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Palladium-Catalyzed Formation of Cyclic Ethers – Regio-, Stereo- and Enantioselectivity of the Reaction

Anna Zawisza,[a] Bernard Fenêt,[b] and Denis Sinou*[a]

Keywords: Cyclization / Palladium / Oxygen heterocycles / Diastereoselectivity / Enantioselectivity

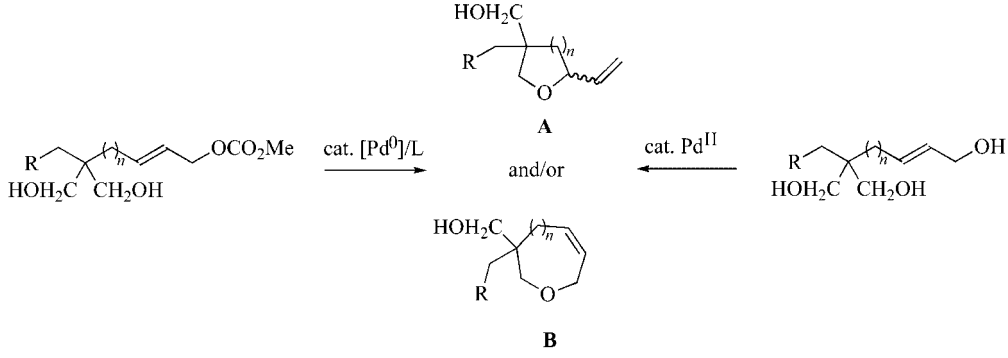
An efficient and stereoselective synthesis of 3-alkyl-3-hydroxymethyl-5-vinyltetrahydrofurans is described by the Pd^0-catalyzed cyclization of the methyl carbonates of ω,ω-bis(hydroxymethyl)-α,β-unsaturated alcohols. The use of chiral ligands gave the corresponding THF derivatives in low to moderate enantiomeric ratios.

Introduction

Pd is one of the most widely used transition metals for the synthesis of heterocyclic compounds.[1] This is mainly due to the mild reaction conditions used, the high yields, the tolerance of a large variety of functional groups, and the high regio- and stereoselectivity observed. One way to synthesize oxygen heterocycles is to build the heterocyclic backbone itself. This approach, based on organometallic catalysis, could be divided into two pathways: (a) the Pd^0-catalyzed intramolecular allylation of oxygen nucleophiles[2–4] and (b) the Pd^{II}-catalyzed intramolecular oxidative cyclization of hydroxyalkene nucleophiles.[2,3,5,6]

Pd^0-catalyzed intramolecular heteroannulation through allylic alkylation, the so-called Tsuji–Trost reaction, generally employs allylic acetates,[7–11] benzoates,[12] carbonates,[13–16] or vinyl epoxides[8,17,18] bearing a hydroxy group. Allylsilanes have also been used as precursors of the η^3-allyl intermediates, starting from $PdCl_2$ and $CuCl_2$, affording the corresponding THF derivatives in quite good yields.[19] This cyclization has also been achieved in an enantioselective way in the presence of chiral ligands.[15,20–25]

The Pd^{II}-catalyzed cyclization of alkenyl alcohols has led to cyclic enols by a β-hydride elimination, or to oxygen heterocycles bearing a vinyl group through a β-hydroxy elimination, if the alkenol possesses an allyl alcohol moiety.[2,3,5] A large variety of oxygen-containing heterocycles have been obtained with this methodology,[26–34] even in an asymmetric fashion.[35–37]



Scheme 1.

In our continuing interest in Pd-catalyzed access to substituted THFs and tetrahydropyrans, we were interested in the synthesis of such functionalized oxygen heterocycles. Recently it was reported that ω-hydroxy-α,β-unsaturated alcohols underwent an intramolecular Pd^{II}-catalyzed cycli-

[a] Laboratoire de Synthèse Asymétrique, associé au CNRS, UMR 5181, CPE Lyon, Université Claude Bernard Lyon 1,
43, boulevard du 11 novembre 1918, 69622 Villeurbanne cedex, France
Fax: +33-4-78898914
E-mail: sinou@univ-lyon1.fr
[b] Centre Commun de RMN, CPE Lyon, Université Claude Bernard Lyon 1,
43, boulevard du 11 novembre 1918, 69622 Villeurbanne cedex, France
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zation to give vinyltetrahydropyrans. We expected that the cyclization of ω,ω-bis(hydroxymethyl)-α,β-unsaturated alcohols or of the corresponding allylic carbonates would afford functionalized oxygen heterocycles (Scheme 1). This cyclization could occur in an *exo*- or *endo*-trigonal fashion to afford heterocycle **A** or **B**. Moreover, since these unsaturated alcohols possess two enantiotopic hydroxymethyl groups, a stereo- and enantioselective cyclization could take place. In this paper, we report a full account of the stereochemical results in the Pd^0- and Pd^{II}-catalyzed cyclization reactions of ω,ω-bis(hydroxymethyl)-α,β-unsaturated alcohols and the corresponding allylic carbonates and preliminary results concerning the asymmetric Pd^0-catalyzed cyclization of the allylic carbonates.

Results and Discussion

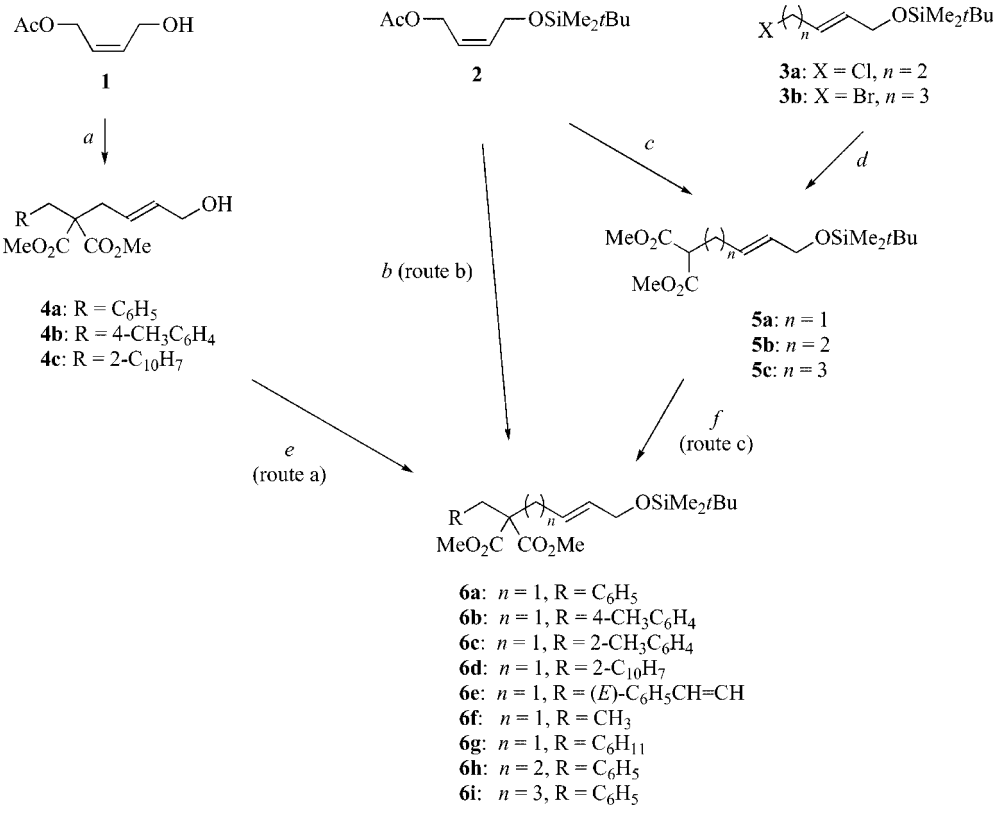
Synthesis of the Starting Materials

The starting bis(hydroxymethyl) allylic alcohols **8a**–**i** and carbonates **9a**–**i** were prepared according to Scheme 2 and Scheme 3. The key intermediates in these syntheses were the unsaturated dimethyl alkyl malonates **6a**–**i** (Scheme 2).

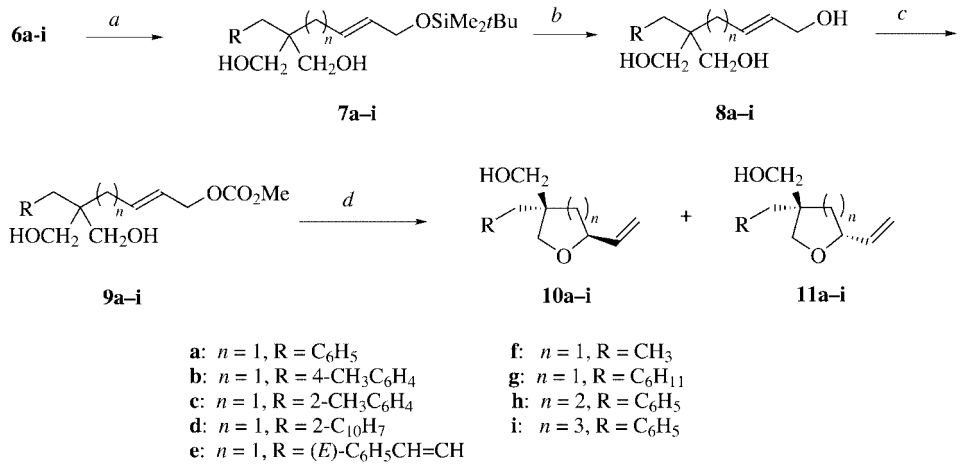
In the first route, Pd^0-catalyzed condensation of (*Z*)-4-hydroxybut-2-en-1-yl acetate (**1**)[38] with dimethyl benzylmalonate, dimethyl (4-methylbenzyl)malonate, or dimethyl (2-naphtylmethyl)malonate in THF at room temp. afforded substituted dimethyl (4-hydroxybut-2-en-1-yl)malonates **4a**–**c** in 54%, 55%, and 50% yield, respectively. Compounds **4a**–**c** were generally obtained as a 90:10 mixture of the (*E*) and (*Z*) stereoisomers, which could be separated by column chromatography. The silylation of (*E*)-allylic alcohols **4a**–**c** with tBuMe$_2$SiCl in CH_2Cl_2 in the presence of Et_3N and imidazole gave the corresponding (*E*)-unsaturated silylated diesters **6a**, **6b**, and **6d**, in 87%, 94%, and 79% yield, respectively.

The second route was the Pd^0-catalyzed alkylation of (*Z*)-4-[(*tert*-butyldimethylsilyl)oxy]but-2-en-1-yl acetate (**2**)[39] with dimethyl [(*E*)-3-phenylprop-2-en-1-yl]malonate, dimethyl ethylmalonate, or dimethyl (cyclohexylmethyl)-malonate, affording directly the corresponding unsaturated, silylated, substituted dimethyl malonates **6e**–**g**, having the (*E*) configuration, in 86%, 86%, and 77% yield, respectively.

The third route used unsaturated, silylated, dimethyl malonates **5a**–**c** as intermediates. The Pd^0-catalyzed alkylation of allylic acetate (**2**)[39] with dimethyl malonate afforded



Scheme 2. Synthesis of silylated dimethyl malonates **6a**–**i**; reagents and conditions: (*a*) (*i*) $Pd_2(dba)_3$, dppb, THF, room temp., 0.5 h; (ii) $RCH_2CH(CO_2Me)_2$ (R = C_6H_5, 4-$CH_3C_6H_4$, or 2-$C_{10}H_7$), NaH, THF; (iii) **1**, THF, room temp., 24 h; (*b*) (i) $Pd_2(dba)_3$, dppb, THF, room temp., 0.5 h; (ii) $RCH_2CH(CO_2Me)_2$ (R = (*E*)-$C_6H_5CH{=}CHCH_2$, CH_3, or C_6H_{11}), NaH, THF; (iii) **2**, THF, room temp., 24 h; (*c*) (i) $Pd_2(dba)_3$, dppb, THF, room temp., 0.5 h; (ii) $CH_2(CO_2Me)_2$, NaH, THF, room temp.; (iii) **2**, THF, room temp., 24 h; (*d*) $CH_2(CO_2Me)_2$, NaH, THF, DMF, reflux, 5 h; (*e*) tBuMe$_2$SiCl, imidazole, Et_3N, CH_2Cl_2, room temp., 15 h; (*f*) (i) **5**, NaH, THF, DMF, room temp., 0.5 h; (ii) RCH_2Br (R = C_6H_5, or 2-$CH_3C_6H_5$), reflux, 5 h.



