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Asymmetric palladium-catalyzed annulation of benzene-1,2-diol and racemic secondary propargylic carbonates bearing two different substituents

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Abstract—The palladium-catalyzed cyclization of benzene-1,2-diol with various racemic secondary propargyl carbonates having no acetylenic hydrogen in the presence of (*R*)-Binap as the chiral ligand afforded the two regioisomers of the corresponding 2,3-dihydro-1,4-dioxin derivatives in quite good yields, and also in enantioselectivities going from 40 to 97%. The cyclization of benzene-1,2-diol with methyl (*R*)-1-methyl-3-phenylpro-2-yn-1-yl carbonate in the presence of dppb as the achiral ligand afforded 2-benzylidene-3-methyl-2,3-dihydro-1,4-benzodioxine as the major product with 15% ee. The use of (*R*)-Binap as the chiral ligand afforded the (+) cyclized compound in 45% ee, when the (−) enantiomer was obtained with 77% ee in the presence of (*S*)-Binap. All the results suggest that in this case the enantioselective step is the diastereoselective protonation of the palladium–carbene intermediates.

1. Introduction

The 1,4-benzodioxin and 1,4-benzodioxan subunits are present in some natural compounds displaying interesting biological properties.[1–5] For example, some 2-substituted 1,4-benzodioxanes exhibit antihyperglycemic properties;[6] others act as inhibitors of 5-lipoxygenase,[7] or can be used as α- or β-blocking agents or in antidepression or anti-hypertension therapy.[8–12] Due to these interesting properties, the synthesis of compounds containing this structure has been the subject of increasing research during the last few years. Moreover, these compounds are also interesting precursors for further synthetic transformations.[13–16]

If the synthesis of 1,4-benzodioxin structures is now well documented in the literature,[13,17–25] the synthetic routes to 2-alkylidene-2,3-dihydro-1,4-benzodioxines are less studied, and the published procedures often required a tedious multistep sequence.[26–32]

Recently two very facile methods for the synthesis of these structures in quite good yields have been developed. Kundu and colleagues.[33,34] described the palladium(II)–copper catalyzed condensation of aryl halides and mono-prop-2-ynilated catechol. We reported also the palladium(0)-catalyzed condensation of catechol with various propargylic carbonates leading regio- and stereoselectively to 2,3-dihydro-2-ylidene-1,4-benzodioxines.[35,36] Moreover, performing the condensation in the presence of a chiral palladium catalyst allowed a very easy access to enantiomerically enriched derivatives with enantioselectivies up to 97%.[37,38] The plausible mechanism for this cyclization process is shown in Scheme 1. The first step is the anti S_N2' attack of the palladium(0) complex on the propargylic carbonate affording the σ-allenyl palladium complex **A**,[39] in equilibrium with the η^3-propargyl palladium complex **B**. Selective attack of the monoanion of benzene-1,2-diol to the central carbon of this η^3-propargyl complex gave the σ-alkyl complex **C** in equilibrium with the carbenic complex **D**. This complex **D** was converted by intramolecular proton transfer to the σ-alkyl complex **E**, which is in equilibrium with the η^3-allyl complex **F**. Internal attack of the nucleophile on one of the termini of this η^3-allylic complex **F** afforded the corresponding benzodioxin derivatives **G** (attack 1) or **H** (attack 2), respectively. In order to apply this synthetic route in an asymmetric way, we

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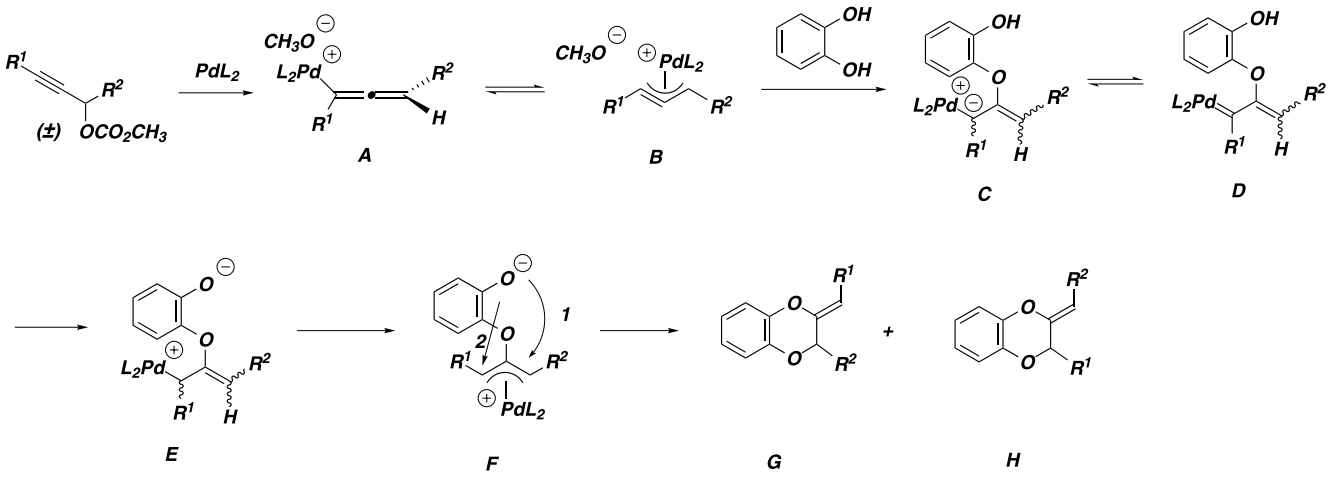


Scheme 1.

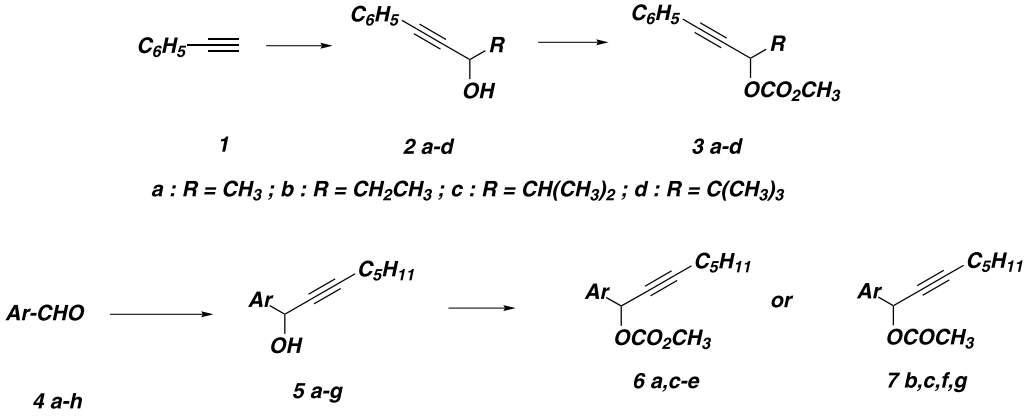
postulated that the enantioselective step was the attack of the nucleophile on the η^3-allyl intermediate. According to the results of the literature,[40] we expected that this η^3-allyl intermediate **E** must have two identical substituents at one of the termini of the η^3-allyl complex, allowing an easy racemization of this complex, or two identical substituents at the two termini of the η^3-allyl complex. We obtained effectively high enantioselectivities, up to 97%, in our palladium catalyzed annulation in these two cases.[38]

However we have also shown that the benzodioxin structures were obtained in quite high enantioselectivity even when the two substituents at the two termini of the η^3-allyl complex were completely different.[41] In this paper we describe in details our results in this field and propose a mechanism for this enantioselective heteroannulation.

