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Stereocontrolled palladium-catalysed umpolung allylation of aldehydes with allyl acetates

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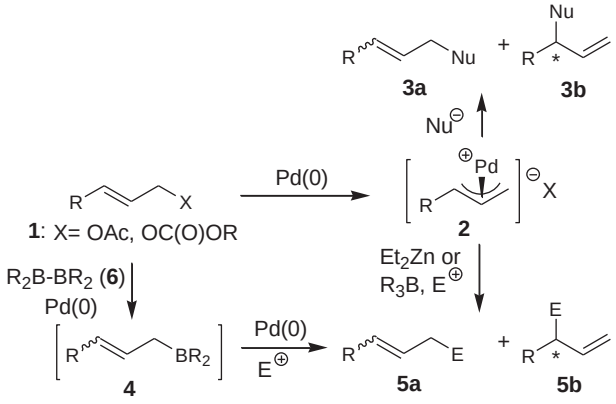
ABSTRACT

In the present work the stereocontrolled palladium-catalysed umpolung allylation of aldehydes is described. Allyl acetates are in situ transformed into the corresponding allyl boronates, which directly react with aldehydes. The question of stereocontrol is raised by employing (a) chiral boronating agents (reagent control) and by (b) utilising chiral aldehydes (substrate control). These studies reveal that the approach based on substrate control is superior to the former one with respect to yields and stereoselectivity. Remarkably, this umpolung protocol often yields the 4,5-*syn* products in high selectivity, which is unprecedented for direct crotylations.

1. Introduction

Trost and Tsuji pioneered the Pd(0)-catalysed asymmetric allylic alkylation of malonic esters and other nucleophiles (Nu^-) (**1**→**2**→**3**; Scheme 1), which has become one of the most studied C–C-bond-forming reactions in current asymmetric catalysis.[1,2]

In 1987, Brown and co-workers[3] published the first example of



Scheme 1. Pd(0)-catalysed electrophilic and nucleophilic allylations.

an umpolung allylation which was studied in detail by Tamaru et al.[4] They showed that the latent reactivity of the palladium allyl complex **2** can be reversed from electrophilic to nucleophilic in the presence of dialkylzinc or trialkylboron species. In situ formation of allylcopper and allyliridium species has recently been added in elegant works mainly by the group of Krische to the list of organometallic nucleophiles.[5] Importantly, Szabó and co-workers disclosed an efficient one-pot electrophilic allylation procedure (**1**→**4**→**5**) applying palladium–pincer complexes and diboranes **6**.[6]

The resulting umpolung reactions represent a complementary reaction to the existing allylation methodologies. In fact, it resembles the nucleophilic allylation of aldehydes (E^+) developed by Hoffmann, Roush and others, except that the allylborane/boronate is formed in situ from an electrophilic allyl precursor **1**.[7d] To date, there have been a few enantioselective examples of the dialkylzinc-mediated umpolung allylation (**2**→**5**) reported in the literature, namely by Zanoni, Zhou, and Feringa,[7] while the Szabó approach has not been tested in asymmetric allylations for constructing complex fragments of natural products.[8] One noteworthy feature of this umpolung reaction is the exclusive generation of the branched product **5b** due to formation of the sterically less hindered allyl boronate **4** (Scheme 1).[4] Thus, a terminal double bond and two new stereogenic centers are formed, which makes the transformation highly attractive for natural product synthesis, namely polyketides. Here, we disclose different strategies to control the relative and absolute configuration of the newly formed stereogenic centers during the palladium-catalysed umpolung with in situ generation of allyl boronates **4**.

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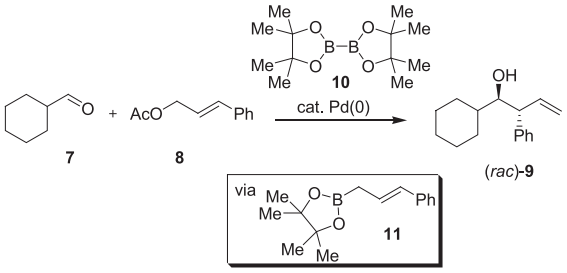
2. Results and discussion

One major advantage of this one-pot procedure stems from the fact that isolation of the labile boronate intermediates can be avoided. Preliminary optimisation studies were carried out based on known procedures[5] using aldehyde **7**, cinnamyl acetate **8**, and diboronate **10** as a model system (Table 1). In addition to different catalytic systems, the catalyst loading and reaction times were modified. Pd_2dba_3 (10 mol %) or $Pd(allyl)_2Cl_2$ in DMSO were found to be the best combinations (entries 4 and 5).[9] Other palladium sources either gave reduced yields of allylation products (entries 3, 5, and 7) or were completely inefficient (entries 1, 2, and 6). Overall, DMSO turned out to be the most suitable solvent, which is in accordance with Szabó's report.[6] The relative configuration of **9** was determined after conducting a short synthetic sequence, which comprises ozonolysis, reduction, and acetonide protection of the intermediate 1,3-diol.[10a] In all cases the anti-product (*rac*)-**9** was formed, which strongly indicates that pinacolallyl boronate **11** must be the reactive intermediate.

In view of this umpolung mechanism, stereocontrol can either be achieved by chiral allyl boronates[11] or by the substrate itself (chiral aldehydes) or by both control elements (double stereo-

Table 1
Optimisation of the model reaction[a]



Entry	Pd(0)	Solvent	Yield[b] [%]
1	$Pd(OAc)_2$, PPh_3	DMSO	0
2	$Pd(PPh_3)_4$	DMSO	0
3	$Pd(OAc)_2$	DMSO	46
4	$Pd_2(dba)_3$	DMSO	75
5	$Pd_2(allyl)_2Cl_2$	DMSO	70
6	Peppsi™	DMSO	0
7	$Pd(CH_3CN)_2Cl_2$	DMSO	38
8	$Pd_2(dba)_3$	Toluene	12
9	$Pd_2(dba)_3$	DMF	14
10	$Pd_2(dba)_3$	MeCN	45
11	$Pd_2(dba)_3$	CH_2Cl_2	0
12	$Pd_2(dba)_3$	THF	0

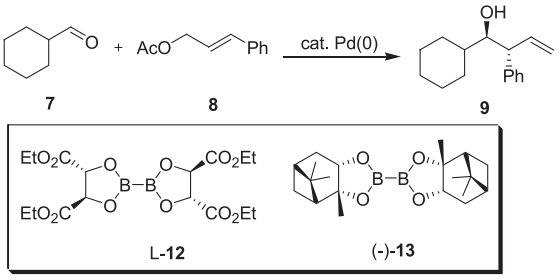
[a] All reactions were carried out using 1.2 equiv of boronate **10**, 1.0 equiv of **7**, 1.2 equiv of **8**, 10 mol % of catalyst, 40 °C, 20 h.
[b] Isolated yield; dr>20:1 (determined by ^{1}H NMR spectroscopy and according to Ref. 10).

differentiation). Initial studies with enantiopure diboronates **12** resulted in low yields and only moderate ee. When diboronate **13** was employed, the isolated yields improved but the ees dropped (Table 2).

One possible rationale for these results may be associated with the reaction temperature since the formation of allyl boronate **4** requires elevated temperatures whereas the allylation should give better stereocontrol at lower temperatures. The low melting point of DMSO (18 °C) prevents from carrying out a two-step procedure at lower temperature. However, similar experiments were conducted with MeCN, which did not give improved results.

