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Domino reaction: Pd(II)-catalyzed cyclization of unsaturated polyols and cross-coupling

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ABSTRACT

The Pd-catalyzed cyclization and cross-coupling of hydroxylated alkenes in domino reactions are described. The alkenols undergo Pd-catalyzed cyclization and subsequent cross-coupling reactions with aryl bromides to afford (poly)hydroxylated tetrahydrofuran derivatives. The relationship between the stereoselectivity of the transformation and the steric and/or electronic effects of the substrates has also been studied. The diastereoselectivity of the cyclization of γ-hydroxyalkenes **1**, **4**–**6** is influenced by the allylic hydroxyl functionality in favor of 2,3-*cis* stereoselectivity. Substitution at the C-1 carbon in alkenitols **7** and **8** ensured the formation of products with 2,5-*trans* diastereoselectivity (up to >19:1), independent of additional substituents.

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1. Introduction

The palladium(II)-catalyzed reactions of unsaturated polyols such as oxycarbonylations[1] or bicyclizations[2] are powerful stereoselective methods for the preparation of heterocyclic structures that are present in many natural or biologically attractive compounds.[3] The key intermediate of these transformations is an alkyl-σ-Pd(II) complex **A**, which is trapped by carbon monoxide and/or by cyclization with the help of a second hydroxyl function specifically placed in the substrate to give bicyclic products **B** and **C** (Scheme 1). As a logical consequence of that, the idea of trapping intermediate **A** with other nucleophilic species to obtain oxa/azaheterocyclic compounds **D** linked with various substituents was raised.

In 1993, Semmelhack[4] reported the trapping of an organo-Pd(II) intermediate by alkenes in a chain extension by vinylation and found out a suitable and efficient system for the reoxidation of the excluded Pd(0). However, this process was limited to substrates which could not undergo β-hydride elimination from an organo-Pd(II) intermediate after cyclization. Later Tietze et al.[5] described the enantioselective domino Wacker–Heck reaction, which was employed as the key step in the enantioselective total synthesis of vitamin E[5a,b] and 4-dehydroxydiversonol.[5c] Wolfe[6] et al. developed a stereoselective method for the synthesis of saturated heterocycles via a Pd-catalyzed carboetherification[7] and carboamination[8] reaction between aryl or alkenyl bromides and γ-hydroxy or γ-aminoalkenes under strongly basic conditions in the presence of a phosphine ligand. In contrast to the related Pd(II)-catalyzed alkoxy-carbonylations, these reactions do not proceed through a Wacker-type mechanism,[7a] but likely involve a rare *syn*-insertion of an alkene into the Pd-O/N bond of a palladium(aryl)(alkoxide)/(amide) intermediate followed by C–C bond-forming reductive elimination and thus, have no previously mentioned limitations on substrates.

Herein, we report a study of domino Wacker-cross coupling reactions of hydroxylated alkenes and their applicability in the stereoselective synthesis of (poly)hydroxylated tetrahydrofurans.

2. Results and discussion

Our initial idea was to integrate an intramolecular Wacker-type cyclization of unsaturated polyols into the cascade with a cross-coupling reaction. This transformation would present a method for the stereoselective installation of an aromatic moiety into saturated heterocyclic skeletons, having a number of potential applications toward the synthesis of many natural products with an incorporated (poly)hydroxylated tetrahydrofuran ring.

The trapping of the cyclic σ-alkylpalladium intermediate **A** by organometallics or alkenes could allow the introduction of an additional *C*-group onto the Pd(II)-complex. We started our investigation with the premise that the coordination of Pd(II) with the allylic hydroxyl group of the substrate (Scheme 2) might ensure the *trans*-arrangement of the β-hydrogen **E** and thus prevent a

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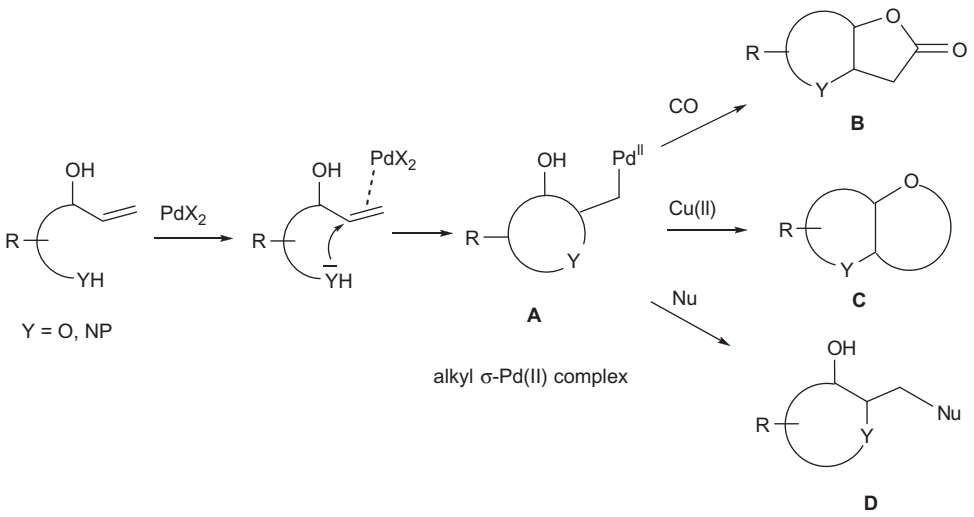


Scheme 1.

competitive β-hydride elimination **F**. The hydroxyl group can also serve as a directing group and due to the potential chelation with palladium could affect the diastereoselectivity as was observed in similar alkoxycarbonylation reactions where the diastereoselectivity was dependent on the participation of allylic hydroxyl group in the process.[9]

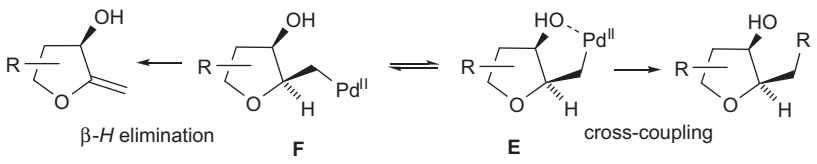
In order to study the domino reactions, the alkenediols **1**–**5** and alkenetriols **6**–**8** were prepared[10] (Fig. 1). The potential complexation of the α-hydroxyl group with palladium and its influence on the course of the reaction and diastereoselectivity were of particular interest. Therefore, the first experiments were carried out with substrates **1**–**3**, which contained a free α-hydroxyl group as a directing neighboring group under the standard reaction conditions for a Wacker-type cyclization.[11] The reactions were accomplished with a Pd(II) salt as a catalyst in AcOH with AcONa and $CuCl_2$ in the presence of organometallic compounds or alkenes with electron withdrawing substituents as coupling partners. Next, we explored the transformation in a Pd(0)–Pd(II) redox system generating a PdArX catalyst from Pd(0)-complexes and aryl halides in situ. However, all of these reaction conditions and modifications of redox system (benzoquinone, O_2), solvents (THF, CH_3CN, CH_2Cl_2, ionic liquids) and temperature did not provide the required tetrahydrofurans and instead gave complex mixtures of β-*H* elimination and consequential products.

The desired products were only observed in the case of substrate **3** by adoption of Semmelhack's conditions[4] (Scheme 3). Product **9** was obtained as a mixture of stereoisomers and product **10** was obtained as a single diastereomer. The structure of bicycle **10** was proven by X-ray analysis[12] (Fig. 2).

A stereoselective synthesis of saturated heterocycles *via* Pd-catalyzed carboetherification[6,7] was recently published. The scope, limitations, and stereoselectivity of this transformation were tested on a wide range of alkyl and aryl substituted γ-hydroxy alkenes. We decided to adopt the described conditions and examine the transformation of model substrates **1**–**8** with aryl bromides (Table 1 and Fig. 3).

We were especially interested in the compatibility of the hydroxyl function with the basic reaction conditions. The first experiments were carried out with substrates **1**–**3** to examine the effect of the possible complexation of an allylic alkoxide and palladium. The desired product **12** was obtained only in the case of substrate **1**, but in low yield (15%) and very poor diastereoselectivity with a slight preference for the *cis*-stereoisomer (1.2:1, entry 1). Substrates **2** and **3** underwent oxidation and did not afford the tetrahydrofuran products (entries 2 and 3). For the successful realization of the desired transformation, the protection of the α-hydroxy group appeared to be crucial. We chose *tert*-butyldimethylsilyl as the protecting group because of its stability under basic conditions. The reactions of partially silyl-protected diols **4** and **5** proceeded in moderate yields (31–52%) and diastereoselectivity (2.3–2.6:1) favoring the *cis*-diastereomer (entries 5, 6, 8 and 9). The relative configuration of *cis*-**15** was confirmed by X-ray analysis[14] after TBS-deprotection (Fig. 4). It is noteworthy that in the presence of the dppb ligand the diastereoselectivity was worse (1:1.2) and opposite to the reactions where dpe-phos and xant-phos ligands were used (entries 4 and 7).

In continuation of our efforts to apply this reaction in the synthesis of target (poly)hydroxylated tetrahydrofurans, we explored the transformation with enantiomerically pure substrates. The transformations of the known triol[10d] **6** with different aryl bromides (entries 10–12) proceeded in a similar manner with good yields (66–72%) albeit with moderate diastereoselectivity (2.3–3:1) in favor of the 2,3-*cis*-stereoisomers. While the reactions of **6** with the electron-neutral and electron-rich aryl bromides (entries 10 and 11) gave Heck products **23** and **24** (Fig. 5) as by-products (<15%), the reaction with an electron-deficient aryl bromide (entry 12) was slower providing **19** as the sole product with slightly higher diastereoselectivity (3:1).