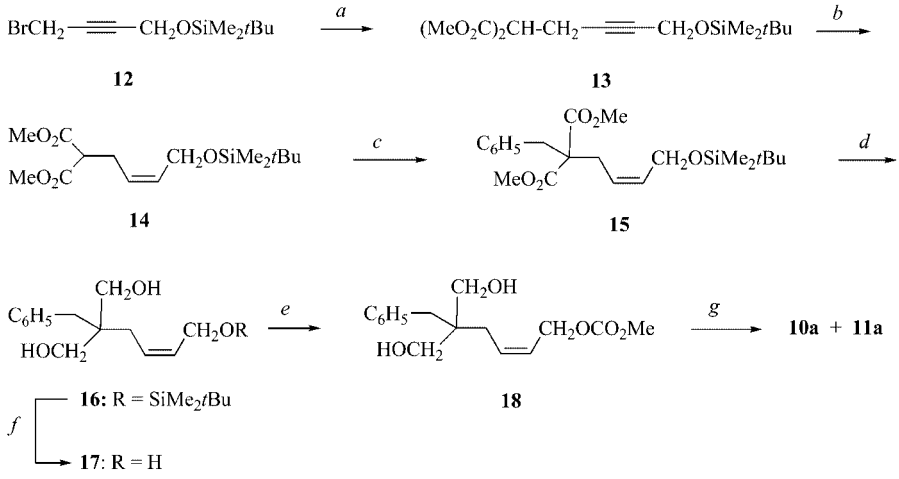
Scheme 3. Synthesis of dihydroxycarbonates **9a**–**i** and Pd-catalyzed cyclization to oxygen heterocycles **10** and **11**; reagents and conditions: (*a*) AlH_4Li, Et_2O, 0 °C → room temp., 0.5 h; (*b*) $Bu_4NF{\cdot}3H_2O$, THF, room temp., 15 h; (*c*) $ClCO_2CH_3$, C_5H_5N, CH_2Cl_2, 0 °C → room temp., 2 h; (*d*) $Pd_2(dba)_3$, ligand, THF, 1 h, room temp.

compound (*E*)-**5a** in 85% yield after purification. Compounds (*E*)-**5b** and (*E*)-**5c** were obtained in 51% and 83% yield, respectively, by the alkylation of dimethyl malonate in THF with unsaturated halides **3a**–**b** with sodium hydride as the base. Finally, the alkylation of dimethyl malonates **5a**–**c** with 2-methylbenzyl bromide or benzyl bromide in THF in the presence of sodium hydride afforded the corresponding (*E*)-dimethyl benzylic malonates **6c**, **6h**, and **6i**, in 82%, 76%, and 93% yield, respectively.

The reduction of substituted, silylated, dimethyl malonates **6a**–**i** with lithium aluminum hydride in diethyl ether afforded unsaturated diols **7a**–**i** in 60–91% yield (Scheme 3). Triols **8a**–**i** were obtained in 66–98% yield after purification by treatment of compounds **7a**–**i** with $Bu_4NF{\cdot}3H_2O$ in THF. Condensation of these triols with one equivalent of methyl chloroformate at 0 °C afforded bis(hydroxymethyl) allylic carbonates **9a**–**i** in 40–72% yield.

Unsaturated dimethyl benzyl malonate **15** having the (*Z*) stereochemistry was prepared according to Scheme 4. Dimethyl acetylenic malonate **13** was obtained in 85% yield by the alkylation of dimethyl malonate with propargylic bromide **12**.[40] Hydrogenation of acetylenic compound **13** in the presence of Lindlar's catalyst afforded the (*Z*)-allylic derivative **14** in 98% yield, whose alkylation with benzyl bromide in the presence of sodium hydride gave ethylenic dimethyl malonate **15** in 96% yield. The sequence of reduction of the diester with lithium aluminum hydride in diethyl ether followed by desilylation in the presence of $Bu_4NF{\cdot}3H_2O$ in THF gave the corresponding triol **17** (55% overall yield), which was transformed into allylic carbonate **18** in 54% yield.

The above synthetic procedures provide a simple access to a wide range of precursors for the catalytic cyclizations.



Scheme 4. Synthesis of dihydroxycarbonate **18** and Pd-catalyzed cyclization; reagents and conditions: (*a*) $CH_2(CO_2Me)_2$, NaH, THF, DMF, reflux, 5 h, 85%; (*b*) H_2, 1 bar, Pd Lindlar, cyclohexane, ethyl acetate, room temp., 48 h, 98%; (*c*) NaH, $C_6H_5CH_2Br$, THF, DMF, reflux, 5h, 96%; (*d*) AlH_4Li, Et_2O, 0 °C → room temp., 0.5 h, 73%; (*e*) $Bu_4NF{\cdot}3H_2O$, THF, room temp., 15 h, 75%; (*f*) $ClCO_2CH_3$, C_5H_5N, CH_2Cl_2, 0 °C → room temp., 2 h, 54%; (*g*) $Pd_2(dba)_3$, ligand, THF, 1 h, room temp.

Pd^0-Catalyzed Cyclization of Bis(hydroxymethyl) Allylic Carbonates 9a–h and 18

The cyclization was first studied with bis(hydroxymethyl) allylic carbonate **9a** as the substrate (Scheme 3). Ring closure of carbonate **9a** occurred readily in THF at room temp. in the presence of a catalytic amount of $Pd_2(dba)_3$ associated with PPh_3, providing exclusively THF derivatives **10a** and **11a** as a 14:86 mixture and in 84% overall yield (Table 1, Entry 1). The configuration assignment of compounds **10a** and **11a** was based on NOESY experiments. The major stereoisomer **11a** showed a particularly strong correlation between the 5-H signal at δ = 4.41 ppm and the CH_2OH group signal at δ = 3.48 ppm, while the minor one **10a** showed a correlation between the 5-H signal at δ = 4.42 ppm and the benzylic proton signals at δ = 2.81 ppm and 2.92 ppm (Figure 1).

Other ligands such as tris(*o*-tolyl)phosphane, dppe [1,2-bis(diphenylphosphanyl)ethane], dppp [1,3-bis(diphenylphosphanyl)propane], dppb [1,4-bis(diphenylphosphanyl)-butane], or dppf [1,1′-bis(diphenylphosphanyl)ferrocene] were associated with Pd in this cyclization reaction (Table 1, Entries 2–6). All these ligands gave almost the same high diastereoselectivities, compound **11a** being obtained as the major stereoisomer; however, dppe and dppf gave lower yields (72% and 35%, respectively), even after a 20 h reaction.

The (*Z*)-configured isomer **18** was also submitted to this cyclization procedure in the presence of dppb as the ligand (Scheme 4, Table 1, Entry 7); THFs **10a** and **11a** were obtained in an overall yield of 95% after 1 h and in a 14:86 ratio, similar to the results observed in the case of the (*E*) isomer.

This Pd^0-catalyzed cyclization was extended to other bis(hydroxymethyl) allylic carbonates **9b**–**g** bearing different substituents. In all cases, the corresponding THFs **10b**–**g** and **11b**–**g** were obtained in quite high yields (91–98%) after a 1 h reaction (Table 1, Entries 8–13). The observed diastereoselectivities were quite similar to those obtained in the cyclization of carbonate **9a**, ranging from 20:80 to 12:88 in favor of the stereoisomer **11**. Only bis(hydroxymethyl) allylic carbonate **9f** gave a lower diastereoselectivity (31:69) in favor of the diastereoisomer **11f**; this difference could be due to the presence of the less bulky ethyl group compared to the other substituents.

Then we extended the cyclization to allylic carbonate **9h**, having two methylenic units between the double bond and the quaternary carbon bearing the two hydroxymethyl

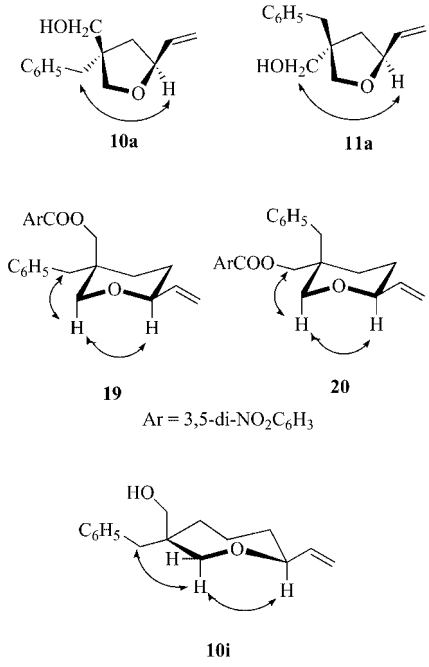


Figure 1. Observed NOE effects.

Table 1. Pd^0-catalyzed cyclization of allylic carbonates **9a**–**i** and **18**.[a]

Entry	Carbonate	Ligand	*T* [°C]	Time [h]	Yield (**10** + **11**) [%][b]	**10/11 [%]**[c]
1	**9a**	PPh_3	25	1	84	14:86
2	**9a**	$P(2\text{-}MeC_6H_4)_3$	25	1.5	84	20:80
3	**9a**	dppe	25	20	72	24:76
4	**9a**	dppp	25	1.5	90	20:80
5	**9a**	dppb	25	1	92	15:85
6	**9a**	dppf	25	20	35	26:74
7	**18**	dppb	25	1	95	14:86
8	**9b**	dppb	25	1	95	17:83
9	**9c**	dppb	25	1	94	15:85
10	**9d**	dppb	25	1	94	13:87
11	**9e**	dppb	25	1	98	20:80
12	**9f**	dppb	25	1	91	31:69
13	**9g**	dppb	25	1	95	12:88
14	**9h**	dppb	25	20	84	57:43
15	**9i**	dppb	25	20	no reaction	–
16	**9i**	dppb	55	20	30	32:68
17	**9i**	dppb	25[d]	20	41	37:63
18	**9i**	dppb	55[d]	20	61	34:66

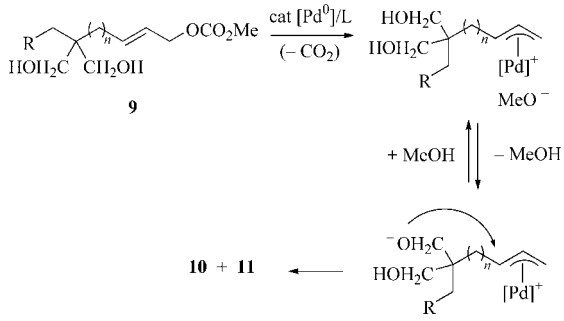
[a] [**9**] Or [**18**]:[$Pd_2(dba)_3$]:[dppb] = 40:1:2, THF or CH_2Cl_2, 1 h. [b] Yields refer to isolated pure products after column chromatography. [c] Determined by ^1H NMR spectroscopy. [d] 12 mL (6 + 6) of THF was used instead of 6 mL (see the Exp. Section).

groups. Bis(hydroxymethyl) carbonate **9h** afforded a 57:43 mixture of tetrahydropyrans **10h** and **11h** in 84% yield after 20 h (Table 1, Entry 14). The relative stereochemistry of stereoisomers **10h** and **11h** was difficult to assign, due to the overlapping of the 6-H and CH_2OH signals at δ = 3.69–3.81 ppm for one stereoisomer and of the 2-H and H–6 signals at δ = 3.78–3.87 ppm for the other stereoisomer. In order to determine this stereochemistry, compounds **10h** and **11h** were transformed into their dinitrobenzoates **19** and **20**, respectively. The NOE spectrum of dinitrobenzoate **19** clearly shows a relation between the axial 2-H (δ = 3.39 ppm) and axial 6-H (δ = 3.78–3.85 ppm) and the axial 2-H and the CH_2OCO hydrogens (δ = 4.03 ppm and 4.10 ppm, Figure 1); this indicates that these hydrogens are on the same side of the molecule. For dinitrobenzoate **20**, the NOE spectrum clearly shows a relation between the axial 2-H (δ = 3.41 ppm) and axial 6-H (δ = 3.70–3.78 ppm) as well as between the axial 2-H and the benzylic hydrogens (δ = 2.53 ppm and 2.64 ppm), indicating that these hydrogens are on the same side of the molecule.

Finally we studied the Pd^0-catalyzed cyclization of allylic carbonate **9i**, having now three methylenic units between the double bond and the quaternary carbon. Under the above-mentioned conditions, the formation of cyclized products was never observed; however a 32:68 mixture of **10i/11i** was obtained in 30% yield when the reaction was performed at 55 °C (Table 1, Entries 15 and 16). Since we expected that an intermolecular reaction could compete in this case, due to the slower cyclization process, we performed the same reaction under more dilute conditions (Table 1, Entries 17 and 18). When the reaction was performed at 25 °C, the yield of **10i/11i** increased to 41% after 20 h, whereas a 61% yield was obtained by performing the reaction at 55 °C; it is to be noted that the stereoselectivity was not dependent on the temperature or the reaction concentration.

The relative stereochemistry for stereoisomers **10i** and **11i** was mainly based on the NOESY spectrum of compound **10i**. The determination of compound **11i** was difficult, due to the overlapping of the signals of the 2-H and CH_2OH signals (δ = 3.54–3.60 ppm). Fortunately, we observed for compound **10i** a relation between the axial 2-H (δ = 3.44 ppm) and the axial 7-H (δ = 3.95–4.05 ppm) and another relation between the axial 2-H and the benzylic hydrogens (δ = 2.48 ppm and 2.64 ppm), in agreement with the proposed structure for this stereoisomer (Figure 1).

The reaction mechanism for this cyclization is shown in Scheme 5. Bis(hydroxymethyl) carbonate **9** reacted with Pd^0 to give an η^3-allylPd complex. Exchange between the methanoate formed and one of the hydroxy groups gave a new cationic complex. Attack of the alcoholate nucleophile on the η^3-allyl intermediate gave the cyclized compounds **10** and **11**. Since the same stereoselectivity was observed starting from the (*E*) isomer **9a** or the (*Z*) isomer **18**, this implies that the *syn-anti* isomerization of the η^3-allylPd intermediate was very fast compared to the attack of the oxygen nucleophile on this complex.



Scheme 5. Mechanism of the Pd^0-catalyzed cyclization.

The observed stereoselectivities could be explained according to Figure 2. In all cases, the η^3-allylPd cationic complexes exist into two diastereoisomeric forms **I** and **II**. For the cyclization of compounds **9a**–**g** and **18**, these η^3-allylPd cationic complexes adopt the conformations **Ia** and **IIa**, with the more bulky substituent in the "equatorial" position. We assume also that there is a hydrogen bond between the hydroxy group and the alcoholate.[41,42] Conformation **Ia** leads to the stereoisomer **10**, whereas conformation **IIa** leads to the stereoisomer **11**. The η^3-allyl complex **Ia** possesses an unfavorable strain between the allylic moiety and the hydroxymethyl group, whereas such strain does not exist for η^3-allyl complex **IIa**. So the cyclization in these cases proceeds by the more likely conformation **IIA**, giving stereoisomer **11** as the major product.

