $3t$ and $3u$ could be isolated in moderate yields from the reactions of the corresponding propiolamides and the C3-unsubstituted cyclobutanol $2b$. The $^1$H NMR spectra of compounds $3s$–$u$ showed an aromatic signal belonging to the oxindole core at a relatively low chemical shift (5.8–6.0 ppm). This shielding on H$_a$ (compound 3u, Scheme 3) is provoked by the phenyl ring on the exocyclic olefine moiety, as observed in related structures reported in the literature. In addition, the NOESY NMR analysis of 3u also confirmed the E-stereochemistry of the exocyclic double bond. The presence of minor Z-stereoisomers in the reaction mixtures leading to $3s$–u cannot be discarded; however, we were unable to isolate such minor components of the crude mixtures and identify their nature unambiguously.

The plausible mechanistic pathway for this reaction is depicted in Scheme 6. The aryl-Pd species A would form upon oxidative addition of the C–Br bond present in the starting material $1a$ to Pd(0) (Chart 1). Next, the intramolecular syn carbopalladation of the tethered alkyne would render the intermediate B. At this stage, Cs$_2$CO$_3$ would assist the deprotonation of the cycloalkanol, along with the removal of the halogen ligand from the coordination sphere, allowing the formation of the alkoxide complex C. The opening of the strained cycloalkanol through $\beta$-C cleavage would render the $\sigma$-alkyl-Pd(II) intermediate D, from which reductive elimination could take place to deliver the substituted olefin $3a$ upon C(sp$^2$)–C(sp$^3$) bond formation.

The fact that propiolamide substrates afford the E-alkenylated oxindoles $3s$–u as main coupling products reveals that in those cases the alkynyl-Pd(II) intermediate, arising from the syn carbopalladation step, could undergo an isomerization process. There are several precedents in the literature of related Pd-catalyzed cascade reactions involving the syn carbopalladation of alkynes and subsequent isomerization prior to the final C–Pd bond functionalization. Generally, the isomerization of the alkynyl-Pd intermediates is driven by steric factors. Nevertheless, $\alpha$-alkyl-substituted alkynyl substrates, such as 1a, require the use of bulky phosphine ligands (Q-Phos, X-Phos, or P$_3$Bu$_3$ among others) to increase the steric hindrance around the Pd center and therefore promote the isomerization.
α-acyl-substituted alkyne substrates, such as propiolamides 1m–o, the isomerization is a frequent feature in a range of different conditions, probably due to the conjugation of the alkynyl-Pd moiety and the carbonyl group, which might lower the energy barrier for the C–C rotation process (Scheme 6).28,62,68,69 Likely the coordination of the carbonyl moiety might facilitate such processes. Nevertheless, the opposite isomerization has been observed in related systems (that is, the steric factors seemed to predominate over the possible coordination of the carbonyl group in intermediates such as E).68,69

We carried out the reaction of substrate 1b with a stoichiometric amount of [Pd(PPh3)4] in CH2Cl2 at 50 °C for 18 h under N2 atmosphere (Scheme 7). From the reaction mixture, the vinyl-Pd(II) complex 4 (analogous to the intermediate B) could be isolated in 84% yield. The complex 4 was subsequently heated in toluene at 100 °C in the presence of cyclobutanol 2a and Cs2CO3. The 1H NMR spectra of the crude reaction mixture confirmed the formation of the functionalized dihydrobenzofuran 3a in 70% yield.

The crystal structure of complex 4 was solved by X-ray diffraction studies (Figure 1, Chart 2). The PPh3 ligands adopted a trans disposition. The palladium atom was in a slightly distorted square-planar environment, with a mean deviation of the Pd(II) coordination plane of 0.088 Å. The exocyclic double bond exhibited an E geometry, with the phenyl...
ring located cis to the methylene group of the dihydrobenzo- 
uran ring. The heterocyclic nucleus formed angles of 38.1° 
and 77.1° with the phenyl substituent at the double bond and 
the Pd(II) coordination plane, respectively. This way, the 
phenyl ring was rotated 23.3° with respect to the exocyclic 
double bond plane.

