Synthesis of alkenyl-2,5-dihydrofurans *via* palladium-catalysed reaction of cyclic alkynyl carbonates

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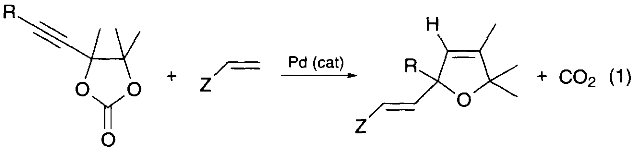
Cyclic alkynyl carbonates react with electron-deficient alkenes in the presence of palladium catalysts to selectively afford alkenyl-2,5-dihydrofurans *via* tandem C–C and C–O bond formation.

New catalytic reactions under mild conditions, without formation of by-products which satisfy the atom economy criteria,[1] have a great potential for organic synthesis. Here we report a new synthesis of alkenyl-2,5-dihydrofuran derivatives **4–6** *via* tandem palladium-catalysed carbon–carbon and intramolecular carbon–oxygen bond forming reactions from cyclic alk-1-ynyl carbonates **1** and electron-deficient alkenes **2–3** [eqn. (1)]. This new methodology contrasts with the previously reported multistep preparations of 2,5-dihydrofurans starting from monosaccharides,[2] or from α-allenols upon addition of electrophiles[3,4] or cyclization in the presence of Ag^I salts.[5]



1a R = Me
b R = Bu
c R= C(Me)=CH$_2$

2 Z = CO$_2$Me
3 Z = CONR$_2$

Z = CO$_2$Me;
4a R = Me; **4b** Bu, **4c** C(Me)=CH$_2$
Z = CONMe$_2$;
5a R = Me; **5c** C(Me)=CH$_2$
Z = CONH$_2$; **6b** R = Bu

The activation of cyclic alkynyl carbonates of type **1** in the presence of palladium(0) complexes is expected to give rise, *via* prop-2-ynylic activation, to the formation of zwiterionic allenylpalladium species **A**, which have been used to give α-allenol derivatives.[6,7] We now show that the Pd^0-catalysed activation of cyclic alkynyl carbonates **1** in the presence of activated alkenes leads to the selective formation of alkenyl dihydrofurans instead of the expected hydroxylated vinyl allenes of type **B** *via* the classical Heck reaction.

Thus, treatment of the cyclic carbonate **1b** (1 mmol) with methyl acrylate (3 mmol) in the presence of Pd(OAc)$_2$ (5 mol%), PPh$_3$ (10 mol%), Et$_3$N (2 equiv.) and KBr (2 equiv.) at 75 °C for 50 h led to the formation of compound **4b** in 42% isolated yield. The catalytic system was dramatically improved to give **4b** in 75% yield in 20 h by the addition of 1 equiv. of tetrabutylammonium fluoride, as already observed in Heck reactions.[8] The ^1H NMR spectra of **4b** clearly showed the vinylic proton of the heterocycle as a quartet [*H*C=C(Me), δ 5.18, ^4J = 1.5 Hz], and the other two ethylenic protons in *trans*-position with a ^3J coupling constant of 15.6 Hz (*H*C=C*H*, δ 5.94 and 6.91).

Under our conditions, 2,5-dihydrofurans **4a–c** were isolated in 69, 75 and 60% respective yields after purification by silica gel column chromatography. The presence of an adequate amount of water (0.1 ml) was necessary to achieve this catalytic transformation as no reaction took place in the absence of H$_2$O, but an excess of water (1 ml) had a negative effect and led to only 20% conversion of the initial carbonate after 70 h at 75 °C.

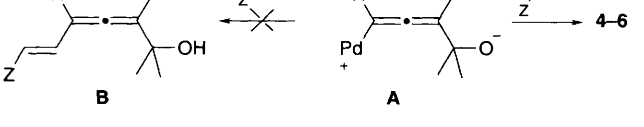
It is noteworthy that linear alkynyl carbonates R^1–C≡C–CR^2–OCO$_2$Me have been shown to give vinyl allenes with activated alkenes in the presence of palladium(0) catalysts under closely related conditions,[9] thus the formation of dihydrofurans **4** appears to be specific of cyclic alkynyl carbonates **1** which bear a masked homoprop-2-ynylic hydroxy group responsible for the cyclization reaction.

Under similar conditions, treatment of carbonates **1** with acrylic amides led to a complete transformation into the amidoalkenyl-2,5-dihydrofurans **5**, **6** at 60 °C. However, these compounds were found to be very water-soluble and difficult to extract from an aqueous phase. Thus, the use of DMF as solvent had to be eliminated to avoid the utilization of water in the subsequent work-up.

In that case, triethylamine itself could be used as the solvent and Bu$_4$NBr gave similar results as the association of Bu$_4$NF with KBr. Compounds **5a,c** and **6b** could thus be obtained in 98, 75 and 97% respective yields, on treatment of the corresponding acryl amide with cyclic alkynyl carbonate **1a–c** using a new catalytic system containing Pd(OAc)$_2$ (5 mol%), PPh$_3$ (10 mol%), Bu$_4$NBr (1.1 equiv.) in Et$_3$N (2.5 ml) at 60 °C for 17–24 h.