As these preliminary results were unsatisfactory, we turned our attention to a substrate-controlled procedure, which relies on α-chiral aldehydes (Table 3). Hoffmann and Roush have extensively

Table 2
Asymmetric allylation using chiral diboronates **12** and **13**[a]



Entry	Boronate	Yield[b] [%] (ee)
1	**12** (D)	41 (40)
2	**12** (L)	39 (37)
3	**13** (+)	60 (21)
4	**13** (−)	50 (19)

[a] All reactions were carried out in degassed DMSO with 1.2 equiv of boronate **12** or **13**, 1.0 equiv of **7**, 1.2 equiv of **8**, 10 mol % of $Pd_2(dba)_3$, 40 °C, 20 h.
[b] Isolated yield; ees were determined by chiral GC (Hydrodex-β PM capillary column, 50 m, 0.25 mm).

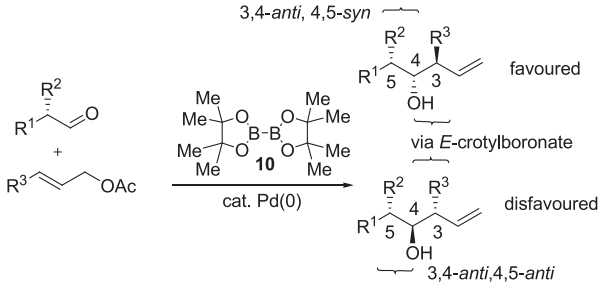
studied the reaction of substituted allyl boronates (like intermediate **11**) to α-chiral aldehydes and determined the resulting 4,5-stereochemistry.[12] (*E*)-Crotylboronates afforded the *anti*,*anti* and the *anti*,*syn* adducts that originate from different facial approaches of the reagent to the aldehyde. In the present study we chose α-siloxy-substituted aldehydes **17** and **18** as well as 2-phenylpropanal **19** as chiral substrates for the palladium-catalysed umpolung allylation with acetates **8** and (*rac*)-**14**, respectively (Table 3). All reactions proceeded with moderate to good yields and with remarkably high 3,4-*anti*-4,5-*syn* selectivities. The 4,5-stereochemistry of coupling products **20** and **24** was determined by comparison with ^{1}H NMR data reported in the literature.[13,14] The configuration of **22** was determined after transformation into the corresponding six-membered acetal.[15] For all other products **21**, **23**, and **25** it is assumed that the addition proceeds with the same diastereocontrol as determined for adducts **20**, **22**, and **24** listed in entries 1, 3, and 5 (Table 3).

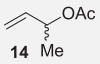
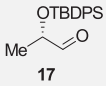
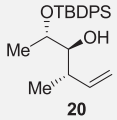
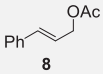
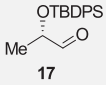
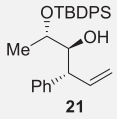
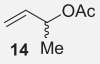
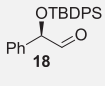
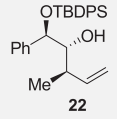
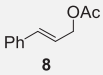
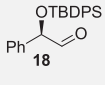
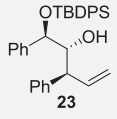
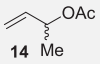
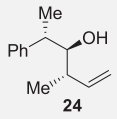
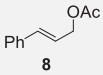
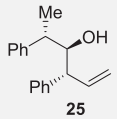
We extended these studies to complex aldehydes **26**, **28**, and **30** that are typical examples for preparing natural product backbones (Scheme 2). Except for the aldehyde **30**, which is relevant for the total synthesis of ansamycin antibiotics[16] such as geldanamycin, the allylations proceeded in good yield and for product **29** with excellent 4,5-*syn* selectivity. The absolute configuration of the secondary alcohol in **27** was determined by Mosher ester analysis.[17] The configuration of the new stereogenic centers in **29** was determined by analysis of the corresponding six-membered acetal.[10b]

Based on steric as well as electronic considerations Roush and co-workers provided a detailed analysis of why (*E*)-crotylboronates favor the formation of 4,5-*anti* adducts in reactions with α-chiral aldehydes.[12b] From a steric point of view transition states (TS) **II** and **III** (Fig. 1) should play a dominant role for generating 4,5-*anti* adducts, while Felkin–Anh transition state **I** should be made responsible for yielding 4,5-*syn* adducts.

Both, Hoffmann and Roush[12] noted that α-alkoxy-substituted aldehydes show a moderate *anti*-selectivity in the reaction with (*E*)-crotylboronates. Therefore, it can be assumed that also the electronic properties of the aldehyde influence diastereofacial selectivity. Thus, favorable electronic activation by the Cornforth-type TS **II** was additionally made responsible for the increased *anti*-selectivity. However, the reversed 4,5-*syn* selectivity for (*E*)-crotylboronate intermediates observed in this communication for the palladium-catalysed umpolung allylation is unprecedented. Remarkably, both types of α-chiral aldehydes, α-oxy aldehydes as well as 2-phenylpropanal preferentially gave the 4,5-*syn* adducts.

Table 3
Substrate-controlled stereoselective allylation using chiral aldehydes **17**–**19**[a]

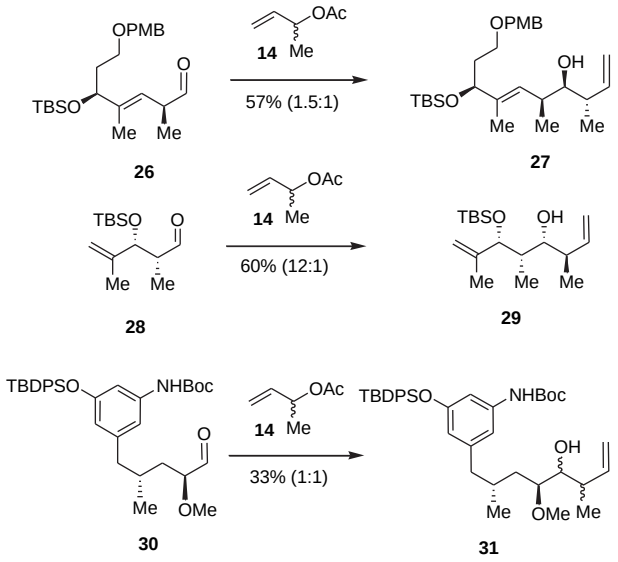


Entry	Acetate	Aldehyde	Major product	Yield [%] (dr) [b]
1	 **14**	 **17**	 **20**	73 (10:1)
2	 **8**	 **17**	 **21**	80 (5:1)
3	 **14**	 **18**	 **22**	65 (7:1)
4	 **8**	 **18**	 **23**	60[c]
5	 **14**	 **19**	 **24**	54 (5:1)
6	 **8**	 **19**	 **25**	58[c]

[a] All reactions were carried out in degassed DMSO with 1.2 equiv of boronate **10**, 1.0 equiv of aldehyde, 1.2 equiv of acetate, 10 mol % of $Pd_2(dba)_3$, 40 °C, 20 h.
[b] Isolated yield; major *syn*-diastereomer depicted; ratios determined by ^{1}H NMR spectroscopy.
[c] The 4,5-*anti*-diastereomer could not be detected.