Scheme 2.

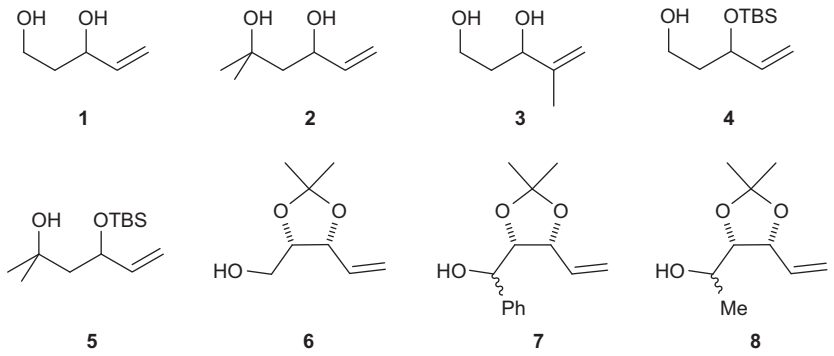
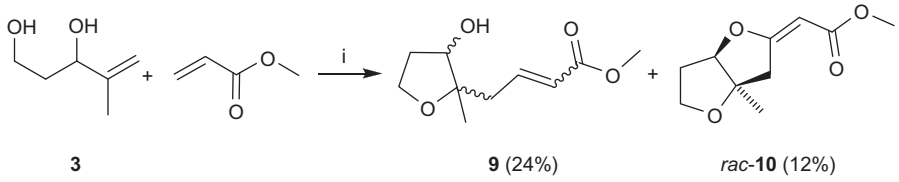


Figure 1. Substrates **1**–**8**.



Scheme 3. Reagents and conditions: (i) methyl acrylate (5 equiv), $Pd(OAc)_2$ (0.1 equiv), CuCl (1 equiv), O_2, DMF (4 mL/mmol **3**), rt, 56 h.

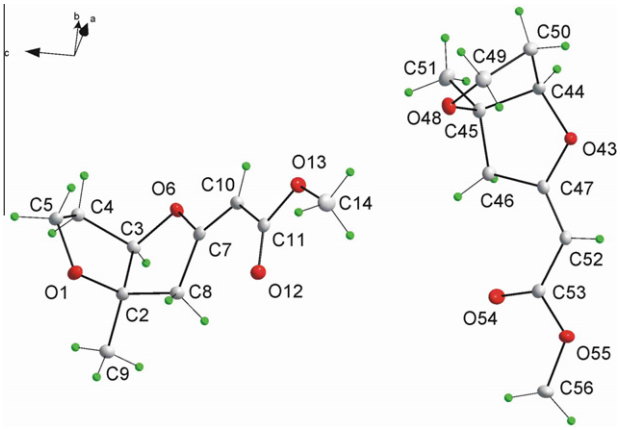


Figure 2. An ORTEP[12] view of the crystal and molecular structure of compound **10**.

The stereoselectivity observed is in contrast to the study published in the literature,[8] where the transformations of pent-4-en-1-ol derivatives bearing an alkyl or aryl substituent at the C3-position afforded the 2,3-*trans*-isomers with fair to excellent diastereoselectivity (1.3–20:1). The yield and the stereoselectivity were dependent on the size of the alkyl or aryl substituent (Scheme 4).[7]

A possible explanation for the opposite stereochemical outcome and lower diastereoselectivity of these transformations of model substrates **1**, **4**–**6** (Scheme 5) could be due to the duality of the reaction pathway as shown in Scheme 6. The *cis*-preference in 5-*exo*-trig cyclizations initiated by an electrophile is directed by an allylic O-function usually with excellent diastereoselectivity (>20:1).[15] The electrophilic attack is preferred on the OH-in-plane conformer **G** (Chamberlein's model of TS) from the face of the π bond *syn* to the allylic hydrogen providing the *cis*-diastereomer.[15c,d] On the other hand, the simultaneous insertion of the alkene into the Pd-O bond on conformer **H** (Wolfe's model of TS) as the *trans*-diastereomer formation determining step is considered to diminish the expected high *cis*-stereoselectivity in our experiments.

In order to enhance the diastereoselectivity of the cyclization, the effect of the substitution at C-1 of alkenol **6** was examined. Triols **7**[11e] and **8**[11f] were synthesized by Swern oxidation of **6** followed by the addition of Grignard reagents to pentenal **26**[11e,f] (Scheme 7). The inseparable mixture of alcohols *syn*-**7**/*anti*-**7** in a ratio of 5:2. and *anti*-**8**/*syn*-**8** in a ratio of 2:3 were obtained, respectively.

The diastereomeric mixtures **7** and **8** were then subjected to a domino process with 2-naphthyl bromide (Scheme 8) providing the desired tetrahydrofurans in moderate to good yields with excellent diastereocontrol (>19:1).

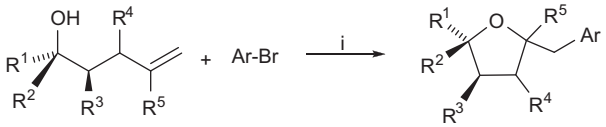
Only the 2,5-*trans* diastereomers (2,3-*trans,* 2,5-*trans* **20a**, **21a**, and 2,3-*cis*, 2,5-*trans* **20b**, **21b**), were identified in the reaction mixtures. The formation of the 2,5-*cis* diastereomers was not observed. The abundance of stereomers **20a**, **20b** and **21a**, **21b** depended on the composition of the starting diastereomeric mixtures of **7** and **8**. The relative configuration of the tetrahydrofuran derivatives **20** and **21** was determined by ^{1}H NMR and NOE experiments. The structure of diastereomer **21b** was confirmed by X-ray analysis[14] (Fig. 6).

Apparently, a substituent at C-1 ensured high 2,5-*trans*- diatereoselectivity for the cyclization (>19:1). Additional ether substituents at C-2 and C-3 in **7** and **8** did not influence the stereochemical course of the transformation. It seems that the stereoselective formation of 2,3,4,5-tetrasubstituted tetrahydrofurans is not effected by the allylic OR group and thus is governed by substitution at the C-1 carbon. The origin of the high diastereoselectivity is rationalized by the energy difference between the transition states of the insertion of an alkene into Pd-O bond (Scheme 9).

3. Conclusion

In conclusion, we have investigated the possibility to utilize the alkyl-σ-Pd(II) intermediate in domino Wacker-type cyclization and *cross-coupling* reactions of hydroxylated alkenes with participation of a neighboring group. Chelation of the palladium with hydroxyl group at the allylic position under the reaction conditions examined appeared to be insufficient to avoid competing β-*H*-elimination. The transformation proceeds toward the desired prod-

Table 1
Domino Pd(II)-catalyzed cyclization/cross-coupling reactions



Entry	Substrate	Ar-Br	Ligand[13]	Time	Product (yield[a]%)	dr (*cis*/*trans*)
1	**1**	2-BrNaph	dpe-phos	8 h	**12** (15)	1.2:1
2	**2**	2-BrNaph	dpe-phos	1 d	**13** (0)	—
3	**3**	2-BrNaph	dpe-phos	30 h	**14** (0)	—
4	**4**	2-BrNaph	dppb	1 d	**15** (32)	1:1.2[g]
5	**4**	2-BrNaph	xant-phos	2 h	**15** (31)	2.3:1[g]
6	**4**	2-BrNaph	dpe-phos	4 h	**15** (52)	2.6:1[g]
7	**5**	2-BrNaph	dppb	1 d	**16** (36)	1:1.2[g]
8	**5**	2-BrNaph	xant-phos	3 h	**16** (39[b,c])	1.2:1[g]
9	**5**	2-BrNaph	dpe-phos	8 h	**16** (48[d])	2:1[g]
10	**6**	2-BrNaph	dpe-phos	2 h	**17** (72[e])	2.5:1[f]
11	**6**	4-BrC_6H_4OMe	dpe-phos	2 h	**18** (66[e])	2.3:1[f]
12	**6**	4-BrC_6H_4CN	dpe-phos	8 h	**19** (72)	3:1[f]
13	*syn*-**7**/*anti*-**7**	2-BrNaph	dpe-phos	3 h	**20** (70)	>1:19[f]
14	*syn*-**8**/*anti*-**8**	2-BrNaph	dpe-phos	3 h	**21** (46)[e]	>1:19[f]

Reaction conditions: (i) Ar-Br (1.5–2 equiv), ^{t}BuONa (1.5–2 equiv), Pd(dba)$_2$ (10 mol %), ligand (12 mol %), THF (2 mL/mmol Ar-Br), 65 °C. Conversions were complete, except in the entries marked.

[a] Yield of isolated product after column chromatography on SiO_2.
[b] Heck product was isolated (<10%).
[c] 82% conversion.
[d] 95% conversion.
[e] Heck product was isolated (<15%).
[f] Dr was determined by ^{1}H NMR of crude product.
[g] Dr and conversions were determined by GC of crude product.