### CONCLUSION

In summary, we have expanded the versatility of Pd cascades 
relying on intramolecular carbopalladation processes through 
its merging with the opening of strained cycloalkanols. Thus, 
the carbopalladation of tethered alkynes followed by an 
intramolecular carbopalladation processes through 
**EXPERIMENTAL SECTION**

**General Remarks.** Infrared spectra were recorded on a 
PerkinElmer spectrum 100 spectrophotometer. High-resolution ESI 
mass spectra were recorded on an Agilent 6220 Accurate Mass TOF 
LC-MS spectrometer. Melting points were determined using a 
Reichert apparatus and are uncorrected. Nuclear magnetic resonance 
(NMR) spectra were recorded on a 300, 400, or 600 MHz Bruker 
NMR spectrometers in CDC1$_3$ at 298 K (unless stated otherwise). All chemical shift values are reported in parts per million (ppm) with 
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1.93 (m, 2 H). 13C NMR (75.45 MHz, CDCl3) δ 197.7 (s, Cq), 166.5 (q, JCF = 10.0 Hz, Cq), 146.7 (s, Cq), 143.5 (s, Cq), 137.7 (s, Cq), 134.2 (s, Cq), 133.2 (s, Cq), 132.6 (s, CH), 128.8 (s, CH), 128.3 (s, CH), 128.2 (s, CH), 127.7 (s, Cq), 127.4 (s, Cq), 127.2 (q, JCF = 3.3 Hz, CH), 126.0 (s, CH), 125.7 (s, Cq), 125.5 (s, CH), 122.6 (q, JCF = 32.1 Hz, CH), 121.3 (q, JCF = 3.9 Hz, CH), 110.4 (s, CH), 76.3 (s, CH), 48.9 (s, CH), 46.7 (s, CH), 42.2 (s, Cq), 24.4 (s, CH). One quaternary carbon signal is overapped. 19F-NMR (376.5 MHz, CDCl3) δ −61.02 (s). HRMS (+ESI) m/z calculated for C30H27NNaO2 [M + Na]+ 535.1855, found 535.1856.

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1H NMR (300 MHz, CDCl3) δ 8.00−7.87 (m, 2 H), 7.65 (dd, J = 7.8, 1.3 Hz, 1 H), 7.43−7.34 (m, 2 H), 7.32−7.27 (m, 1 H), 7.24−7.15 (m, 3 H), 7.15−7.05 (m, 2 H), 6.93 (dd, J = 7.6, 1.1 Hz, 1 H), 4.91 (s, 2 H). 13C NMR (75.45 MHz, CDCl3) δ 197.8 (s, Cq), 160.3 (s, Cq), 156.9 (d, JCF = 235.4 Hz, Cq), 147.0 (s, Cq), 143.5 (s, Cq), 137.7 (s, Cq), 135.4 (d, J = 2.9 Hz, Cq), 132.6 (s, Cq), 132.2 (s, Cq), 128.7 (s, CH), 128.1 (s, CH), 127.7 (s, CH), 127.5 (s, CH), 127.1 (s, CH), 125.9 (s, CH), 125.6 (s, Cq), 116.0 (d, J = 24.6 Hz, CH), 110.8 (d, J = 26.5 Hz, CH), 110.4 (d, J = 8.7 Hz, CH), 76.1 (s, CH), 49.3 (s, CH), 46.0 (s, CH), 42.0 (s, Cq), 24.3 (s, CH). The signal of one Cq is overapped. 19F-NMR (376.5 MHz, CDCl3) δ −123.57 (s). HRMS (+ESI) m/z calculated for C32H25FNaO2 [M + Na]+ 485.1887, found 485.1868.

