Homogeneous Catalysis

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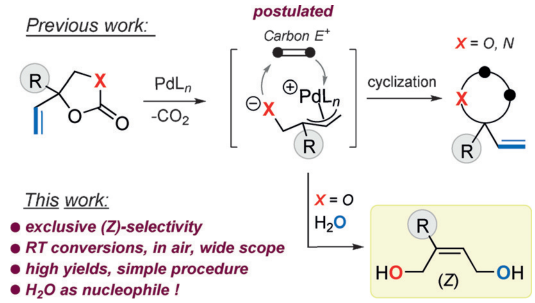
Highly Efficient Catalytic Formation of (Z)-1,4-But-2-ene Diols Using Water as a Nucleophile

*Wusheng Guo[+], Luis Martínez-Rodríguez[+], Eddy Martin, Eduardo C. Escudero-Adán, and Arjan W. Kleij**

Abstract: *The first general catalytic and highly stereoselective formation of (Z)-1,4-but-2-ene diols is described from readily available and modular vinyl-substituted cyclic carbonate precursors using water as a nucleophilic reagent. These 1,4-diol scaffolds can be generally prepared in high yields and with ample scope in reaction partners using a simple synthetic method that does not require the presence of any additive or any special precaution unlike the stoichiometric approaches reported to date. Control experiments support the mechanistic view that hyperconjugation within the catalytic intermediate after decarboxylation plays an imperative role to control the stereoselective outcome of these reactions.*

Diols are among the most ubiquitous scaffolds in chemistry, being of eminent value to synthetic and polymer chemistry and typically encompassing a wide structural diversity.[1] The stereoselective and enantioselective preparation of 1,2-diols has undoubtedly received most of the attention of the synthetic community with the development of the hydrolytic kinetic resolution of epoxides[2] and the asymmetric *cis*-dihydroxylation of alkenes[3] being important milestones in this area. Although established for 1,3-diols,[1a] diastereoselective preparation of other diol scaffolds still remains a challenge to synthetic chemists. In this respect, acyclic unsaturated (*Z*)-configured 1,4-diols have found important applications as transient scaffolds towards the stereocontrolled preparation of vinylcyclopropanes,[4] vinyl glycinols,[5] and the formation of lactones.[6] A recent contribution from Hoveyda[7] has exposed further growth potential of these 1,4-diol synthons in catalytic and stereoselective cross-metathesis furnishing valuable acyclic (*Z*)-allylic alcohols.

Up to now, the limited amount of available strategies for (*Z*)-1,4-but-2-ene diols synthesis have in common that they require stoichiometric chemistry and/or air-sensitive reagents such as DIBAL-H (diisobutylaluminum hydride).[4,5] Despite the increasing incentive of (*Z*)-1,4-but-2-ene diols in synthetic chemistry, the quest towards an efficient and mild catalytic procedure focusing on such (substituted) 1,4-diol scaffolds still continues.[8] Inspired by the dearth of catalytic solutions for the stereocontrolled construction of substituted (*Z*)-but-2-ene diols, we anticipated the use of vinyl-substituted cyclic carbonates as key reaction partners. Previous success with these latter scaffolds demonstrated that decarboxylative functionalization with suitable electrophiles such as Michael acceptors[9] is feasible under mild reaction conditions giving access to furans,[9a] tertiary vinylglycols,[9b] and highly functional pyrrolidines.[9c] As an intermediate in these Pd-mediated processes a zwitterionic structure was postulated (Scheme 1). Conceptually, such a charged-separated structure should possess ambivalent reactivity, with the Pd-allyl fragment being highly electrophilic and amenable to react with (very) weak nucleophiles such as water. Examples of catalytic conversions that are based on the use of water as nucleophilic reagent are, however, extremely rare.[1f,2,10] A successful development of a new catalytic method towards selective (*Z*)-but-2-ene diol formation by nucleophilic hydration of allyl surrogates formed in situ would provide a highly attractive new route towards these synthetically useful scaffolds. Herein we disclose such a conceptually new and highly efficient approach for (*Z*)-but-2-ene diols that is based on a decarboxylative hydration of readily available vinyl-based cyclic carbonates under mild operating conditions (Scheme 1).



Scheme 1. A previously postulated zwitterionic Pd-allyl intermediate and current approach towards (*Z*)-1,4-but-2-ene diols using H_2O as nucleophile.