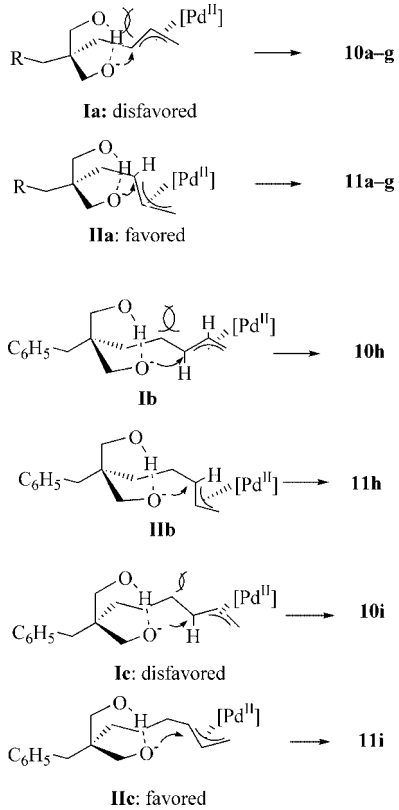


Figure 2. Models for Pd^0-catalyzed cyclization.

In the case of the cyclization of carbonate **9h**, the conformations of the η^3-allylPd cationic complexes are **Ib** and **IIb**. Again, molecular models show unambiguously an unfavorable strain between the allylic moiety and the hydroxymethyl group in conformation **Ib**; however, in conformation **IIb**, there is a 1,3-diaxial repulsive interaction for the η^3-allyl moiety. In this case, the stabilities of the two conformers are probably very close, affording a 1:1 mixture of two stereoisomers **10h** and **11h**.

Finally the cyclization of carbonate **9i** affords predominantly diastereoisomer **11i**. This stereoselectivity could be also related to the two conformations **Ic** and **IIc**; some unfavorable strain between the allylic moiety and the hydroxymethyl group was observed for conformation **Ic**.

Pd^{II}-Catalyzed Cyclization of Bis(hydroxymethyl) Allylic Alcohols 8a–i and 17

We expected that the Pd^{II}-catalyzed cyclization of bis(hydroxymethyl) allylic alcohols **8a**–**i** and **17** would also afford the corresponding oxygen heterocyclic compounds[43] through an intramolecular oxypalladation reaction, according to the recent work of Uenishi et al.[30–33] When bis(hydroxymethyl) allylic alcohol **8a** was treated with 5 mol-% of $PdCl_2(MeCN)_2$ in THF at room temp., stereoisomeric THFs **10a** and **11a** were obtained as a 10:90 mixture in 32% yield, together with dioxabicyclo[2.2.2]octane **21a** in 68% yield (Table 2, Entry 1, Scheme 6). When the reaction was performed in methanol, CH_2Cl_2, acetonitrile, or benzene, a mixture of these three compounds was also obtained (Table 2, Entries 2–5); however, the amount of bicyclic compound **21a** decreased drastically, and the stereoisomeric THFs **10a** and **11b** were obtained as a 1:1 mixture.

Performing the reaction in THF in the presence of Et_3N afforded THFs **10a** and **11a** only as a 1:1 mixture, although the chemical yield decreased to 42% (Table 2, Entry 6). Addition of 1 equiv. of $CuCl_2$ to the reaction gave a 30:70 mixture of THFs **10a** and **11a**, together with dioxabicyclooctane **21a** in 39% yield (Table 2, Entry 7). Finally, with $Pd(OAc)_2$ as the catalyst instead of $PdCl_2(CH_3CN)_2$ gave a very low yield (Table 2, Entry 8).

The Pd^{II}-catalyzed cyclization of (*Z*)-bis(hydroxymethyl) allylic alcohol **17** in THF gave results very similar to those obtained with the (*E*) stereoisomer; dioxabicyclooctane derivative **21a** was obtained in 70% yield, together with a 9:91 mixture of **10a** and **11a** in 27% yield (Table 2, Entry 9).

Table 2. Pd^{II}-catalyzed transformation of allylic alcohols **8a–i** and **17**.[a]

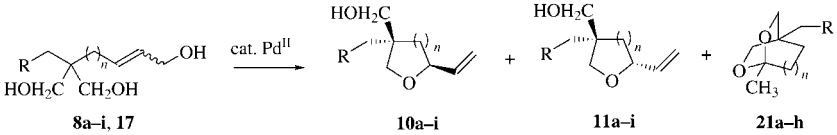
Entry	Alcohol	Solvent	Yield (**10** + **11**) [%][b]	**10/11** [%][c]	Yield **21** [%][b]
1	**8a**	THF	32	10:90	68
2	**8a**	CH_3OH	63	47:53	30
3	**8a**	CH_2Cl_2	83	52:48	14
4	**8a**	CH_3CN	86	54:46	13
5	**8a**	C_6H_6	80	52:48	15
6	**8a**	THF[d]	42	48:52	0
7	**8a**	THF[e]	58	30:70	39
8	**8a**	THF[f]	4	50:50	0
9	**17**	THF	27	9:91	70
10	**8b**	THF	31	9:91	61
11	**8c**	THF	23	9:91	75
12	**8d**	THF	19	0:100	78
13	**8e**	THF	75	20:80	19
14	**8f**	THF	51	27:73	46
15	**8g**	THF	36	7:93	60
16	**8h**	THF	72	57:43	23
17	**8i**	THF	89	56:44	0

[a] [**8**]:[$PdCl_2(CH_3CN)_2$] = 20:1, room temp., 24 h. [b] Yields refer to isolated pure products after column chromatography. [c] Determined by ^1H NMR spectroscopy. [d] NEt_3 (2 equiv./Pd) was added. [e] $CuCl_2$ (1 equiv./**8a**) was added. [f] $Pd(OAc)_2$ was used as a catalyst.

This methodology was also extended to other allylic alcohols. Bis(hydroxymethyl) allylic alcohols **8b**, **8c**, and **8d**, afforded the corresponding dioxabicyclooctanes **21b**, **21c**, and **21d** as the major products, respectively (61%, 75%, and 78% yield, respectively, Table 2, Entries 10–12); THFs **10b**–**c** and **11b**–**c** were obtained in 31% and 23% yields as a 9:91 mixture, while stereoisomer **11d** was exclusively formed in 19% yield starting from allylic alcohol **8d**.

The Pd^{II}-catalyzed reaction of compound **8e** bearing a cinnamyl group as the substituent, gave a quite different result (Table 2, Entry 13); dioxabicyclooctane derivative **21e** was now obtained as the minor compound (19% yield), and a 20:80 mixture of THFs **10e** and **11e** was formed in 75% yield. Bis(hydroxymethyl) allylic alcohol **8f** afforded bicyclic derivative **21f** in 46% yield together with a 27:73 mixture of THFs **10f** and **11f** in 51% yield (Table 2, Entry 14), whereas bicyclic compound **21g** was obtained in 60% yield together with a 7:93 mixture of THFs **10g** and **11g** in 36% yield starting from allylic alcohol **8g** (R = C_6H_{11}, Table 2, Entry 15).

Finally, allylic alcohols **8h** and **8i** were also treated by $PdCl_2(CH_3CN)_2$ in THF. Compound **8h** gave predomi-



a: n = 1, R = C_6H_5; **b**: n = 1, R = 4-$CH_3C_6H_4$; **c**: n = 1, R = 2-$CH_3C_6H_4$; **d**: n = 1, R = 2-$C_{10}H_7$;

e: n = 1, R = (*E*)-C_6H_5CH=CH; **f**: n = 1, R = CH_3; **g**: n = 1, R = C_6H_{11}; **h**: n = 2, R = C_6H_5; **i**: n = 3, R = C_6H_5

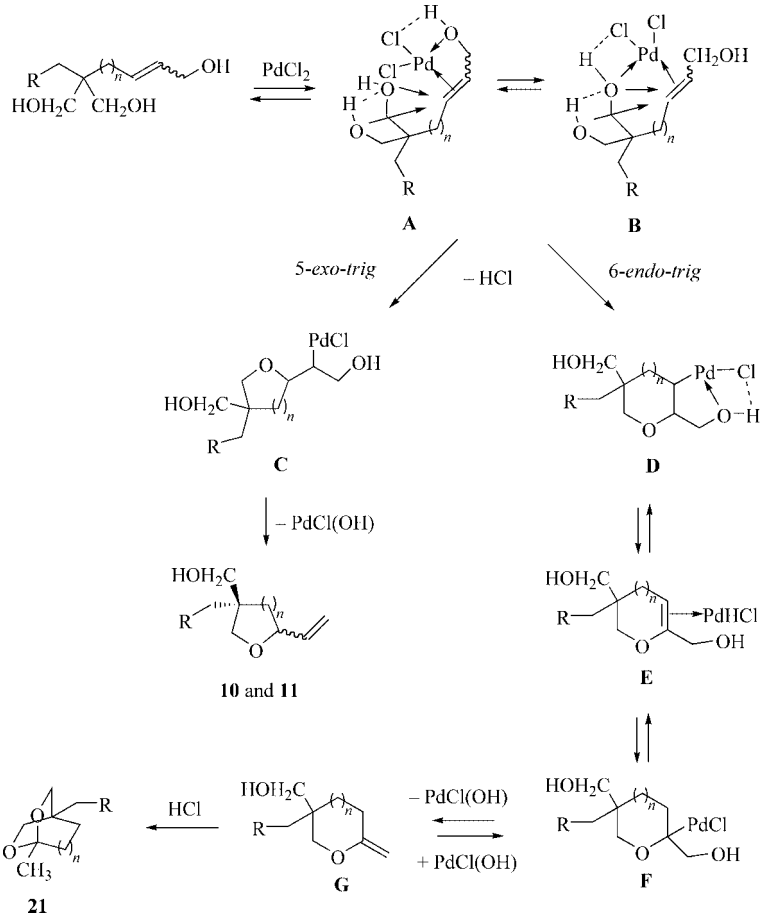
Scheme 6. Pd^{II}-catalyzed cyclization of triols **8a**–**i** and **17**.

nantly a 57:43 mixture of THFs **10h** and **11h** in 72% yield, together with dioxabicyclo derivative **21h** in 23% yield (Table 2, Entry 16). The formation of the dioxabicyclo derivative was never observed in the cyclization of allylic alcohol **8i** (Table 2, Entry 17), and only a 56:44 mixture of THF derivatives **10i** and **11i** was obtained in 89% yield.

The reaction mechanism we proposed is quite similar to the mechanism postulated recently by Uenishi et al.[33] (Scheme 7). The first step is the coordination of $PdCl_2$ to the double bond and to the allylic hydroxy group to give the π complex **A**, which is in equilibrium with the π complex **B** obtained by a simple hydroxy group exchange at Pd. The next step is an intramolecular *syn* attack of this hydroxy group from the same side of the Pd complex[44,45] occurring in a 5-*exo*-*trig* or a 6-*endo*-*trig* fashion to give the σ-Pd complexes **C** and **D**, respectively. A *syn* elimination of PdCl(OH) from intermediate **C** generates the oxygen heterocycles **10** and **11**. On the other hand, a β-hydride elimination from intermediate **D** gives the new π-Pd complex **E**. Subsequent hydropalladation of this intermediate affords the σ-Pd complex **F**; a *syn* elimination of PdCl(OH) affords the oxygen heterocycle **G**, which is readily cyclized to the dioxabicyclo derivative **21** in the presence of a catalytic amount of HCl. It is to be noted that this cyclization was not observed in the presence of Et_3N. Such an intramolecular oxypalladation of hydroxyalkenes leading to dioxabicyclo compounds has already been published.[46–48]

The high stereoselectivities observed in the formation of heterocycles **10** and **11** in the Pd^{II}-catalyzed cyclization of allylic alcohols **8a**–**g** could be explained according to Figure 3. The π complex adopts on of the two conformations **A** or **B**, the bulky substituent being in an equatorial position, if we assume that the hydroxymethyl group is associated with the Pd. Conformation **A** leads to the THF **11**, whereas conformation **B** leads to THF **10**. Since the conformation **B** possess an unfavorable interaction between the double bond and the hydroxymethyl group, the cyclization proceeds through conformation **A** to give THF **11** as the major product. This reaction pathway is in good agreement with the formation of stereoisomer **11d** only when R = β-naphthyl and the increase in the formation of **10f** when R = CH_3.

In the cyclization of allylic alcohol **8h**, the two possible conformations are **C** and **D**, with the bulky benzyl substituent in the equatorial position and avoiding any 1,3-diaxial interaction involving the olefin. Since there is no preferable conformation, the cyclization leads to an equal mixture of tetrahydropyrans **10h** and **11h**. The same scheme could be applied to the cyclization of allylic alcohol **8i**, leading to a mixture of oxygen heterocycles **10i** and **11i**.



Scheme 7. Mechanism of the Pd^{II}-catalyzed cyclization.

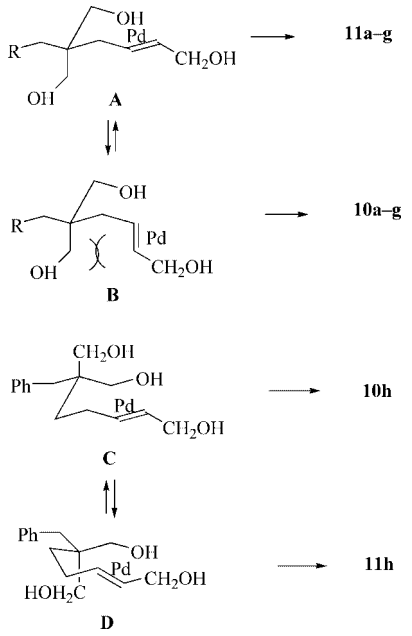


Figure 3. Models for Pd^{II}-catalyzed cyclization.

