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Heterocycles by $PtCl_2$-Catalyzed Intramolecular Carboalkoxylation or Carboamination of Alkynes

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During the course of our studies on noble metal catalyzed skeletal rearrangements,[1] it was found that alkynes bearing lateral allyl ether moieties form tetrahydrofuran rings with concomitant O → C allyl transfer on treatment with $PtCl_2$ (Scheme 1).[2] In an attempt to explore the scope of this net carboalkoxylation of the triple bond,[2,3] we now present a versatile and convenient entry into aromatic heterocycles and extend the concept of carboalkoxylation beyond the original allyl shift reaction.

Given the efficient activation of alkynes by late transition metal species toward nucleophilic attack,[4] it comes as no surprise that phenol derivatives **1** bearing an alkyne moiety at the *ortho*-position smoothly convert into the corresponding benzofurans on exposure to catalytic amounts of $PtCl_2$ in toluene. The reaction proceeds at ambient temperature, although it is significantly faster when performed at 80 °C. Low catalyst loadings (0.5−1 mol %) usually suffice to obtain almost quantitative yields with an assortment of examples (Table 1). In contrast to most other catalysts used for similar purposes,[5] no external base is necessary to promote the reaction. Workup is therefore greatly simplified with only filtration of the crude mixture through a plug of silica necessary. The fact that the cyclization even proceeds in air using an easy-to-handle, nonhygroscopic salt constitutes an additional bonus in practical terms.

Gratifyingly, protection of the phenolic −OH in **1** as the corresponding allyl ethers **3** does not preclude the heteroannulation. Rather, the allyl substituent is transferred to the 3-position of the resulting benzofuran **4** via an efficient intramolecular "*endo*-mode" *trans*-carboalkoxylation (Table 2). The reaction is best performed under an atmosphere of CO, which we have recently shown to accelerate certain $PtCl_2$-catalyzed skeletal rearrangements to a significant extent.[6,7] Entries 9−12 witness that benzyl ether derivatives are also well behaved substrates. Furthermore, Scheme 2 shows that related reactions can be achieved with suitable aniline derivatives **5**, thus opening a novel entry into substituted indoles **6** by intramolecular (hydro)carboamination.[8]

At first sight, the overall transformation formally resembles the benzofuran (indole) synthesis pioneered by Cacchi and Balme using $Pd(PPh_3)_4$ cat. (Scheme 3).[9,10] It is important to note, however, that this palladium-based methodology generates the actual catalyst in situ by oxidative addition into the allyl ether group and hence relies on a redox cycle, whereas the $PtCl_2$-catalyzed procedure does not. This particular feature pays off in dealing with substrates containing additional sites prone to oxidative insertion as evident from entry 7 (Table 2). In this case, the $PtCl_2$-catalyzed reaction proceeds without affecting the vinyl bromide entity, thus leaving options for subsequent manipulation.

The proposed catalytic cycle (Scheme 4) implies activation of the alkyne by the electrophilic metal species which enables nucleophilic attack by the heteroelement, resulting in *trans*-alkoxyplatination. This process *formally* generates an allyl cation fragment[11] that shifts to the most nucleophilic position on the incipient ring to give the product and regenerate the catalyst. This notion suggests that other entities R^3, able to stabilize positive charge, might transfer in a similar fashion.

To probe this concept, a series of appropriate phenolic MOM-acetals was subjected to the $PtCl_2$-catalyzed rearrangement. All of them afforded the corresponding 2,3-disubstituted benzofuran derivatives in good to excellent yield after short reaction times

Scheme 1. $PtCl_2$-Catalyzed Carboalkoxylation[2]

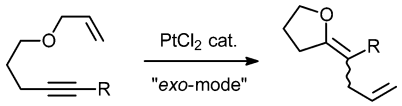
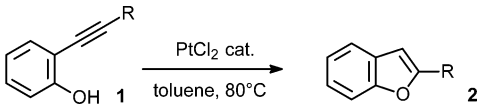


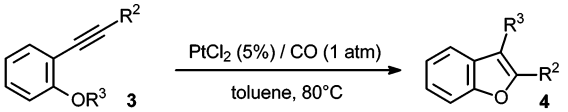
Table 1. $PtCl_2$-Catalyzed Synthesis of 2-Substituted Benzofurans

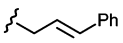


Entry	R	$PtCl_2$	*t* (h)	Yield
1	-C_3H_7	5 mol %	1	88% (83%)[a]
2	-C_5H_{11}	0.5 mol %	5	98%
3	cyclopropyl	1 mol %	1	98%
4	-CH_2CH_2Ph	1 mol %	5	98%
5	-$CH_2CH(COOMe)_2$	5 mol %	1	92%
6	-C_6H_5	5 mol %	1.5	97%
7	*p*-MeO-C_6H_4-	0.5 mol %	2	95%
8	*m*-F_3C-C_6H_4-	0.5 mol %	5	94%

[a] Under air at ambient temperature, 3 h.