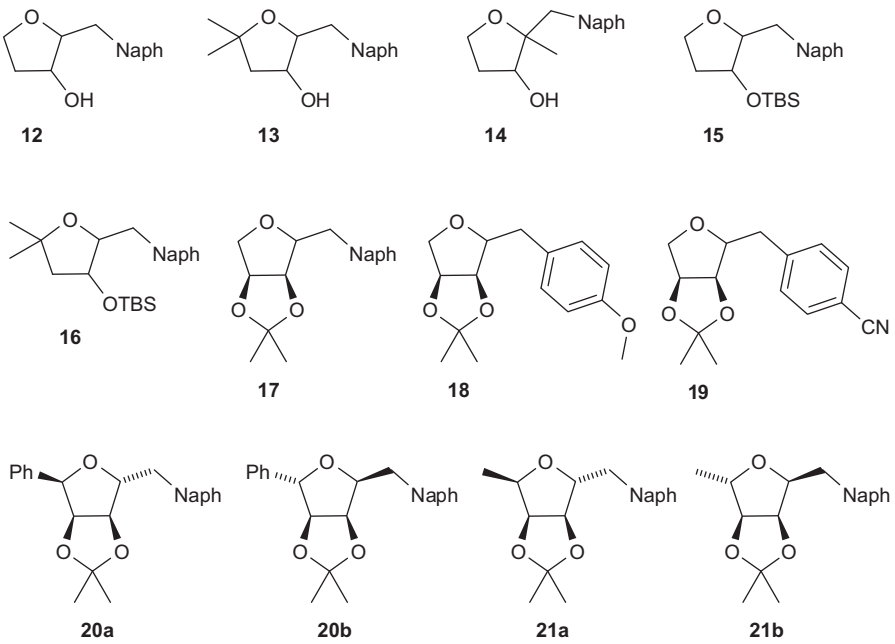


Figure 3. Products of the domino Pd-cyclization/cross-coupling **12**–**21**.

ucts only on substrates with terminal unsymmetrically disubstituted alkenes.

We also explored the synthesis of (poly)hydroxylated tetrahydrofurans by the palladium-catalyzed reaction of aryl bromides with substituted γ-hydroxyalkenes under basic conditions in the presence of phosphine ligands. The protection of the hydroxyl groups, except for the γ-hydroxyl, is a prerequisite for obtaining the tetrahydrofuran products in satisfactory yields. Substitution at the C-1 carbon had a significant impact on the stereocontrol of the reaction and ensured the formation of products with 2,5-*trans* diastereoselectivity, independent of additional substitutions. This suggests that the domino transformation of corresponding alkene triols could be used in the synthesis of natural compounds such as goniothalesdiol, varitriol, etc. and/or their analogues. The

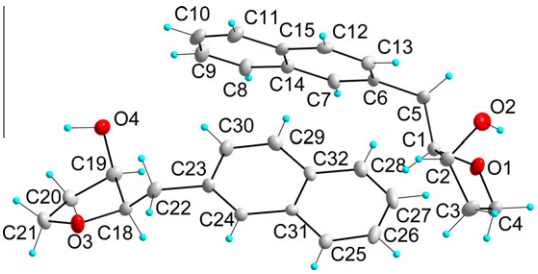
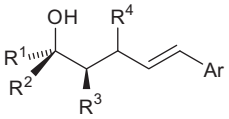


Figure 4. An ORTEP[14] view of the crystal and molecular structure of the deprotected compound *cis*-**15**.



22 R^1, R^2= Me; R^3= H; R^4= OTBS; Ar = 2-Naph
23 R^1, R^2= H; R^3, R^4= *O*-isopropylidene; Ar = 2-Naph
24 R^1, R^2= H; R^3, R^4= *O*-isopropylidene; Ar = 4-C_6H_4OMe
25 R^1= H or Me; R^2= H or Me; R^3, R^4= *O*-isopropylidene; Ar = 2-Naph

Figure 5. Heck products **22**–**25**.

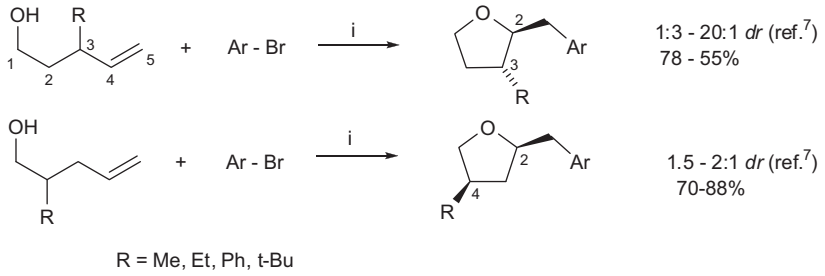
cyclization of γ-hydroxyalkenes without a substituent at the C-1 carbon is influenced by allylic hydroxyl functionality in favor of 2,3-*cis* diastereoselectivity.

4. Experimental

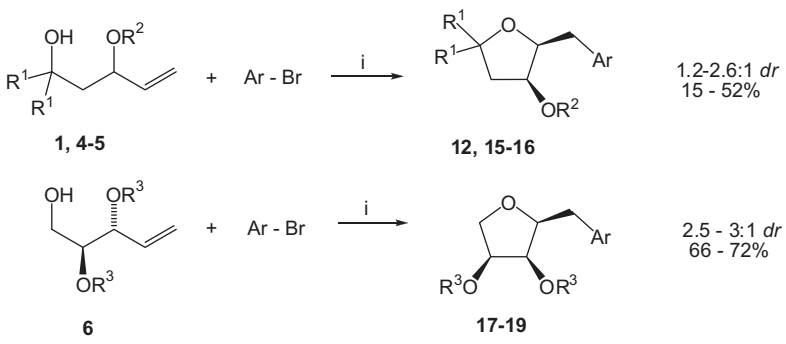
All syntheses were performed using standard Schlenk techniques under an argon atmosphere. Solvents were commercially obtained at the highest commercial quality and were used without further purification. Column chromatography was performed on silica gel grade 60 (230–400 mesh). Analytical TLC was performed using Silica Gel 60, F254 plates from Merck, which were visualized by UV and phosphomolybdic acid staining. Optical rotations were measured with a POLAR L-μP polarimeter (IBZ Messtechnik) with a water-jacketed 10.000 cm cell at the wavelength of sodium line D (λ = 589 nm) and 25 °C. Specific rotations are given in units of 10^{-1} deg cm^2 g^{-1} and concentrations are given in g/100 mL. Melting points were determined using a Büchi Melting Point B-540 instrument and are uncorrected. Fourier transform infra red spectra were recorded on a Philips Analytical PU9800 FTIR spectrometer or a Perkin Elmer Spectrum One FT-IR spectrometer. HRMS were recorded on a micrOTOF-Q II (Bruker) spectrometer by electrospray ionization (ESI) using tandem quadrupole coupled with a time-of-flight mass analyzer. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR-300 or Varian Inova 600 spectrometer; chemical shifts (δ) are given in ppm and are referenced to residual solvent peaks. Compounds **1**–**6** were prepared by previously described methods.[11a–d]

4.1. General procedure for the addition of MeMgI to esters

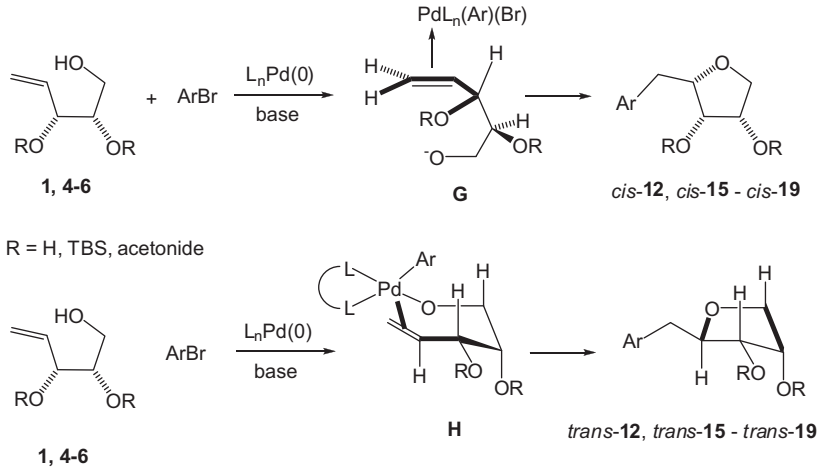
An oven or flame-dried flask was purged with argon and charged with MeMgI (23 mL, 69 mmol, 3.0 M in diethyl ether). Additional ether was then added to provide a 1.0 M solution of MeMgI, which was then cooled to 0 °C. The appropriate ester (17.3 mmol) was added dropwise via syringe, and the resulting mixture was warmed to rt and stirred for 4–5 h until the starting



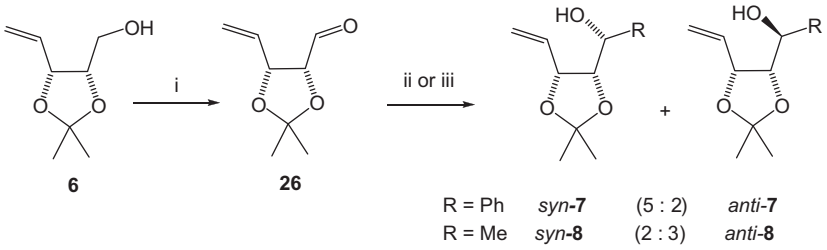
Scheme 4. Reagents and conditions: (i) Ar-Br (2 equiv), ^{t}BuONa (2 equiv), $Pd_2(dba)_3$ (0.01 equiv), dpe-phos (0.02 equiv), THF, 65 °C.