Pd^0-Catalyzed Asymmetric Cyclization

In the Pd^0-catalyzed cyclization depicted in Scheme 5, the two hydroxymethyl groups are enantiotopic, so we expected that the asymmetric cyclization could occur if the cyclization reaction is performed in the presence of a Pd complex associated with a chiral catalyst.

We first studied the Pd^0-catalyzed cyclization of bis(hydroxymethyl) carbonate **9a** in the presence of (*R*,*R*)-Trost's ligand. When the reaction was performed in THF, we observed the same diastereoselectivity as that obtained previously with dppb as the ligand (Table 3, Entry 1); the major diastereoisomer **11a** was obtained with an enantiomeric ratio (*er*) of 59:41, while the minor diastereoisomer **10a** exhibited an *er* of 43:57. With CH_2Cl_2 as the solvent, the *er* of the minor stereoisomer increased to 64:36, the other enantiomer now being obtained as the major one; under these conditions, the major stereoisomer **11a** was obtained as an essentially racemic mixture (Table 3, Entry 2). No modification was observed when acetic acid was added to the reaction mixture in CH_2Cl_2 (Table 3, Entry 3).[49] The use of (*R*,*S*)-Josiphos as the chiral ligand afforded quite similar diastereoselectivity (**10a/11a** 32:68), although the yield was lower (only 39% after 20 h); the minor isomer was obtained in an *er* of 25:75, while the major one exhibited an *er* of 59:41 (Table 3, Entry 4). Increasing the reaction time to 48 h increased the yield to 82%, with the same diastereo- and enantioselectivities being observed. Performing the reaction at 55 °C gave the cyclized products in 83% yield after 20 h, with a 82:18 diastereoselectivity in favor of stereoisomer **11a**; the minor isomer was obtained in a higher *er* of 15:85, while the major isomer exhibited an *er* of 64:36 (Table 3, Entry 5). The same diastereoselectivities were obtained with (*S*,*S*)-BDPP or (*R*)-PheBox as the ligands (a **10a/11a** of 24:76 and 25:75, respectively); the *er* values of the major isomer **11a** were very low, while those of the minor isomer **10a** were 66:34 and 65:35, respectively (Table 3, Entries 6 and 7).

The Pd^0-catalyzed cyclization of bis(hydroxymethyl) allylic carbonates **9b–d** and **9d** in the presence of Trost's ligand in THF or in CH_2Cl_2 gave the cyclized products **10b–d** and **11b–d** in high yields, stereoisomer **11** being the major one (Table 3, Entries 8–13). In the cyclization of compounds **9b** and **9d**, quite low *er* values were obtained for the two stereoisomers when the reaction was performed in THF (Table 3, Entries 8 and 12); however, when CH_2Cl_2 was used as the solvent, these values were increased to 80:20 and 23:77 for the minor stereoisomers **10b** and **10d**, respec-

Table 3. Asymmetric Pd^0-catalyzed cyclization of some allylic carbonates.[a]

Entry	Carbonate	Ligand	Solvent	Time [h]	Yield (**10** + **11**) [%][b]	**10/11** [%][c]	*er* of **10**[d]	*er* of **11**[d]
1	**9a**	(*R*,*R*)-Trost	THF	1	99	20:80	43:57	59:41
2	**9a**	(*R*,*R*)-Trost	CH_2Cl_2	1.5	96	20:80	64:36	51:49
3	**9a**	(*R*,*R*)-Trost	CH_2Cl_2[e]	1.5	94	23:77	66:34	48:52
4	**9a**	(*R*,*S*)-Josiphos	THF	20 (48)	39 (82)	32:68 (36:64)	25:75	59:41
5[f]	**9a**	(*R*,*S*)-Josiphos	THF	20	83	18:82	15:85	64:36
6	**9a**	(*S*,*S*)-BDPP	THF	20	76	24:76	66:34	41:59
7	**9a**	(*R*)-PheBox	THF	20	50	25:75	65:35	52:48
8	**9b**	(*R*,*R*)-Trost	THF	1	95	17:83	48:52	62:38
9	**9b**	(*R*,*R*)-Trost	CH_2Cl_2	1.5	90	23:77	80:20	48:52
10	**9c**	(*R*,*R*)-Trost	THF	1	92	15:85	42:58	60:40
11	**9c**	(*R*,*R*)-Trost	CH_2Cl_2	1.5	87	25:75	58:42	48:52
12	**9d**	(*R*,*R*)-Trost	THF	1.5	99	13:87	40:60	53:47
13	**9d**	(*R*,*R*)-Trost	CH_2Cl_2	1.5	94	17:83	23:77	47:53
14	**9h**	(*R*,*S*)-Josiphos	THF	48	63	69:31	60:40	34:66
15[f]	**9h**	(*R*,*S*)-Josiphos	THF	20	83	69:31	61:39	35:65
16[g]	**9i**	(*R*,*S*)-Josiphos	THF	20	45	28:72	66:34	33:67

[a] [**9**]:[$Pd_2(dba)_3$]:[ligand] = 40:1:2, room temp., 1 h; (*R*,*R*)-Trost's ligand: (*1R*, *2R*)-1,2-bis[(2′-diphenylphosphanyl)benzoylamino]cyclohexane; (*R*,*S*)-Josiphos: (*R*)-1-{(*S*)-2-diphenylphosphanyl]ferrocenyl}ethyldicyclohexylphosphane; (*S*,*S*)-BDPP: (*2S*,*4S*)-2,4-bis(diphenylphosphanyl)pentane; (*R*)-PheBox: (*R*)-2,2′-Isopropylidenebis(4-phenyl-2-oxazoline). [b] Yields refer to isolated pure products after column chromatography. [c] Determined by ^1H NMR spectroscopy. [d] Enantioselectivity (*er*) was measured by chiral stationary phase HPLC on a Chiral OD-H column; the first value corresponds to the enantiomer being eluted first. [e] Acetic acid (1 equiv./Pd) was added. [f] Reaction performed at 55 °C. [g] 12 mL (6 + 6) of THF was used instead of 6 mL (see the Exp. Section).

tively, while the *er* values of the major stereoisomers **11b** and **11d** were quite low (Table 3, Entries 9 and 13). In the cyclization of allylic carbonate **9c**, bearing a *o*-tolyl substituent, the minor stereoisomer **10c** was obtained with the same *er* but with a reversal of configuration going from THF (42:58) to CH_2Cl_2 (58:42), while the major stereoisomer **11c** was obtained in an *er* of 60:40 in THF (Table 3, Entries 10–11).

Finally the asymmetric cyclization of allylic carbonates **9h** and **9i** was performed in THF in the presence of (*R*,*S*)-Josiphos as the chiral ligand. The cyclization of compound **9h** at room temp. or at 55 °C, afforded a 69:31 mixture of stereoisomers **10h** and **11h**, moderate *er* values for the two stereoisomers **10h** and **11h** being obtained (60:40 and 34:66 for **10h** and **11h**, respectively, Table 3, Entries 14 and 15). Oxepanes **10i** and **11i** were obtained in 45% yield under the same conditions, in a 28:72 ratio, with *er* values of 66:34 and 33:67, respectively, starting from allylic carbonate **9i** (Table 3, Entry 16).

Conclusions

We have described a Pd^0-catalyzed synthesis of 3-alkyl-3-hydroxymethyl-5-vinyltetrahydrofurans in very high yields with good diastereoselectivities starting from 5-alkyl-6-hydroxy-5-(hydroxymethyl)hexenyl methyl carbonates, the major product isomers being those where the vinyl and the alkyl group are on the same side of the heterocycle. The use of chiral ligands in association with Pd afforded the corresponding THF stereoisomers in low to moderate *er* values (up to 80:20). On the other hand, the Pd^{II}-catalyzed cyclisation of 5-alkyl-5-(hydroxymethyl)hex-2-ene-1,6-diol, the precursor of the above mentioned carbonates, afforded a mixture of 3-alkyl-3-hydroxymethyl-5-vinyltetrahydrofurans and 1-methyl-4-alkyl-2,6-dioxobicyclo[2.2.2]-octanes, the latter generally being obtained as the major products.

Experimental Section

General: All commercially available chemical reagents were used without further purification. Technical solvents were distilled by standard literature methods before use.[50] Dimethyl ethylmalonate,[51] dimethyl benzylmalonate,[52] dimethyl (4-methylbenzyl)malonate,[52] dimethyl (2-naphtylmethyl)malonate,[53] dimethyl [(*E*)-3-phenylprop-2-en-1-yl]malonate,[54] dimethyl (cyclohexylmethyl)-malonate,[55] (*Z*)-4-hydroxybut-2-en-1-yl acetate (**1**),[38] (*Z*)-4-{[*tert*-butyl(dimethyl)silyl]oxy}but-2-en-1-yl acetate (**2**),[39] (*E*)-5-chloropent-2-en-1-ol,[56] (*E*)-6-bromohex-2-en-1-ol,[57] and [(4-bromobut-2-yn-1-yl)oxy](*tert*-butyl)dimethylsilane (**12**)[40] were prepared by literature methods. Tin-layer chromatography was performed on aluminum-backed plates Merck silica gel 60 F_{254}. Silica gel 60 (40–63 μm, Merck) was used for column chromatography. Chiral HPLC analyses were performed with a Chiraldex OD-H column (0.46 cm X 25 cm) at 25 °C, flow rate: 0.5 mL/min with *n*-hexane/2-propanol as the eluent. ^1H and ^{13}C NMR spectra were recorded with 300 MHz or 500 MHz spectrometers. Mass spectra were obtained with a Micromass ZABSpecTOF spectrometer.

General Procedures for the Preparation of Malonates 6a–i and 15

Route A: To a solution of unsaturated alcohol **4a**–**c** (10 mmol) in CH_2Cl_2 (50 mL) were successively added at 0 °C, imidazole (34.7 mg, 5 mmol), Et_3N (1.87 mL, 13.4 μmol), and *t*$BuMe_2SiCl$ (2.02 g, 13.4 mmol). The mixture was stirred for 15 h at room temp. Water (5 mL) was added, and the organic phase was separated and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel to give the *O*-silylated dimethyl malonate **6a**, **6b**, or **6d**.

Dimethyl Benzyl{(*E*)-[4-(*tert*-butyldimethylsilyl)oxy]but-2-en-1-yl}-malonate (6a): Colorless oil, 3.53 g, 87% yield. R_f = 0.84 (petroleum ether/ethyl acetate, 3:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, $SiMe_2$), 0.84 (s, 9 H, CMe_3), 2.47 (d, J = 6.2 Hz, 2 H, CH_2-CH=), 3.15 (s, 2 H, CH_2Ph), 3.62 (s, 3 H, OMe), 4.05–4.11 (m, 2 H, CH_2O), 5.50 (dt, J = 15.3, 6.2 Hz, 1 H, -CH=), 5.58 (dt, J = 15.3, 4.3 Hz, 1 H, -CH=), 6.95–7.05 (m, 2 H, H_{arom}), 7.10–7.15 (m, 3 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.8, 18.7, 26.3, 35.3, 38.6, 52.7, 59.6, 63.8, 127.4, 128.7, 130.3, 134.6, 136.3, 171.6 ppm. $C_{22}H_{34}O_5Si$ (406.58): calcd. C 64.99, H 8.43; found C 64.82, H 8.50.

Route B: A solution of $Pd_2(dba)_3$ (13.6 mg, 0.02 mmol) and dppb (17.1 mg, 0.04 mmol) in THF (3 mL) in a Schlenk tube was stirred at room temp. for 30 min. This solution was then added to a mixture of the corresponding alkylated dimethyl malonate (1.1 mmol) and sodium hydride (26.4 mg, 1.1 mmol) in THF (3 mL), followed by a solution of allylic acetate **2** (244.4 mg, 1 mmol) in THF (1 mL). After completion as shown by chromatography, the reaction was quenched with water (20 mL), the organic product was extracted with diethyl ether (100 mL), and the organic layers were dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave a residue that was purified by flash column chromatography on silica gel to give dimethyl malonate **6e**, **6f**, or **6g**.

Dimethyl {(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]but-2-en-1-yl}[(*E*)-3-phenylprop-2-en-1-yl]malonate (6e): Colorless oil, 398 mg, 86% yield. R_f = 0.75 (petroleum ether/ethyl acetate, 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, $SiMe_2$), 0.82 (s, 9 H, CMe_3), 2.61 (d, J = 7.2 Hz, 2 H, CH_2-CH=), 2.71 (d, J = 7.5 Hz, 2 H, CH_2-CH=), 3.66 (s, 6 H, OMe), 4.07 (d, J = 4.5 Hz, 2 H, CH_2O), 5.47 (dt, J = 15.3, 7.2 Hz, 1 H, -CH=), 5.60 (dt, J = 15.3, 4.5 Hz, 1 H, -CH=), 5.97 (dt, J = 15.6, 7.5 Hz, 1 H, -CH=), 6.38 (d, J = 15.6 Hz, 1 H, PhC*H*=), 7.10–7.30 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.8, 18.8, 26.3, 36.0, 36.7, 52.8, 58.5, 63.8, 124.1, 124.3, 126.6, 127.8, 128.9, 134.4, 134.6, 137.5, 171.6 ppm. $C_{24}H_{36}O_5Si$ (432.63): calcd. C 66.63, H 8.39; found C 66.49, H 8.33.

Route C: A mixture of dimethyl malonate **5a**–**c** or **14** (12.5 mmol) and sodium hydride (0.38 g, 16 mmol, 60% in mineral oil) in THF (20 mL) and *N*,*N*-dimethylformamide (5 mL) was stirred at room temp. for 30 min. Benzyl bromide (for substrates **5b**–**c** or **14**) or 1-(bromomethyl)-2-methylbenzene (for substrate **5a**, 18 mmol) was then added, and the mixture was refluxed for 5 h. Hexane (5 mL) and water (30 mL) were added at room temp., and the aqueous phase was separated and extracted with a 1:1 mixture of diethyl ether and hexane (2 × 20 mL). The combined organic phases were dried (Na_2SO_4). Evaporation of the solvents under reduced gave a residue that was purified by flash chromatography on silica gel to give dimethyl malonate **6c**, **6h**, **6i**, or **15**.