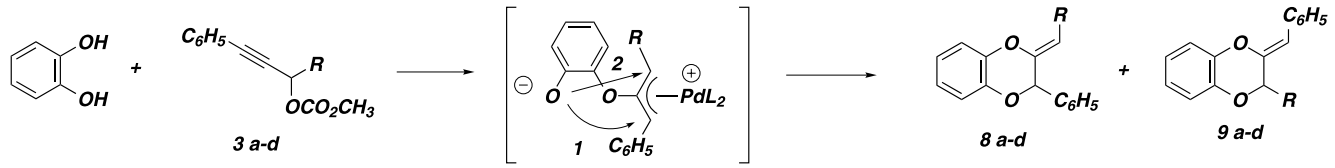
2. Results and discussion

In order to study the influence of both the alkyl and the aryl substituents on the regio-, stereo- and enantioselectivities of this cyclization, we prepared the corresponding propargylic carbonates **3a–d**, **6a**, **6c–e**, and acetates **7b**, **7c**, **7f**, and **7g** (Scheme 2). Reaction of propargylic alcohols **2a–d** with methyl chloroformate in CH_2Cl_2 in the presence of pyridine and dimethylaminopyridine gave the corresponding carbonates **3a–d** in quite good yields. Condensation of the lithium derivative of hept-1-yne with the corresponding aromatic aldehyde in THF afforded the propargylic alcohols **5a–g**. Reaction of methyl chloroformate with alcohols **5a**, and **5c–e**, in CH_2Cl_2 in the presence of pyridine and dimethylaminopyridine afforded the corresponding propargylic carbonates **6a**, and **6c–e**, in moderate chemical yields. Since the carbonates derived from propargylic alcohols **5b**, **5f**, and **5g**, were unstable, we prepared the corresponding acetates **7b**, **7f**, and **7g**, together with acetate **7c**.

The palladium-catalyzed condensation of carbonates **3a–d** with benzene-1,2-diol was conducted at rt in THF as the solvent, $Pd_2(dba)_3$ associated with dppb as the catalyst (Scheme 3). The results summarized in Table 1 showed that the cyclized products **8** and **9** were obtained in high chemical yields for R = CH_3 and CH_2CH_3 (Table 1, entries 1 and 3), in moderate yield for R = $CH(CH_3)_2$ (Table 1, entry 5), when no reaction occurred when the alkyl substituent was a *tert*-butyl group. For R = CH_3, the major regioisomer **9a** (95%)) occurred from the attack of the phenate on the termini of the η^3-allylpalladium complex bearing the alkyl substituent; this is in quite good agreement with the



Scheme 2.



Scheme 3.

Table 1. Palladium-catalyzed condensation of benzene-1,2-diol with propargylic carbonates **3a–c**[a]

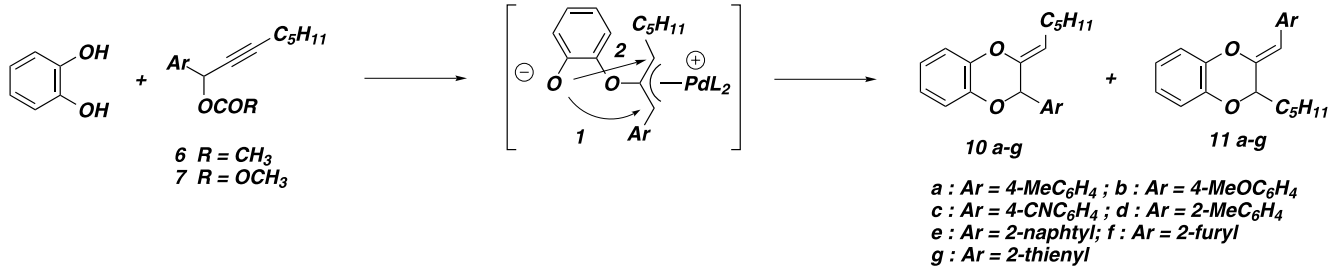
Entry	Carbonate **3**	Phosphine	Yield (%) of (**8**+**9**)[b]	% **8**/% **9**[c]	ee (%) **8**[d]	ee (%) **9**[d]
1	**3a**	dppb	90	5:95		
2	**3a**	(*R*)-Binap	70	20/80	nd	70
3	**3b**	dppb	90	14/86		
4	**3b**	(*R*)-Binap	95	32/68	nd	85
5	**3c**	dppb	66	60/40		
6	**3c**	(*R*)-Binap	70	68/32	93	83

[a] Conditions: [benzene-1,2-diol]/[**3**]/[$Pd_2(dba)_3$]/[phosphine]=48:40:1:4; 25 °C; THF as the solvent.
[b] After column chromatography.
[c] Determined by GC.
[d] Determined by HPLC using a chiral column Chiralpak AD (25 cm×4.6 mm) using hexane/2-propanol as the eluent; nd means that no separation could be observed whatever the conditions used.

previous published results.[36] Increasing the steric bulk of the substituent R and going from -CH_3 or -C_2H_5 to –$CH(CH_3)_2$ reversed the regioselectivity of the cyclization, the regioisomer **8c** being predominantly obtained in this last case. The stereochemistry at the double bond for the two regioisomers was *Z*, as shown using NOE NMR experiments. Irradiation of the signal of the methyl group for **9a** or of the proton on the carbon near the oxygen for **9b** and **9c** showed an enhancement of 6, 8, and 14% of the signal of the ethylenic proton; for compounds **8b** and **8c**, irradiation of the benzylic proton showed an enhancement of the signal of the ethylenic proton of 2 and 7%, respectively.

The use of (*R*)-Binap as the ligand gave quite similar chemical yields; the observed regioselectivity of the cyclization was lower using carbonates **3a** (Table 1, entry 2) and **3b** (Table 1, entry 4), when the reverse selectivity was also observed for **3c** (Table 1, entry 6). The enantioselectivities of the cyclized products **9a** and **9b** were 70 and 85%, respectively (Table 1, entries 2 and 4); unfortunately, the two enantiomers of the minor regioisomers **8a** and **8b** could not be separated, whatever the conditions used. The enantiomeric excesses of the two regioisomers **8c** and **9c** were 93 and 83% ee, respectively (Table 1, entry 6). We also studied the influence of the amount of carbonate used on the enantioselectivity in the cyclization of catechol and carbonate **3c**; we always obtained the same results using 1.2 or 2 equiv of carbonate **3c**.

Then we turned our attention on the influence of the nature of the aromatic ring on both the regio- and the enantioselectivity of the cyclization (Scheme 4). We have previously shown that propargylic carbonate **6a** and acetate **7b**, bearing an electron-donating group on the ring, afforded a 25:75 and 38:62 mixture of regioisomers **10a/11a** and **10b/11b** in 96 and 88% chemical yield, respectively (Table 2, entries 1 and 3), while carbonate **6c** or acetate **7c**, bearing an electron-withdrawing group, gave almost exclusively the regioisomer **11c** in 96 and 56% chemical yield, respectively (Table 2, entries 5 and 6); in the case of acetate **7c** the chemical yield was increased to 84% when the reaction was performed at reflux (Table 2, entry 7). Carbonates **6d** and **6e**, bearing a 2-methylphenyl and a naphthyl substituent, gave also a mixture of the two regioisomers **10d–e** and **11d–e** in quite good yields (65 and 93%, respectively), the last one being the major isomer (94 and 79%, respectively) (Table 2, entries 9 and 11). The palladium-catalyzed cyclisation of acetates **7f** and **7g** gave the corresponding 2-alkylidene-2,3-dihydro-1,4-benzodioxines in moderate



Scheme 4.