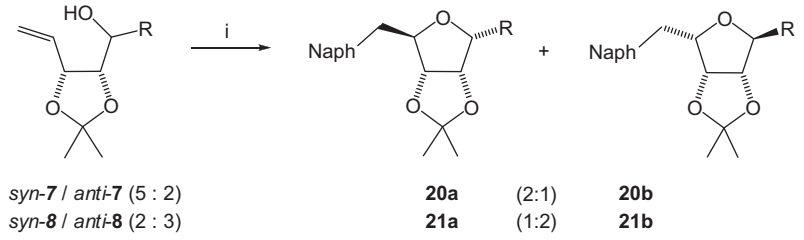
Scheme 5. Reagents and conditions: (i) Ar-Br (2 equiv), ^{t}BuONa (2 equiv), $Pd(dba)_2$ (0.01 equiv), dpe-phos (0.02 equiv), THF, 65 °C.



Scheme 6. Reaction pathways considered.



Scheme 7. Reagents and conditions: (i) $(COCl)_2$, DMSO, Et_3N, DCM, −78 °C; (ii) (1) PhMgBr, Et_2O, rt; (2) NH_4Cl, H_2O, 48% over two steps from **6**, dr 5:2; (iii) (1) MeMgI, Et_2O, rt; (2) NH_4Cl, H_2O, 31% over two steps from **6**, dr 2:3.



Scheme 8. Reagents and conditions: (i) 2-BrNaph (2 equiv), ^{t}BuONa (2 equiv), $Pd(dba)_2$ (10 mol %), dpe-phos (12 mol %), THF (2 mL/mmol Ar-Br), 65 °C, combined yield 70% for **20**, 46% for **21** (drs of isolated products).

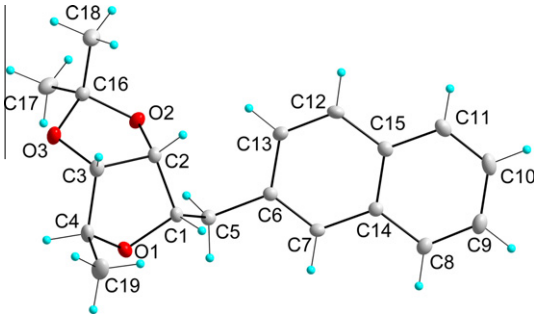


Figure 6. An *ORTEP*14 view of crystal and molecular structure of diastereomer **21b**.

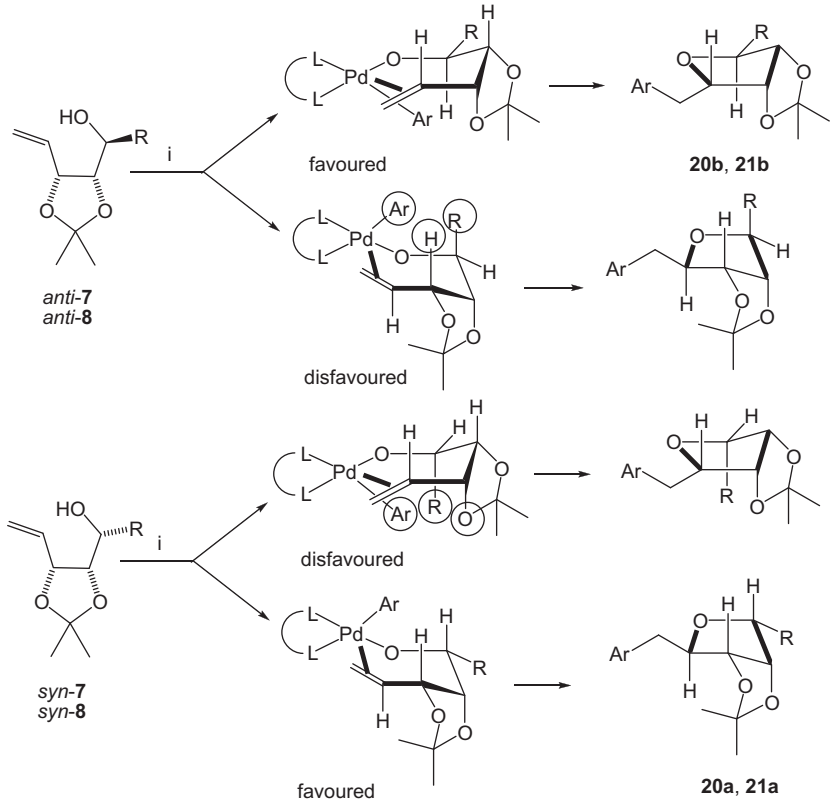
material was found to be completely consumed as judged by TLC analysis. A saturated solution of aqueous NH_4Cl (1:1 by volume with the reaction mixture) was added dropwise and the resulting mixture was then diluted with ethyl acetate (70 mL). The layers were separated, and the aqueous layer extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude tertiary alcohol product was then purified by flash chromatography on silica gel.

4.1.1. 2-Methylhex-5-ene-2,4-diol 2

Yellowish liquid (72%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (s, 3H), 1.34 (s, 3H), 1.55 (dd, 1H, J = 2.5, 14.6 Hz), 1.73 (dd, 1H, J = 14.6, 10.8 Hz), 3.76 (br s, 1H), 3.96 (br s, 1H), 4.47–4.52 (m, 1H), 5.08 (d, 1H, J = 10.4 Hz), 5.24 (d, 1H, J = 17.2 Hz), 5.86 (ddd, 1H, J = 17.2, 10.4, 5.8 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.6, 31.6, 47.5, 70.7, 71.4, 114.1, 140.9 ppm. IR (KBr): ν 3320, 2971, 1381, 1366, 1150, 989, 910, 850 cm^{-1}.

4.1.2. 2-Methyl-4-*tert*butyldimethylsilyloxy-hex-5-en-2-ol 5

Colorless liquid (74%); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.06 (s, 3H), 0.12 (s, 3H), 0.89 (s, 9H), 1.19 (s, 3H), 1.28 (s, 3H), 1.49 (dd, 1H, J = 14.5, 3.2 Hz), 1.81 (dd, 1H, J = 14.5, 10.4 Hz), 4.12 (br s, 1H), 4.50 (ddd, 1H, J = 10.5, 7.7, 3.2 Hz), 5.04 (d, 1H, J = 10.2 Hz), 5.12



Scheme 9. Reagents and conditions: (i) Ar-Br (2 equiv), ^{t}BuONa (2 equiv), $Pd(dba)_2$ (0.01 equiv), dpe-phos (0.02 equiv), THF, 65 °C.

(d, 1H, *J* = 17.2 Hz), 5.80 (ddd, 1H, *J* = 17.2, 10.2, 7.7 Hz) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.8, −3.3, 17.9, 25.8, 28.0, 31.1, 48.6, 70.4, 74.1, 114.8, 141.7 ppm. IR (KBr): ν 2930, 1252, 1073, 921, 835, 776 cm^{-1}; HRMS (ESI): calcd for $C_{13}H_{28}O_2Si$ $[M+Na]^+$ 267.1756; found $[M+Na]^+$ 267.1747.

4.2. (4*R*,5*R*)-2,2-Dimethyl-5-vinyl-1,3-dioxolane-4-carbaldehyde 26[10g–i]

To a −78 °C solution of oxalyl chloride (0.55 mL, 6.4 mmol) in dichloromethane (13 mL) was added DMSO (0.6 mL, 8.0 mmol) in dichloromethane (1.6 mL). The reaction was stirred at −78 °C for 15 min, then alcohol **6**[11d] (500 mg, 3.2 mmol) in dichloromethane (1.6 mL) was added. The reaction was stirred for 20 min at −78 °C followed by the addition of triethylamine (2.7 mL, 19.2 mmol). The mixture was stirred at −78 °C for 10 min and then allowed to warm to 0 °C. After 30 min of stirring, the reaction was diluted with diethyl ether (50 mL) upon which a white precipitate of triethylamine hydrochloride was formed. The slurry was filtered through a pad of celite and concentrated to afford the crude aldehyde **26** which was immediately used in the next reaction without purification. Crude yield: 485 mg (contaminated with DMSO), volatile liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 (s, 1H); 1.63 (s, 1H); 4.42 (dd, 1H, *J* = 7.5, 3.1 Hz); 4.87 (t, 1H, *J* = 7.2 Hz); 5.33 (dt, 1H, *J* = 10.4, 1.1 Hz); 5.47 (dt, 1H, *J* = 17.2, 1.2 Hz); 5.76 (ddd, 1H, *J* = 17.2, 10.4, 7.2 Hz); 9.56 (d, 1H, *J* = 3.1 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.3, 27.3, 79.0, 82.2, 111.2, 119.7, 131.2, 200.6 ppm; IR (KBr): ν 3307, 1715, 1405, 1005, 949 cm^{-1}.

4.3. General procedure for the addition of Grignard reagents to carbaldehyde 26

A three-necked flask equipped with a condenser was filled with magnesium chips (45 mg, 1.8 mmol) and a small iodine grain. After the activation, bromobenzene or iodomethane (1.8 mmol) in diethyl ether (3.5 mL) was added. The discoloration of the reaction mixture indicated the start of reaction. The mixture was stirred at rt until complete consumption of magnesium. To a solution of Grignard reagent the crude aldehyde **26** (168 mg, 1.1 mmol) was added at 0 °C. The reaction mixture was stirred for 2 h and quenched with satd NH_4Cl (10 mL). The water phase was extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude alcohol was purified by flash chromatography on silica gel (ethyl acetate/hexanes 1:5).