**Compound (Z)-5-(Furo(3,2-b)pyridine-3(2H)-ylidene)-1,3-diphenylpentan-1-one (3f).** Prepared according to the representative procedure A from 0.14 mmol of substrate 1a and 0.17 mmol of 3-methyl-1,3-diphenylclobutan-1-ol (2a). The crude was purified by column chromatography over silica gel using 0 to 10% gradient EtOAc in n-hexane containing 1% Et3N to afford the heterocycle 3f as a light-yellow oil (32 mg, 0.086 mmol, 72%). IR (cm−1) ν 3376, 3061, 2933 (m, m), 1682 (s), 1599 (s), 1504 (m), 1408 (m), 1228 (s), 1156 (m), 1098 (w), 832 (w), 747 (s), 700 (s). 1H NMR (300 MHz, CDCl3) δ 8.00−7.87 (m, 2 H), 7.65 (dd, J = 7.8, 1.3 Hz, 1 H), 7.43−7.34 (m, 2 H), 7.32−7.27 (m, 1 H), 7.24−7.15 (m, 3 H), 7.15−7.05 (m, 2 H), 6.93 (dd, J = 7.6, 1.1 Hz, 1 H), 4.91 (s, 2 H), 3.01 (td, J = 7.2, 1.1 Hz, 2 H), 2.93−2.62 (m, 2 H), 2.40 (s, 3 H), 2.06−1.78 (m, 2 H). 13C NMR (75.45 MHz, CDCl3) δ 199.6 (s, Cq), 164.2 (s, Cq), 152.2 (s, Cq), 143.7 (s, Cq), 143.0 (s, Cq), 134.5 (s, Cq), 133.4 (s, Cq), 133.5 (s, Cq), 129.5 (s, CH), 129.2 (s, CH), 128.8 (s, CH), 128.1 (s, CH), 127.4 (s, CH), 127.2 (s, CH), 124.1 (s, CH), 120.7 (s, CH), 110.4 (s, CH), 75.2 (s, CH), 38.0 (s, CH), 33.7 (s, CH), 22.6 (s, CH), 21.6 (s, CH). HRMS (+ESI) m/z calculated for C21H16F2NaO2 [M + Na]+ 391.1609, found 391.1606.

**Compound (Z)-5-(Furo(3,2-b)pyridine-3(2H)-ylidene)-1,5-di-phenylpentan-1-one (3j).** Prepared according to the representative procedure A from 0.11 mmol of substrate 1g and 0.17 mmol of 1-phenylclobutan-1-ol (2b). The crude was purified by column chromatography over silica gel using 0 to 10% gradient EtOAc in n-hexane containing 1% Et3N to afford the heterocycle 3j as a yellow oil (23 mg, 0.065 mmol, 46%). IR (cm−1) ν 3376, 3061, 2933 (m, m), 1682 (s), 1599 (s), 1408 (m), 1228 (s), 1156 (m), 1098 (w), 832 (w), 747 (s), 700 (s). 1H NMR (300 MHz, CDCl3) δ 8.00−7.87 (m, 2 H), 7.65 (dd, J = 7.8, 1.3 Hz, 1 H), 7.43−7.34 (m, 2 H), 7.32−7.27 (m, 1 H), 7.24−7.15 (m, 3 H), 7.15−7.05 (m, 2 H), 6.93 (dd, J = 7.6, 1.1 Hz, 1 H), 4.91 (s, 2 H), 3.01 (td, J = 7.2, 1.1 Hz, 2 H), 2.93−2.62 (m, 2 H), 2.40 (s, 3 H), 2.06−1.78 (m, 2 H). 13C NMR (75.45 MHz, CDCl3) δ 199.6 (s, Cq), 164.2 (s, Cq), 152.2 (s, Cq), 143.7 (s, Cq), 143.0 (s, Cq), 134.5 (s, Cq), 133.4 (s, Cq), 133.5 (s, Cq), 129.5 (s, CH), 129.2 (s, CH), 128.8 (s, CH), 128.1 (s, CH), 127.4 (s, CH), 127.2 (s, CH), 124.1 (s, CH), 120.7 (s, CH), 110.4 (s, CH), 75.2 (s, CH), 38.0 (s, CH), 33.7 (s, CH), 22.6 (s, CH), 21.6 (s, CH). HRMS (+ESI) m/z calculated for C21H16F2NaO2 [M + Na]+ 391.1609, found 391.1606.

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yellow oil (17 mg, 0.053 mmol, 44%). IR (cm⁻¹) 1708 (s), 1685 (s), 1648 (s), 1489 (s), 1387 (s), 1253 (m), 1124 (m), 876 (s), 787 (s), 695 (s). ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.77 (m, 2 H), 7.29–7.25 (m, 3 H), 6.99–6.95 (m, 1 H), 6.86–6.64 (m, 2 H), 4.87 (s, 1 H), 4.8 (s, 1 H), 4.09 (d, J = 7.1 Hz, 2 H), 2.24 (s, 6 H), 1.00–0.80 (m, 3 H). MS (+ESI) m/z calculated for C₃₇H₃₁NNaO₃ [M + Na]⁺ 620.2238, found 620.2235.