These results are difficult to rationalise as one would expect the same principal Zimmermann–Traxler transition state for all three procedures. Therefore, we repeated Hoffmann's and Roush's experiments in our laboratories. We particularly added aldehydes **32** and **33** (entries 1 and 3) to the list of aldehydes because these have been studied by both groups before.[12b,14] We could reproduce their results with respect to yields and selectivities (Table 4). In all cases, the one-pot umpolung protocol gave increased 4,5-*syn* selectivities, very pronounced for α-siloxy aldehyde **17** (entry 2).

Having confirmed the unprecedented high 4,5-*syn* selectivity we finally focused on the parameters and selected additives that are relevant for the umpolung protocol and studied their influence on the stereochemical outcome of the classical Hoffmann crotylation using chiral α-siloxy aldehyde **17** (Table 5). This aldehyde had provided selectivities in the range of 5:1 to 10:1 in the umpolung protocol. However, this aldehyde reacted under Hoffmann conditions with boronate **34** without stereochemical preference (entry 1). No stereochemical change took place when the Pd source was added or DMSO was used as solvent except that the yield dropped



Scheme 2. Palladium-catalysed umpolung allylation with complex aldehydes.

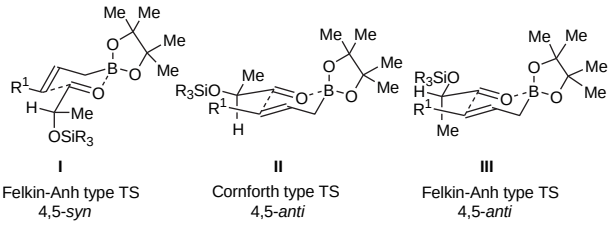
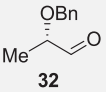
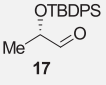
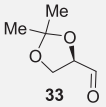
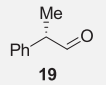


Figure 1. Relevant transition states **I**–**III**.

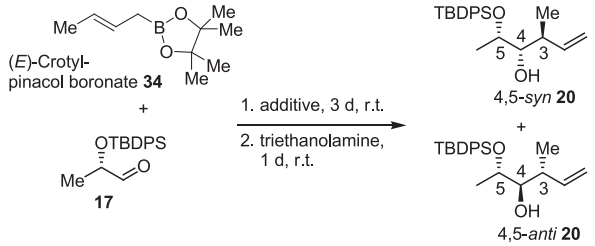
(entries 2–4). When a combination of Pd complex, DMSO, and boronate **10** was added the crotylation proceeded in excellent yield but again without any stereochemical preference (entry 5). Finally, we added boronate Lewis acids, which could be expected to be

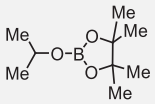
Table 4
Comparison of Hoffmann's and Roush's allylation protocol with the Pd-catalysed umpolung

Entry	Aldehyde	Conditions	Yield [%]	dr (*syn*:*anti*)
1	 **32**	Hoffmann[a,d]	97	1:1.1
		Pd-catalysed[b] umpolung	79	3:1
2	 **17**	Hoffmann[a]	Quant	1:1
		Roush[c]	97	1.3:1
		Pd-catalysed umpolung[b]	73	10:1
3	 **33**	Roush[c]	50	1:1
		Pd-catalysed umpolung[b]	58	1.3:1
4	 **19**	Hoffmann[a,d]	53	3:1
		Roush[c]	88	3:1
		Pd-catalysed umpolung[b]	54	5:1

[a] *Hoffmann conditions*[14]: 1.0 equiv of the aldehyde and 1.0 equiv of (*E*)-crotyl pinacol boronate **34** were stirred for 3 days at rt (neat).
[b] *Palladium-catalysed umpolung*: for details refer to Table 3 and the Experimental section.
[c] *Roush conditions*[12b]: 1.2 equiv of the aldehyde were dissolved in dry CH_2Cl_2 under nitrogen atmosphere and cooled to −78 °C. Then 1.0 equiv of (*E*)-crotyl pinacol boronate **34** was added and the reaction was stirred over night at −78 °C.
[d] Literature value.[14]

Table 5
Influence of additives on the stereochemical outcome of crotylating aldehyde **17** with boronate **34**



Entry	Additives or modified conditions	Yield [%]	dr (*syn*/*anti*)
1	None (*Hoffmann conditions*)	Quantitative	1:1
2	Pd_2dba_3 (10 mol %)	79	1:1
3	DMSO	47	1.3:1
4	40 °C	49	1:1
5	**10** (1.2. equiv), Pd_2dba_3 (10 mol %), DMSO, 40 °C	Quantitative	1:1
6	 (1.2 equiv)	80	1.7:1
7	Pinacol borane (1.2 equiv)	66	1:1

byproducts from the umpolung protocol. However, only a minor effect toward 4,5-*syn* selectivity was encountered, far away from the 10:1 ratio observed in the Pd-catalysed umpolung (entry 1, Table 3).

At this stage, we have to encounter doubt whether the transition state or the course of the umpolung reaction is identical with those for the direct crotylation developed by Roush and Hoffmann, respectively. As none of the altered reaction conditions had a profound influence on the selectivity further studies are necessary to unravel the mechanistic details of the palladium-catalysed umpolung reaction.

3. Conclusion

In summary, we disclosed the stereochemical outcome of the palladium-catalysed umpolung allylation of aldehydes with allyl acetates. This protocol has several beneficial features compared to classical crotylations such as the possibility of the in situ generation of allyl boronates and the option of employing racemic allyl acetates.[18] Remarkably, an unprecedented high 4,5-*syn* selectivity was found for selected chiral aldehydes. In conclusion, the umpolung procedure can become a promising tool for the stereoselective synthesis of complex structural fragments that are present in many polyketides. Investigations on improved catalytic conditions and the extension of this one-pot umpolung methodology on more elaborated allyl acetates and aldehydes that would allow to merge large polyketide fragments are currently under way in our laboratories.

4. Experimental

4.1. General

All experiments were performed under a nitrogen atmosphere in oven-dried glassware. Anhydrous THF was obtained by distillation from sodium and benzophenone. All other chemicals and solvents were purchased from Acros, Sigma–Aldrich, and ABCR. HRMS data were obtained on a Micromass LCT electrospray ionisation spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 (400 MHz and 100 MHz). Compounds **7**, **8**, **10**, L-**12**, and (−)-**13** are commercially available. Compounds **26**, **28**, and **30** were prepared according to literature procedures.[19]

4.2. Preparation of allyl acetates and aldehydes

*4.2.1. (rac)-3-Butene-2-methylacetate (**14**)*[20]. 3-Butene-2-ol (5.0 g, 69.3 mmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (157 ml) under a nitrogen atmosphere and cooled to 0 °C. Dry pyridine (5.4 mL, 76.3 mmol, 1.1 equiv) was added and then acetyl chloride (6.0 mL, 74.1 mmol, 1.07 equiv) was added dropwise. After 90 min the reaction was hydrolysed with water (40 mL). The organic phase was washed with brine and water, dried (Na_2SO_4), and concentrated in vacuo. As a result, 7.8 g (68.3 mmol, 99%) of the product were obtained as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.82 (ddd, J=17.2, 10.6, 6.2 Hz, 1H, H-3), 5.32 (dq, J=6.6, 6.2 Hz, 1H, H-2), 5.22 (d, J=17.2 Hz, 1H, H-4a), 5.12 (d, J=10.6 Hz, 1H, H-4b), 2.04 (s, 3H, COMe), 1.29 (d, J=6.6 Hz, 3H, H-1); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.4 (q, CO), 137.8 (t, C-3), 115.8 (s, C-4), 71.0 (t, C-2), 21.4 (p, C-1), 20.0 (p, COMe).