Table 2. Palladium-catalyzed condensation of benzene-1,2-diol with propargylic carbonates **6** and acetates **7**[a]

Entry	Propargylic compound	Phosphine	Yield (%) of **10**+**11**[b]	% **10**/% **11**[c]	ee (%) **10**[d]	ee (%) **11**[d]
1	**6a**	dppb	96	25/75		
2	**6a**	(*R*)-Binap	84	24/76	nd	86
3	**7b**	dppb	88	38/62		
4	**7b**	(*R*)-Binap	35	39/61	78	80
5	**6c**	dppb	96	0/100		
6	**7c**	dppb	56	0/100		
7	**7c**	dppb/reflux	84	0/100		
8	**7c**	(*R*)-Binap	49	10/90	52	85
9	**6d**	dppb	65	6/94		
10	**6d**	(*R*)-Binap	77	63/37	40	97
11	**6e**	dppb	93	21/79		
12	**6e**	(*R*)-Binap	74	42/58	76	64
13	**7f**	dppb	34	4/96		
14	**7f**	(*R*)-Binap	30	3/97	nd	85
15	**7g**	dppb	45	7/93		
16	**7g**	(*R*)-Binap	49	8/92	88	90

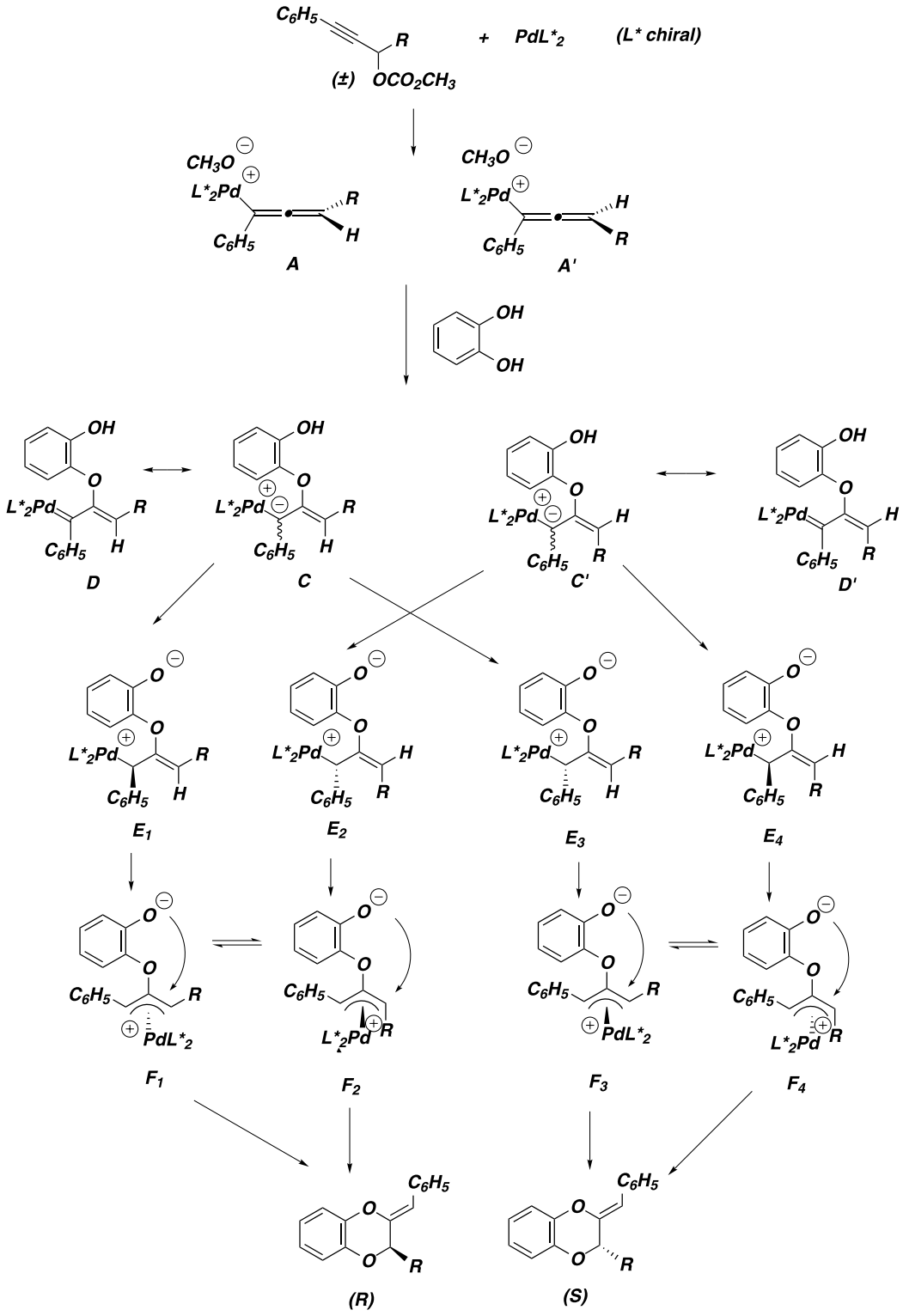
[a] Conditions: [benzene-1,2-diol]/[**3**]/[$Pd_2(dba)_3$]/[phosphine]=48:40:1:4; 25 °C; THF as the solvent.
[b] After column chromatography.
[c] Determined by GC.
[d] Determined by HPLC using a chiral column Chiralpak AD (25 cm×4.6 mm) using hexane/2-propanol as the eluent; nd means that no separation could be observed whatever the conditions used.

chemical yields (34 and 45%, respectively) (Table 2, entries 13 and 15); the major regioisomer was compound **11** (96% **11f** and 93% **11g**, respectively). As described previously, the attack occurred predominantly on the terminus of the π-allyl bearing the alkyl substituent, the regioisomer **11** being the predominant one; however the ratio of the two regioisomers depends strongly on the nature of the aryl ring. The different regioselectivities observed in the cyclization of carbonates **6a** and **6d** could be due probably to steric effects. It is to be noticed that the stereochemistry at the double bond for the two regioisomers was again *Z*, as shown using NOE NMR experiments.

When the cyclization was performed in the presence of (*R*)-Binap as the chiral ligand the ratios of the two regioisomers obtained were generally quite similar, except for carbonate **6d**, where a reversal of the regioselectivity was observed, the regioisomer **10d** being now the major one. In each case, the enantiomeric excess of the regioisomer **11** could be determined, when the separation of the enantiomers for regioisomers **10a** and **10f** was unsuccessful. Enantioselectivities in the range 80–90% ee were obtained when the phenyl ring is *para*-substituted with a methyl, a methoxy, or a cyano group, or when this ring was a heteoatomic one (Table 2, entries 2, 4, 8, 14, and 16); the presence of a methyl group at the *o*-position gave a higher ee (up to 97%) (Table 1, entry 10), whereas the naphtyl group lowered this enantioselectivity (64% ee) (Table 2, entry 12). The highest enantioselectivity obtained for regioisomer **10** was 88% using heterocyclic acetate **7g** (Table 2, entry 16); acetate **7b** and carbonate **6e** afforded the corresponding regioisomers **10b** and **10e** with 78 and 76% ee, respectively (Table 2, entries 4 and 12), whereas acetate **7c** and carbonate **6d** gave lower enantioselectivities (52 and 40% ee, respectively) (Table 2, entries 8 and 10).

All these results (one major isomer, high enantioselectivities for the two regioisomers) could not be explained using the model shown in Scheme 1. Since the palladium intermediate **F** bears two different substituents at the two termini of the η^3-allyl complex, the enantioselective step could not be the attack of the nucleophile on this η^3-allyl intermediate. A possible mechanism that could be invoked is the epimerization of this η^3-allyl complex **F** via a nucleophilic substitution of PdL_n by another PdL_n molecule with inversion of configuration. Although such a mechanism has been proposed by different groups in the case of intermolecular palladium-catalyzed alkylation reactions,[42–51] we postulated a quite different mechanism in our case (Scheme 5).