**Compound (2a)** 1-Methyl-3-(3-methyl-5-oxo-1,3,5-triphenyl-5-(1-tosylindolin-3-ylidene)-1-phenyl-5-(1H)-yldiene)pentan-1-one (2a). Prepared according to the representative procedure A from 0.14 mmol of substrate 1m and 0.17 mmol of 1,3-diphenylcyclobutan-1-ol (2a). The crude was purified by column chromatography over silica gel using 0 to 30% gradient EtOAc in n-hexane as a yellow oil (38 mg, 0.081 mmol, 58%). IR (cm⁻¹) δ 1699 (s), 1616 (s), 1595 (s), 1490 (s), 1122 (s), 904 (s), 787 (s), 693 (s). ¹H NMR (600 MHz, CDCl₃) δ 7.69–7.67 (m, 2 H), 7.45 (dtt, J = 8.7, 1.3, 1.0 Hz, 1 H), 7.40–7.37 (m, 2 H), 7.35–7.31 (m, 3 H), 7.31–7.28 (m, 3 H), 7.16–7.10 (m, 4 H), 7.00 (m, 4 H), 5.97–5.93 (d, J = 7.7, 1.1 Hz, 1 H), 5.47 (d, J = 7.1 Hz, 1 H), 5.09–5.03 (m, 2 H), 3.74–3.36 (m, 4 H), 3.45–3.30 (m, 1 H), 2.66–2.42 (m, 2 H), 1.37 (m, 3 H), 1.04–0.84 (m, 6 H), 0.70–0.59 (m, 2 H), 0.43–0.26 (m, 2 H), 0.32–0.17 (m, 3 H), 0.29 (d, J = 17.2 Hz, 2 H), 0.28 (s, 3 H), 0.15 (s, 3 H). MS (+ESI) m/z calculated for C₃₇H₃₁NO₃ [M + H]⁺ 571.2387, found 571.2388.

**Compound (1b)** 1-Methyl-3-(3-methyl-1,3,5-triphenyl-5-(1-tosylindolin-3-ylidene)-5-(1H)-yldiene)-1,3,5-triphenylpentan-1-one (1b). Prepared according to the representative procedure A from 0.14 mmol of substrate 1k and 0.17 mmol of 1,3-diphenylcyclobutan-1-ol (2a). The crude was purified by column chromatography over silica gel using 0 to 20% gradient EtOAc in n-hexane containing 1% Et₃N to afford the heterocycle 3b as a yellow oil (40 mg, 0.10 mmol, 73%). mp 130 °C. IR (cm⁻¹) δ 1708 (s), 1606 (s), 1576 (s), 1519 (s), 1487 (s), 1449 (s), 1424 (s), 1365 (s), 1342 (s), 1337 (s), 1326 (s), 1321 (s), 1296 (s), 1291 (s), 1288 (s), 1282 (s), 1276 (s), 1274 (s), 1271 (s), 1268 (s), 1258 (s), 125 (s), 120 (s), 110 (s), 75 (s), 38 (s), 31 (s), 23 (s), 21.5 (s), CH₃. Some Cq signals are overlapped. HRMS (+ESI) m/z calculated for C₃₉H₃₃NNaO₃ [M + Na]⁺ 655.2178, found 655.2178.

**Compound (1c)** 1-Methyl-3-(3-methyl-1,3,5-triphenyl-5-(1-tosylindolin-3-ylidene)-5-(1H)-yldiene)-1,3,5-triphenylpentan-1-one (1c). Prepared according to the representative procedure A from 0.14 mmol of substrate 1k and 0.17 mmol of 3-methyl-1,3-diphenylcyclobutan-1-ol (2a). The crude was purified by column chromatography over silica gel using 0 to 20% gradient EtOAc in n-hexane containing 1% Et₃N to afford the heterocycle 3c as a yellow oil (40 mg, 0.10 mmol, 73%). mp 130 °C. IR (cm⁻¹) δ 1708 (s), 1606 (s), 1576 (s), 1519 (s), 1487 (s), 1449 (s), 1424 (s), 1365 (s), 1342 (s), 1337 (s), 1326 (s), 1321 (s), 1296 (s), 1291 (s), 1288 (s), 1282 (s), 1276 (s), 1274 (s), 1271 (s), 1268 (s), 1258 (s), 125 (s), 120 (s), 110 (s), 75 (s), 38 (s), 31 (s), 23 (s), 21.5 (s), CH₃. Some Cq signals are overlapped. HRMS (+ESI) m/z calculated for C₃₉H₃₃NNaO₃ [M + Na]⁺ 655.2178, found 655.2178.
CH2Cl2/Et2O to give analytically pure monochromated Mo Kα 125.6 (s, C6H4), 127.4 (t, Cq), 167.4 (s, Cq), 160.3 (s, Cq), 140.8 (s, Cq), 140.5 (s, Cq), as a yellow oil (25 mg, 0.06 mmol, 43%). IR (cm⁻¹ (400.9 MHz, CDCl3) 1.96 (q, φ) scan mode. Multiscan absorption correction was applied.