The screening phase towards appropriate reaction conditions for the synthesis of unsaturated 1,4-diol compound **1** started off with the use of vinyl carbonate **A** and using various Pd precursors and phosphine ligands (Table 1). Several Pd precursors were tested including the well-known and reactive White catalyst.[11] We first screened various mono- and bidentate ligands (**L1**–**L8**) combined with this precursor using DMF as solvent.[12] Whereas the use of mono-

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[*] Dr. W. Guo,[+] L. Martínez-Rodríguez,[+] Dr. E. Martin,
E. C. Escudero-Adán, Prof. Dr. A. W. Kleij
Institute of Chemical Research of Catalonia (ICIQ)
The Barcelona Institute of Science and Technology
Av. Països Catalans 16, 43007 Tarragona (Spain)
E-mail: akleij@iciq.es

Prof. Dr. A. W. Kleij
Catalan Institute of Research and Advanced Studies (ICREA)
Pg. Lluís Companys 23, 08010 Barcelona (Spain)

[+] These authors contributed equally to this work.

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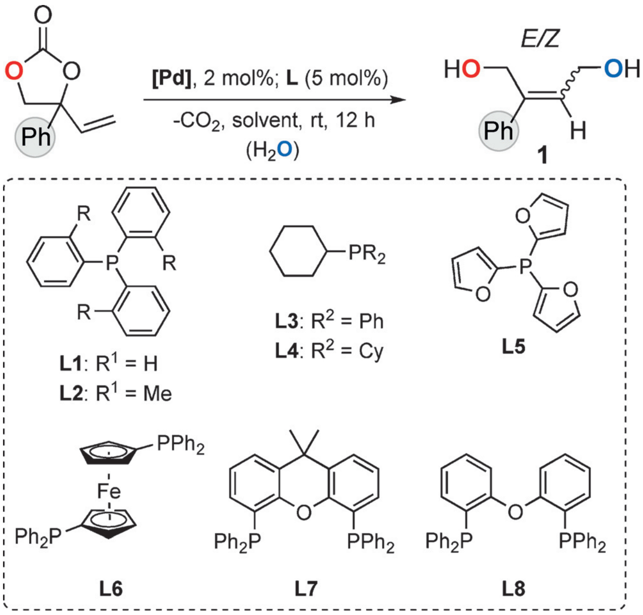
Table 1: Optimization of conditions in the synthesis of (*Z*)-but-2-ene diol **1** varying the Pd precursor, ligand **L**, and solvent.[a]



Entry	Pd precursor	L	Solvent [1 M]	Yield[b,c] [%]
1	Pd/bis(sulfoxide)	**L1**	DMF	0
2	Pd/bis(sulfoxide)	**L2**	DMF	0
3	Pd/bis(sulfoxide)	**L3**	DMF	0
4	Pd/bis(sulfoxide)	**L4**	DMF	0
5	Pd/bis(sulfoxide)	**L5**	DMF	0
6	Pd/bis(sulfoxide)	**L6**	DMF	90
7	Pd/bis(sulfoxide)	**L7**	DMF	95
8	Pd/bis(sulfoxide)	**L8**	DMF	98
9	$[Pd_2(dba)_3]\cdot CHCl_3$	**L8**	DMF	97
10	$Pd(dba)_2$	**L8**	DMF	99
11	$Pd(OAc)_2$	**L8**	DMF	94
12	Pd/C	**L8**	DMF	0
13	$Pd(PPh_3)_2Cl_2$	**L8**	DMF	70
14	Pd/bis(sulfoxide)	**L8**	CH_3CN	40
15	Pd/bis(sulfoxide)	**L8**	MeOH	<1
16	Pd/bis(sulfoxide)	**L8**	CH_2Cl_2	0
17	Pd/bis(sulfoxide)	**L8**	THF	0

[a] Reaction conditions: 0.20 mmol of carbonate, 0.20 mL of solvent, rt. [b] NMR yield using toluene as internal standard; see the Supporting Information for details. [c] In all cases, the *Z*/*E* ratio was $>99:1$ as determined by ^{1}H NMR spectroscopy.

dentate phosphine ligands **L1**–**L5** (entries 1–5) did not result in any observable formation, to our delight the presence of bidentate phosphines **L6**–**L8** (entries 6–8) proved to be highly beneficial for the formation of the desired 1,4-but-2-ene diol **1** under ambient conditions (see also the Supporting Information, Table S1). Moreover, ^{1}H NMR analysis supported the exclusive formation of the (*Z*)-configured product ($Z/E >$ 99:1). Further screening (entries 9–13) of other Pd precursors in the presence of **L8** showed $Pd(dba)_2$ and $[Pd_2(dba)_3\cdot CHCl_3]$ (dba = dibenzylideneacetone) to be competitive precursors, but to avoid any potential problem related to the stability of these Pd precursors we decided to continue with the air-stable White catalyst precursor. Other solvents than DMF were probed (entries 14–17) but these showed inferior yields of **1** underlining the crucial importance of the polarity of the medium.