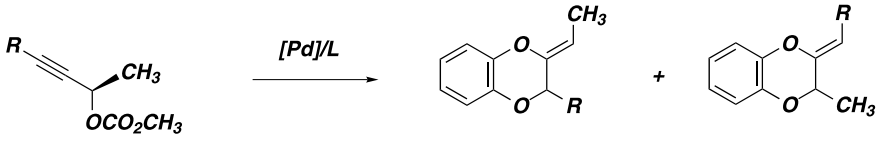
The first step is the formation of the two diastereoisomeric σ-allenyl complexes **A** and **A′** via a S_N2' mechanism from the propargylic carbonate and the palladium(0) complex. These σ-allenyl complexes are in equilibrium with the corresponding diastereoisomeric η^3-propargylic palladium complexes **B** and **B′** (not shown here). Attack of the monoanion of benzene-1,2-diol on the central atom of these σ-allenyl complexes gave the diastereoisomeric σ-alkyl complexes **C** and **C′** in equilibrium with the diastereoisomeric carbenic complexes **D** and **D′**. Since this anion attacked probably on the less hindered site, the major diastereoisomers will be isomers **C′** and **D′**. Protonation of these intermediates **C** and **C′** (or of the corresponding carbene complexes **D** and **D′**) gave four diastereoisomeric σ-alkyl complexes $\mathbf{E_1}$–$\mathbf{E_4}$, in equilibrium with the corresponding diastereoisomeric η^3-allyl complexes $\mathbf{F_1}$–$\mathbf{F_4}$. If interconversion occurred readily between complexes $\mathbf{F_1}$ and $\mathbf{F_2}$, and complexes $\mathbf{F_3}$ and $\mathbf{F_4}$, there is no possibility of interconversion between the diastereoisomeric complexes $\mathbf{F_1}$ and $\mathbf{F_3}$ or $\mathbf{F_4}$, and $\mathbf{F_2}$ and $\mathbf{F_3}$ or $\mathbf{F_4}$, since the two substituents at the two termini of the η^3-allyl are different. The attack of the nucleophile on the terminus of intermediates $\mathbf{F_1}$ or $\mathbf{F_2}$ bearing the alkyl group afforded the (*R*) cyclized product, whereas the (*S*) enantiomer was obtained from intermediates $\mathbf{F_3}$ and $\mathbf{F_4}$. We postulated that the enantioselection occurred during the step of protonation of the intermediates **C**,**C′** or **D**,**D′**, when the new chiral center was created. For example, the diastereoisomeric complexes $\mathbf{E_1}$ and $\mathbf{E_3}$, and so the η^3-allyl intermediates $\mathbf{F_1}$



Scheme 5.

and $\mathbf{F_3}$, are probably formed in quite different amounts, affording the corresponding cyclized enantiomers also in different amounts. It is the same scheme starting from complexes $\mathbf{E_2}$ and $\mathbf{E_4}$. The proposed mechanism is different from that of Yoshida and colleagues.[52,53] These authors observed a cascade chirality transfer process in the palladium-catalyzed reaction of substituted chiral propargylic carbonates with phenols, affording chiral cyclic carbonates in a highly enantiospecific manner. If their mechanism is a general one, the reaction of a racemic propargylic carbonate such as **3** or **6** will give the cyclized product as a racemate, even in the presence of a chiral ligand, since no racemization of the different intermediates could occur.

In order to have a deeper insight into our possible



(R)-12 R = H
(R)-3a R = C6H5

13 R = H
8a R = C6H5

14 R = H
9a R = C6H5

Scheme 6.

mechanism, we performed the palladium-cyclization of benzene-1,2-diol with two chiral propargylic carbonates (*R*)-**3a** and (*R*)-**12** in the presence of both an achiral ligand (dppb) and a chiral ligand [(*R*)- or (*S*)-Binap] (Scheme 6). Enantiopure carbonate (*R*)-**3a** was obtained from commercial (*R*)-but-3-yn-2-ol in the presence of methyl chloroformate, whereas (*R*)-4-phenylbut-3-yn-2-ol, obtained from (*R*)-but-3-yn-2-ol via a Sonogashira coupling,[54] afforded carbonate (*R*)-**12** under the same conditions. The results are summarized in Table 3. Reaction of enantiopure propargylic carbonate (*R*)-**12** with benzene-1,2-diol in the presence of $Pd_2(dba)_3$ associated with dppb afforded the cyclized products **13** and **14** in a 3:97 ratio (Table 3, entry1); however, compound **14** was obtained as a racemate. When the same condensation was performed in the presence of (*R*)-Binap, compound (−)-**14** was obtained with an enantioselectivity up to 60% (Table 3, entry 2). Using (*S*)-Binap as the chiral ligand afforded compound (+)-**14** with 62% ee (Table 3, entry 3). These results could be explained by a rapid racemization of the intermediate η^3-allyl palladium complex bearing in this case two hydrogens on one of the termini of the η^3-allyl system, the rate of the racemization being fast compared to the rate of the attack of the nucleophile.

The palladium-condensation of enantiopure propargylic carbonate (*R*)-**3a** with catechol in the presence of dppb gave the cyclized products **8a/9a** in a 4:96 ratio, compound **9a** being obtained with an enantioselectivity up to 15% in the (−) enantiomer (Table 3, entry 4). When the cyclization was performed in the presence of (*R*)-Binap, compound **9a** was obtained as the (+) enantiomer with an ee up to 45 and 49%, at 25 and 50 °C, respectively (Table 3, entries 5 and 7). The use of (*S*)-Binap afforded the (−) enantiomer with ee up to 77 and 75% at 25 and 50 °C, respectively (Table 3, entries 6 and 8). We have previously shown that the cyclization of racemic propargylic carbonate **3a** in the presence of (*R*)-Binap gave compound **9a** with 70% ee in the (−) enantiomer (Table 1, entry 2). These results clearly showed that the cyclization occurred via two different mechanisms. The first one is similar to the one proposed by Yoshida and colleagues,[52,53] with a transfer of chirality from the carbonate to the cyclized product; however since we observed only 15% of transfer of chirality, this mechanism is not the major one. The other mechanism is the one proposed in Scheme 5. Using (*R*)- or (*S*)-Binap as the chiral ligand gave, respectively, lower and higher ee in the cyclized product, indicating that (*S*)-Binap/(*R*)-**3a** is a match pair, and (*R*)-Binap/(*R*)-**3a** is a mismatch pair. This quite different behaviour between the two mechanisms could be due to the presence of a propargylic hydroxy function in the carbonates used by Yoshida et al,[52,53] function which could stabilize the η^3-propargylic and η^3-allylic intermediates by complexation, and so allowing the transfer of chirality.