Figure 1: An illustration of the X-ray diffraction pattern of the complex 1b, showing the peaks at different wavelengths.

Synthesis of Complex 4. A Carius tube was charged with the substrate 1b (100 mg, 0.30 mmol), [Pd(PPh3)4] (350 mg, 0.30 mmol), and a magnetic stirrer. The tube was sealed, and the mixture was stirred at 50 °C for 18 h. After the tube was cooled, the solution was filtered through a Celite plug. The filtrate was concentrated to ca. 2 mL, and n-pentane (15 mL) was added. The suspension was filtered, and the solid was washed with n-pentane (2 × 3 mL) and air-dried to give crude 4 as a bright yellow solid. Yield: 243 mg, 0.25 mmol, 84%. Compound 4 was recrystallized from CH2Cl2/Et2O to give analytically pure 4. mp 204 °C (dec). 1H NMR (400.9 MHz, CDCl3) δ 9.24 (d, JH = 7.2 Hz, 1 H, H6, C6H4), 7.57–7.42 (m, 5 H, p-H, PPh3), 7.37–7.30 (m, 6 H, p-H, PPh3), 7.25–7.18 (m, 12 H, m-H, PPh3), 7.03 (td, JH = 7.8, 12 Hz, 1 H, H4, C6H4), 6.98 (t, JH = 7.3 Hz, 1 H, m-H, Ph), 6.87 (td, JH = 7.4, 1 H, H5, C6H4), 6.84 (t, JH = 0.8 Hz, 1 H, H3, C6H4). 13C NMR (100 MHz, CDCl3) δ 163.2 (c, N), 155.5 (t, JCP = 2 Hz, 2 H, CH2), 143.9 (t, JCP = 2.9 Hz, i-C, Phh), 135.2 (t, JCP = 5.9 Hz, o-C, PPh3), 134.4 (t, JCP = 5.1 Hz, C1), 131.9 (t, JCP = 22.9 Hz, i-C, PPh3), 130.2 (s, C1), 130.0 (s, p-C, PPh3), 129.0 (s, o-C, Phh), 128.7 (s, CH4, C6H4), 127.4 (t, JCP = 5.0 Hz, m-C, PPh3), 126.9 (s, m-C, Phh), 125.6 (s, p-C, Phh), 121.9 (s, CH6, C6H4), 119.4 (s, CH5, C6H4), 109.1 (s, CH3, 77.1 (s, CHh4). IR (Nujol, cm⁻¹) v 1590 (w), 1231 (m), 1093 (m), 742 (s), 691 (s), 520 (s), 509 (s), 494 (m). Anal. Calcd for C51H41IOP2Pd: C, 63.47; H, 4.28. Found: C, 63.55; H, 4.33.

Single-Crystal X-ray Structure Determination. Single crystals of complex 4, suitable for an X-ray diffraction study, were obtained by slow diffusion of n-pentane into a solution of 4 in CHCl3.

Data Collection. A crystal suitable for X-ray diffraction was mounted in an insert on a glass fiber and transferred to a Bruker diffractometer. Data were recorded at 100(2) K, using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) and omega and phi scan mode. Multiscan absorption correction was applied.

Structure Solution and Refinements. The crystal structure was solved by dual method, and all non-hydrogen atoms were refined anisotropically on F² using the program SHELXL-2018/3. Hydrogen atoms were refined using the riding model.

ASSOCIATED CONTENT

Supporting Information. The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.2c00015.

The Supporting Information contains the following:

- Table S1: Crystallographic data for several compounds.
- Table S2: A summary of the crystallographic data.
- Table S3: A summary of the atomic coordinates.
- Table S4: A summary of the bond lengths and angles.
- Table S5: A summary of the hydrogen bond interactions.
- Table S6: A summary of the packing interactions.

Accession Codes.

CCDC 2132049 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes
The authors declare no competing financial interest.

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