The optimized conditions reported in entry 8 of Table 1 were then used to investigate the product scope in detail (Figure 1). The R-groups of the vinyl carbonate reagent were systematically varied (for their preparation, see the Supporting Information) and provided a series of substituted (*Z*)-but-2-ene diols **1**–**28**. In most cases excellent yields of isolated product (up to 98 %) and selectivity (> 99:1) towards the (*Z*) isomer were noted. This user-friendly procedure does not require any additive and can be operated in air at ambient temperature. The introduction of various aryl groups in the olefinic unit is tolerated, including *para*-, *meta*-, and *ortho*-substituted (di)halo aryls (**2**, **3**, **7**, **18**–**21**, **23**, and **24**), benzoic ester (**9**), and even thioether (**12**) groups. The use of 2- and 3-furyl, thiophene-, and 3-pyridyl-substituted cyclic carbonates smoothly leads to (*Z*)-1,4-diols **13**–**16** in high yield, despite the

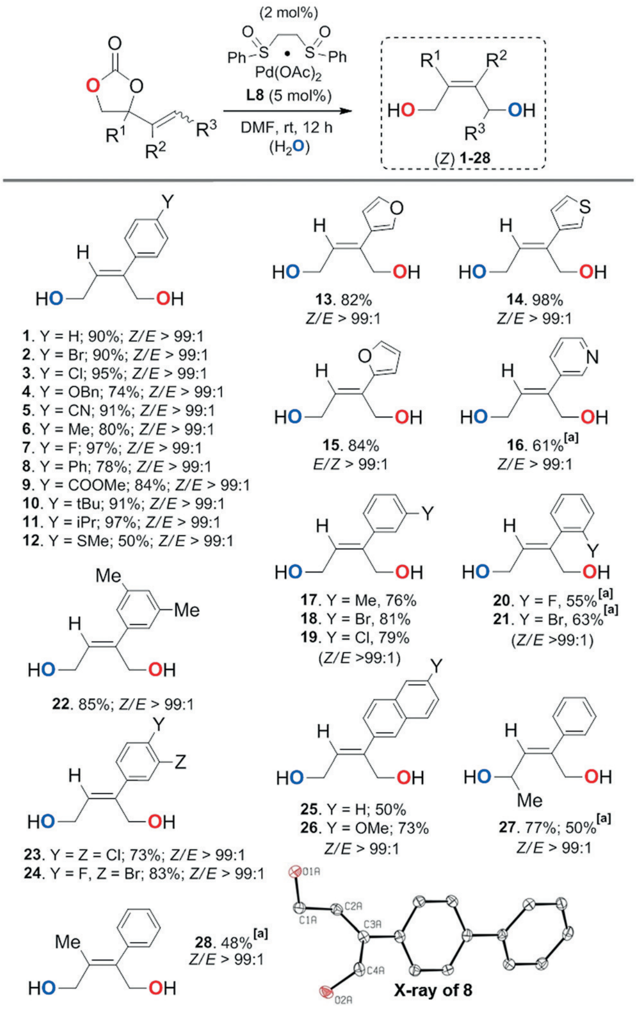
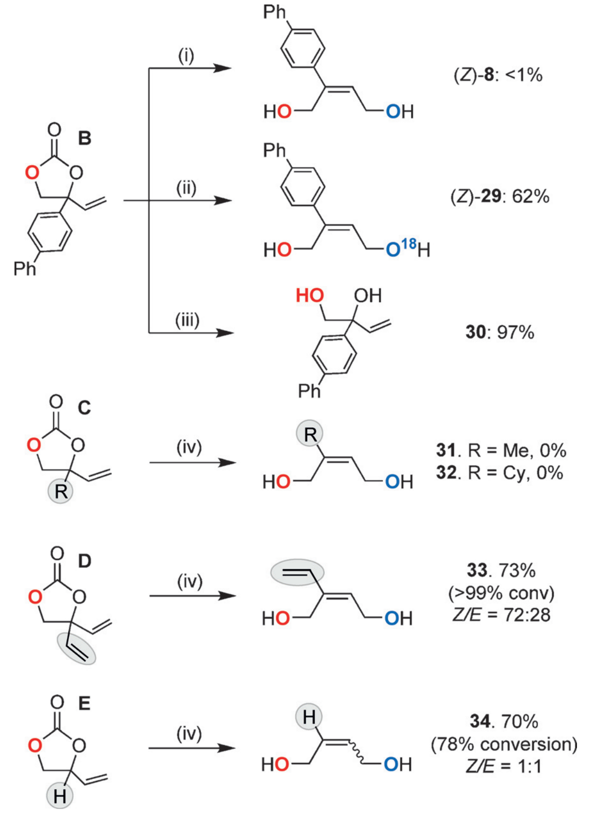