Dimethyl {(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]but-2-en-1-yl}(2-methylbenzyl)malonate (6c): Colorless oil, 4.22 g, 82% yield. R_f = 0.65 (petroleum ether/ethyl acetate, 5:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, $SiMe_2$), 0.83 (s, 9 H, CMe_3), 2.23 (s, 3 H, CH_3),

2.58 (d, J = 6.0 Hz, 2 H, CH_2-CH=), 3.25 (s, 2 H, ArCH_2), 3.61 (s, 6 H, OMe), 4.05 (d, J = 4.5 Hz, 2 H, CH_2O), 5.55 (dt, J = 15.4, 4.5 Hz, 1 H, -CH=), 5.60 (dt, J = 15.4, 6.0 Hz, 1 H, -CH=), 6.92–7.08 (m, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.8, 18.7, 20.3, 26.3, 35.1, 36.3, 52.7, 59.8, 63.8, 126.1, 127.2, 130.4, 131.0, 134.4, 135.0, 137.6, 172.1 ppm. $C_{23}H_{36}O_5Si$ (420.61): calcd. C 65.68, H 8.63, found C 65.94, H 8.76.

Typical Procedure for the Synthesis of Diols 7a–i and 16: A solution of *O*-silylated dimethyl malonates **6** or **15** (13 mmol) in diethyl ether (10 mL) was added at 0 °C to a stirred suspension of $LiAlH_4$ (0.43 g, 13 mmol) in diethyl ether (15 mL). The reaction mixture was stirred at room temp. for 30 min and then quenched by the addition of water (1 mL) at 0 °C, followed by aqueous sodium hydroxide (15%, 4 mL). The mixture was extracted with ethyl acetate (3 × 10 mL). The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure to give a residue that was purified by flash column chromatography on silica gel to give diol **7a**–**i** or **16**.

2-Benzyl-2-{(*E*)-4-[(*tert*-butyldimethylsilyl)oxy]but-2-en-1-yl}-propane-1,3-diol (7a): Colorless oil, 3.65 g, 80% yield. R_f = 0.46 (petroleum ether/ethyl acetate, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, $SiMe_2$), 0.84 (s, 9 H, CMe_3), 1.92 (d, J = 7.0 Hz, 2 H, CH_2-CH=), 2.53 (s, 1 H, OH), 2.59 (s, 2 H, CH_2Ph), 3.40–3.55 (m, 4 H, CH_2OH), 4.06 (br. d, J = 4.9 Hz, 2 H, CH_2O), 5.55 (dt, J = 15.3, 4.9 Hz, 1 H, -CH=), 5.70 (dt, J = 15.3, 7.0 Hz, 1 H, -CH=), 7.12–7.19 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.7, 18.8, 26.4, 35.0, 38.0, 43.4, 64.1, 68.2, 126.3, 126.6, 128.5, 128.5, 130.8, 130.9, 133.3, 138.0 ppm. $C_{20}H_{34}O_3Si$ (350.57): calcd. C 68.52, H 9.78; found C 68.63, H 9.65.

Typical Procedure for the Synthesis of Triols 8a–i and 17: A mixture of silylated diol **7** or **16** (4.8 mmol) and $Bu_4NF{\cdot}3H_2O$ (1.5 g, 4.8 mmol) in THF (50 mL) was stirred at room temp. for 15 h. After evaporation of the solvent, diethyl ether (30 mL) was added, and the organic phase was washed with brine (2 × 25 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel to give triol **8a**–**i** or **17**.

(*E*)-5-Benzyl-5-(hydroxymethyl)hex-2-ene-1,6-diol (8a): Colorless oil, 1.11 g, 98% yield. R_f = 0.45 (ethyl acetate/methanol, 25:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.01 (d, J = 6.8 Hz, 2 H, CH_2-CH=), 2.63 (s, 2 H, CH_2Ph), 3.53 (s, 4 H, CH_2OH), 3.69 (s, 3 H, OH), 4.09 (d, J = 5.1 Hz, 2 H, =CHCH_2OH), 5.70 (dt, J = 15.3, 5.1 Hz, 1 H, -CH=), 5.80 (dt, J = 15.3, 6.8 Hz, 1 H, -CH=), 7.19–7.27 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 34.7, 38.0, 43.4, 63.6, 67.0, 126.7, 128.3, 128.5, 128.6, 130.9, 132.7, 137.8 ppm. HRMS (ESI): calcd. for $C_{14}H_{21}O_3$ $[M + H]^+$ 237.1491; found 237.1493.

Typical Procedure for the Synthesis of Allylic Carbonates 9a–i and 18: A solution of triol **8a**–**i** or **17** (4.7 mmol) in CH_2Cl_2 (50 mL) cooled to 0 °C was treated with pyridine (0.4 mL, 9.3 mmol) and methyl chloroformate (0.36 mL, 4.7 mmol). After 2 h at room temp., the reaction mixture was quenched with water (10 mL) and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phases were dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to give allylic carbonate **9a**–**i** or **18**.

(*E*)-5-Benzyl-6-hydroxy-5-(hydroxymethyl)hex-2-en-1-yl Methyl Carbonate (9a): Colorless oil, 926 mg, 67% yield. R_f = 0.48 (ethyl acetate/petroleum ether, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07 (d, J = 7.5 Hz, 2 H, CH_2-CH=), 2.63 (s, 2 H, OH), 2.67 (s, 2 H, PhCH_2), 3.57 (br. s, 4 H, CH_2OH), 3.80 (s, 3 H, CH_3), 4.61 (d, J = 6.4 Hz, 2 H, CH_2OCO_2), 5.69 (dt, J = 15.3, 6.4 Hz, 1 H, -CH=), 5.91 (dt, J = 15.3, 7.5 Hz, 1 H, -CH=), 7.19–7.27 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.1, 38.2, 43.4, 55.2, 67.9, 68.8, 126.7, 127.2, 128.5, 130.8, 132.7, 137.8, 156.1 ppm. $C_{16}H_{22}O_5$ (294.34): calcd. C 65.29, H 7.53; found C 65.47, H 7.72.

Typical Procedure for the Pd^0-Catalyzed Cyclization Reaction: The Pd catalyst was prepared by stirring $Pd_2(dba)_3$ (6.8 mg, 0.01 mmol) and dppb (8.6 mg, 0.02 mmol) or the chiral ligand (0.02 mmol) at room temp. in THF (3 mL) for 30 min. To this solution was added allylic carbonate **9** or **18** (0.8 mmol) dissolved in THF (3 mL). After being stirred for the indicated time, the solvent was evaporated, and the residue was purified by column chromatography on silica gel.

3-Benzyl-3-hydroxymethyl-5-vinyltetrahydrofuran (10a) and (11a): Colorless oil, 160 mg, 90% yield. Mixture of ***rac*-(3*R*,5*S*)-10a** and ***rac*-(3*S*,5*S*)-11a**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10a:** Colorless oil. R_f = 0.32 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48 (dd, J = 13.0, 8.3 Hz, 1 H, CH_2), 1.57 (s, 1 H, OH), 2.07 (dd, J = 13.0, 7.5 Hz, 1 H, CH_2), 2.81 (d, J = 13.4 Hz, 1 H, $C_6H_5CH_2$), 2.92 (d, J = 13.4 Hz, 1 H, $C_6H_5CH_2$), 3.46 (d, J = 10.5 Hz, 1 H, CH_2OH), 3.52 (d, J = 10.5 Hz, 1 H, CH_2OH), 3.67 (d, J = 8.9 Hz, 1 H, CH_2O), 3.83 (d, J = 8.9 Hz, 1 H, CH_2O), 4.42 (ddd, J = 8.3, 7.5, 6.4 Hz, 1 H, CH-CH=), 5.12 (ddd, J = 10.4, 1.1, 1.1 Hz, 1 H, CH=CH_2), 5.27 (ddd, J = 17.0, 1.1, 1.1 Hz, 1 H, CH=CH_2), 5.88 (ddd, J = 17.0, 10.4, 6.4 Hz, 1 H, CH=CH_2), 7.20–7.40 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.2, 40.9, 50.3, 66.9, 75.4, 80.3, 116.0, 126.8, 128.7, 130.3, 130.5, 138.5, 139.2 ppm. $C_{14}H_{18}O_2$ (218.29): calcd. C 77.03, H 8.31; found C 76.78, H 8.22.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (90:10) as the eluent: t_R = 18.7 min and t_R = 22.8 min.

***rac*-(3*S*,5*S*)-(11a):** Colorless oil. R_f = 0.24 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.64 (dd, J = 12.8, 8.8 Hz, 1 H, CH_2), 1.85 (s, 1 H, OH), 1.97 (dd, J = 12.8, 7.0 Hz, 1 H, CH_2), 2.78 (d, J = 13.4 Hz, 1 H, $C_6H_5CH_2$), 2.88 (d, J = 13.4 Hz, 1 H, $C_6H_5CH_2$), 3.48 (s, 2 H, CH_2OH), 3.68 (d, J = 8.9 Hz, 1 H, CH_2O), 3.77 (d, J = 8.9 Hz, 1 H, CH_2O), 4.41 (ddd, J = 8.8, 7.0, 6.6 Hz, 1 H, CH-CH=), 5.10 (ddd, J = 10.4, 1.3, 1.3 Hz, 1 H, CH=CH_2), 5.24 (ddd, J = 17.0, 1.3, 1.3 Hz, 1 H, CH=CH_2), 5.86 (ddd, J = 17.0, 10.4, 6.6 Hz, 1 H, CH=CH_2), 7.15–7.35 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.9, 50.3, 65.5, 75.0, 80.3, 115.7, 126.8, 128.7, 130.3, 130.5, 138.6, 139.5 ppm. HRMS (EI): calcd. for $C_{14}H_{18}O_2$ $[M]^{+\cdot}$ 218.1307; found 218.1305.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (90:10) as the eluent: t_R = 17.2 min and t_R = 18.7 min.

3-Hydroxymethyl-3-(4-methylbenzyl)-5-vinyltetrahydrofuran (10b) and (11b): Colorless oil, 176 mg, 95% yield. Mixture of ***rac*-(3*R*,5*S*)-10b** and ***rac*-(3*S*,5*S*)-11b**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10b:** Colorless oil. R_f = 0.31 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (dd, J = 13.0, 8.3 Hz, 1 H, CH_2), 1.64 (s, 1 H, OH), 2.03 (dd, J = 13.0, 7.5 Hz, 1 H, CH_2), 2.33 (s, 3 H, CH_3), 2.75 (d, J = 13.6 Hz, 1 H, ArCH_2), 2.84 (d, J = 13.6 Hz, 1 H, ArCH_2), 3.47 (br. s, 2 H, CH_2OH), 3.64 (d, J = 9.0 Hz, 1 H, CH_2O), 3.80 (d, J = 9.0 Hz, 1 H, CH_2O), 4.40 (ddd, J = 8.3, 7.5, 6.4 Hz, 1 H, CH-CH=), 5.09 (d, J = 10.4 Hz, 1 H, CH=CH_2), 5.24 (d, J = 17.1 Hz, 1 H, CH=CH_2), 5.86 (ddd, J

= 17.1, 10.4, 6.4 Hz, 1 H, C*H*=CH_2), 7.10 (s, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 39.8, 40.3, 50.0, 66.9, 75.5, 80.4, 116.0, 129.5, 130.4, 135.4, 136.4, 139.2 ppm. $C_{15}H_{20}O_2$ (232.32): calcd. C 77.55, H 8.68; found C 77.41, H 8.93.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (95:5) as the eluent: t_R = 24.7 min and t_R = 33.3 min.

***rac*-(3*S*,5*S*)-11b:** Colorless oil. R_f = 0.23 (petroleum ether/diethyl ether, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.61 (dd, *J* = 12.6, 8.7 Hz, 1 H, CH_2), 1.96 (dd, *J* = 12.6, 6.9 Hz, 1 H, CH_2), 2.02 (br. s, 1 H, OH), 2.32 (s, 3 H, CH_3), 2.73 (d, *J* = 13.5 Hz, 1 H, ArCH_2), 2.83 (d, *J* = 13.5 Hz, 1 H, ArCH_2), 3.46 (s, 2 H, CH_2OH), 3.69 (d, *J* = 8.7 Hz, 1 H, CH_2O), 3.75 (d, *J* = 8.7 Hz, 1 H, CH_2O), 4.41 (ddd, *J* = 8.7, 6.9, 6.6 Hz, 1 H, C*H*-CH=), 5.10 (d, *J* = 10.4 Hz, 1 H, CH=CH_2), 5.22 (d, *J* = 17.0 Hz, 1 H, CH=CH_2), 5.87 (ddd, *J* = 17.0, 10.4, 6.6 Hz, 1 H, C*H*=CH_2), 7.09 (s, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 40.5, 40.9, 50.3, 65.5, 75.0, 80.3, 115.7, 129.4, 130.2, 135.5, 136.3, 139.5 ppm. HRMS (EI): calcd. for $C_{15}H_{20}O_2$ $[M]^{+\cdot}$ 232.1463; found 232.1467.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (95:5) as the eluent: t_R = 23.2 min and t_R = 25.1 min.