*4.2.2. (2S)-(tert-Butyldiphenylsiloxy)-propanal (**17**).* (2*S*)-(*tert*-Butyldiphenylsiloxy)-*N*-methoxy-*N*-methyl-propionamid[21] (30 mg, 0.081 mmol, 1.0 equiv) was dissolved in dry THF (0.6 mL) under a nitrogen atmosphere and cooled to −78 °C. DIBAL-H (0.4 mL, 0.404 mmol, 1.0 M in hexane, 5.0 equiv) was added dropwise over 5 min and the mixture was stirred for 30 min at −78 °C. The reaction was hydrolysed by addition of ethyl acetate (0.1 mL) and diluted with a solution of K–Na–tartrate (10%, aq) and CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2 and the combined organic extracts were dried ($MgSO_4$). After removal of the solvent aldehyde **17** was obtained quantitatively as a colorless oil and directly submitted to the umpolung reaction.

*4.2.3. (R)-(tert-Butyldiphenylsiloxy)-phenyl-acetaldehyde (**18**).* Aldehyde **18** (0.16 mmol) was prepared from the corresponding Weinreb amide according to the procedure described for aldehyde **17**. It was obtained in quantitative yield (60 mg, 0.16 mmol) as a colorless oil.

*4.2.4. (2R)-Phenyl-propionaldehyde (**19**).* (2*R*)-Phenyl-propanol (40 mg, 294 μmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 (30 mL) under nitrogen atmosphere and cooled to 0 °C. Then $NaHCO_3$ (30 mg, 353 μmol, 1.2 equiv) and Dess–Martin-periodinane (149 mg, 353 μmol, 1.2 equiv) were added and the reaction was stirred for 1 h at room temperature. The reaction was hydrolysed by addition of a 1:1 mixture of $Na_2S_2O_3$ (satd, aq) and $NaHCO_3$ (satd, aq). The aqueous phase was extracted with CH_2Cl_2 and the combined organic extracts were washed with $NaHCO_3$ (aq) and dried ($MgSO_4$). After removal of the solvent 32 mg (235 μmol, 80%) of the product were obtained as a colorless oil, which was directly submitted to the umpolung reaction.

*4.2.5. (2S, 5R)-5-(tert-Butyldimethylsiloxy)-7-(4-methoxy-benzyloxy)-2,4-dimethyl-hept-3-enal (**26**).* Aldehyde **26** (49 μmol) was prepared by Dess–Martin oxidation from the corresponding alcohol according to the procedure described for aldehyde **19** and was directly submitted to the umpolung reaction. The aldehyde was obtained in quantitative yield (20 mg, 49 μmol) as a colorless oil.

*4.2.6. (2R, 3R)-3-(tert-Butyldimethylsiloxy)-2,4-dimethyl-pent-4-enal (**28**).* Aldehyde **28** (269 μmol) was prepared by reduction with DIBAL-H from the corresponding Weinreb amide as a colorless oil according to the procedure described for aldehyde **17** and was

directly submitted to the umpolung reaction. The aldehyde was obtained in quantitative yield (65 mg, 269 μmol) as a colorless oil.

*4.2.7. (2S, 4R)-5-[tert-Butoxycarbonylamino-3-(tert-butyldiphenylsiloxy)-phenyl]-4-methyl-2-methoxy-1-pentanal (**30**).* Aldehyde **30** (26 μmol) was prepared by Dess–Martin oxidation from the corresponding alcohol according to the procedure described for aldehyde **19** and was directly submitted to the umpolung reaction. It was obtained in quantitative yield (15 mg, 26 μmol) as a colorless oil.

4.3. General procedure for the palladium-catalysed umpolung

Procedure A: $Pd_2(dba)_3$–chloroform adduct (29 mg, 28.8 μmol, 0.1 equiv) was dissolved in degassed DMSO (3 mL) under a nitrogen atmosphere. The aldehyde (288 μmol, 1.0 equiv) and the allyl acetate (346 μmol, 1.2 equiv) were added and the reaction mixture was stirred for 10 min at room temperature. After addition of bis(pinacol)boronate **10** (88 mg, 346 μmol, 1.2 equiv) the reaction was warmed to 40 °C and stirred for 20 h. The reaction was hydrolysed with water (3 mL). After stirring for 1 h at room temperature, the mixture was extracted with diethylether. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography.[22]

Procedure B: $Pd_2(dba)_3$–chloroform adduct (29 mg, 28.8 μmol, 0.1 equiv) was dissolved in degassed DMSO (3 mL) under a nitrogen atmosphere. The allyl acetate (346 μmol, 1.2 equiv) was added and the reaction mixture was stirred for 10 min at room temperature. After addition of bis(pinacol)boronate (88 mg, 346 μmol, 1.2 equiv) the reaction was warmed to 40 °C. After stirring for 15 min the aldehyde (288 μmol, 1.0 equiv) was added and the reaction mixture was stirred at 40 °C for 20 h. The reaction was hydrolysed with water (3 mL). After stirring for 1 h at room temperature, the mixture was extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography.[21]

4.4. Analytical data of the coupling products

*4.4.1. (rac)-1-Cyclohexyl-2-phenylbut-3-en-1ol (**9**).* Compound **9** was prepared as a colorless oil according to procedure A and was obtained in 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32–7.18 (m, 5H, Ph), 6.13 (ddd, J=19.7, 17.0, 8.9 Hz, 1H, H-3), 5.20 (dd, J=10.7, 1.7 Hz, 1H, H-4a), 5.17 (ddd, J=17.0, 1.7, 0.7 Hz, 1H, H-4b), 3.58–3.53 (m, 1H, H-1), 3.44 (dd, J=8.9, 7.1 Hz, 1H, H-2), 1.83–1.81 (m, 1H, Cy), 1.70–1.57 (m, 4H, Cy), 1.26–1.05 (m, 6H, Cy); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.2 (t, C-3), 138.6 (q, Ph), 128.9 (t, Ph), 128.0 (t, Ph), 126.7 (t, Ph), 117.8 (s, C-4), 78.2 (t, C-1), 53.8 (t, C-2), 39.7 (t, Cy), 30.3 (s, Cy), 26.7 (s, Cy), 26.6 (s, Cy), 26.5 (s, Cy), 26.1 (s, Cy); HRMS $[M+Na]^+$ calcd for $C_{16}H_{22}ONa$: 253.1568, found 253.1564.