4.3.1. (2*S*,3*R*)-2,3-*O*-Isopropylidene-1-phenyl-pent-4-en-1,2,3-triol 7[10e]

Colorless oil (48% over two steps from **6**); dr *syn*-**7**/*anti*-**7**, 5:2. ^{1}H NMR (600 MHz, $CDCl_3$): δ (*syn*-**7**) 1.42 (s, 3H); 1.60 (s, 3H); 2.75 (d, 1H, *J* = 4.6 Hz); 4.41 (dd, 1H, *J* = 6.5, 5.7 Hz); 4.55 (dd, 1H, *J* = 7.2, 6.6 Hz); 4.64 (t, 1H, *J* = 4.8 Hz); 5.25 (dt, 1H, *J* = 10.2, 1.0 Hz); 5.29 (dt, 1H, *J* = 17.4, 1.1 Hz); 5.96 (ddd, 1H, *J* = 17.4, 10.2, 7.5 Hz); 7.32–7.40 (m, 5H) ppm; δ (*anti*-**7**) 1.31 (s, 3H); 1.47 (s, 3H); 2.05 (d, 1H, *J* = 3.4 Hz); 4.31 (dd, 1H, *J* = 8.7, 6.2 Hz); 4.68 (dd, 1H, *J* = 8.7, 3.2 Hz); 4.75 (dd, 1H, *J* = 7.2, 6.2 Hz); 5.35 (dt, 1H, *J* = 10.4, 1.0 Hz); 5.49 (dt, 1H, *J* = 17.2, 1.4 Hz); 6.16 (ddd, 1H, *J* = 17.4, 10.4, 7.2 Hz); 7.32–7.40 (m, 5H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ (*syn*-**7**) 25.1, 27.5, 72.2, 78.8, 81.4, 108.9, 119.2, 127.3, 128.0, 128.3, 133.7, 140.4; δ (*anti*-**7**) 25.2, 27.8, 72.4, 78.9, 80.8, 108.9, 118.3, 127.0, 128.0, 128.3, 134.1, 141.2 ppm. IR (KBr): ν 3369, 1452, 1214, 1025, 992, 699 cm^{-1}.

4.3.2. (3*S*,4*R*)-3,4-*O*-Isopropylidene-hex-5-ene-2,3,4-triol 8[10f]

Yellowish oil (31% over two steps from **6**); dr *anti*-**8**/*syn*-**8**, 3:2. ^{1}H NMR (600 MHz, $CDCl_3$): δ (*anti*-**8**) 1.28 (d, 3H, *J* = 6.6 Hz); 1.38 (s, 3H); 1.48 (s, 3H); 3.82–3.87 (m, 1H); 3.93 (dd, 1H, *J* = 9.6, 6.5 Hz); 4.66 (dd, 1H, *J* = 7.4, 6.5 Hz); 5.32 (ddd, 1H, *J* = 10.8, 1.3, 1.0 Hz); 5.44 (dt, 1H, *J* = 17.4, 1.3 Hz); 6.04 (ddd, 1H, *J* = 17.4,

10.2, 7.8 Hz). δ (*syn*-**8**) 1.16 (d, 3H, *J* = 6.6 Hz); 1.40 (s, 3H); 1.52 (s, 3H); 3.74–3.79 (m, 1H); 3.95 (dd, 1H, *J* = 8.2, 6.5 Hz); 4.56 (t, 1H, *J* = 6.5 Hz); 5.29 (ddd, 1H, *J* = 10.2, 1.3, 1.0 Hz); 5.34 (dt, 1H, *J* = 17.3, 1.3 Hz); 5.93 (ddd, 1H, *J* = 17.3, 10.2, 8.1 Hz) ppm; IR (KBr): *ν* 3367, 2960, 2924, 1259, 1016, 797 cm^{-1}.

4.4. General procedure for the Pd(II) catalyzed cyclization and cross-coupling

A flame-dried Schlenk tube was cooled under a stream of argon and charged with $Pd(dba)_2$ (0.1 equiv), dpe-phos (0.12 equiv), *t*BuONa (2.0 equiv), and the aryl bromide (2.0 equiv) The tube was purged with argon, and the unsaturated alcohol substrate (1.0 equiv), and THF (4 mL/mmol aryl bromide) were added. The reaction mixture was heated to 65 °C until the alcohol substrate was consumed as judged by TLC. The reaction mixture was cooled to rt and filtered through a pad of Celite. After the addition of silica gel (1 g/mmol of alcohol substrate), the solvent was evaporated and the crude product purified by flash column chromatography.

4.4.1. (±)-*cis*-2-(Naphthalen-2-ylmethyl)tetrahydrofuran-3-ol *cis*-12

Recrystallization from hexane provided a white solid, mp 75–79 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.89 (br s, 1H), 1.94 (m, 1H), 2.16 (m, 1H), 3.15 (d, 1H, *J* = 6.6 Hz), 3.79 (ddd, 1H, *J* = 9.6, 8.4, 4.8 Hz), 3.91 (ddd, 1H, *J* = 7.2, 7.2, 3.0 Hz), 4.10 (ddd, 1H, *J* = 8.4, 7.8, 7.8 Hz), 4.17 (m, 1H), 7.40–7.45 (m, 3H), 7.73 (s, 1H); 7.77–7.80 (m, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 35.3, 35.6, 65.8, 72.1, 83.8, 125.3, 125.9, 127.4, 127.5, 127.6, 127.6, 128.0, 132.2, 133.6, 136.2 ppm. HRMS (ESI): calcd for $C_{15}H_{16}O_2$ $[M+Na]^+$ 251.1048; found $[M+Na]^+$ 251.1038.

4.4.2. (±)-*trans*-(2-Naphthalen-2-ylmethyl)tetrahydrofuran-3-ol *trans*-12

Yellowish oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.78 (m, 1H), 1.96 (br s, 1H), 2.01 (m, 1H), 2.88 (dd, 1H, *J* = 13.8, 6.6 Hz), 2.97 (dd, 1H, *J* = 13.8, 7.2 Hz), 3.89 (ddd, 1H, *J* = 9.0, 9.0, 6.6 Hz), 3.93 (ddd, 1H, *J* = 8.4, 8.4, 3.6 Hz), 4.01 (ddd, 1H, *J* = 6.6, 6.6, 3.0 Hz), 4.11 (m, 1H), 7.35 (dd, 1H, *J* = 8.4, 1.8 Hz), 7.43 (m, 2H), 7.65 (s, 1H), 7.77 (m, 3H) ppm; ^{13}C NMR (75 150 MHz, $CDCl_3$): δ 34.6, 39.9, 66.4, 75.3, 86.6, 125.4, 126.0, 127.5, 127.5, 127.6, 127.6, 128.0, 132.2, 133.5, 135.5 ppm. HRMS (ESI): calcd for $C_{15}H_{16}O_2$ $[M+Na]^+$ 251.1048; found $[M+Na]^+$ 251.1041.

4.4.3. (±)-*cis*-3-(*tert*Butyldimethylsilyloxy)-2-(naphthalen-2-ylmethyl)tetrahydrofuran *cis*-15

Yellowish oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.08 (s, 3H), 0.10 (s, 3H), 0.96 (s, 9H), 1.89–1.93 (m, 1H), 2.07–2.13 (m, 1H), 3.03 (dd, 1H, *J* = 14.3, 4.9 Hz), 3.09 (dd, 1H, *J* = 14.3, 8.2 Hz), 3.78 (ddd, 1H, *J* = 12.8, 8.5, 4.4 Hz), 4.01 (ddd, 1H, *J* = 8.4, 4.9, 3.7 Hz), 4.07 (dd, 1H, *J* = 15.6, 8.0 Hz), 4.31–4.33 (m, 1H), 7.38–7.44 (m, 3H), 7.71–7.79 (m, 4H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ −4.9, −4.4, 18.2, 25.9, 36.0, 36.1, 66.0, 73.0, 83.8, 125.1, 125.7, 127.3, 127.5, 127.5, 127.8, 127.8, 132.1, 133.6, 137.2 ppm. HRMS (ESI): calcd for $C_{21}H_{30}O_2Si$ $[M+Na]^+$ 365.1913; found $[M+Na]^+$ 365.1890.

4.4.4. (±)-*trans*-3-(*tert*-Butyldimethylsilyloxy)-2-(naphthalen-2-ylmethyl)tetrahydrofuran *trans*-15

Yellowish oil; ^{1}H NMR (600 MHz, $CDCl_3$): δ −0.09 (s, 3H), −0.05 (s, 3H), 0.82 (s, 9H), 1.75–1.80 (m, 1H), 1.96–2.02 (m, 1H), 2.93 (dd, 1H, *J* = 14.0, 7.0 Hz), 2.96 (dd, 1H, *J* = 14.0, 6.0 Hz), 3.91 (ddd, 1H, *J* = 15.2, 8.5, 7.0 Hz), 3.95 (ddd, 1H, *J* = 12.2, 8.2, 4.0 Hz), 4.00 (ddd, 1H, *J* = 6.8, 6.2, 3.7 Hz), 4.08–4.10 (m, 1H), 7.38–7.45 (m, 3H), 7.66–7.80 (m, 4H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ −4.9, −4.7, 17.9, 25.7, 35.2, 40.0, 66.8, 75.7, 86.7, 125.2, 125.8, 127.5, 127.5, 127.6, 127.8, 127.9, 132.2, 133.6, 136.1 ppm. HRMS (ESI): calcd for $C_{21}H_{30}O_2Si$ $[M+Na]^+$ 365.1913; found $[M+Na]^+$ 365.1891.