Figure 1. Product scope in the Pd-mediated formation of (*Z*)-but-2-ene diols **1**–**28**. Substrate amounts used: carbonate (0.20 mmol), DMF (0.20 mL). The *Z*/*E* ratios were determined by ^{1}H NMR spectroscopy ($CDCl_3$). Although following the same stereochemical formation pathway, compound **15** has formally an (*E*) configuration. [a] Using 5 mol % of Pd precursor and 10 mol % of **L8**, 60 °C, 200 μL DMF, 60 μL H_2O.

potential of the heteroatoms to coordinate and deactivate the Pd catalyst.

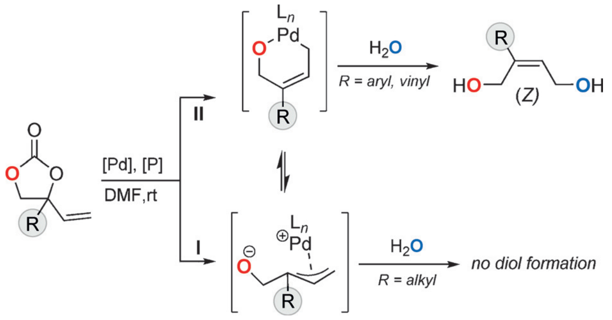
Interestingly, the presence of other substitution patterns is also allowed, producing an α-functionalized diol (**27**) and a tetra-substituted olefin derivative (**28**). Generally, to prepare these latter compounds with more elaborate substitutions and those incorporating *ortho*-functionalized aryl groups (cf., **20** and **21**) and 3-pyridyl-based **16**, a higher reaction temperature and additional water in the medium was required; for these more challenging conversions a higher amount of Pd catalyst (5 mol%) was also necessary. The (*Z*) configuration was deduced from 1D and 2D NMR analysis, whereas in the case of **8** further evidence for the preferred stereoisomer formation was obtained from X-ray diffraction studies (Figure 1).[13]

Intrigued by the highly stereoselective nature of these conversions and to gain mechanistic insight, we performed a series of control experiments. Vinyl carbonate **B** (Scheme 2) was subjected to the same reaction conditions as used for **1**–**28** using anhydrous DMF; no conversion into diol (*Z*)-**8** could be noted. Using a combination of anhydrous DMF with ^{18}O-labeled water (9:1 *v*/*v*) and treatment of vinyl carbonate **B** under these conditions afforded the labeled diol (*Z*)-**29** in 62% yield: these combined results support the key role of water in the stereoselective formation of the 1,4-diols. Further to this, when carbonate **B** is treated with H_2O under basic conditions in the absence of Pd catalyst the 1,2-diol **30** is produced that results from the hydrolysis of the carbonate unit.[3c,14] Therefore, the presence of a suitable Pd catalyst is essential to produce the 1,4-diol products. To examine whether other vinyl-substituted carbonates (that is, **C**–**E**) would equally convert into their corresponding (*Z*)-but-2-ene diols, the synthesis of **31**–**34** was attempted under the optimized reaction conditions. When alkyl-substituted carbonates were probed (**C**; R = alkyl) no conversion into the targeted diols **31** and **32** could be observed up to 60 °C. Interestingly, diol **33** derived from carbonate **D** that incorporates an additional vinyl substituent was obtained in 74% yield as a 72:28 mixture of both (*Z*) and (*E*) isomers. When carbonate **E** was employed, the corresponding diol **34** (*Z*/*E* = 1:1) was obtained under even lower stereocontrol.