3. Conclusion

In conclusion, we have extended the previous asymmetric palladium-catalyzed annulation of benzene-1,2-diol with racemic secondary propargylic carbonates and acetates bearing two different substituents (≠H), both on the sp carbon and on the carbon bearing the carbonate (or acetate) function. The high enantioselectivities observed could be explained by a highly stereospecific protonation of the

Table 3. Palladium-catalyzed condensation of benzene-1,2-diol with propargylic carbonates (*R*)-**12** and (*R*)-**3a**[a]

Entry	Propargylic carbonate	Phosphine	*T* (°C)	Yield (%) of cyclized products[b]	%**14**/%**13** or %**9a**/%**8a**[c]	ee (%) **9a** or **14**[d]
1	(*R*)-**12**	dppb	25	96	97/3 (**14/13**)	0
2	(*R*)-**12**	(*R*)-Binap	25	80	82/18 (**14/13**)	60 (−)[e]
3	(*R*)-**12**	(*S*)-Binap	5	60	83/17 (**14/13**)	62 (+)[f]
4	(*R*)-**3a**	dppb	25	74	96/4 (**9a/8a**)	15 (−)[g]
5	(*R*)-**3a**	(*R*)-Binap	25	32	90/10 (**9a/8a**)	45 (+)
6	(*R*)-**3a**	(*S*)-Binap	25	25	90/10 (**9a/8a**)	77 (−)
7	(*R*)-**3a**	(*R*)-Binap	50	50	85/15 (**9a/8a**)	49 (+)
8	(*R*)-**3a**	(*S*)-Binap	50	50	83/17 (**9a/8a**)	75 (−)

[a] Conditions: [benzene-1,2-diol]/[propargylic carbonate]/[$Pd_2(dba)_3$]/[phosphine]=48:40:1:4; THF as the solvent.
[b] After column chromatography.
[c] Determined by GC.
[d] Determined by HPLC using a chiral column Chiralpak AD (25 cm×4.6 mm) using hexane/2-propanol as the eluent; nd means that no separation could be observed irrespective of the conditions used.
[e] $[\alpha]_D^{25}=-22.5$ (*c* 1.1, CH_2Cl_2).
[f] $[\alpha]_D^{25}=+19.8$ (*c* 1.1, CH_2Cl_2).
[g] $[\alpha]_D^{25}=-3.6$ (*c* 1, diethyl ether).

intermediate palladium–carbene complexes. The results obtained in the palladium-catalyzed annulation of benzene-1,2-diol with methyl (*R*)-1-methyl-3-phenylpro-2-yn-1-yl carbonate in the presence of an achiral (dppb) or a chiral ligand [(*R*)- or (*S*)-Binap] are in agreement with such a mechanism. Extension of this work to other bisnucleophiles is actually in progress.

4. Experimental

General remarks. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were obtained using a Bruker AM 300 spectrometer. Chemical shifts are reported with reference to $SiMe_4$ or $CDCl_3$ as an internal standard. Optical rotations were determined using a Perkin–Elmer 241 polarimeter. All reactions were monitored by thin-layer chromatography carried out on 0.25 mm silica gel plates (60 F-254, Merck). Compounds were exposed under UV light (254 nm). Column chromatography was carried out using Merck silica gel 60 (40–63 μm). HPLC analysis was performed on a Shimatzu apparatus LC-6A combined with a UV detector SPD-6A. Reactions involving palladium complexes were carried out in a Schlenk tube under an argon atmosphere. Tetrahydrofuran was distilled from sodium/benzophenone and stored under argon.

Propargylic alcohols **2a**, **2b**, **2c**, **2d**, **5a**, **5b**, **5c**, propargylic carbonates **3a**, **6a**, **6c**, and propargylic acetates **7b** and **7c**, have already been described, as well as benzodioxins **10a–c**, and **11a–c**.[36]

4.1. Synthesis of propargylic alcohols

To a solution of hept-1-yne (726 mg, 7.4 mmol) in THF (10 mL) maintained at −30 °C was added a 2.5 M solution of *n*-butyllithium in hexane (3.2 mL, 7.8 mmol) and 1,3-dimethyltetahydro-2-[1]pyrimidinone (1.36 g, 10.4 mmol). After being stirred for 2 h at −30 °C, the aromatic aldehyde (7.4 mmol) was added, and the solution was stirred for 24 h at −10 °C. A saturated aqueous ammonium chloride solution (50 mL) was added, and the mixture was extracted with diethyl ether (3×50 mL). Evaporation of the solvent under reduced pressure gave a residue which was purified by flash-chromatography on silica using the appropriate eluent.

4.1.1. 1-(2-Methylphenyl)oct-2-yn-1-ol 5d. Yield 60%; oil; R_f 0.34 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J=7.0 Hz, 3H, CH_3), 1.24–1.42 (m, 4H, CH_2), 1.48–1.58 (m, 2H, CH_2), 2.17 (d, J=5.5 Hz, 1H, OH), 2.24 (dt, J=7.0, 2.0 Hz, 2H, =C–CH_2), 2.43 (s, 3H, CH_3), 5.58 (dt, J=5.5, 2.0 Hz, 1H, CHO), 7.13–7.25 (m, 3H, H_{arom}), 7.62–7.67 (m, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 19.2, 19.3, 22.6, 28.7, 31.5, 63.0, 80.1, 87.9, 126.5, 126.8, 128.6, 131.1, 136.3, 139.4. Anal. Calcd for $C_{15}H_{20}O$: C, 83.29; H, 9.32. Found: C, 82.94; H, 9.39.

4.1.2. 1-(2-Naphtyl)oct-2-yn-1-ol 5e. Yield 72%; oil; R_f 0.24 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, J=7.0 Hz, 3H, CH_3), 1.24–1.40 (m, 4H, CH_2), 1.51–1.61 (m, 2H, CH_2), 2.10 (s, 1H, OH), 2.25 (dt, J=7.2, 2.1 Hz, 2H, =C–CH_2), 5.50 (t, J=2.1 Hz, 1H, CHO), 7.46–7.49 (m, 2H, H_{arom}), 7.64 (dd, J=8.6, 1.7 Hz, 1H, H_{arom}), 7.81–7.86 (m, 3H, H_{arom}), 7.97 (s, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.0, 18.8, 22.1, 28.2, 31.1, 64.9, 79.9, 88.0, 124.7, 125.3, 126.2, 127.6, 128.2, 128.3, 133.1, 133.2, 138.6. Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.40; H, 8.05.

4.1.3. 1-(2-Furyl)oct-2-yn-1-ol 5f. Yield 69%; oil; R_f 0.30 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92 (t, J=7.1 Hz, 3H, CH_3), 1.24–1.44 (m, 4H, CH_2), 1.56 (tt, J=7.1, 7.1 Hz, 2H, CH_2), 2.28 (dt, J=7.1, 2.1 Hz, 2H, =C–CH_2), 2.38 (bs, 1H, OH), 5.40 (t, J=2.1 Hz, 1H, CHO), 6.36 (dd, J=3.2, 1.9 Hz, 1H, =CH–), 6.45 (bd, J=3.2 Hz, 1H, =CH–), 7.42 (dd, J=1.9, 1.0 Hz, 1H, =CH–),); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.3, 19.1, 22.6, 28.5, 31.4, 58.7, 87.4, 107.8, 110.7, 115.0, 143.2, 154.1. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.58; H, 8.42.

4.1.4. 1-(2-Thienyl)oct-2-yn-1-ol 5g. Yield 29%; oil; R_f=0.50 (petroleum ether/ethyl acetate 8:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (t, J=7.0 Hz, 3H, CH_3), 1.29–1.44 (m, 4H, CH_2), 1.55 (tt, J=7.0, 7.0 Hz, 2H, CH_2), 2.26 (dt, J=7.0, 1.9 Hz, 2H, =C–CH_2), 2.50 (bs, 1H, OH), 5.63 (t, J=1.9 Hz, 1H, CHO), 6.95 (dd, J=5.1, 3.6 Hz, 1H, =CH–), 7.14 (bd, J=3.6 Hz, 1H, =CH–), 7.26 (dd, J=5.1, 1.3 Hz, 1H, =CH–); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 19.1, 22.6, 28.5, 31.4, 60.8, 79.6, 87.6, 107.8, 125.7, 126.2, 127.1, 146.0.