4.4.5. (±)-*cis*/*trans*-3-(*tert*-Butyldimethylsilyloxy)-5,5-dimethyl-2-(naphthalen-2ylmethyl)-tetrahydrofuran 16

Non-separable mixture of diastereomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer *cis*-**16**) 0.04 (s, 3H), 0.09 (s, 3H), 0.99 (s, 9H), 1.26 (s, 3H), 1.45 (s, 3H), 1.89 (dd, 1H, *J* = 13.2, 2.3 Hz), 1.98 (dd, 1H, *J* = 13.2, 5.1 Hz), 3.10 (dd, 1H, *J* = 14.2, 6.7 Hz), 3.16 (dd, 1H, *J* = 14.2, 6.1 Hz), 4.22 (dd, 1H, *J* = 10.2, 6.5 Hz), 4.29 (m, 1H), 7.41–7.45 (m, 3H), 7.71–7.82 (m, 4H) ppm; ^{1}H NMR (300 MHz, $CDCl_3$): δ (minor isomer *trans*-**16**) −0.13 (s, 3H), −0.04 (s, 3H), 0.84 (s, 9H), 1.26 (s, 3H), 1.37 (s, 3H), 1.71 (dd, 1H, *J* = 12.7, 4.3 Hz), 1.87 (dd, 1H, *J* = 12.7, 7.0 Hz), 3.02 (d, 2H, *J* = 6.0 Hz, 4.08 (ddd, 1H, *J* = 6.8, 4.5, 4.5 Hz), 4.16–4.24 (m, 1H), 7.39–7.48 (m, 3H), 7.69–7.83 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer *cis*-**16**) −5.1, −4.2, 18.2, 25.9, 29.3, 30.1, 36.3, 48.2, 74.2, 79.6, 82.9, 125.0, 125.7, 127.3, 127.4, 127.5, 127.6, 128.0, 132.0, 133.6, 137.2 ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ (minor isomer *trans*-**16**) −5.1, −4.7, 17.8, 25.6, 28.5, 30.1, 40.3, 47.4, 76.2, 80.4, 85.8, 125.1, 125.7, 127.5, 127.6, 127.6, 127.8, 128.3, 132.2, 133.5, 136.0 ppm. HRMS (ESI): calcd for $C_{23}H_{34}O_2Si$ $[M+Na]^+$ 393.2220; found $[M+Na]^+$ 393.2208.

4.4.6. (*E*)-4-*tert*-Butyldimethylsilyloxy-2-methyl-6-(naphthalen-3-yl)hex-5-ene-2-ol 22

Yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.09 (s, 3H), 0.18 (s, 3H), 0.93 (s, 9H), 1.25 (s, 3H), 1.37 (s, 3H), 1.63 (dd, 1H, *J* = 14.3, 3.1 Hz), 1.98 (dd, 1H, *J* = 14.3, 10.6 Hz), 4.27 (br s, 1H), 4.76 (ddd, 1H, *J* = 10.6, 8.0, 2.9 Hz), 6.27 (dd, 1H, *J* = 15.9, 8.0 Hz), 6.64 (d, 1H, *J* = 15.9 Hz), 7.44–7.48 (m, 2H), 7.58 (dd, 1H, *J* = 8.6, 1.7 Hz), 7.71–7.73 (m, 1H), 7.79–7.83 (m, 3H) ppm; IR (film on NaCl): *ν* 3516, 2959, 2930, 2857, 1471, 1257, 1150, 965, 837, 666 cm^{-1}.

4.4.7. (3*R*,4*S*)-3,4-*O*-Isopropylidene-2-((naphtalene-2-yl)methyl) tetrahydrofuran-3,4-diol 17

Non-separable mixture of diastereomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer *cis*-**17**) 1.36 (s, 3H), 1.59 (s, 3H), 3.17 (dd, 1H, *J* = 13.8, 7.2 Hz), 3.25 (dd, 1H, *J* = 13.8, 6.5 Hz), 3.45 (dd, 1H, *J* = 10.8, 3.9 Hz), 3.70 (ddd, 1H, *J* = 6.8, 6.8, 3.5 Hz), 4.04 (d, 1H, *J* = 10.8 Hz), 4.57 (dd, 1H, *J* = 6.1, 3.6 Hz), 4.76 (dd, 1H, *J* = 6.1, 3.7 Hz), 7.41–7.49 (m, 3H), 7.77–7.80 (m, 4H) ppm; ^{1}H NMR (300 MHz, $CDCl_3$): δ (minor isomer *trans*-**17**) 1.30 (s, 3H), 1.50 (s, 3H), 2.87 (dd, 1H, *J* = 14.1, 6.9 Hz), 2.96 (dd, 1H, *J* = 14.1, 7.8 Hz), 3.96 (dd, 1H, *J* = 10.6, 3.6 Hz), 4.00 (dd, 1H, *J* = 10.6, 2.0 Hz), 4.42 (ddd, 1H, *J* = 7.4, 7.4, 1.6 Hz), 4.54–4.58 (m, 1H), 4.82 (ddd, 1H, *J* = 6.0, 3.7, 2.2 Hz), 7.35–7.49 (m, 3H), 7.77–7.80 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer *cis*-**17**) 25.0, 26.2, 35.0, 72.8, 80.8, 81.0, 83.6, 112.0, 125.3, 125.8, 127.5, 127.6, 127.6, 127.8, 127.9, 132.2, 133.5, 136.0 ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ (minor isomer *trans*-**17**) 25.1, 26.6, 37.2, 72.0, 81.0, 84.1, 85.1, 112.8, 125.5, 126.0, 127.4, 127.5, 127.6, 127.9, 128.2, 132.2, 133.5, 135.0 ppm. HRMS (ESI): calcd for $C_{18}H_{20}O_3$ $[M+Na]^+$ 307.1305; found $[M+Na]^+$ 307.1301.

4.4.8. (*E*)-(2*S*,3*R*)-2,3-*O*-Isopropylidene-5-(naphtalene-2-yl)pent-4-ene-1,2,3-triol 23

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.46 (s, 3H), 1.58 (s, 3H), 3.68 (d, 2H, *J* = 5.5 Hz), 4.35 (dt, 1H, *J* = 6.6, 5.7 Hz), 4.88 (ddd, 1H, *J* = 7.8, 6.9, 0.8 Hz), 6.34 (dd, 1H, *J* = 15.9, 7.8 Hz), 6.85 (d, 1H, *J* = 15.9 Hz), 7.43–7.47 (m, 2H), 7.76–7.81 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.2, 27.8, 62.1, 78.2, 78.6, 108.9, 123.6, 124.2, 126.1, 126.4, 126.9, 127.7, 128.0, 132.1, 133.5, 134.2 ppm.

4.4.9. (3*R*,4*S*)-3,4-*O*-Isopropylidene-2-(4-methoxybenzyl)tetrahydrofuran-3,4-diol 18

Non-separable mixture of diastereomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer *cis*-**18**) 1.35 (s, 3H), 1.55 (s, 3H), 2.95 (dd, 1H, J = 13.8, 6.9 Hz), 3.04 (dd, 1H, J = 13.8, 6.9 Hz), 3.43 (dd, 1H, J = 10.8, 3.9 Hz), 3.55 (dt, 1H, J = 6.8, 3.6 Hz), 3.78 (s, 3H), 4.01 (d, 1H, J = 10.8 Hz), 4.53 (dd, 1H, J = 6.1, 3.5 Hz), 4.74 (dd, 1H, J = 6.1, 3.7 Hz), 6.84 (d, 2H, J = 8.7 Hz), 7.23 (d, 2H, J = 8.7 Hz). ^{1}H NMR (300 MHz, $CDCl_3$): δ (minor isomer *trans*-**18**) 1.31 (s, 3H), 1.50 (s, 3H), 2.65 (dd, 1H, J = 14.1, 7.2 Hz), 2.73 (dd, 1H, J = 14.1, 7.5 Hz), 3.78 (s, 3H), 3.91 (d, 1H, J = 4.2 Hz), 3.89 (dd, 1H, J = 10.7, 4.1 Hz), 3.95 (dd, 1H, J = 10.7, 1.8 Hz), 4.25 (dt, 1H, J = 7.4, 1.6 Hz), 4.50 – 4.54 (m, 1H), 4.79 (ddd, 1H, J = 6.0, 4.1, 1.8 Hz), 6.84 (d, 2H, J = 8.7 Hz), 7.12 (d, 2H, J = 8.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer *cis*-**18**) 25.0, 26.1, 33.9, 55.2, 72.8, 80.7, 81.0, 83.9, 112.0, 113.8, 130.2, 130.5, 158.1; ^{13}C NMR (75 MHz, $CDCl_3$): δ (minor isomer *trans*-**18**) 25.1, 26.6, 36.2, 55.2, 72.0, 80.9, 84.0, 85.3, 112.8, 114.0, 130.0, 130.5, 158.2 ppm. HRMS (ESI): calcd for $C_{15}H_{20}O_4$ $[M+Na]^+$ 287.1254; found $[M+Na]^+$ 287.1246.