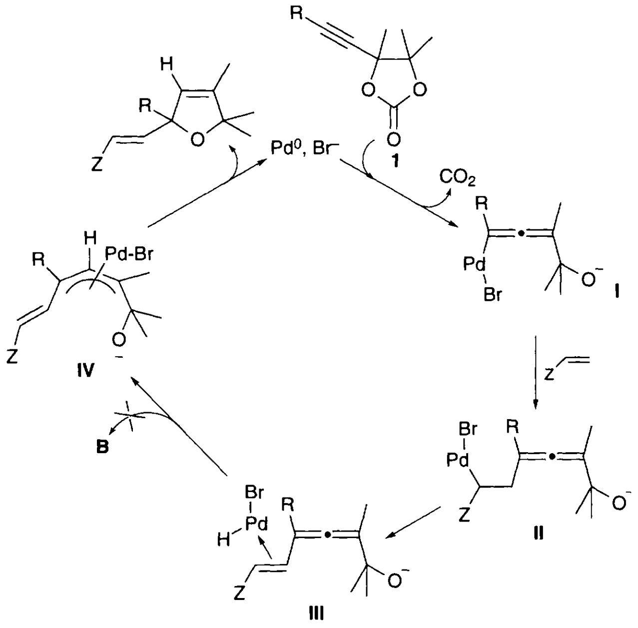
Although the mechanism of this reaction cannot be proved, it is likely to involve the prop-2-ynylic activation of the cyclic alkynyl carbonate **1** to produce an intermediate of type **I** Scheme 1, and the selective insertion of the C=C double bond of the activated alkene into the Pd–C bond to give **II** as in a classical Heck reaction. β-Elimination leading to the intermediate **III** might happen but the decoordination of the ligand to give a hydroxy vinyl allene of type **B** was not observed. From the intermediate **III**, the reactive allylpalladium **IV** can be generated *via* the insertion of the conjugated double bond of the allene system into the Pd–H bond, as has been shown for the addition of carbonucleophiles to allenes.[10] Intramolecular nucleophilic addition of the alcoholate to the external carbon of the allylic moiety in **IV** is then expected to lead to the favoured formation of the five-membered dihydrofuran ring.

In conclusion, this selective transformation of cyclic alk-1-ynyl carbonates takes advantage of the ability of palladium(0) catalysts to successively perform three different reactions in one pot; prop-2-ynylic activation, Heck reaction and allylic activation of unsaturated substrates to afford 2,5-dihydrofurans. This reaction represents an example of the involvement of the homoprop-2-ynylic oxygen atom of cyclic carbonates into a palladium-catalysed transformation. The above reaction has potential for use in organic synthesis as the starting acetylenic carbonates are readily prepared in three steps from prop-



B **A**

2-ynylic alcohol, CO_2 and terminal alkyne,[6] or from diols and phosgene derivatives.[11]



Scheme 1

The authors wish to thank the Ministère de la Recherche for a thesis grant to C. Darcel, and the European Union for an Erasmus grant to M. Albert from the University of Graz (Austria), and for a HCM Network (ERB-CHRXCT930147) financial support.

References

1 B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 259.
2 C. Paolucci, C. Mazzini and A. Fava, *J. Org. Chem.*, 1995, **60**, 169; S. Hanessian, *The Total Synthesis of Natural Products: The Chiron Approach*, Pergamon Press, Oxford, 1983; T. L. Boivin, *Tetrahedron*, 1987, **43**, 3309.
3 R. Gelin, S. Gelin and M. Albrand, *Bull. Soc. Chim. Fr.*, 1972, 720; R. Whitby and P. Kocienski, *Tetrahedron Lett.*, 1987, **28**, 3619.
4 P. L. Beaulieu, V. M. Morisset and D. G. Garatt, *Tetrahedron Lett.*, 1980, 129; J. A. Marshall and X. Wang, *J. Org. Chem.*, 1990, **55**, 2995.
5 J. A. Marshall and X. Wang, *J. Org. Chem.*, 1991, **56**, 4913; J. A. Marshall and K. G. Pinney, *J. Org. Chem.*, 1993, **58**, 7180.
6 C. Darcel, S. Bartsch, C. Bruneau and P. H. Dixneuf, *Synlett*, 1994, 457.
7 S.-K. Kang, D.-C. Park, D.-G. Cho, J.-U. Chung and K.-Y. Jung, *J. Chem. Soc., Perkin Trans. 1*, 1994, 237.
8 T. Jeffery, *J. Chem. Soc., Chem. Commun.*, 1984, 1287.
9 T. Mandai, M. L. Ogawa, H. Yamaoki, T. Nakata, H. Murayama, M. Kawoda and J. Tsuji, *Tetrahedron Lett.*, 1991, **32**, 3397.
10 B. M. Trost and V. J. Gerusz, *J. Am. Chem. Soc.*, 1995, **117**, 5156.
11 S.-K. Kang, J.-H. Jeon, K.-S. Nam, C.-H. Park and H.-W. Lee, *Synth. Commun.*, 1994, **24**, 305.

Received, 15th January 1996; Com. 6/00291I