3-Hydroxymethyl-3-(2-methylbenzyl)-5-vinyltetrahydrofuran (10c) and (11c): Colorless oil, 175 mg, 94% yield. Mixture of ***rac*-(3*R*,5*S*)-10c** and ***rac*-(3*S*,5*S*)-11c**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10c:** Colorless oil. R_f = 0.27 (petroleum ether/diethyl ether, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.55 (dd, *J* = 12.8, 7.9 Hz, 1 H, CH_2), 1.58 (s, 1 H, OH), 2.03 (dd, *J* = 12.8, 7.7 Hz, 1 H, CH_2), 2.36 (s, 3 H, CH_3), 2.87 (s, 2 H, ArCH_2), 3.48–3.60 (m, 2 H, CH_2OH), 3.60 (d, *J* = 9.0 Hz, 1 H, CH_2O), 3.80 (d, *J* = 9.0 Hz, 1 H, CH_2O), 4.37 (ddd, *J* = 7.9, 7.7, 6.4 Hz, 1 H, C*H*-CH=), 5.09 (dd, *J* = 10.4, 1.1 Hz, 1 H, CH=CH_2), 5.23 (dd, *J* = 17.2, 1.1 Hz, 1 H, CH=CH_2), 5.87 (ddd, *J* = 17.2, 10.4, 6.4 Hz, 1 H, C*H*=CH_2), 7.08–7.20 (m, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 35.9, 40.1, 50.6, 67.6, 74.7, 80.4, 115.9, 126.2, 126.9, 131.1, 131.3, 137.5, 139.3 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}O_2$ $[M + H]^+$ 233.1542; found 233.1545.

***rac*-(3*S*,5*S*)-11c:** Colorless oil. R_f = 0.19 (petroleum ether/diethyl ether, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.61 (dd, *J* = 12.8, 8.7 Hz, 1 H, CH_2), 2.04 (dd, *J* = 12.8, 7.0 Hz, 1 H, CH_2), 2.16 (s, 1 H, OH), 2.33 (s, 3 H, CH_3), 2.81 (d, *J* = 13.9 Hz, 1 H, ArCH_2), 2.84 (d, *J* = 13.9 Hz, 1 H, ArCH_2), 3.54 (s, 2 H, CH_2OH), 3.68 (d, *J* = 8.9 Hz, 1 H, CH_2O), 3.72 (d, *J* = 8.9 Hz, 1 H, CH_2O), 4.42 (ddd, *J* = 8.7, 7.0, 6.6 Hz, 1 H, C*H*-CH=), 5.05 (d, *J* = 10.4 Hz, 1 H, CH=CH_2), 5.20 (d, *J* = 17.1 Hz, 1 H, CH=CH_2), 5.79 (ddd, *J* = 17.1, 10.4, 6.6 Hz, 1 H, C*H*=CH_2), 7.05–7.18 (m, 4 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 36.4, 40.4, 50.8, 66.4, 74.0, 80.1, 115.7, 126.1, 126.9, 131.1, 131.2, 136.9, 137.4, 139.5 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}O_2$ $[M + H]^+$ 233.1542; found 233.1545.

3-Hydroxymethyl-3-(2-naphtylmethyl)-5-vinyltetrahydrofuran (10d) and (11d): Colorless oil, 201 mg, 94% yield. Mixture of ***rac*-(3*R*,5*S*)-10d** and ***rac*-(3*S*,5*S*)-11d**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10d:** Colorless oil. R_f = 0.74 (ethyl acetate/petroleum ether, 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.48 (dd, *J* = 12.8, 8.3 Hz, 1 H, CH_2), 1.57 (s, 1 H, OH), 2.13 (dd, *J* = 12.8, 7.5 Hz, 1 H, CH_2), 2.96 (d, *J* = 13.4 Hz, 1 H, ArCH_2), 3.05 (d, *J* = 13.4 Hz, 1 H, ArCH_2), 3.46–3.55 (m, 2 H, CH_2OH), 3.72 (d, *J* = 8.9 Hz, 1 H, CH_2O), 3.84 (d, *J* = 8.9 Hz, 1 H, CH_2O), 4.44 (ddd, *J* = 8.3, 7.5, 6.4 Hz, 1 H, C*H*-CH=), 5.10 (dd, *J* = 10.4, 1.1 Hz, 1 H, CH=CH_2), 5.25 (dd, *J* = 17.0, 1.1 Hz, 1 H, CH=CH_2), 5.87 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2), 7.30–7.90 (m, 7 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.3, 50.5, 65.6, 75.1, 80.4, 116.1, 125.9, 126.5, 128.0, 128.2, 128.8, 128.9, 132.6, 133.8, 136.23, 139.5 ppm. $C_{18}H_{20}O_2$ (268.35): calcd. C 80.56, H 7.51; found C 80.29, H 7.46.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (98:2) as the eluent: t_R = 42.3 min and t_R = 44.7 min.

***rac*-(3*S*,5*S*)-11d:** Colorless oil. R_f = 0.69 (ethyl acetate/petroleum ether, 2:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.69 (dd, *J* = 12.8, 8.7 Hz, 1 H, CH_2), 1.86 (s, 1 H, OH), 1.98 (dd, *J* = 12.8, 7.1 Hz, 1 H, CH_2), 2.92 (d, *J* = 13.4 Hz, 1 H, ArCH_2), 3.03 (d, *J* = 13.4 Hz, 1 H, ArCH_2), 3.49 (br. s, 2 H, CH_2OH), 3.72 (d, *J* = 8.9 Hz, 1 H, CH_2O), 3.82 (d, *J* = 8.9 Hz, 1 H, CH_2O), 4.41 (ddd, *J* = 8.7, 7.1, 6.4 Hz, 1 H, C*H*-CH=), 5.11 (d, *J* = 10.4 Hz, 1 H, CH=CH_2), 5.24 (d, *J* = 17.0 Hz, 1 H, CH=CH_2), 5.86 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2), 7.20–7.90 (m, 7 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 41.0, 50.5, 65.5, 75.0, 80.3, 115.8, 125.9, 126.5, 128.0, 128.1, 128.2, 128.8, 128.9, 132.6, 133.8, 136.3, 139.5 ppm. HRMS (EI): calcd. for $C_{18}H_{20}O_2$ $[M]^{+\cdot}$ 268.1463; found 268.1463.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (98:2) as the eluent: t_R = 84.6 min and t_R = 88.6 min.

3-[(*E*)-Cinnamyl]-3-hydroxymethyl-5-vinyltetrahydrofuran (10e) and (11e): Colorless oil, 191 mg, 98% yield. Mixture of ***rac*-(3*R*,5*S*)-10e** and of ***rac*-(3*S*,5*S*)-11e**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10e:** Colorless oil. R_f = 0.27 (petroleum ether/diethyl ether, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.53 (dd, *J* = 12.8, 8.3 Hz, 1 H, CH_2), 1.69 (s, 1 H, OH), 2.01 (dd, *J* = 12.8, 7.5 Hz, 1 H, CH_2), 2.40 (ddd, *J* = 13.9, 7.7, 1.1 Hz, 1 H, CH_2-CH=), 2.48 (ddd, *J* = 13.9, 7.7, 1.1 Hz, 1 H, CH_2-CH=), 3.58 (s, 2 H, CH_2OH), 3.59 (d, *J* = 9.0 Hz, 1 H, CH_2O), 3.88 (d, *J* = 9.0 Hz, 1 H, CH_2O), 4.38 (ddd, *J* = 8.3, 7.4, 6.4 Hz, 1 H, C*H*-CH=), 5.11 (ddd, *J* = 10.4, 1.5, 1.5 Hz, 1 H, CH=CH_2), 5.25 (ddd, *J* = 17.1, 1.5, 1.5 Hz, 1 H, CH=CH_2), 5.88 (ddd, *J* = 17.1, 10.4, 6.4 Hz, 1 H, C*H*=CH_2), 6.22 (ddd, *J* = 15.8, 7.5, 7.5 Hz, 1 H, CH_2-C*H*=), 6.50 (d, *J* = 15.8 Hz, 1 H, C_6H_5C*H*=CH), 7.18–7.38 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 38.5, 40.5, 49.5, 67.9, 75.4, 80.5, 116.1, 126.5, 127.4, 127.7, 128.9, 133.5, 137.6, 138.9 ppm. HRMS (ESI): calcd. for $C_{16}H_{21}O_2$ $[M + H]^+$ 245.1542; found 245.1545.

***rac*-(3*S*,5*S*)-11e:** Colorless oil. R_f = 0.18 (petroleum ether/diethyl ether, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.60 (dd, *J* = 12.8, 8.6 Hz, 1 H, CH_2), 1.80 (s, 1 H, OH), 2.08 (dd, *J* = 12.8, 7.0 Hz, 1 H, CH_2), 2.44 (ddd, *J* = 14.1, 7.7, 0.8 Hz, 1 H, CH_2-CH=), 2.58 (ddd, *J* = 14.1, 7.7, 0.8 Hz, 1 H, CH_2-CH=), 3.63 (s, 2 H, CH_2O), 3.76 (s, 2 H, CH_2OH), 4.43 (ddd, *J* = 8.6, 7.0, 6.4 Hz, 1 H, C*H*-CH=), 5.14 (d, *J* = 10.4 Hz, 1 H, CH=CH_2), 5.27 (d, *J* = 17.0 Hz, 1 H, CH=CH_2), 5.90 (ddd, *J* = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2), 6.21 (ddd, *J* = 15.8, 7.5, 7.5 Hz, 1 H, CH_2-C*H*=), 6.50 (d, *J* = 15.8 Hz, 1 H, C_6H_5C*H*=CH), 7.20–7.40 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 39.4, 40.8, 49.7, 67.0, 75.1, 80.5, 115.9, 126.5, 126.7, 127.7, 128.9, 133.4, 137.6, 139.2 ppm. HRMS (EI): calcd. for $C_{16}H_{21}O_2$ $[M]^{+\cdot}$ 244.1463; found 244.1479.

3-Ethyl-3-hydroxymethyl-5-vinyltetrahydrofuran (10f) and (11f): Colorless oil, 113.7 mg, 91% yield. Mixture of ***rac*-(3*R*,5*S*)-10f** and ***rac*-(3*S*,5*S*)-11f**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10f:** Colorless oil. R_f = 0.30 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.5 Hz, 3 H, CH_3), 1.48 (dd, J = 12.6, 8.5 Hz, 1 H, CH_2), 1.54 (q, J = 7.5 Hz, 2 H, CH_3CH_2), 1.62 (s, 1 H, OH), 1.88 (dd, J = 12.6, 7.4 Hz, 1 H, CH_2), 3.46 (d, J = 8.9 Hz, 1 H, CH_2O), 3.54 (s, 2 H, CH_2OH), 3.85 (d, J = 8.9 Hz, 1 H, CH_2O), 4.32 (ddd, J = 8.5, 7.4, 6.4 Hz, 1 H, C*H*-CH=), 5.12 (ddd, J = 10.4, 1.5, 1.1 Hz, 1 H, CH=CH_2), 5.24 (ddd, J = 17.0, 1.5, 1.1 Hz, 1 H, CH=CH_2), 5.88 (ddd, J = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.5, 27.2, 40.5, 49.1, 67.3, 75.7, 80.6, 116.1, 139.1 ppm. HRMS (ESI): calcd. for $C_9H_{17}O_2$ [M + H]$^+$ 157.1229; found 157.1227.

***rac*-(3*S*,5*S*)-11f:** Colorless oil. R_f = 0.25 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.5 Hz, 3 H, CH_3), 1.46 (dd, J = 12.6, 8.5 Hz, 1 H, CH_2), 1.54 (q, J = 7.5 Hz, 2 H, CH_3CH_2), 1.76 (s, 1 H, OH), 1.99 (dd, J = 12.6, 6.8 Hz, 1 H, CH_2), 3.58 (s, 2 H, CH_2OH), 3.61 (d, J = 8.9 Hz, 1 H, CH_2O), 3.71 (d, J = 8.9 Hz, 1 H, CH_2O), 4.39 (ddd, J = 8.5, 6.8, 6.4 Hz, 1 H, C*H*-CH=), 5.09 (ddd, J = 10.4, 1.5, 1.1 Hz, 1 H, CH=CH_2), 5.23 (ddd, J = 17.0, 1.5, 1.1 Hz, 1 H, CH=CH_2), 5.86 (ddd, J = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.6, 27.9, 40.8, 49.4, 66.3, 75.3, 80.5, 115.6, 139.4 ppm. HRMS (ESI): calcd. for $C_9H_{17}O_2$ [M + H]$^+$ 157.1229; found 157.1228.

3-Cyclohexylmethyl-3-hydroxymethyl-5-vinyltetrahydrofuran (10g) and (11g): Colorless oil, 170 mg, 95% yield. Mixture of ***rac*-(3*R*,5*S*)-10g** and ***rac*-(3*S*,5*S*)-11g**, which were separated by column chromatography.

***rac*-(3*R*,5*S*)-10g:** Colorless oil. R_f = 0.37 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82–1.46 (m, 6 H, C_6H_{11}), 1.38 (d, J = 5.5 Hz, 2 H, $CH_2C_6H_{11}$), 1.57 (dd, J = 12.8, 7.9 Hz, 1 H, CH_2), 1.60–1.68 (m, 6 H, C_6H_{11}, OH), 1.90 (dd, J = 12.8, 7.7 Hz, 1 H, CH_2), 3.39 (d, J = 9.0 Hz, 1 H, CH_2O), 3.54 (s, 2 H, CH_2OH), 3.89 (d, J = 9.0 Hz, 1 H, CH_2O), 4.32 (ddd, J = 7.9, 7.7, 6.4 Hz, 1 H, C*H*-CH=), 5.10 (ddd, J = 10.4, 1.3, 1.3 Hz, 1 H, CH=CH_2), 5.24 (ddd, J = 17.0, 1.3, 1.3 Hz, 1 H, CH=CH_2), 5.88 (ddd, J = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.6, 26.8, 34.9, 35.4, 35.5, 41.8, 42.6, 48.8, 67.8, 76.7, 80.6, 116.1, 139.1 ppm. $C_{14}H_{24}O_2$ (224.34): calcd. C 74.95, H 10.78; found C 74.62, H 10.89.