*4.4.2. (2S, 3S, 4S)-2-(tert-Butyldiphenylsiloxy)-4-methyl-5-hexen-3-ol (**20**).* Compound **20** was prepared according to procedure A and was obtained in 73% yield as a pale yellow oil (dr 10:1). $[\alpha]_D^{20}$ −5.6 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70–7.68 (m, 4H, Ph), 7.45–7.35 (m, 6H, Ph), 5.80 (ddd, J=16.5, 10.3, 7.5 Hz, 1H, H-5), 4.96 (d, J=10.3 Hz, 1H, H-6a), 4.93 (d, J=16.5 Hz, 1H, H-6b), 3.85 (dq, J=6.0, 5.5 Hz, 1H, H-2), 3.20 (ddd, J=5.9, 5.5, 4.7 Hz, 1H, H-3), 2.51 (d, J=4.7 Hz, 1H, O*H*), 2.29 (ddq, J=7.5, 6.9, 5.9 Hz, 1H, H-4), 1.06 (s, 9H, Si^{t}Bu), 1.01 (d, J=6.0 Hz, 3H, H-1), 0.97 (d, J=6.9 Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.3 (t, C-5), 136.0 (t, Ph), 136.0 (t, Ph), 135.4 (q, Ph), 134.3 (q, Ph), 129.9 (t, Ph), 127.8 (t, Ph), 115.0 (s, C-6), 79.5 (t, C-3), 71.1 (t, C-2), 40.5 (t, C-4), 27.2 (p, Si^{t}Bu), 20.1 (p, Me), 19.5 (q, Si^{t}Bu), 17.6 (p, C-1); HRMS $[M-{}^t\text{Bu}]^+$ calcd for $C_{19}H_{23}O_2Si$: 311.1462, found 311.1465.

*4.4.3. (2S, 3S, 4S)-2-(tert-Butyldiphenylsiloxy)-4-phenyl-5-hexen-3-ol (**21**).* Compound **21** was prepared according to procedure A and was obtained in 80% yield as a colorless oil (dr 5:1). The diastereoisomers could not be separated. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64–7.56 (m, 4H, SiPh), 7.47–7.32 (m, 6H, SiPh), 7.15–7.11 (m, 3H, Ph), 6.81–6.79 (m, 2H, Ph), 6.03 (ddd, J=17.1, 8.1, 8.0 Hz, 1H, H-5), 4.98 (dd, J=17.1, 8.0 Hz, 2H, H-6), 3.86 (ddd, J=9.0, 2.9, 1.4 Hz, 1H, H-3), 3.58 (dq, J=6.4, 2.9 Hz, 1H, H-2), 3.18 (dd, J=9.0, 8.1 Hz, 1H, H-4), 2.54 (d, J=1.4 Hz, 1H, O*H*), 1.04 (br s, 12H, H-1 and Si^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.2 (q, Ph), 139.9 (t, C-5), 135.9 (t, SiPh), 135.9 (t, SiPh), 133.9 (q, SiPh), 133.6 (q, SiPh), 129.9 (t, SiPh), 129.7 (t, SiPh), 128.7 (t, Ph), 127.9 (t, SiPh), 127.8 (t, Ph), 127.6 (t, SiPh), 126.5 (t, Ph), 116.1 (s, C-6), 76.8 (t, C-3), 70.1 (t, C-2), 52.6 (t, C-4), 27.2 (p, Si^{t}Bu), 19.2 (q, Si^{t}Bu), 15.5 (p, C-1); HRMS $[M+Na]^+$ calcd for $C_{28}H_{34}O_2SiNa$: 453.2226, found 453.2218.

*4.4.4. (1R, 2R, 3R)-1-(tert-Butyldiphenylsiloxy)-3-methyl-1-phenyl-pent-4-en-2-ol (**22**).* Compound **22** was prepared according to procedure A and was obtained in 65% yield as a pale yellow oil (dr 7:1). $[\alpha]_D^{20}$ −43.5 (*c* 2.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63–7.07 (m, 15H, Ph), 5.76 (ddd, J=17.0, 10.2, 9.2 Hz, 1H, H-4), 4.91 (d, J=11.0 Hz, 1H, H-5a), 4.78 (d, J=17.9 Hz, 1H, H-5b), 4.54 (d, J=8.1 Hz, 1H, H-1), 3.66 (ddd, J=8.1, 2.5 Hz, 1H, H-2), 2.81 (br s, 1H, O*H*), 1.87 (ddq, J=9.2, 6.7 Hz, 1H, H-3), 1.01 (s, 9H, Si^{t}Bu), 0.96 (d, J=6.7 Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 140.9 (q, Ph), 139.1 (t, C-4), 136.1 (t, Ph), 135.9 (t, Ph), 133.7 (q, Ph), 133.0 (q, Ph), 129.8 (t, Ph), 129.6 (t, Ph), 128.1 (t, Ph), 127.8 (t, Ph), 127.7 (t, Ph), 115.6 (s, C-5), 80.7 (t, C-2), 79.7 (t, C-1), 38.8 (t, C-3), 27.1 (p, Si^{t}Bu), 19.5 (q, Si^{t}Bu), 18.8 (p, Me); HRMS $[M+Na]^+$ calcd for $C_{28}H_{34}O_2SiNa$: 453.2226, found 453.2237.

*4.4.5. (1R, 2R, 3S)-1-(tert-Butyldiphenylsiloxy)-1,3-diphenyl-pent-4-en-2-ol (**23**).* Compound **23** was prepared according to procedure A and was obtained in 60% yield as a colorless oil (only one diastereoisomer could be detected). $[\alpha]_D^{20}$ −21.3 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64–7.62 (m, 2H, Ph), 7.45–7.30 (m, 6H, Ph), 7.21–7.14 (m, 8H, Ph), 7.08–7.05 (m, 4H, Ph), 6.17 (ddd, J=17.3, 9.8, 9.4 Hz, 1H, H-4), 5.08 (dd, J=9.8, 1.5 Hz, 1H, H-5a), 4.87 (dd, J=17.3, 1.5 Hz, 1H, H-5b), 4.61 (d, J=7.9 Hz, 1H, H-1), 4.07–4.03 (m, 1H, H-2), 3.03 (dd, J=9.4, 3.1 Hz, 1H, H-3), 3.00 (d, J=3.1 Hz, 1H, O*H*), 1.00 (s, 9H, Si^{t}Bu); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.1 (q, Ph), 141.1 (q, Ph), 136.9 (t, C-4), 136.4 (t, Ph), 136.2 (t, Ph), 133.8 (q, Ph), 133.1 (q, Ph), 130.1 (t, Ph), 129.9 (t, Ph), 128.6 (t, Ph), 128.5 (t, Ph), 128.3 (t, Ph), 128.2 (t, Ph), 128.1 (t, Ph), 127.9 (t, Ph), 127.6 (t, Ph), 126.6 (t, Ph), 117.8 (s, C-5), 79.5 (t, C-2), 78.1 (t, C-1), 50.8 (t, C-3), 27.3 (p, Si^{t}Bu), 19.7 (q, Si^{t}Bu); HRMS $[M+Na]^+$ calcd for $C_{33}H_{36}O_2Si_1Na$: 515.2392, found 515.2382.