Scheme 2. Control experiments using vinyl carbonates **B**–**E** as substrates under different conditions: i) anhydrous DMF (0.2 mL), White catalyst (2.0 mol%), **L8** (5.0 mol%), rt, 12 h; ii) anhydrous DMF/$H_2{}^{18}O$ (0.2 mL; 9:1), White catalyst (2.0 mol%), **L8** (5.0 mol%), rt, 12 h; iii) DMF/H_2O, NaOH (5 equiv), rt, 8 h; iv) conditions as under (i) but using commercial DMF.

From the results presented in Scheme 2, a mechanistic rationale is proposed taking the previously postulated zwitterionic Pd-allyl intermediate **I**[9] as starting point (Scheme 3).

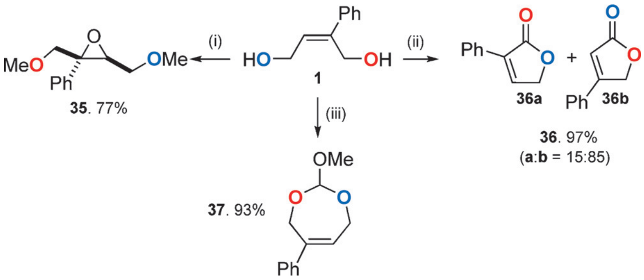


Scheme 3. Proposed mechanistic manifolds related to the Pd intermediates formed after decarboxylation.

Equilibration of η^3-allyl-Pd species **I** to η^1-palladacyclic intermediate **II** is electronically biased, as the presence of an aryl/vinyl substituent allows for hyperconjugation of the double bond: this in turn controls the (*Z*) configuration of the palladacycle and thus the stereocontrol towards the 1,4-diol product. In turn, the lack of reactivity towards diol formation when R is an alkyl group (compare **31** and **32**; Scheme 2) is explained by a larger charge delocalization in intermediate **I** onto which nucleophilic attack by water is disfavored for electronic reasons. Thus, clearly electron-donating groups are unable to mediate the formation of intermediate **II** and no conversion is observed, as was indeed noted experimentally.

In the case of the non-substituted carbonate **E** (Scheme 2), relatively slower conversion towards diol product is observed. The low *Z*/*E* ratio of this latter conversion is the result of a non-stereospecific nucleophilic attack governed by steric rather than electronic considerations.

Finally, the post-modification potential of these (*Z*)-1,4-but-2-ene diols was investigated using **1** as starting material (Scheme 4). Simple oxidation of the double bond (after alcohol protection) in **1** by *meta*-chloroperoxybenzoic acid afforded **35** as a single diastereoisomer in 77% yield. Oxidative lactonization of **1** using a radical initiator (9-azabicyclo[3.3.1]nonane *N*-oxyl) under Cu catalysis in the presence of *N*-methyl-imidazole produced the lactone **36** in 97% yield.[6] The cyclic *ortho*-ester **37** was prepared by combining **1** with trimethyl orthoformate[4] under acid



Scheme 4. Examples of post-use of (*Z*)-1,4-but-2-ene diol **1** in the synthesis of other interesting scaffolds (**35**–**37**). Conditions/reagents used: i) NaH (3 equiv.), MeI (4 equiv.), DMF, rt; then *m*-CPBA (1.1 equiv.), DCM, rt, 18 h; ii) CuI (5 mol%), 2,2′-bipy (5 mol%), 9-azabicyclo[3.3.1]nonane *N*-oxyl (1 mol%), *N*-methyl imidazole (10 mol%), MeCN, rt, 3 h; iii) Camphorsulfonic acid (1 mol%), trimethyl orthoformate (2 equiv.), DCM, rt, 5 h.

catalysis providing a well-known protection of this diol useful in synthetic chemistry.[15]

In summary, we here describe a user-friendly, highly mild and stereoselective method towards the formation of synthetically useful (*Z*)-1,4-but-2-ene diols in high yield and under exclusive stereocontrol. This procedure utilizes readily available and modular vinyl-based cyclic carbonates and simple water as reactants, can be operated in air, and does not require any additive. Such privileged conditions may greatly advance the use of these diol synthons in preparative chemistry as demonstrated herein.

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