4.4.10. (*E*)-(2*S*,3*R*)-2,3-*O*-Isopropylidene-5-(4-methoxybenzyl) pent-4-ene-1,2,3-triol 24

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.43 (s, 3H), 1.56 (s, 3H), 1.86 (t, 1H, J = 6.1 Hz), 3.65 (dd, 2H J = 5.7, 5.4 Hz), 3.81 (s, 3H), 4.31 (dt, 1H, J = 6.9, 5.4 Hz), 4.82 (ddd, 1H, J = 7.2, 7.2, 0.5 Hz), 6.08 (dd, 1H, J = 15.9, 8.1 Hz), 6.64 (d, 1H, J = 15.9 Hz), 6.86 (d, 2H, J = 8.7 Hz), 7.33 (d, 2H, J = 8.7 Hz) ppm.

4.4.11. (3*R*,4*S*)-3,4-*O*-Isopropylidene-2-(4-cyanobenzyl)tetrahydrofuran-3,4-diol 19

Non-separable mixture of diastereomers; ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer *cis*-**19**) 1.35 (s, 3H), 1.55 (s, 3H), 3.03–3.15 (m, 2H), 3.45 (dd, 1H, J = 10.8, 3.6 Hz), 3.59 (dt, 1H, J = 6.6, 3.6 Hz), 4.03 (d, 1H, J = 10.8 Hz), 4.54 (dd, 1H, J = 6.0, 3.6 Hz), 4.77 (dd, 1H, J = 6.3, 3.9 Hz), 7.43 (d, 2H, J = 8.4 Hz), 7.59 (d, 2H, J = 8.4 Hz); ^{1}H NMR (300 MHz, $CDCl_3$): δ (minor isomer *trans*-**19**) 1.33 (s, 3H), 1.50 (s, 3H), 2.80–2.82 (m, 2H), 3.93 (dd, 1H, J = 10.7, 3.9 Hz), 3.97 (dd, 1H, J = 10.7, 2.3 Hz), 4.22–4.27 (m, 1H), 4.49 (dd, 1H, J = 6.3, 2.1 Hz), 4.83 (ddd, 1H, J = 6.2, 3.9, 2.2 Hz), 7.33 (d, 2H, J = 8.4 Hz), 7.60 (d, 2H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer *cis*-**19**) 24.9, 26.0, 35.1, 72.8, 80.7, 81.0, 82.7, 110.2, 112.2, 119.0, 130.1, 132.1, 144.3; ^{13}C NMR (75 MHz, $CDCl_3$): δ (minor isomer *trans*-**19**) 25.1, 26.6, 37.2, 71.9, 80.8, 84.3, 84.6, 110.4, 113.2, 118.9, 129.9, 132.2, 143.4 ppm. HRMS (ESI): calcd for $C_{15}H_{17}NO_3$ $[M+Na]^+$ 282.1101; found $[M+Na]^+$ 282.1089.

4.4.12. (2*R*,3*R*,4*S*,5*R*)-3,4-*O*-Isopropylidene-5-phenyl-2-((naphthalene-2-yl)methyl)tetrahydrofuran-3,4-diol 20a

$[\alpha]_D^{25} = -19.5$ (*c* 0.83, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.22 (s, 3H), 1.42 (s, 3H), 2.96 (dd, 1H, J = 14.1, 8.1 Hz), 3.12 (dd, 1H, J = 14.1, 7.2 Hz), 4.63 (t, 1H, J = 7.5 Hz), 4.75 (d, 1H, J = 5.9 Hz), 4.84 (dd, 1H, J = 5.9, 3.8 Hz), 5.05 (d, 1H, J = 3.8 Hz), 7.27–7.46 (m, 8H), 7.68–7.81 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 24.8, 26.1, 37.3, 82.0, 82.6, 84.6, 84.6, 112.6, 125.5, 126.0, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.3, 132.3, 133.6, 134.9, 136.1 ppm. HRMS (ESI): calcd for $C_{24}H_{24}O_3$ $[M+Na]^+$ 383.1618; found $[M+Na]^+$ 383.1604.

4.4.13. (2*S*,3*R*,4*S*,5*S*)-3,4-*O*-Isopropylidene-5-phenyl-2-((naphtalene-2-yl)methyl)tetrahydrofuran-3,4-diol 20b

Recrystallization from hexane provided a white solid mp 105–107 °C; $[\alpha]_D^{26} = +26.8$ (*c* 0.31, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.40 (s, 3H), 1.68 (s, 3H), 3.27 (dd, 1H, J = 14.0, 7.1 Hz), 3.32 (dd, 1H, J = 14.0, 6.6 Hz), 4.16 (dt, 1H J = 6.9, 3.6 Hz), 4.58 (dd, 1H, J = 6.0, 3.6 Hz), 4.95 (d, 1H, J = 6.0 Hz), 5.23 (s, 1H), 7.22–7.34 (m, 5H), 7.41–7.52 (m, 3H), 7.78–7.82 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 26.3, 26.5, 35.4, 81.7, 81.8, 84.6, 87.5, 112.6, 125.3, 125.5, 125.9, 127.3, 127.5, 127.6, 127.8, 127.9, 128.6, 132.2, 133.6, 136.1, 138.8 ppm. HRMS (ESI): calcd for $C_{24}H_{24}O_3$ $[M+Na]^+$ 383.1618; found $[M+Na]^+$ 383.1610.

4.4.14. (2*R*,3*R*,4*S*,5*R*)-3,4-*O*-Isopropylidene-5-methyl-2-((naphtalene-2-yl)methyl)tetrahydrofuran-3,4-diol 21a

^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (s, 3H), 1.33 (d, 3H, J = 6.3 Hz), 1.48 (s, 3H), 2.84 (dd, 1H, J = 14.0, 7.8 Hz), 3.00 (dd, 1H, J = 14.0, 7.6 Hz), 4.10 (dd, 1H, J = 7.5, 3.8 Hz), 4.42 (t, 1H, J = 7.7 Hz), 4.62–4.65 (m, 2H), 7.40–7.47 (m, 3H), 7.75–7.80 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 25.2, 26.3, 37.4, 75.8, 82.3, 84.4, 84.9, 119.8, 125.2, 125.8, 127.5, 127.6, 127.8, 127.9, 132.2, 134.5, 135.1 ppm; IR (film on NaCl): ν 3059, 2964, 1373, 1267, 1207, 1072, 749 cm^{-1}. HRMS (ESI): calcd for $C_{19}H_{22}O_3$ $[M+Na]^+$ 321.1461; found $[M+Na]^+$ 321.1456.

4.4.15. (2*S*,3*R*,4*S*,5*S*)-3,4-*O*-Isopropylidene-5-methyl-2-((naphtalene-2-yl)methyl)tetrahydrofuran-3,4-diol 21b

Recrystallization from hexane provided a white solid mp 93–95 °C; $[\alpha]_D^{26} = +77.2$ (*c* 0.246, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.11 (d, 3H, J = 7.2 Hz), 1.35 (s, 3H), 1.60 (s, 3H), 3.11 (dd, 1H, J = 13.7, 6.3 Hz), 3.25 (dd, 1H, J = 13.7, 7.2 Hz), 4.10 (dt, 1H, J = 6.6, 3.9 Hz), 4.29 (q, 1H, J = 6.9 Hz), 4.43 (d, 1H, J = 6.0 Hz), 4.58 (dd, 1H, J = 6.0, 3.6 Hz), 7.41–7.48 (m, 3H), 7.76–7.81 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 16.9, 25.1, 26.4, 35.3, 79.6, 80.3, 81.2, 86.4, 112.3, 125.3, 125.8, 127.5, 127.6, 127.8, 127.9, 132.2, 133.5, 136.2 ppm; IR (KBr): ν 3059, 2964, 1373, 1267, 1207, 1072, 749 cm^{-1}. HRMS (ESI): calcd for $C_{19}H_{22}O_3$ $[M+Na]^+$ 321.1461; found $[M+Na]^+$ 321.1456.

4.4.16. (*E*)-(3*S*,4*R*)-3,4-*O*-Isopropylidene-6-(naphthalene-2-yl)hex-5-ene-2,3,4-triol 25

^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer) 1.20 (d, 3H, J = 6.3 Hz), 1.46 (s, 3H), 1.60 (s, 3H), 3.87 (qi, 1H, J = 6.2 Hz), 4.03 (dd, 1H, J = 6.3, 4.3 Hz), 4.81 (ddd, 1H, J = 8.4, 6.6, 0.5 Hz), 6.40 (dd, 1H, J = 15.8, 8.5 Hz), 6.81 (d, 1H, J = 15.8 Hz), 7.45–7.48 (m, 2H), 7.62–7.63 (m, 1H), 7.76–7.82 (m, 4H) ppm; ^{1}H NMR (300 MHz, $CDCl_3$): δ (major isomer) 1.31 (d, 3H, J = 6.1 Hz), 1.44 (s, 3H), 1.56 (s, 3H), 3.96 (q, 1H, J = 6.2 Hz), 4.22 (dd, 1H, J = 5.9, 3.7 Hz), 4.90 (ddd, 1H, J = 7.4, 6.3, 0.9 Hz), 6.49 (dd, 1H, J = 15.9, 7.8 Hz), 6.89 (d, 1H, J = 15.9 Hz), 7.45–7.48 (m, 2H); 7.59–7.60 (m, 1H); 7.76–7.82 (m, 4H) ppm.