*4.4.6. (2R, 3R, 4R)-2-Phenyl-4-methyl-hex-5-en-3-ol (**24**).* Compound **24** was prepared according to procedure A and was obtained in 54% yield as a pale yellow oil (dr 5:1). $[\alpha]_D^{20}$ +22.5 (*c* 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.43–7.39 (m, 1H, Ph), 7.35–7.29 (m, 2H, Ph), 7.23–7.19 (m, 2H, Ph), 5.83 (ddd, J=17.4, 11.0, 7.2 Hz, 1H, H-5), 5.13 (d, J=11.0 Hz, 1H, H-6a), 5.04 (d, J=17.4 Hz, 1H, H-6b), 3.50 (dd, J=6.1, 6.1 Hz, 1H, H-3), 2.85 (dq, J=7.0, 6.1 Hz, 1H, H-2), 2.20 (ddq, J=7.2, 6.8, 6.1 Hz, 1H, H-4), 1.51 (d, J=5.4 Hz, 1H, O*H*), 1.32 (d, J=7.0 Hz, 3H, H-1), 1.05 (d, J=6.8 Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.1 (q, Ph), 139.5 (t, C-5), 128.6 (t, Ph), 127.8 (t, Ph), 126.4 (t, Ph), 116.6 (s, C-6), 79.4 (t, C-3), 43.2 (t, C-2), 40.6 (t, C-4), 17.4 (p, C-1), 16.4 (p, Me); HRMS $[M+H]^+$ calcd for $C_{13}H_{19}O$: 191.1430, found 191.0863.

*4.4.7. (2R, 3R, 3R)-2,4-Diphenyl-hex-5-en-3-ol (**25**).* Compound **25** was prepared according to procedure A and was obtained in 58%

yield as a pale yellow oil (only one diastereomer could be detected). $[\alpha]_D^{20}$ +14.6 (*c* 1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.18 (m, 10H, Ph), 6.17 (ddd, *J*=17.6, 9.9, 9.2 Hz, 1H, H-5), 5.22 (dd, *J*=9.9, 1.7 Hz, 1H, H-6a), 5.09 (d, *J*=17.6 Hz, 1H, H-6b), 3.99–3.94 (m, 1H, H-3), 3.32 (dd, *J*=9.2, 6.8 Hz, 1H, H-4), 2.78–2.71 (m, 1H, H-2), 1.75 (d, *J*=3.4 Hz, 1H, O*H*), 1.30 (d, *J*=7.2 Hz, 3H, H-1); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 145.4 (q, Ph), 142.5 (q, Ph), 138.1 (t, C-5), 129.2 (t, Ph), 128.8 (t, Ph), 128.2 (t, Ph), 128.1 (t, Ph), 127.0 (t, Ph), 126.7 (t, Ph), 118.3 (p, C-6), 78.8 (t, C-3), 54.1 (t, C-4), 42.2 (t, C-2), 15.3 (p, C-1); HRMS $[M+H]^+$ calcd for $C_{18}H_{21}O$: 253.1587, found 253.1570.

*4.4.8. (3S, 4S, 5S, 8R)-8-(tert-Butyldimethylsiloxy)-10-(4-methoxybenzyloxy)-3,5,7-trimethyl-deca-1,6-dien-4-ol (**27**).* Compound **27** was prepared according to procedure B and was obtained in 57% yield as a yellow oil (dr 1.5:1). $[\alpha]_D^{20}$ −4.3 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.26–7.24 (m, 2H, Ph), 6.88–6.86 (m, 2H, Ph), 5.79 (ddd, *J*=17.2, 10.3, 7.2 Hz, 1H, H-2), 5.20 (d, *J*=9.8 Hz, 1H, H-6), 5.09 (dd, *J*=17.2, 10.3 Hz, 2H, H-1), 4.42 (d, *J*=11.4 Hz, 1H, C*H*$_2$PMB), 4.36 (d, *J*=11.4 Hz, 1H, C*H*$_2$PMB), 4.13 (dd, *J*=7.3, 5.6 Hz, 1H, H-8), 3.80 (s, 3H, OMe), 3.49–3.38 (m, 2H, H-10), 3.19–3.15 (m, 1H, H-4), 2.46 (ddq, *J*=9.8, 6.9, 6.6 Hz, 1H, H-5), 2.36 (ddq, *J*=7.2, 7.1, 4.4 Hz, 1H, H-3), 1.80–1.70 (m, 2H, H-9), 1.55 (s, 3H, Me), 1.38 (d, *J*=6.1 Hz, 1H, O*H*), 1.06 (d, *J*=7.0 Hz, 3H, Me), 0.94 (d, *J*=6.4 Hz, 3H, Me), 0.87 (s, 9H, Si^{t}Bu), 0.02 (s, 3H, SiMe), −0.01 (s, 3H, SiMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.2 (q, $C_{aromat.}$), 139.4 (t, C-2), 137.3 (q, C-7), 130.8 (q, $C_{aromat.}$), 129.4 (t, $C_{aromat.}$), 128.1 (t, C-6), 116.5 (s, C-1), 113.8 (t, $C_{aromat.}$), 79.2 (t, C-4), 75.1 (t, C-8), 72.8 (s, *C*H$_2$PMB), 67.1 (s, C-10), 55.4 (p, OMe), 40.8 (t, C-5), 36.8 (s, C-9), 36.0 (t, C-3), 25.9 (p, Si^{t}Bu), 18.3 (q, Si^{t}Bu), 17.4 (p, Me), 16.2 (p, Me), 11.7 (p, Me), −4.4 (p, SiMe), −4.9 (p, SiMe); HRMS $[M+Na]^+$ calcd for $C_{27}H_{46}O_4SiNa$: 485.3063, found 485.3052.

*4.4.9. (3R, 4R, 5S, 6R)-6-(tert-Butyl-dimethyl-siloxy)-3,5,7-trimethyl-octa-1,7-dien-4-ol (**29**).* Compound **29** was prepared according to procedure A and was obtained in 60% yield as a colorless oil (dr 12:1). $[\alpha]_D^{20}$ −4.1 (*c* 1.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.72 (ddd, *J*=17.1, 9.6, 9.3 Hz, 1H, H-2), 5.11 (d, *J*=17.1 Hz, 1H, H-1a), 5.09 (d, *J*=9.67 Hz, 1H, H-1b), 4.93 (s, 1H, H-8a), 4.87 (s, 1H, H-8b), 4.07 (d, *J*=7.9 Hz, 1H, H-6), 3.22 (d, *J*=7.9 Hz, 1H, H-4), 2.90 (br s, 1H, O*H*), 2.29–2.23 (m, 1H, H-3), 1.77–1.73 (m, 1H, H-5), 1.66 (s, 3H, H$_2$CCC*H*$_3$), 0.94–0.90 (m, 15H, 2× C*H*$_3$, Si^{t}Bu), 0.07 (s, 6H, SiMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.1 (q, C-7), 142.1 (t, C-2), 116.1 (s, C-1), 113.2 (s, C-8), 80.3 (t, C-7), 75.0 (t, C-4), 42.5 (t, C-5), 38.0 (t, C-3), 26.1 (p, Si^{t}Bu), 18.4 (q, Si^{t}Bu), 17.5 (p, C-7), 16.7 (p, C-5), 8.1 (p, C-3), −4.4 (p, SiMe), −4.9 (p, SiMe); HRMS $[M+Na]^+$ calcd for $C_{17}H_{34}O_2SiNa$: 321.2226, found 321.2226.