4.1.5. Synthesis of (*R*)-4-phenylbut-3-yn-2-ol. A suspension of iodobenzene (971 mg, 4.76 mmol), CuI (36.2 mg, 0.2 mmol), $Pd(PPh_3)_2Cl_2$ (70.2 mg, 0.1 mmol), and Et_3N (1 mL, 7.14 mmol), in THF (7 mL) was stirred for 45 min at rt. A solution of (*R*)-but-3-yn-2-ol (350 mg, 5 mmol) in THF (5 mL) was then added dropwise, and the stirring was continued for 5 h at rt. After evaporation of the solvent, the residue was diluted with water (10 mL), and the mixture was extracted with diethyl ether (3×10 mL). The combined organic phases were washed with brine (5 mL), and then dried over Na_2SO_4. Evaporation of the solvent under reduced pressure afforded an oil that was purified by flash-chromatography on silica to give 502 mg (yield 62%) of (*R*)-4-phenylbut-3-yn-2-ol. Oil; R_f 0.32 (petroleum ether/CH_2Cl_2 1:2); $[\alpha]_D^{25}=+43.6$ (*c* 0.8, diethyl ether) [Ref. 54 (*S*)-4-phenylbut-3-yn-2-ol: $[\alpha]_D^{25}=-44.8$ (*c* 1.0, Et_2O)]; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.47 (d, J=6.0 Hz, 3H, CH_3), 2.05 (bs, 1H, OH), 4.68 (q, J=6.0 Hz, 1H, C*H*OH), 7.15–7.25 (m, 3H, H_{arom}), 7.33–7.40 (m, 2H, H_{arom}), in agreement with the literature data.[54]

4.2. Typical procedure for the preparation of propargylic carbonates

To a solution of propargylic alcohol **2a–d**, **6a**, or **6c–e** (17.8 mmol), dimethylaminopyridine (436 mg, 3.6 mmol), pyridine (6.7 mg, 71.4 mmol), in CH_2Cl_2 (40 mL) cooled at 0 °C wad added methyl chloroformate (5.6 mg, 71.4 mmol). After stirring for 24 h at rt, the reaction mixture was poured into a saturated aqueous copper sulfate solution (30 mL), and the aqueous phase was extracted with diethyl ether (3× 30 mL). Evaporation of the solvent under reduced pressure

afforded an oil that was purified by flash-chromatography on silica to give the corresponding propargylic carbonate.

4.2.1. 1-Ethyl-3-phenylprop-2-yn-1-yl methyl carbonate 3b. Yield 77%; oil; R_f 0.64 (petroleum ether/ethyl acetate 7:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.08 (t, J=7.4 Hz, 3H, CH_3), 1.91 (dq, J=7.4, 6.4 Hz, 2H, CH_2), 3.75 (s, 3H, OCH_3), 5.42 (t, J=6.4 Hz, 1H, CHO), 7.24–7.29 (m, 3H, H_{arom}), 7.39–7.45 (m, 2H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 9.6, 28.6, 55.1, 69.9, 86.2, 86.5, 122.6, 128.7, 132.2, 129.1, 155.4. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.53; H, 6.47. Found: C, 71.29; H, 6.61.

4.2.2. 1-Isopropyl-3-phenylprop-2-yn-1-yl methyl carbonate 3c. Yield 84%; oil; R_f 0.73 (petroleum ether/ethyl acetate 7:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (d, J=6.8 Hz, 3H, CH_3), 1.15 (d, J=6.6 Hz, 3H, CH_3), 2.25 (m, 1H, C*H*Me_2), 3.82 (s, 3H, OCH_3), 5.30 (d, J=5.7 Hz, 1H, CHO), 7.22–7.29 (m, 3H, H_{arom}), 7.39–7.47 (m, 2H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 17.9, 18.6, 33.2, 55.3, 74.1, 84.9, 87.3, 122.7, 128.6, 129.0, 132.3, 155.6. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.22; H, 6.98.

4.2.3. 1-*ter*-Butyl-3-phenylprop-2-yn-1-yl methyl carbonate 3d. Yield 86%; mp 71 °C; R_f 0.65 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.10 (s, 9H, CH_3), 3.83 (s, 3H, OCH_3), 5.18 (s, 1H, CHO), 7.27–7.35 (m, 3H, H_{arom}), 7.41–7.49 (m, 2H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 30.8, 35.4, 55.2, 70.4, 85.6, 89.5, 122.5, 128.6, 129.2, 132.4, 155.6. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.35; H, 7.08.

4.2.4. Methyl 1-(2-methylphenyl)oct-2-yn-1-yl carbonate 6d. Yield 56%; oil; R_f 0.73 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J=7.0 Hz, 3H, CH_3), 1.27–1.37 (m, 4H, CH_2), 1.50–1.55 (m, 2H, CH_2), 2.35 (dt, J=7.1, 2.0 Hz, 2H, =C–CH_2), 2.43 (s, 3H, CH_3), 3.80 (s, 3H, OCH_3), 6.42 (t, J=2.0 Hz, 1H, CHO), 7.16–7.26 (m, 3H, H_{arom}), 7.58–7.62 (m, 2H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.3, 19.2, 19.4, 22.5, 28.4, 31.4, 55.4, 68.7, 78.7, 89.8, 126.6, 128.4, 129.3, 131.1, 135.6, 136.6, 155.4. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.52; H, 8.18.

4.2.5. Methyl 1-(2-naphtyl)oct-2-yn-1-yl carbonate 6e. Yield 46%; oil; R_f 0.56 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, J=7.0 Hz, 3H, CH_3), 1.31–1.49 (m, 4H, CH_2), 1.56–1.65 (m, 2H, CH_2), 2.35 (dt, J=7.0, 2.0 Hz, 2H, =C–CH_2), 3.83 (s, 3H, CH_3), 6.63 (t, J=2.0 Hz, 1H, CHO), 7.84–7.92 (m, 3H, H_{arom}), 7.77 (dd, J=8.7, 2.0 Hz, 1H, H_{arom}), 7.49–7.55 (m, 2H, H_{arom}), 8.12 (s, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 19.3, 22.6, 28.5, 31.5, 55.3, 70.9, 78.2, 90.2, 125.5, 126.8, 127.1, 127.6, 128.1, 128.8, 129.0, 133.5, 134.0, 135.0, 155.5. HRMS (EI) calcd for $C_{20}H_{23}O_3$ $[M+H]^+$: 311.1647. Found: 311.1646.

4.2.6. Methyl (*R*)-1-methylprop-2-yn-1-yl carbonate. Yield 82%; oil; R_f 0.72 (petroleum ether/ethyl acetate 5:1); $[\alpha]_D^{25}=+109$ (c 1, diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.65 (d, J=6.7 Hz, 3H, CH_3), 3.83 (s, 3H, CH_3), 5.57 (q, J=6.7 Hz, 1H, C*H*O), 7.26–7.36 (m, 3H, H_{arom}), 7.42–7.50 (m, 2H, H_{arom}), in agreement with the literature data.[36]

4.2.7. Methyl (*R*)-1-methyl-3-phenylprop-2-yn-1-yl carbonate. Yield 91%; oil; R_f 0.56 (petroleum ether/ethyl acetate 6:1); $[\alpha]_D^{25}=+167.4$ (c 1, diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.65 (d, J=6.7 Hz, 3H, CH_3), 3.83 (s, 3H, CH_3), 5.57 (q, J=6.7 Hz, 1H, C*H*O), 7.26–7.36 (m, 3H, H_{arom}), 7.42–7.50 (m, 2H, H_{arom}), in agreement with the literature data.[36]

4.3. Typical procedure for the preparation of propargylic acetates

To a solution of propargylic alcohol (1.6 mmol), and pyridine (514 mg, 6.5 mmol), in CH_2Cl_2 (10 mL) cooled at 0 °C wad added acetyl chloride (521 mg, 6.5 mmol). After stirring for 24 h at rt, the mixture was poured into a saturated aqueous copper sulfate solution (10 mL), and the aqueous phase was extracted with diethyl ether (3×10 mL). Evaporation of the solvent under reduced pressure afforded an oil that was purified by flash-chromatography on silica to give the corresponding propargylic acetate.