Table 2. $PtCl_2$-Catalyzed Benzofuran Synthesis by Intramolecular Carboalkoxylation (Allyl/Benzyl Shift Reactions)

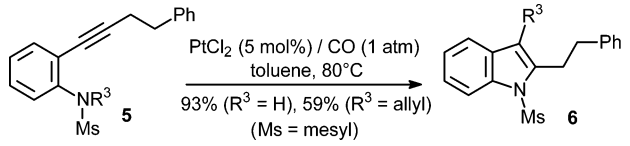


Entry	R^2	R^3	*t* (h)	Yield
1	-C_3H_7		4	88%
2	-CH_2CH_2Ph		4	94%[a]
3	*m*-MeO-C_6H_4-		1	98%
4	*m*-F_3C-C_6H_4-		1	94%
5	-C_5H_{11}		12	73%
6	-CH_2CH_2Ph		8	71%[a]
7	-C_5H_{11}		5	54%
8	-C_5H_{11}		3	68%[b]
9	-C_5H_{11}	-Bn	6	66%[a]
10	-C_5H_{11}	*p*-MeO(C_6H_4)CH_2-	4	76%[a]
11	*m*-F_3C-C_6H_4-	*p*-MeO(C_6H_4)CH_2-	4	78%[a]
12	-cyclopropyl	*p*-MeO(C_6H_4)CH_2-	3	77%[a]

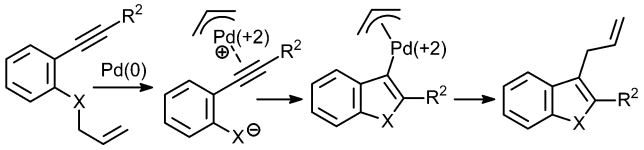
[a] Using 10 mol % of $PtCl_2$. [b] Linear cinnamyl entity in the product.

10.1021/ja055659p CCC: $30.25

Scheme 2. $PtCl_2$-Catalyzed Indole Synthesis



Scheme 3. Heterocycle Synthesis by Oxidative Insertion[9,10]



Scheme 4. Proposed Reaction Mechanism

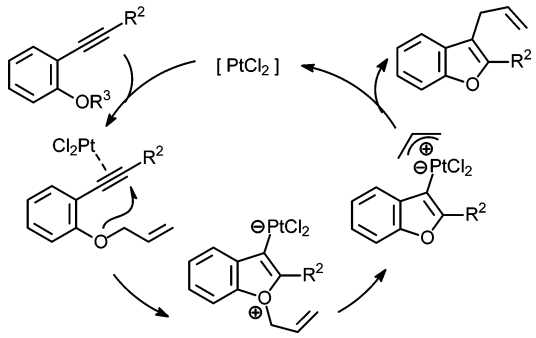
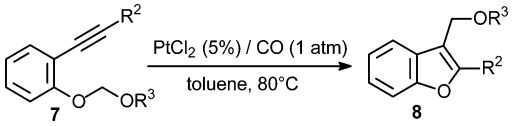
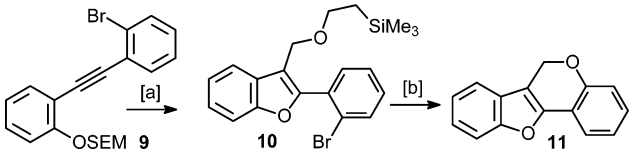


Table 3. $PtCl_2$-Catalyzed Benzofuran Synthesis by Intramolecular Carboalkoxylation (MOM/BOM/SEM Shift Reactions)



Entry	R^2	R^3	*t* (h)	Yield
1	$-C_5H_{11}$	Me	2	91%
2	$-CH_2CH_2Ph$	Me	0.5	84%
3		Bn	0.5	78%
4		$CH_2CH_2SiMe_3$	0.5	81%
5	cyclopropyl	Me	2	84%
6	$-C_6H_5$	Me	0.5	95%
7	*m*-MeO-C_6H_4-	Me	2	62%
8	*m*-F_3C-C_6H_4-	Me	2	74%
9		Bn	0.5	84%
10	*o*-(*i*-PrO)-C_6H_4-	Bn	2	94%

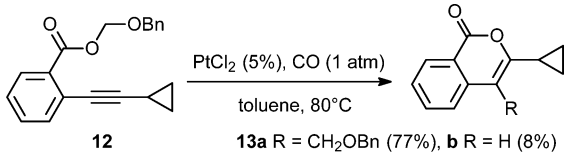
Scheme 5. Preparation of the Pterocarpane Skeleton[a]



[a] Conditions: (a) $PtCl_2$ (5 mol %), CO (1 atm), toluene, 80 °C, 3 h, 75%; (b) (i) HF, pyridine; (ii) $Pd(OAc)_2$ cat., Cs_2CO_3, (tBu)$_2$P(2-biphenyl).

(Table 3). Analogous transfer of the BOM group (entries 3, 9, and 10) opens further options for subsequent manipulation of the protected hydroxymethyl substituent at C-3 of the heterocycle, either by oxidative (CAN) or hydrogenolytic cleavage of the benzyloxy entity. Along the same lines, SEM-ethers are valuable substituents susceptible to selective cleavage with fluoride after O → C transfer (entry 4). The application in Scheme 5 illustrates this point. Since the aryl bromide group of substrate **9** is compatible with the $PtCl_2$-catalyzed cyclization, the resulting product **10** allows for subsequent

Scheme 6. Carboalkoxylation of a Benzoate



intramolecular etherification,[12] affording the polycyclic skeleton **11** of the pterocarpane family of phytoalexins.[13] Furthermore, preliminary experiments indicate that $PtCl_2$-catalyzed carboalkoxylation reactions are not limited to phenolic substrates. The successful cyclization of the benzoic acid ester **12** to isochromene-1-one **13** illustrates this point (Scheme 6). In any case, it is important to note that none of the acetalic substrates described in this paper is amenable to heteroannulation using $Pd(PPh_3)_4$[9,10] because they are unable to generate a catalytically competent species by oxidative addition. Therefore, the $PtCl_2$-catalyzed protocol is not only more convenient but also significantly broader in scope and constitutes a useful supplement to existing methodology for the preparation of physiologically relevant heterocycles.[14]

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

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