*4.4.10. (2S, 4R)-5-[tert-Butoxycarbonylamino-3-(tert-butyldiphenylsiloxy)-phenyl]-4-hydroxy-5-methoxy-3,7-dimethyl-oct-2-en (**31**).* Compound **31** was prepared according to procedure B and was obtained in 33% yield as a yellow oil (dr 1:1). The diastereoisomers could not be separated. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71–7.68 (m, 7H, SiPh), 7.43–7.33 (m, 11H, SiPh), 6.81 (s, 1H, Ph), 6.77 (s, 1H, Ph), 6.66 (s, 1H, Ph), 6.63 (s, 1H, Ph), 6.25 (s, 2H, NH), 6.15 (s, 1H, Ph), 6.14 (s, 1H, Ph), 5.90–5.75 (m, 2H, H-2), 5.12–4.93 (m, 4H, H-1), 3.53 (dd, *J*=7.8, 3.7 Hz, 1H, H-4), 3.30 (s, 3H, OMe), 3.27 (s, 3H, OMe), 3.23–3.20 (m, 2H, H-4 and H-5a), 3.18–3.12 (m, 1H, H-5b), 2.43 (dd, *J*=13.3, 5.8 Hz, 1H, H-8a), 2.34 (dd, *J*=13.3, 6.1 Hz, 1H, H-8a), 2.28–2.17 (m, 2H, H-3), 2.14–2.05 (m, 2H, H-8b), 1.76–1.72 (m, 1H, H-7), 1.67–1.62 (m, 1H, H-7), 1.60–1.58 (m, 1H, H-6a), 1.53 (s, 15H, ^{t}Bu), 1.47–1.44 (m, 1H, H-6a), 1.37–1.10 (m, 2H, H-6b), 1.07 (s, 15H, 2×Si^{t}Bu), 1.04 (d, *J*=6.8 Hz, 3H, H-9), 0.94 (d, *J*=6.8 Hz, 3H, H-9), 0.69 (d, *J*=6.4 Hz, 3H, H-10), 0.63 (d, *J*=6.8 Hz, 3H, H-10); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.9 (q, NCO), 155.9 (q, NCO), 152.6 (q, $C_{aromat.}$), 143.0 (q, $C_{aromat.}$), 142.9 (q, $C_{aromat.}$), 141.3 (t, C-2), 140.1 (t, C-2), 139.1 (q, $C_{aromat.}$), 139.0 (q, $C_{aromat.}$), 135.6 (t, $C_{aromat.}$), 135.6 (t, $C_{aromat.}$), 135.6 (t, $C_{aromat.}$), 133.1 (q, $C_{aromat.}$), 133.0 (q, $C_{aromat.}$), 133.0 (q, $C_{aromat.}$), 129.9 (t, $C_{aromat.}$), 129.9 (t, $C_{aromat.}$), 129.9 (t, $C_{aromat.}$), 129.9 (t, $C_{aromat.}$), 127.8 (t, $C_{aromat.}$), 127.8 (t, $C_{aromat.}$), 127.8 (t, $C_{aromat.}$), 115.5 (s, C-1), 115.5 (s, C-1), 115.4 (t, $C_{aromat.}$), 115.3 (t, $C_{aromat.}$), 112.3 (t, $C_{aromat.}$), 112.2 (t, $C_{aromat.}$), 107.6 (t, $C_{aromat.}$), 80.4 (q, ^{t}Bu), 79.9 (t, C-5), 79.8 (t, C-5), 76.1 (t, C-4), 73.8 (t, C-4), 57.6 (p, OMe), 57.2 (p, OMe), 44.6 (s, C-8), 44.3 (s, C-8), 40.7 (t, C-3), 39.8 (t, C-3), 37.2 (s, C-6), 35.3 (s, C-6), 31.3 (t, C-7), 30.9 (t, C-7), 28.4 (p, ^{t}Bu), 26.6 (p, Si^{t}Bu), 19.7 (p, C-10), 19.5 (q, Si^{t}Bu), 18.7 (p, C-10), 17.7 (p, C-9), 16.2 (p, C-9); HRMS $[M+H]^+$ calcd for $C_{38}H_{54}NO_5Si$: 632.3771, found 632.3770.

4.5. General procedure for the Hoffmann procedure[14]

(*E*)-Crotyl pinacol boronate **34** (30 μL, 138 μmol, 1.0 equiv) and the aldehyde (138 μmol, 1.0 equiv) were mixed in a flask and stirred for 3 days at room temperature. The reaction was hydrolysed with triethanolamine (19 μL, 138 μmol, 1.0 equiv) and diluted with petroleum ether and CH_2Cl_2 (1 mL, 1:1). After stirring for 1 day the solvents were evaporated and the residue was purified by flash chromatography.

Analytical data for the product of the reaction of aldehyde **32** with boronate **34** can be found in Ref. 14.

4.6. General procedure for the Roush procedure

(*E*)-Crotyl pinacol boronate **34** (66 μL, 320 μmol, 1.0 equiv) was dissolved in dry CH_2Cl_2 under an argon atmosphere and cooled to −78 °C. The aldehyde (384 μmol, 1.2 equiv) was added and stirring was continued at −78 °C for 2 h. The mixture was allowed to warm to room temperature over night and was hydrolysed with H_2O (1 mL). The aqueous phase was extracted with ethyl acetate and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by flash chromatography.

Analytical data for the product of the reaction of aldehyde **33** with boronate **34** can be found in Ref. 12b.

4.7. General procedure for mechanistic investigation experiments (Table 5)

(*E*)-Crotyl pinacol boronate **34** (42 μL, 192 μmol, 1.0 equiv) and (2*S*)-(*tert*-butyldiphenylsiloxy)-propanal **17** (60 mg, 192 μmol, 1.0 equiv) were mixed in a flask. Then the particular additive was added (amounts given in Table 5) and the reaction mixture was stirred for 3 days at room temperature. The reaction was hydrolysed with triethanolamine (19 μL, 138 μmol, 1.0 equiv) and diluted with petroleum ether and CH_2Cl_2 (1 mL, 1:1). After stirring for 1 day the solvents were evaporated and the residue was purified by flash chromatography.

When DMSO was added the hydrolysed reaction mixture was submitted to usual aqueous workup before it was purified by flash chromatography.

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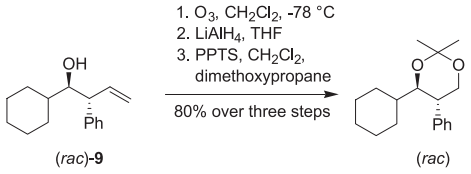
Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.04.133.

References and notes

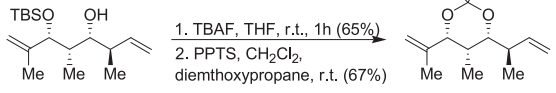
1. (a) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2944; (b) Review Trost, B. M. *J. Org. Chem* **2004**, *69*, 5813–5873.