4.3.1. 1-(2-Furyl)oct-2-yn-1-yl acetate 7f. Yield 93%; oil; R_f 0.56 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, J=7.2 Hz, 3H, CH_3), 1.31–1.38 (m, 4H, CH_2), 1.55 (m, 2H, CH_2), 2.10 (s, 3H, $COCH_3$), 2.26 (dt, J=7.2, 2.1 Hz, 2H, =C–CH_2), 6.36 (dd, J=3.2, 1.7 Hz, 1H, =CH–), 6.49–6.52 (m, 2H, =CH-, CHO), 7.41 (m, 1H, =CH–). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.3, 19.1, 21.3, 22.5, 28.3, 31.4, 59.3, 74.6, 88.0, 110.2, 110.8, 143.7, 150.6, 170.0. Anal. Calcd for $C_{14}H_{19}O_3$ $[M+H]^+$ 235.1334. Found: 235.1335.

4.3.2. 1-(2-Thienyl)oct-2-yn-1-yl acetate 7g. Yield 82%; oil; R_f 0.50 (petroleum ether/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, J=7.0 Hz, 3H, CH_3), 1.30–1.40 (m, 4H, CH_2), 1.53 (tt, J=7.1, 7.1 Hz, 2H, CH_2), 2.03 (s, 3H, $COCH_3$), 2.25 (dt, J=7.1, 1.9 Hz, 2H, =C–CH_2), 6.67 (t, J=1.9 Hz, 1H, CHO), 6.93 (dd, J=5.1, 3.6 Hz, 1H, =CH–), 7.19 (bd, J=3.6 Hz, 1H, =CH–), 7.27 (dd, J=5.1, 1.1 Hz, 1H, =CH–). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.3, 19.1, 21.3, 22.5, 28.4, 31.4, 61.4, 76.8, 88.2, 127.0, 127.1, 127.8, 141.3, 169.9. Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.17; H, 7.25. Found: C, 67.44; H, 7.18.

4.4. Typical procedure for the palladium-catalyzed annulation reaction

A mixture of $Pd_2(dba)_3$ (20.8 mg, 2.2×10^{-2} mmol), and diphosphine (9.1×10^{-2} mmol) in THF (7 mL) was stirred under a nitrogen atmosphere at rt for 30 min. This catalyst solution was added to a mixture of benzene-1,2-diol (100 mg, 0.9 mmol) and the corresponding propargylic carbonate (1.1 mmol), or propargylic acetate (1.1 mmol) in the presence of triethylamine (269 mg, 2.6 mmol). The resulting solution was stirred at rt for 24 h. The solvent was evaporated and the residue was chromatographed over silica with petroleum ether/ethyl acetate as the eluent to afford the corresponding 2,3-dihydro-1,4-benzodioxine.

4.4.1. (3*Z*)-2-Ethylidene-3-phenyl-2,3-dihydro-1,4-benzodioxine (8a) and (2*Z*)-2-benzylidene-3-methyl-2,3-dihydro-1,4-benzodioxine (9a). R_f 0.63 (petroleum ether/ethyl acetate 40:1).

For **8a**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.71 (d, J=6.8 Hz, 3H, CH_3), 4.54 (q, J=6.8 Hz, 1H, =CH–), 5.50 (s, 1H, OCH), 6.89–7.86 (m, 9H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.0, 76.4, 105.4, 120.8, 122.0, 126.4, 127.1, 131.3, 132.9, 133.5, 138.9, 146.7, 147.5, 151.6.

For **9a**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.65 (d, J=6.5 Hz, 3H, CH_3), 4.72 (q, J=6.5 Hz, 1H, OCH), 5.72 (s, 1H, =CH–), 6.89–7.86 (m, 9H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 22.2, 74.9, 109.7, 120.8, 122.0, 126.4, 127.1, 131.3, 132.9, 133.5, 138.9, 146.7, 147.5, 151.6. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.61; H, 5.99.

4.4.2. (2*Z*)-2-Phenyl-3-propylidene-2,3-dihydro-1,4-benzodioxine (8b) and (2*Z*)-2-benzylidene-3-ethyl-2,3-dihydro-1,4-benzodioxine (9b). R_f 0.68 (petroleum ether/ethyl acetate 40:1).

For **8b**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (d, J=7.5 Hz, 3H, CH_3), 2.32 (m, 2H, CH_2), 4.50 (m, 1H, =CH–), 5.49 (s, 1H, OCH), 6.90–7.90 (m, 9H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 18.0, 76.4, 112.7, 117.9, 122.3, 122.4, 128.0, 128.7, 128.8, 129.3, 137.2, 143.8, 145.3, 146.0.

For **9b**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (t, J=7.3 Hz, 3H, CH_3), 1.91 (m, 2H, CH_2), 4.50 (m, 1H, OCH), 5.64 (s, 1H, =CH–), 6.90–7.90 (m, 9H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 10.4, 25.0, 76.6, 106.8, 116.6, 118.1, 122.2, 123.1, 127.2, 128.7, 129.3, 134.8, 142.5, 142.6, 146.0. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 81.13; H, 6.34.

4.4.3. (2*Z*)-2-(2-Methylpropylidene)-3-phenyl-2,3-dihydro-1,4-benzodioxine (8c) and (2*Z*)-2-benzylidene-3-isopropyl-2,3-dihydro-1,4-benzodioxine (9c). R_f=0.80 (petroleum ether/ethyl acetate 40:1).

For **8c**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (d, J=4.9 Hz, 6H, CH_3), 2.91 (m, 1H, C*H*Me$_2$), 4.27 (d, J=9.0 Hz, 1H, =CH–), 5.33 (s, 1H, OCH), 6.72–7.65 (m, 9H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 23.2, 23.4, 24.6, 76.3, 118.4, 116.7, 118.0, 118.4, 122.3, 122.4, 128.0, 128.8, 134.8, 137.3, 143.7, 143.9.

For **9c**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.00 (d, J=6.6 Hz, 6H, CH_3), 1.95 (m, 1H, CH_2), 4.04 (d, J=9.8 Hz, 1H, OCH), 5.46 (s, 1H, =CH–), 6.72–7.65 (m, 9H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 18.9, 19.0, 29.2, 81.6, 108.4, 116.6, 118.1, 122.1, 123.2, 127.2, 128.7, 129.3, 142.2, 142.8, 143.3, 144.7. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.06; H, 6.78.

4.4.4. (2*Z*)-2-Hexylidene-3-(2-methylphenyl)-2,3-dihydro-1,4-benzodioxine (10d) and (2*Z*)-2-(2-methylbenzylidene)-3-pentyl-2,3-dihydro-1,4-benzodioxine (11d). R_f, 0.46 for **10d** and 0.38 for **11d** (petroleum ether/ethyl acetate 60:1).

For **10d**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.78 (t, J=6.8 Hz, 3H, CH_3), 1.19–1.31 (m, 6H, CH_2), 2.08–2.12 (m, 2H, CH_2), 2.28 (s, 3H, CH_3), 4.16 (t, J=7.3 Hz, 1H, =CH–), 5.45 (s, 1H, OCH), 6.77–7.22 (m, 7H, H_{arom}), 7.37–7.40 (m, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 20.7, 23.0, 25.6, 31.8, 31.9, 75.4, 104.3, 116.8, 118.0, 122.3, 122.9, 126.2, 127.3, 129.9, 130.4, 133.1, 136.3, 142.5, 142.6, 142.9.

