A General Synthesis of Alkenyl-Substituted Benzofurans, Indoles, and Isoquinolones by Cascade Palladium-Catalyzed Heterocyclization/Oxidative Heck Coupling

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Figure 1. ORTEP diagram of 11a with thermal ellipsoids at 50% probability.

In the Full Paper by A. R. de Lera^[1a] et al. the structures of the products derived from benzamides **7** are incorrectly displayed in Schemes 3, 5, 7, and the schemes of Tables 2–4. The authors have now determined with X-ray diffraction analysis data (Figure 1)^[1b] that those reactions proceed by *O*-cyclization and not through the *N*-cyclization pathway

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originally reported. However, the conclusions of the paper do not change. The authors apologize for this oversight.

As a result, corrected versions of Schemes 2, 3, 5, 7, and the schemes of Tables 2–4 are provided here, and the following amendments are needed in the main text of the paper:

- Page 12747, left column, lines 23–24: "...The synthesis of 3-(3-oxoprop-2-enyl)benzofurans..." replaces "...The synthesis of 3-(3-oxoprop-2-enyl)benzofurans and corresponding 4-alkenylisoquinolones...".
- 2) References [7c,d] and [8] in the original manuscript are no longer applicable.
- 3) The term "1*H*-isochromen-1-imine" replaces the term "isoquinolone" throughout the rest of the paper.
- 4) Page 12750, right column, line 48: The term "5-*exo-trig*-derived" replaces the term "isoindolone-type".
- 5) Page 12752, left column, line 24 and Scheme 7 legend: The term "carboximidate" replaces the term "amide".
- 6) For the legend of Scheme 2 "Strategy for the preparation of heterocyclic derivatives 9–12" replaces "Strategy for



Scheme 2. Strategy for the preparation of heterocyclic derivatives 9–12.



Scheme 3. Preparation of 1*H*-pyrano[4,3-*c*]pyridin-1-imine 11 h.

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Scheme 5. Olefins **8c–n** used in the oxidative Heck coupling reactions and side-products **17–19** obtained in the cyclization/coupling reactions (Table 4).



Scheme 7. Formation of lactone 23 e from carboximidate 11 e.

Table 2.	Test	of the	standard	reaction	conditions	for	aniline	and	benza-
mide sub	ostrat	es. ^[a]							



the preparation of benzofurans 9, indoles 10, and isoquinolones 11". Scheme 2 is reproduced here for clarity.

11

12

13

14

15

16

17

18

8n 5b

8c 6a

8d 6a

8e 6a B

8i 6a B

8k 6a

8m 6a

8e 7b

A

 $\mathbf{B}^{[i,j]}$

 $\mathbf{B}^{[k,l]}$

 $B^{\left[f,i\right] }$

 $B^{[k]}$

 $\mathbf{C}^{[j]}$

- 7) For the legend of Scheme 3 "Preparation of 1*H*-pyrano-[4,3-*c*]pyridin-1-imine **11h**" replaces "Preparation of 6azaisoquinolone (a 2,6-naphthyridine-1-one) **11h**".
- 8) Footnote [o] in Table 4 is corrected. The whole table is reproduced here for clarity.

Table 3. General preparation of 3-alkenylbenzofurans, 3-alkenylindoles, and 4-alkenyl-1*H*-isochromen-1-imines from alkynyl substrates **5–7** and *n*-butyl (**8a**) or ethyl acrylate (**8b**).^[a]



Table 4. General preparation of 3-alkenylbenzofurans, 3-alkenylindoles, and 4-alkenyl-1*H*-isochromen-1-imines from alkynyl substrates **5–7** and alkenes **8c–n** (Scheme 5).^[a]



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Ph

CO₂Me

CO₂Me

COMe

CONH₂

SO₂Me

COMe

CN

9q

10^h

10 i

10 j

10 k

10 I

10 m

11 i

Н

Me H

Η

Н Н

н н

н н

H H 87

н н

Η

Me 67

60

51

79

95

77^[m]

71^[n]

Table 4.	(Continued)
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Entry	8	5–7	Conditions ^[a]	9–11	\mathbf{R}^1	\mathbf{R}^2	\mathbb{R}^3	Yield [%] ^{[b}
19	8i	7b	С	11 j	$CONH_2$	Н	Н	78
20	8 n	7b	$C^{[d]}$	11 k	Ph	Н	Н	39 ^[0]

[a] Unless otherwise indicated, reactions were conducted with Pd^{II} complex (5 mol%), KI (0.5 equiv), and alkene (6 equiv) in DMF under an air atmosphere for the indicated time. Conditions A: PdCl₂, 80 °C, 20 h. Conditions B: PdCl₂, 100°C, 20 h. Conditions C: [PdCl₂(PPh₃)₂], 80°C, 21-23 h. [b] Isolated yield. [c] A 1:1 mixture of 9g and 17a (Scheme 5) was obtained. [d] Reaction conducted at 100°C. [e] A 1:1.5 mixture of 9m and 17b (Scheme 5) was obtained. [f] Reaction conducted in a sealed tube. [g] A 3:1 E/Z mixture was obtained. [h] A 1.2:1 E/Z mixture was obtained. [i] Reaction conducted with 12 equiv of olefin. [j] Reaction time: 8 h. [k] $[PdCl_2(PPh_3)_2]$ was used as catalyst. [l] Reaction conducted at 60 °C. [m] A 13:1 E/Z mixture was obtained. [n] The conjugate addition product 18 (20%) was also obtained (Scheme 5). [o] A 5:1 mixture of regioisomers tentatively assigned as 11k and 19 (Scheme 5) was obtained

Accordingly, revised names and structures for all products derived from benzamides 7 are also provided in the new Supporting Information file.

Additional Discussion

Palladium-catalyzed cycloisomerization reactions of 2-alkynylbenzamides 7 have been shown in various instances to proceed with formation of isoindolone or isoquinolone products through 5-exo- or 6-endo-dig-N-cyclizations, respectively.^[2] Recently, the alternative 5-exo-dig-O-cyclization mode has also been observed, resulting in the regioselective formation of iminoisobenzofuran derivatives by Pd⁰catalyzed cyclization/coupling with aryl halides^[3] or cyclizative dimerization using Cu^{II} as both stoichiometric oxidant and co-catalyst.^[4] In the present case, the initial heterocyclization from 7 is followed by an oxidative intermolecular Heck-type coupling (Scheme 6 in the original manuscript, in which Y = -CONR) leading to 1*H*-isochromen-1-imine derivatives (11). These are interesting compounds^[5] not only for being the nitrogen analogues of the biologically important isocoumarins but also because of their own properties.^[5a,d] The same isochromen-1-imine core structure is also generated in analogous reactions where the Heck-type coupling is performed intramolecularly.^[6a] In the manuscript in ref. [6a], the structures were also incorrectly displayed, therefore this paper is corrected by another Addendum/Correction.^[6b] In any event, in common with the processes leading to iminoisobenzofurans mentioned above,^[3,4] the Pd-catalyzed formation of 11 from 2-alkynylbenzamides 7 also follows an initial O-cyclization pathway, albeit of the 6-endodig type, therefore giving rise to a regiochemically different family of products. An even more fundamental difference arises in the nature of the catalytic cycle, which is shared by all products 9-11, and incorporates a coupling with an external alkene, thus providing a new strategic element in the synthesis of various heterocyclic motifs.

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