## Palladium-Catalyzed Allylating Heteroannulation of *o*-Alkynyl-Allyloxybenzenes. A Route to 2-Substituted-3-Allylbenzo[b]furans

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Received 16 March 1998

**Abstract**: In the presence of palladium(0), *o*-alkynyl allyloxybenzenes produce 2-substituted 3-allylbenzo[b]furans in fair yields. This heteroannulation is promoted by the  $\eta^3$ -allyl palladium species issued from early reaction of the catalyst with the starting allyl aryl ether.

Benzo[b]furans are of great interest due to their widespread occurrence in nature as well as their remarkable physiological properties.<sup>1</sup> Among the various synthetic approaches developed toward the benzofuran nucleus,<sup>2</sup> recent efforts have focused on palladium catalyzed heteroannulation processes involving acetylenic compounds.<sup>3</sup> In particular, cyclization of *o*-alkynylphenols promoted by  $\sigma$ -aryl(or vinyl) palladium complexes has recently opened a valuable new route toward 2, 3-disubstituted benzo[b]furans.<sup>4</sup> This annulation process can be seen as an attack of the phenoxide onto the triple bond from the opposite side of the activating  $\sigma$ -unsaturated palladium species generated from oxidative addition of the palladium(0) complex to an unsaturated halide or triflate. A reductive elimination gives the cyclization product and regenerates the catalyst (Scheme 1).



## Scheme 1

As part of our ongoing interest in the development of conceptually related processes<sup>5</sup> aimed in particular at the synthesis of heterocycles, we found that such annulation reaction can equally be effected by using  $\eta^3$ -allyl palladium complexes as activating species thus leading to 3allylbenzofurans.<sup>6a</sup> Only in rare occasions has this type of activating species been used in the past and it concerned the cyclization of alkynylcarboxylic acids.<sup>6b</sup> We were aware of the fact that in the case of o-alkynylphenols direct endo-dig cyclization might occur under basic conditions to give the corresponding benzo[b]furans even in the absence of catalysis.<sup>3a,4</sup> We decided to avoid this potentially competitive reaction by starting from o-alkynylallyloxybenzenes of type 1 taking advantage of the ability of such species to form  $\eta^3$ -allyl palladium complexes.<sup>7</sup> In this way, the allyl moiety would be internally delivered allowing the reaction to occur in a complete neutral medium. A reasonable reaction path is depicted in Scheme 2: oxidative addition of the palladium(0) complex to 1 and displacement of one ligand of the resulting  $\eta^3$ -allyl palladium species by the proximal triple bond would allow activation and thus promote the attack of the phenoxide. Subsequent coupling of the  $\eta^3$ -allyl and the furanyl moiety would give 2 and regenerate the palladium(0) complex. We present herein our successful preliminary results toward this goal.

A range of o-alkynylallyloxybenzenes **1a-f** were prepared and their reactivity toward palladium catalysts studied. Compounds **1a-e** were readily synthesized in three steps as depicted in Scheme 3. The procedure is based on the Corey-Fuchs dibromomethylenation<sup>8</sup> applied to 2-allyloxybenzaldehydes derived from salicylaldehyde, followed by



Scheme 2

treatment with n-Buli and quenching with various electrophiles  $^{9}$  (H<sup>2</sup>O, Me<sup>3</sup>SiCl, (MeO)<sup>2</sup>SO<sup>2</sup>).





Scheme 3

Compound **1f** was prepared from **1a** by coupling with allyl bromide in the presence of catalytic copper iodide (Scheme 4).





Acceptable rates of cyclization were obtained for **1c-f** using Pd(PPh<sub>3</sub>)<sub>4</sub> as catalyst (5 mol%) in a mixture of MeCN:THF (4:1) at 80°C (Table, entries 3-6).The corresponding benzofurans were isolated in good yield and only traces of products **3** resulting from direct cyclization were formed in these reactions (Scheme 5). A longer reaction time was needed in the case of allyl fragments bearing a substituent on the central carbon (entry 5). In line with previous results<sup>6b</sup> and concerning the cinnamyl group in **1d**, the carbon-carbon bond formation toward the  $\eta^3$ – allyl palladium species took place regioselectively to the less crowded

allyl terminus. The stereochemistry of the allylic moiety in 2d was found to be exclusively E (entry 4).



Scheme 5

Table . Heteroannulation of o-alkynyl-allyloxybenzenesa

entry	/	allyloxybenzenes	time (h)	benzofuran	yield (%) <sup>C</sup>
1	1a	R <sup>1</sup> ,R <sup>2</sup> ,R <sup>3</sup> =H	8	b	-
2	1b	$R^1$ , $R^2$ =H; $R^3$ =SiMe <sub>3</sub>	8	b	-
3	1c	$R^{1},R^{2}=H; R^{3}=Me$	1	2 c	76
4	1d	R <sup>1</sup> =H; R <sup>2</sup> =Ph; R <sup>3</sup> =Me	1	2 d	87
5	1e	$R^1$ , $R^3$ =Me; $R^2$ =H	6	2 e	70
6	1f	$R^1$ , $R^2=H$ ; $R^3=allyl$	3	2 f	71

a) All reactions were carried out at 80°C in MeCN:THF (4:1) using 5 mol% of catalyst (on half mmol scale). b) see text. c) Isolated yield

However cyclization of compounds **1a,b** proved problematic (entries 1, 2), always giving rise to complex mixtures of products. In the case of **1a** it was nevertheless possible to identify the bis-allylic derivative **2f** as the only product possessing the expected 3-allylbenzo[b]furan structure, a compound which could not be cleanly isolated. We thus believe that competitive palladium-catalyzed allylation of the acetylenic moiety<sup>10</sup> is responsible for the unsuccessful cyclization of terminal acetylene **1a**. Unfortunately, rapid desilylation of **1b** occurred under the same cyclization conditions which again led to a complex mixture of products. Further work will be undertaken in order to find conditions allowing cyclization of terminal acetylenes.

In conclusion, we have shown that 2-substituted 3-allylbenzo[b]furans can be easily obtained from readily available *o*-alkynylallyloxy benzenes by simple treatment with a palladium catalyst.<sup>11</sup> Although the reaction is so far limited to the cyclization of internal alkynes we believe that the simple procedure described herein will find wide application for the elaboration of more complex molecules possessing the benzofuran nucleus.

## **References and Notes**

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