For **11d**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82 (t, J=6.8 Hz, 3H, CH_3), 1.19–1.31 (m, 6H, CH_2), 1.66–1.81 (m, 2H, CH_2), 2.26 (s, 3H, CH_3), 4.50 (t, J=7.3 Hz, 1H, OCH), 5.63 (s, 1H, =CH–), 6.77–7.22 (m, 7H, H_{arom}), 7.79 (d, J=7.6 Hz, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.5, 19.7, 22.8, 24.5, 29.3, 74.0, 110.4, 116.7, 117.9, 122.2, 122.4, 126.7, 128.0, 128.9, 130.8, 135.2, 136.7, 143.4, 144.5, 145.5. Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.56; H, 8.02.

4.4.5. (2*Z*)-2-Hexylidene-3-(2-naphthyl)-2,3-dihydro-1,4-benzodioxine (10e) and (2*Z*)-2-(2-naphthylmethylene)-3-pentyl-2,3-dihydro-1,4-benzodioxine (11e). R_f 0.74 (petroleum ether/ethyl acetate 40:1).

For **10e**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, J=6.8 Hz, 3H, CH_3), 1.46–1.65 (m, 6H, CH_2), 2.28 (dt, J=7.2, 7.2 Hz, 2H, CH_2), 4.53 (t, J=7.2 Hz, 1H, =CH–), 5.64 (s, 1H, OCH), 6.85–8.13 (m, 11H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1, 22.5, 22.6, 24.2, 29.0, 76.1, 111.1, 116.4, 117.6, 122.0, 122.1, 125.3, 126.3, 126.4, 127.1, 127.7, 128.3, 133.1, 133.2, 134.4, 143.0, 143.4, 145.2.

For **11e**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, J=6.8 Hz, 3H, CH_3), 1.25–1.44 (m, 6H, CH_2), 1.75–1.95 (m, 2H, CH_2), 4.61 (dd, J=7.9, 6.2 Hz, 1H, OCH), 5.77 (s, 1H, =CH–), 6.85–8.13 (m, 11H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1, 22.6, 25.2, 31.5, 31.6, 74.9, 106.4, 116.3, 117.8, 121.9, 122.8, 125.8, 126.1, 127.2, 127.6, 127.8, 127.9, 128.1, 132.1, 132.4, 133.6, 142.2, 142.3, 146.3. Anal. Calcd for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.29; H, 6.98.

4.4.6. (3*Z*)-2-(2-Furyl)-3-hexylidene-2,3-dihydro-1,4-benzodioxine (10f) and (2*Z*)-2-(2-furylmethylene)-3-pentyl-2,3-dihydro-1,4-benzodioxine (11f). R_f 0.5 (petroleum ether/ethyl acetate 60:1+0.5% Et_3N).

For **10f**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (t, J=6.8 Hz, 3H, CH_3), 1.27–1.36 (m, 4H, CH_2), 1.41–1.58 (m, 2H, CH_2), 1.69–1.86 (m, 2H, CH_2), 4.74 (t, J=7.5 Hz, 1H, =CH–), 5.54 (s, 1H, OCH), 6.45–6.47 (m, 1H, H_{arom}), 6.85 (d, J=3.2 Hz, 1H, H_{arom}), 6.92–7.12 (m, 4H, H_{arom}), 7.35–7.36 (m, 1H, H_{arom}).

For **11f**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (t, J=6.8 Hz, 3H, CH_3), 1.27–1.36 (m, 4H, CH_2), 1.41–1.58 (m, 2H, CH_2), 1.69–1.86 (m, 2H, CH_2), 4.49 (dd, J=8.1, 6.0 Hz, 1H, OCH), 5.68 (s, 1H, =CH–), 6.45–6.47 (m, 1H, H_{arom}), 6.85 (d, J=3.2 Hz, 1H, H_{arom}), 6.92–7.12 (m, 4H, H_{arom}), 7.35–7.36 (m, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.4, 22.9, 25.4, 31.7, 31.8, 74.3, 96.8, 109.9, 112.1, 116.6, 118.1, 122.3, 123.2, 141.2, 142.5, 142.7, 145.1, 150.0.

HRMS (EI) calcd for $C_{18}H_{21}O_3$ $[M+H]^+$: 285.1491. Found: 285.1493.

4.4.7. (2*Z*)-2-Hexylidene-3-(2-thienyl)-2,3-dihydro-1,4-benzodioxine (10g) and (3*Z*)-2-pentyl-3-(2-thienylmethylene)-2,3-dihydro-1,4-benzodioxine (11g). R_f 0.46 (petroleum ether/ethyl acetate 60:1+0.5% Et_3N).

For **10g**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82 (t, J=6.8 Hz, 3H, CH_3), 1.10–1.18 (m, 4H, CH_2), 1.32–1.55 (m, 2H, CH_2), 1.63–1.85 (m, 2H, CH_2), 4.70 (t, J=7.4 Hz, 1H, =CH–), 5.66 (s, 1H, OCH), 6.84–6.93 (m, 4H, H_{arom}), 7.03 (d, J=3.6 Hz, 1H, H_{arom}), 7.05–7.10 (m, 1H, H_{arom}), 7.18–7.21 (m, 1H, H_{arom}).

For **11g**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82 (t, J=6.8 Hz, 3H, CH_3), 1.24–1.26 (m, 4H, CH_2), 1.32–1.55 (m, 2H, CH_2), 1.63–1.85 (m, 2H, CH_2), 4.45 (dd, J=7.9, 6.2 Hz, 1H, OCH), 5.87 (s, 1H, =CH–), 6.84–6.93 (m, 4H, H_{arom}), 7.03 (d, J=3.6 Hz, 1H, H_{arom}), 7.05–7.10 (m, 1H, H_{arom}), 7.18–7.21 (m, 1H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 16.8, 25.3, 27.8, 34.2, 34.3, 76.8, 103.7, 119.2, 120.5, 124.7, 125.6, 128.5, 129.2, 129.3, 139.6, 144.9, 145.1, 146.8. Anal. Calcd for $C_{18}H_{20}O_2S$: C, 71.97; H, 6.71. Found: C, 71.81; H, 6.58.

4.5. Separation of the enantiomers

The enantiomeric excesses of the obtained compounds were determined by HPLC on a chiral column Chiralpak AD (25 cm×4.6 mm).

8a/9a (hexane/2-propanol 98:2): **8a**: non-separated; **9a**: R_t=14.5 min for the (−) enantiomer and 16.2 min for the (+) enantiomer.

8b/9b (hexane/2-propanol 98:2): **8b**: non-separated; **9b**: R_t=15.3 and 17.8 min.

8c/9c (hexane/2-propanol 99:1): **8c**: R_t=10.2 and 20.9 min; **9c**: R_t=32.4 and 35.0 min.

10a/11a (hexane/2-propanol 96:4): **10a**: non-separated; **11a**: R_t=44.8 and 51.7 min.

10b/11b (hexane/2-propanol 96:4): **10b**: R_t=15.6 and 19.8 min; **11b**: R_t=11.8 and 12.3 min.

10c/11c (hexane/2-propanol 96:4): **10c**: R_t=27.7 and 32.6 min; **11c**: R_t=15.8 and 17.4 min.

10d/11d (hexane): **10d**: R_t=24.9 and 32.1 min; **11d**: R_t= 13.8 and 14.8 min.

10e/11e (hexane/2-propanol, 150:1): **10e**: R_t=32.0 and 42.9 min; **11e**: R_t=19.7 and 20.4 min.

10f/11f (hexane/2-propanol 98:2) **10f**: non-separated; **11g**: R_t=13.4 and 14.6 min.

10g/11g (hexane): **10g**: R_t=15.3 and 16.2 min; **11g**: R_t= 29.4 and 38.7 min.

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