2. Tsuji, J. *Pure Appl. Chem* **1982**, *54*, 197–206.
3. Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1987**, *52*, 3702–3704.
4. (a) Kimura, M.; Shimizu, M.; Shibata, K.; Tazoe, M.; Tamaru, Y. *Angew. Chem., Int. Ed.* **2003**, *42*, 3392–3395; (b) Tamaru, Y. *J. Organomet. Chem.* **1999**, *576*, 215–231; (c) Tamaru, Y.; Tanaka, A.; Yasui, K.; Goto, S.; Tanaka, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 787–789; (d) Yasui, Y. G.; Yajima, T.; Taniseki, Y.; Fugami, A.; Tamaru, Y. *Tetrahedron Lett.* **1993**, *34*, 7619–7622; (e) Qiao, X.-C.; Zhu, S.-F.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2009**, *20*, 1254–1261; (f) Ito, H.; Okura, T.; Matsuura, K.; Sawamura, M. *Angew. Chem.* **2010**, *122*, 570–573; *Angew. Chem., Int. Ed.* **2010**, *49*, 560–563.
5. (a) Itoh, J.; Han, S. B.; Krische, M. J. *Angew. Chem.* **2009**, *121*, 6431–6434; *Angew. Chem., Int. Ed.* **2009**, *48*, 6313–6316; (b) Lu, Y.; Krische, M. J. *Org. Lett.* **2009**, *11*, 3108–3111; (c) Han, S. B.; Kim, I. S.; Krische, M. J. *Chem. Commun.* **2009**, 7278–7287.
6. (a) Selander, N.; Kipke, A.; Sebelius, S.; Szabó, K. J. *J. Am. Chem. Soc.* **2007**, *129*, 13723–13731; (b) Sebelius, S.; Olsson, V. J.; Wallner, O. A.; Szabó, K. J. *J. Am. Chem. Soc.* **2006**, *128*, 8150–8151.
7. Asymmetric umpolung examples: (a) Zanoni, G.; Gladiali, S.; Marchetti, A.; Piccinini, P.; Tredici, I.; Vidari, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 846–849; (b) Zhu, S. F.; Yang, Y.; Wang, L. X.; Liu, B.; Zhou, Q. L. *Org. Lett.* **2005**, *7*, 2333–2335; (c) Howell, G. P.; Minnaard, A. J.; Feringa, B. L. *Org. Biomol. Chem.* **2006**, *4*, 1278–1283 For a recent review on asymmetric allylations of aldehydes and applications in synthesis, see: (d) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763–2794.
8. Selander, N.; Sebelius, S.; Estay, C.; Szabó, K. J. *Eur. J. Org. Chem.* **2006**, 4085–4087.
9. Ishiyama, T.; Ahiko, T.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 6889–6892.
10. (a) The relative stereochemistry was determined after a three-step modification of product **9** and analysis was carried out according to Rychnowsky et al.: Rychnovsky, S.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945–948 Thus, the anti-configuration was assigned based on the large coupling constant $J_{H\text{-}4,\ H\text{-}5}$=10.8 Hz; see also Lombardo, M.; Morganti, S.; Tozzi, M.; Trombini, C. *Eur. J. Org. Chem.* **2002**, 2823–2830 who determined a J=10.6 Hz for a related case.



(*rac*)-**9** (*rac*)

(b) The relative stereochemistry was determined after a two-step modification of compound **29** and analysis was carried out according to Rychnowsky, et al. (see Ref. 10a). Based on the ^{13}C NMR signals of the methyl groups (δ: 30.1, 19.6 ppm) the *syn* configuration was assigned.



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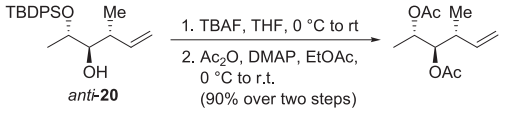
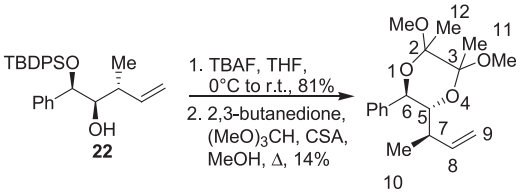
11. Earlier studies by Szabó and co-workers revealed similar moderate enantioselectivities: Sebelius, S.; Szabó, K. J. *Eur. J. Org. Chem.* **2005**, 2539–2547.
12. (a) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, 3966–3979; (b) Roush, W. R.; Adam, M. A.; Walts, A. E.; Harris, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 3422–3434.
13. The minor *anti*, *anti*-diastereomer of **20** was converted into the corresponding diacetate.



anti-**20**

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.68 (ddd, J=17.7, 9.5, 8.5 Hz, 1H, H-5), 5.04–4.95 (m, 4H, H-6, H-3, H-2), 2.43 (dq, J=7.1, 8.5 Hz, 1H, H-4), 2.07 (s, 3H, OAc), 2.01 (s, 3H, OAc), 1.20 (d, J=6.4 Hz, 3H, H-1), 1.02 (d, J=7.1 Hz, 3H, Me); $[\alpha]_D^{20}$ −40 (*c* 0.2, CH_2Cl_2) and the analytical data were identical with those reported by: Toshima, K.; Jyojima, T.; Yamaguchi, H.; Noguchi, Y.; Yoshida, T.; Murase, H.; Nakata, M.; Matsumura, S. *J. Org. Chem.* **1997**, *62*, 3271–3284.

14. Brinkmann, H.; Hoffmann, R. W. *Chem. Ber.* **1990**, 2395–2401.
15. (a) Liu, H.; Nasi, R.; Jayakanthan, K.; Sim, L.; Heipel, H.; Rose, D. R.; Pinto, B. M. *J. Org. Chem.* **2007**, *72*, 6562–6572; (b) Priepke, H. W. M.; Warriner, S. L.; Ley, S. V. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2290–2292;



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^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.39 (m, 2H, Ph), 7.36–7.30 (m, 3H, Ph), 6.00 (ddd, J=17.2, 10.3, 9.0 Hz, 1H, H-8), 5.06 (d, J=10.3 Hz, 1H, H-9), 4.91 (d, J=17.2 Hz, ^{1}H, H-9), 4.54 (d, J=9.8 Hz, 1H, H-6), 3.71 (dd, J=9.8, 2.0 Hz, 1H, H-5), 3.27 (s, 3H, H-11), 3.25 (s, 3H, H-11), 1.93 (ddq, J=9.0, 7.1, 2.0 Hz, 1H, H-7), 1.33 (s, 3H, H-12), 1.30 (s, 3H, H-12), 1.00 (d, J=7.1 Hz, 3H, H-10).

16. Kirschning, A.; Harmrolfs, K.; Knobloch, T. *C.R. Chim.* **2008**, 1523–1543.
17. Dale, A. J.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *24*, 512–519.
18. Utilisation of the corresponding allyl carbonates is also possible but resulted in lower yields which is presumably due to the lower stability of compared to the acetates: Mennecke, K.; Vogt, M.; Kirschning, A. Unpublished results.
19. (a) For the preparation of compound **26** see: Frenzel, T.; Brünjes, M.; Kirschning, A. *Org. Lett.* **2006**, *8*, 135–138; (b) The synthesis of compound **28** is reported in: Schöning, K.-U.; Wittenberg, R.; Kirschning, A. *Synlett* **1999**, 1624–1626.
(c) A detailed procedure for the synthesis of compound **30** will be published elsewhere.
20. Potuzak, J. S.; Moilanen, S. B. *J. Am. Chem. Soc.* **2005**, *127*, 13769–13797.
21. Paterson, I.; Wallace, D. J.; Cowden, C. J. *Synthesis* **1998**, 639–652.
22. For removing impurities derived from dba traces the crude product was submitted to a DIBAL-H reduction before it was purified by flash chromatography.