***rac*-(3*S*,5*S*)-11g:** Colorless oil. R_f = 0.27 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80–1.40 (m, 8 H, C_6H_{11}, $CH_2C_6H_{11}$), 1.46 (dd, J = 12.8, 8.9 Hz, 1 H, CH_2), 1.55–1.75 (m, 5 H, C_6H_{11}), 1.96 (s, 1 H, OH), 2.10 (dd, J = 12.8, 6.8 Hz, 1 H, CH_2), 3.55 (d, J = 8.9 Hz, 1 H, CH_2O), 3.58 (s, 2 H, CH_2OH), 3.76 (d, J = 8.9 Hz, 1 H, CH_2O), 4.40 (ddd, J = 8.9, 6.8, 6.4 Hz, 1 H, C*H*-CH=), 5.09 (ddd, J = 10.4, 1.3, 1.3 Hz, 1 H, CH=CH_2), 5.22 (ddd, J = 17.0, 1.3, 1.3 Hz, 1 H, CH=CH_2), 5.84 (ddd, J = 17.0, 10.4, 6.4 Hz, 1 H, C*H*=CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.6, 26.8, 34.8, 35.3, 35.4, 42.3, 43.1, 49.2, 66.5, 76.0, 80.1, 115.5, 139.5 ppm. HRMS (ESI): calcd. for $C_{14}H_{25}O_2$ [M + H]$^+$ 225.1855; found 225.1855.

3-Benzyl-3-hydroxymethyl-6-vinyltetrahydro-2*H*-pyran (10h) and (11h): Colorless oil, 156 mg, 84% yield. Mixture of ***rac*-(3*S*,6*S*)-10h** and ***rac*-(3*R*,6*S*)-11h**, which were separated by column chromatography.

***rac*-(3*S*,6*S*)-10h:** Colorless oil. R_f = 0.55 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.43–1.59 (m, 3 H, CH_2), 1.63–1.72 (m, 1 H, CH_2), 1.84 (s, 1 H, OH), 2.41 (d, J = 13.2 Hz, 1 H, $C_6H_5CH_2$), 2.63 (d, J = 13.2 Hz, 1 H, $C_6H_5CH_2$), 3.31 (d, J = 11.5 Hz, 1 H, CH_2O), 3.50 (d, J = 10.9 Hz, 1 H, CH_2OH), 3.69–3.81 (m, 2 H, CH_2OH, C*H*-CH=), 3.88 (dd, J = 11.5, 2.5 Hz, 1 H, CH_2O), 5.10 (br. d, J = 10.6 Hz, 1 H, CH=CH_2), 5.23 (br. d, J = 17.1 Hz, 1 H, CH=CH_2), 5.84 (ddd, J = 17.1, 10.6, 5.5 Hz, 1 H, C*H*=CH_2), 7.10–7.40 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1, 30.2, 38.2, 41.7, 63.3, 73.2, 78.9, 115.4, 126.7, 128.5, 130.8, 137.5, 139.2 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}O_2$ [M + H]$^+$ 233.1541; found 233.1544.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (95:5) as the eluent: t_R = 28.4 min and t_R = 29.5 min.

***rac*-(3*R*,6*S*)-11h:** Colorless oil. R_f = 0.44 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38–1.48 (m, 1 H, CH_2), 1.53–1.71 (m, 3 H, CH_2, OH), 1.72–1.89 (m, 1 H, CH_2), 2.84 (d, J = 13.4 Hz, 1 H, $C_6H_5CH_2$), 2.98 (d, J = 13.4 Hz, 1 H, $C_6H_5CH_2$), 3.25 (d, J = 11.0 Hz, 1 H, CH_2OH), 3.30 (d, J = 11.0 Hz, 1 H, CH_2OH), 3.36 (d, J = 11.5 Hz, 1 H, CH_2O), 3.78–3.87 (m, 2 H, CH_2O, C*H*-CH=), 5.18 (br. d, J = 10.6 Hz, 1 H, CH=CH_2), 5.32 (br. d, J = 17.3 Hz, 1 H, CH=CH_2), 5.97 (ddd, J = 17.3, 10.6, 5.5 Hz, 1 H, C*H*=CH_2), 7.15–7.35 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.6, 29.1, 36.6, 38.7, 67.4, 73.3, 79.1, 115.6, 126.5, 128.6, 130.9, 138.7, 139.5 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}O_2$ [M + H]$^+$ 233.1541; found 233.1543.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (95:5) as the eluent: t_R = 23.9 min and t_R = 25.4 min.

3-Benzyl-3-hydroxymethyl-7-vinyloxepan (10i) and (11i): Colorless oil, 120 mg, 61% yield. Mixture of ***rac*-(3*R*,7*S*)-10i** and ***rac*-(3*S*,7*S*)-11i**, which were separated by column chromatography.

***rac*-(3*S*,7*S*)-10i:** Colorless oil. R_f = 0.87 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35–1.76 (m, 5 H, CH_2), 1.81–1.97 (m, 1 H, CH_2), 2.28 (s, 1 H, OH), 2.48 (d, J = 13.2 Hz, 1 H, $C_6H_5CH_2$), 2.64 (d, J = 13.2 Hz, 1 H, $C_6H_5CH_2$), 3.40 (d, J = 10.9 Hz, 1 H, CH_2OH), 3.44 (d, J = 12.8 Hz, 1 H, CH_2O), 3.52 (d, J = 10.9 Hz, 1 H, CH_2OH), 3.90 (d, J = 12.8 Hz, 1 H, CH_2O), 3.95–4.05 (m, 1 H, C*H*-CH=), 5.09 (br. d, J = 10.6 Hz, 1 H, CH=CH_2), 5.20 (br. d, J = 17.3 Hz, 1 H, CH=CH_2), 5.85 (ddd, J = 17.3, 10.6, 5.3 Hz, 1 H, C*H*=CH_2), 7.15–7.35 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8, 34.0, 36.9, 40.1, 43.9, 67.9, 74.2, 82.6, 114.6, 126.5, 128.4, 130.9, 138.1, 139.9 ppm. $C_{16}H_{22}O_2$ (246.34): calcd. C 78.01, H 9.00; found C 77.86, H 8.91.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (95:5) as the eluent: t_R = 26.1 min and t_R = 27.6 min.

***rac*-(3*R*,7*S*)-11i:** Colorless oil. R_f = 0.45 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.30–1.95 (m, 7 H, CH_2, OH), 2.50 (d, J = 13.2 Hz, 1 H, $C_6H_5CH_2$), 2.76 (d, J = 13.2 Hz, 1 H, $C_6H_5CH_2$), 3.32 (d, J = 11.0 Hz, 1 H, CH_2OH), 3.54 (d, J = 12.8 Hz, 1 H, CH_2O), 3.56 (d, J = 11.0 Hz, 1 H, CH_2OH), 3.60 (d, J = 12.8 Hz, 1 H, CH_2O), 4.10–4.19 (m, 1 H, C*H*-CH=), 5.10 (br. d, J = 10.6 Hz, 1 H, CH=CH_2), 5.24 (br. d, J = 17.3 Hz, 1 H, CH=CH_2), 5.88 (ddd, J = 17.3, 10.6, 4.7 Hz, 1 H, C*H*=CH_2), 7.15–7.20 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1, 35.3, 36.5, 41.1, 43.9, 65.9, 70.1, 80.0, 114.4, 126.5, 128.4, 131.0, 138.4, 139.8 ppm. $C_{16}H_{22}O_2$ (246.34): calcd. C 78.01, H 9.00; found C 77.96, H 8.95.

The separation of the enantiomers was performed by HPLC with *n*-hexane/2-propanol (95:5) as the eluent: t_R = 22.1 min and t_R = 28.4 min.

Preparation of 3-Benzyl-6-vinyltetrahydro-2*H*-pyran-3-yl]methyl 3,5-Dinitrobenzoates (19) and (20): A solution of compound **10h** or **11h**

(23.2 mg, 0.1 mmol) in pyridine (2 mL), cooled to 0 °C, was treated with 3,5-dinitrobenzoyl chloride (46 mg, 2 mmol). After 12 h at room temp., the reaction mixture was quenched with water (5 mL) and extracted with CH_2Cl_2 (2 × 5 mL). The combined organic phases were dried with Na_2SO_4 and concentrated under reduced pressure to give a residue that was purified by column chromatography on silica gel to give the corresponding dinitrobenzoate **19** or **20**.

***rac*-(3*S*,6*S*)-19:** Colorless solid. M.p. 88–90 °C. 37.5 mg, 88% yield. R_f = 0.83 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40–1.85 (m, 4 H, CH_2), 2.53 (d, J = 13.5 Hz, 1 H, $C_6H_5CH_2$), 2.64 (d, J = 13.5 Hz, 1 H, $C_6H_5CH_2$), 3.41 (d, J = 11.7 Hz, 1 H, CH_2O), 3.70–3.78 (m, 1 H, C*H*-CH=), 3.92 (br. d, J = 11.7 Hz, 1 H, CH_2O), 4.37 (d, J = 11.3 Hz, 1 H, CH_2OCO), 4.43 (d, J = 11.3 Hz, 1 H, CH_2OCO), 5.04 (br. d, J = 10.6 Hz, 1 H, CH=CH_2), 5.16 (br. d, J = 17.3 Hz, 1 H, CH=CH_2), 5.78 (ddd, J = 17.3, 10.7, 5.5 Hz, 1 H, C*H*=CH_2), 6.95–7.20 (m, 5 H, H_{arom}), 8.91 (s, 2 H, H_{arom}), 9.14 (s, 1 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.9, 30.8, 37.2, 43.1, 67.6, 73.2, 78.9, 115.9, 126.9, 128.8, 129.6, 130.4, 138.7, 134.2, 136.6, 149.0, 139.2, 162.7 ppm. HRMS (ESI): calcd. for $C_{22}H_{23}O_7N_2$ [M + H]$^+$ 427.1505; found 427.1507.

***rac*-(3*R*,6*S*)-20:** Colorless oil, 38.3 mg, 90% yield. R_f = 0.83 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.40–1.80 (m, 4 H, CH_2), 2.85 (d, J = 13.7 Hz, 1 H, $C_6H_5CH_2$), 3.04 (d, J = 13.7 Hz, 1 H, $C_6H_5CH_2$), 3.39 (d, J = 11.7 Hz, 1 H, CH_2O), 3.78–3.85 (m, 1 H, C*H*-CH=), 3.98 (br. d, J = 11.7 Hz, 1 H, CH_2O), 4.03 (d, J = 11.4 Hz, 1 H, CH_2OCO), 4.10 (d, J = 11.4 Hz, 1 H, CH_2OCO), 5.15 (br. d, J = 10.6 Hz, 1 H, CH=CH_2), 5.30 (br. d, J = 17.3 Hz, 1 H, CH=CH_2), 5.90 (ddd, J = 17.3, 10.6, 5.5 Hz, 1 H, C*H*=CH_2), 7.09–7.19 (m, 5 H, H_{arom}), 8.93 (s, 2 H, H_{arom}), 9.17 (s, 1 H, H_{arom}) ppm. HRMS (ESI): calcd. for $C_{22}H_{23}O_7N_2$ [M + H]$^+$ 427.1505; found 427.1507.

Typical Procedure for the Pd^{II}-Catalyzed Cyclization Reaction: A solution of $PdCl_2(CH_3CN)_2$ (5.2 mg, 0.02 mmol) in THF (3 mL) was added to a solution of alcohol **8** or **17** (0.4 mmol) in THF (3 mL) at room temp. under an argon atmosphere. The mixture was stirred at room temp. for 24 h. The solvent was evaporated, and the residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate as the eluent to afford compounds **10**, **11**, and **21**.

4-Benzyl-1-methyl-2,6-dioxobicyclo[2.2.2]octane (21a): Colorless solid. M.p. 78–80 °C. 59.3 mg, 68% yield. R_f = 0.52 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.60–1.70 (m, 2 H, CH_2), 1.85–1.96 (m, 2 H, CH_2), 2.45 (s, 2 H, C$H_2C_6H_5$), 3.78 (br. d, J = 8.1 Hz, 2 H, CH_2O), 3.89 (br. d, J = 8.1 Hz, 2 H, CH_2O), 6.97–7.33 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 28.3, 32.2, 33.2, 41.0, 73.3, 95.1, 127.0, 128.7, 130.3, 136.3 ppm. $C_{14}H_{18}O_2$ (218.29): calcd. C 77.03, H 8.31; found C 77.15, H 8.35.

1-Methyl-4-(4-methylbenzyl)-2,6-dioxobicyclo[2.2.2]octane (21b): Colorless solid. M.p. 68–69 °C. 56.7 mg, 61% yield. R_f = 0.73 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.57–1.72 (m, 2 H, CH_2), 1.88–1.97 (m, 2 H, CH_2), 2.34 (s, 3 H, CH_3), 2.42 (s, 2 H, CH_2Ar), 3.78 (br. d, J = 8.1 Hz, 2 H, CH_2O), 3.90 (br. d, J = 8.1 Hz, 2 H, CH_2O), 6.92 (d, J = 7.9 Hz, 2 H, H_{arom}), 7.10 (d, J = 7.9 Hz, 2 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 25.5, 28.2, 32.2, 33.2, 40.5, 73.3, 95.1, 129.3, 130.2 ppm. $C_{15}H_{20}O_2$ (232.32): calcd. C 77.55, H 8.69; found C 77.37, H 8.77.