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References

1. (a) Hegedus, L. S. *Tetrahedron* **1984**, *40*, 2415–2434; (b) Hegedus, L. S. *Coord. Chem. Rev.* **1996**, *147*, 443–545; (c) Heumann, A.; Réglier, M. *Tetrahedron* **1996**, *52*, 9289–9346; (d) Hegedus, L. S. *Coord. Chem. Rev.* **1997**, *161*, 129–255; (e) Hegedus, L. S. *Coord. Chem. Rev* **1998**, *175*, 159–270; (f) Muzart, J. *Tetrahedron* **2005**, *61*, 4179–4212; (g) Muzart, J. *Tetrahedron* **2005**, *61*, 5955–6008; (h) Muzart, J. *Tetrahedron* **2005**, *61*, 9423–9463; (i) Muzart, J. *J. Mol. Catal. A: Chem.* **2010**, *319*, 1–29; (j) Beccalli, E. M.; Broggini, G.; Fasana, A.; Rigamonti, M. *J. Organomet. Chem.* **2011**, *696*, 277–295; (k) Kapitán, P.; Gracza, T. *Arkivoc* **2008**, *viii*, 8–17; (l) Kapitán, P.; Gracza, T. *Tetrahedron: Asymmetry* **2008**, *19*, 38–44.
2. (a) Szolcsányi, P.; Gracza, T. *Chem. Commun.* **2005**, 3948–3950; (b) Babjak, M.; Remeň, Ľ.; Szolcsányi, P.; Zálupský, P.; Miklóš, M.; Gracza, T. *J. Organomet. Chem.* **2006**, *691*, 928–940.

3. (a) Palík, M.; Karlubíková, O.; Lásiková, A.; Kožíšek, J.; Gracza, T. *Eur. J. Org. Chem.* **2009**, 709–715; (b) Gracza, T.; Jäger, V. *Synlett* **1992**, 191–193.
4. Semmelhack, M. F.; Epa, W. R. *Tetrahedron Lett.* **1993**, *34*, 7205–7208.
5. (a) Tietze, L. F.; Sommer, K. M.; Zinngrebe, J.; Stecker, F. *Angew. Chem., Int. Ed.* **2005**, *44*, 257–259; (b) Tietze, L. F.; Stecker, F.; Zinngrebe, J.; Sommer, K. *Chem. Eur. J.* **2006**, *12*, 8770–8776; (c) Tietze, L. F.; Spiegl, D. A.; Stecker, F.; Major, J.; Raith, C.; Große, C. *Chem. Eur. J.* **2008**, *14*, 8956–8963.
6. For reviews see: (a) Wolfe, J. P. *Eur. J. Org. Chem.* **2007**, 571–582; (b) Wolfe, J. P. *Synlett* **2008**, 2913–2937.
7. (a) Wolfe, J. P.; Rossi, M. A. *J. Am. Chem. Soc.* **2004**, *126*, 1620–1621; (b) Hay, M. B.; Hardin, A. R.; Wolfe, J. P. *J. Org. Chem.* **2005**, *70*, 3099–3107; (c) Hay, M. B.; Wolfe, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 16468–16476; (d) Hay, M. B.; Wolfe, J. P. *Tetrahedron Lett.* **2006**, *47*, 2793–2796; (e) Ward, A. F.; Wolfe, J. P. *Org. Lett.* **2010**, *12*, 1268–1271.
8. (a) Ney, J. E.; Wolfe, J. P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3605–3608; (b) Lira, R.; Wolfe, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 13906–13907; (c) Beaudoin Bertrand, M.; Wolfe, J. P. *Tetrahedron* **2005**, *61*, 6447–6459; (d) Ney, J. E.; Wolfe, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 8644–8651; (e) Yang, Q.; Ney, J. E.; Wolfe, J. P. *Org. Lett.* **2005**, *7*, 2575–2578; (f) Ney, J. E.; Hay, M. B.; Yang, Q.; Wolfe, J. P. *Adv. Synth. Catal.* **2005**, *347*, 1614–1620; (g) Beaudoin Bertrand, M.; Wolfe, J. P. *Org. Lett.* **2006**, *8*, 2353–2356; (h) Beaudoin Bertrand, M.; Leathen, M. L.; Wolfe, J. P. *Org. Lett.* **2007**, *9*, 457–460; (i) Beaudoin Bertrand, M.; Neukom, J. D.; Wolfe, J. P. *J. Org. Chem.* **2008**, *73*, 8851–8860; (j) Neukom, J. D.; Perch, N. S.; Wolfe, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 6276–6277; (k) Rosen, B. R.; Ney, J. E.; Wolfe, J. P. *J. Org. Chem.* **2010**, *75*, 2756–2759; (l) Mai, D. N.; Wolfe, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 12157–12159; (m) Lemen, G. S.; Wolfe, J. P. *Org. Lett.* **2010**, *12*, 2322–2325; (n) Mai, D. N.; Rosen, B. R.; Wolfe, J. P. *Org. Lett.* **2011**, *13*, 2932–2935; (o) Fritz, J. A.; Nakhla, J. S.; Wolfe, J. P. *Org. Lett.* **2006**, *8*, 2531–2534; (p) Fritz, J. A.; Wolfe, J. P. *Tetrahedron* **2008**, *64*, 6838–6852; (q) Hay, M. B.; Wolfe, J. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 6492–6494; (r) Lemen, G. S.; Giampietro, N. C.; Hay, M. B.; Wolfe, J. P. *J. Org. Chem.* **2009**, *74*, 2533–2540; (s) Ward, A. F.; Wolfe, J. P. *Org. Lett.* **2011**, *13*, 4728–4731; (t) Giampietro, N. C.; Wolfe, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 12907–12911; (u) Nakhla, J. S.; Wolfe, J. P. *Org. Lett.* **2007**, *9*, 3279–3282; (v) Nakhla, J. S.; Schultz, D. M.; Wolfe, J. P. *Tetrahedron* **2009**, *65*, 6549–6570; (w) Leathen, M. L.; Rosen, B. R.; Wolfe, J. P. *J. Org. Chem.* **2009**, *74*, 5107–5110; (x) Neukom, J. D.; Aquino, A. S.; Wolfe, J. P. *Org. Lett.* **2011**, *13*, 2196–2199.
9. (a) Semmelhack, M. F.; Bodurow, C.; Baum, M. *Tetrahedron Lett.* **1984**, *25*, 3171–3174; (b) Semmelhack, M. F.; Kim, C.; Zhang, N.; Bodurow, C.; Sanner, M.; Dobler, W.; Meier, M. *Pure Appl. Chem.* **1990**, *62*, 2035–2040.
10. (a) Ling, T.; Chowdhury, Ch.; Kramer, B. A.; Binh, G. V. *J. Org. Chem.* **2001**, *66*, 8843–8853; (b) Song, J.; Hollingsworth, R. I. *Tetrahedron: Asymmetry* **2001**, *12*, 387–391; (c) Barco, A.; Baricordi, N.; Benetti, S.; De Risi, C.; Pollini, G. P.; Zanirato, V. *Tetrahedron* **2007**, *63*, 4278–4283; (d) Jäger, V.; Häfele, B. *Synthesis* **1987**, 801–806; (e) Robertson, J.; Unsworth, W. P.; Lamont, S. G. *Tetrahedron* **2010**, *66*, 2363–2372; (f) Gallos, J. K.; Stathakis, Ch. I.; Salapassidou, M. J.; Grammatoglou, C. E.; Koumbis, A. E. *Carbohydr. Res.* **2007**, *342*, 744–748; (g) Hall, A.; Meldrum, K. P.; Therond, P. R.; Wightman, R. H. *Synlett* **1997**, 123–125; (h) Yang, M.; Ye, W.; Schneller, S. W. *J. Org. Chem.* **2004**, *69*, 3993–3996; (i) Va, P.; Roush, W. R. *Tetrahedron* **2007**, *63*, 5768–5796.
11. (a) Gracza, T.; Hasenöhrl, T.; Stahl, U.; Jäger, V. *Synthesis* **1991**, 1108–1118; (b) Babjak, M.; Zálupský, P.; Gracza, T. *Arkivoc* **2005**, *v*, 45–57; (c) Gracza, T.; Jäger, V. *Synthesis* **1994**, 1359–1368; (d) Dixon, D. J.; Ley, S. V.; Gracza, T.; Szolcsányi, P. *J. Chem. Soc., Perkin Trans. 1* **1999**, *8*, 839–841; (e) Babjak, M.; Kapitán, P.; Gracza, T. *Tetrahedron Lett.* **2002**, *43*, 6983–6985; (f) Babjak, M.; Kapitán, P.; Gracza, T. *Tetrahedron* **2005**, *61*, 2471–2479.
12. Bellovičová, L.; Kožíšek, J.; Doháňošová, J.; Lásiková, A.; Gracza, T. *Acta Crystallogr., Sect. E* **2010**, *66*(9), O2381. U930.
13. Ligand abbreviations: dppb = 1,4-bis(diphenylphosphino)butane; xanthphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxantene; dpephos = bis(2-diphenylphosphinophenyl)ether.
14. CCDC-88254 (for *cis*-**15**) and CCDC-882585 [for compound **21b**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
15. (a) Cardillo, G.; Orena, M. *Tetrahedron* **1990**, *46*, 3321–3408; (b) Orena, M., 4th ed. In *Houben-Weyl*; Helmchen, G., Hoffmann, R., Mulzer, J., Eds.; Thieme: Stuttgart, 1995; Vol. 2, pp 4698–4817; (c) Chamberlin, A. R.; Mulholland, R. L., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672–677; (d) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 666–671.