1-Methyl-4-(4-methylbenzyl)-2,6-dioxobicyclo[2.2.2]octane (21c): Colorless solid. M.p. 46–47 °C. 69.7 mg, 75% yield. R_f = 0.80 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.67–1.75 (m, 2 H, CH_2), 1.88–1.96 (m, 2 H, CH_2), 2.26 (s, 3 H, CH_3), 2.49 (s, 2 H, CH_2Ar), 3.82 (br. d, J = 8.1 Hz, 2 H, CH_2O), 3.93 (br. d, J = 8.1 Hz, 2 H, CH_2O), 6.90–7.12 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 25.5, 28.6, 32.3, 34.4, 37.2, 73.4, 94.8, 126.0, 127.1, 131.1, 131.4, 134.9, 136.9 ppm. $C_{15}H_{20}O_2$ (232.32): calcd. C 77.55, H 8.69; found C 77.39, H 8.84.

1-Methyl-4-naphtylmethyl-2,6-dioxobicyclo[2.2.2]octane (21d): Colorless solid. M.p. 111–112 °C. 81.2 mg, 78% yield. R_f = 0.56 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.67–1.78 (m, 2 H, CH_2), 1.87–1.97 (m, 2 H, CH_2), 2.60 (s, 2 H, CH_2Ar), 3.83 (br. d, J = 8.1 Hz, 2 H, CH_2O), 3.96 (br. d, J = 8.1 Hz, 2 H, CH_2O), 7.10–7.90 (m, 7 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 28.3, 32.2, 33.6, 41.1, 73.4, 95.1, 126.0, 126.6, 127.9, 128.0, 128.2, 128.7, 128.8, 132.6, 133.7, 134.0 ppm. $C_{18}H_{20}O_2$ (268.35): calcd. C 80.56, H 7.53; found C 80.60, H 7.70.

1-Methyl-4-[(*E*)-2-phenylvinyl]-2,6-dioxobicyclo[2.2.2]octane (21e): Colorless oil, 18.5 mg, 19% yield. R_f = 0.58 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (s, 3 H, CH_3), 1.72–1.82 (m, 2 H, CH_2), 1.96–2.04 (m, 2 H, CH_2), 2.07 (d, J = 7.7 Hz, 2 H, CH_2-CH=), 3.85 (br. d, J = 7.2 Hz, 2 H, CH_2O), 3.88 (br. d, J = 7.2 Hz, 2 H, CH_2O), 6.07 (dt, J = 15.6, 7.7 Hz, 1 H, =C*H*-CH_2), 6.40 (d, J = 15.6 Hz, 1 H, C_6H_5CH=), 7.20–7.38 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 28.5, 32.4, 33.2, 37.8, 73.3, 95.1, 124.3, 126.5, 127.8, 129.0, 133.7, 137.4 ppm. HRMS (ESI): calcd. for $C_{16}H_{21}O_2$ [M + H]$^+$ 245.1542; found 245.1543.

4-Ethyl-1-methyl-2,6-dioxobicyclo[2.2.2]octane (21f): Colorless oil, 28.7 mg, 46% yield. R_f = 0.78 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (t, J = 7.9 Hz, 3 H, CH_3), 1.17 (q, J = 7.9 Hz, 2 H, CH_2CH_3), 1.28 (s, 3 H, CH_3), 1.62–1.70 (m, 2 H, CH_2), 1.94–2.00 (m, 2 H, CH_2), 3.77 (br. d, J = 9.6 Hz, 2 H, CH_2O), 3.79 (br. d, J = 9.6 Hz, 2 H, CH_2O) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.9, 25.5, 26.6, 27.7, 32.3, 32.3, 73.42, 94.7 ppm. HRMS (ESI): calcd. for $C_9H_{15}O_2$ [M – H]$^+$ 155.1072; found 155.1075.

4-Cyclohexylmethyl-1-methyl-2,6-dioxobicyclo[2.2.2]octane (21g): Colorless oil, 53.8 mg, 60% yield. R_f = 0.85 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82–1.35 (m, 6 H, C_6H_{11}), 0.98 (d, J = 5.5 Hz, 2 H, $C_6H_{11}CH_2$), 1.27 (s, 3 H, CH_3), 1.54–1.75 (m, 7 H, CH_2, C_6H_{11}), 1.93–2.02 (m, 2 H, CH_2), 3.77–3.85 (m, 4 H, CH_2O) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.5, 26.4, 28.7, 32.4, 32.7, 33.3, 35.8, 42.1, 73.7, 94.7 ppm. HRMS (ESI): calcd. for $C_{14}H_{25}O_2$ [M + H]$^+$ 225.1855; found 225.1853.

1-Benzyl-5-methyl-6,9-dioxabicyclo[3.2.1]nonane (21h): Colorless solid. M.p. 59–61 °C. 21.3 mg, 23% yield. R_f = 0.82 (petroleum ether/diethyl ether, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (s, 3 H, CH_3), 1.48–1.90 (m, 6 H, CH_2), 2.45 (s, 2 H, C$H_2C_6H_5$), 3.77 (br. d, J = 8.1 Hz, 2 H, CH_2O), 3.89 (br. d, J = 8.1 Hz, 2 H, CH_2O), 6.95–7.30 (m, 5 H, H_{arom}) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1, 28.1, 29.9, 31.7, 33.4, 41.0, 73.2, 96.8, 126.9, 128.6, 130.3, 136.4 ppm. HRMS (ESI): calcd. for $C_{15}H_{21}O_2$ [M + H]$^+$ 233.1542; found 233.1542.

Supporting Information (see also the footnote on the first page of this article): Preparation and spectroscopic data for compounds **3a**–**b**, **4a**–**c**, **5a**–**c**, **13**, and **14**. Spectroscopic data for compounds **6b**, **6d**, **6f**–**i**, **7b**–**i**, **8b**–**i**, **9b**–**i**, and **15**–**18**. Copies of ^{1}H spectra for compounds **10a**–**i** and **11a**–**i**, ^{1}H and ^{13}C spectra for compounds **21a**–**h**, and NOESY 1D and 2D for compounds **10a**, **11a**, **10i**, **11i**, **19**, and **20**.

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[1] J. J. Li, G. W. Gribble, *Palladium in Heterocyclic Chemistry*, Pergamon, New York, **2000**.
[2] I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127–2198.
[3] J. Muzart, *Tetrahedron* **2005**, *61*, 5955–6008.
[4] C. Hyland, *Tetrahedron* **2005**, *61*, 3457–3471.
[5] G. Zeni, R. Larock, *Chem. Rev.* **2004**, *104*, 2285–2309.
[6] T. Osokawa, S.-I. Murahashi in *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E.-i. Negishi), John Wiley & Sons, New York, **2002**, vol. 2, pp. 2169–2192.
[7] S. A. Stanton, S. W. Felman, C. S. Parkhurst, S. A. Godleski, *J. Am. Chem. Soc.* **1983**, *105*, 1964–1969.
[8] B. M. Trost, A. Tenaglia, *Tetrahedron Lett.* **1988**, *29*, 2927–2930.
[9] A. B. Smith III, M. Ohta, W. M. Clark, J. W. Leahy, *Tetrahedron Lett.* **1993**, *34*, 3033–3036.
[10] E. Keinan, K. K. Seth, R. Lamed, *J. Am. Chem. Soc.* **1986**, *109*, 3474–3480.
[11] M. J. Zacuto, J. L. Leighton, *Org. Lett.* **2005**, *7*, 5525–5527.
[12] G. Stork, J. M. Poirier, *J. Am. Chem. Soc.* **1983**, *105*, 1073–1074.
[13] C. Fournier-Nguefack, P. Lhoste, D. Sinou, *Tetrahedron* **1997**, *53*, 4353–4362.
[14] C. Fournier-Nguefack, P. Lhoste, D. Sinou, *J. Chem. Res.* **1998**, *105*, 0610–0618.
[15] M. Massacret, P. Lhoste, R. Lakhmiri, T. Parella, D. Sinou, *Eur. J. Org. Chem.* **1999**, 2665–2674.
[16] E. C. Hansen, D. Lee, *Tetrahedron Lett.* **2004**, *45*, 7151–7155.
[17] T. Suzuki, O. Sato, M. Hirama, *Tetrahedron Lett.* **1990**, *31*, 4747–4750.
[18] J. E. Harvey, S. A. Raw, R. J. K. Taylor, *Org. Lett.* **2004**, *6*, 2611–2614.
[19] I. Macsari, J. K. Szabo, *Chem. Eur. J.* **2000**, *7*, 4097–4106.
[20] M. Massacret, C. Goux, P. Lhoste, D. Sinou, *Tetrahedron Lett.* **1994**, *35*, 6093–6096.
[21] J. F. Labrosse, C. Poncet, P. Lhoste, D. Sinou, *Tetrahedron: Asymmetry* **1999**, *10*, 1069–1078.
[22] B. S. Lucas, S. D. Burke, *Org. Lett.* **2003**, *5*, 3915–3918.
[23] L. Jiang, S. D. Burke, *Org. Lett.* **2002**, *4*, 3411–3414.
[24] S. D. Burke, L. Jiang, *Org. Lett.* **2001**, *3*, 1953–1955.
[25] B. M. Trost, H. C. Shen, L. Dong, J.-P. Surivet, C. Sylvain, *J. Am. Chem. Soc.* **2004**, *126*, 11966–11983.
[26] F. M. Semmelhack, W. R. Epa, A. W.-H. Cheung, Y. Gu, C. Kim, N. Zhang, W. Lew, *J. Am. Chem. Soc.* **1994**, *116*, 7455–7456.
[27] M. Rönn, J.-E. Bäckvall, P. G. Anderson, *Tetrahedron Lett.* **1995**, *36*, 7749–7752.
[28] G. M. V. Sharma, A. S. Chander, K. Krishnudu, P. R. Krishna, *Tetrahedron Lett.* **1998**, *39*, 6957–6960.
[29] T. Hosakawa, M. Hirata, S.-I. Murahashi, A. Sonoda, *Tetrahedron Lett.* **1976**, *17*, 1821–1824.
[30] J. Uenischi, M. Ohmi, A. Ueda, *Tetrahedron: Asymmetry* **2005**, *16*, 1299–1303.
[31] J. Uenischi, M. Ohmi, *Angew. Chem. Int. Ed.* **2005**, *44*, 2756–2760.
[32] J. Uenischi, M. Ohmi, A. Ueda, *Tetrahedron Lett.* **2005**, *16*, 1299–1303.
[33] N. Kawai, J.-M. Lagrange, M. Ohmi, J. Uenischi, *J. Org. Chem.* **2006**, *71*, 4530–4537.
[34] M. Miyazawa, Y. Hirose, M. Narantsetseg, H. Yokoyama, S. Yamaguchi, Y. Hirai, *Tetrahedron Lett.* **2004**, *45*, 2883–2886.
[35] M. A. Arai, M. Kuraishi, T. Arai, H. Sasai, *J. Am. Chem. Soc.* **2001**, *123*, 2907–2908.
[36] R. M. Trend, Y. K. Ramtohul, B. M. Stoltz, *J. Am. Chem. Soc.* **2005**, *127*, 17778–17788.
[37] Y. Uozumi, H. Kyota, K. Kato, M. Ogasawara, T. Hayashi, *J. Org. Chem.* **1999**, *64*, 1620–1625.
[38] J. P. Genêt, S. Juge, S. Achi, S. Mallart, J. Ruiz Montes, G. Levif, *Tetrahedron* **1988**, *44*, 5263–5275.
[39] G. D. K. Kumar, S. Baskaran, *J. Org. Chem.* **2005**, *70*, 4520–4523.
[40] N. E. Schore, S. D. Najdi, *J. Org. Chem.* **1987**, *52*, 5296–5298.
[41] G. R. Cook, M. Saraswathiamma, *Tetrahedron Lett.* **2005**, *46*, 6491–6494.
[42] G. R. Cook, H. Yu, S. Sankaranarayanan, P. S. Shanker, *J. Am. Chem. Soc.* **2003**, *125*, 5115–5120.
[43] A. Zawisza, D. Sinou, *Tetrahedron Lett.* **2006**, *47*, 3271–3274.
[44] T. Hayashi, K. Yamasaki, M. Mimura, Y. Uosumi, *J. Am. Chem. Soc.* **2004**, *126*, 3036–3037.
[45] R. M. Trend, Y. K. Ramtohul, E. M. Ferreira, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2003**, *42*, 2892–2895.
[46] N. T. Byrom, R. Grigg, B. Kongkathip, *J. Chem. Soc., Chem. Commun.* **1976**, 216–217.
[47] N. T. Byrom, R. Grigg, B. Kongkathip, G. Reimer, A. R. Wade, *J. Chem. Soc., Perkin Trans. 1* **1984**, 1643–1653.
[48] B. Kongkathip, N. Kongkathip, *Tetrahedron Lett.* **1984**, *25*, 2175–2176.
[49] B. M. Trost, H. C. Shen, L. Dong, J.-P. Surivet, C. Sylvain, *J. Am. Chem. Soc.* **2004**, *126*, 11966–11983.
[50] D. D. Perrin, W. L. F. Armarego, *Purification of Laboratory Chemicals*, 3rd ed., Pergamon Press Ltd., Oxford, **1988**.
[51] A. Rahman, J. A. Beisler, J. Harley-Mason, *Tetrahedron* **1980**, *36*, 1063–1070.
[52] H. Ledon, G. Linstrumelle, S. Julia, *Bull. Soc. Chim. Fr.* **1973**, 2065–2071.
[53] J.-Y. Legros, J.-C. Fiaud, *Tetrahedron Lett.* **1992**, *33*, 2509–2510.
[54] S. Ma, B. Xu, B. Ni, *J. Org. Chem.* **2000**, *65*, 8532–8543.
[55] B. Giese, S. Lachhein, *Chem. Ber.* **1985**, *118*, 1616–1620.
[56] M. Nagao, N. Sato, T. Akashi, T. Yoshida, *J. Am. Chem. Soc.* **1966**, *88*, 3447–3449.
[57] J. A. Hunt, W. R. Roush, *J. Org. Chem.* **1997**, *62*, 1112–1124.

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