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Enantioselective γ-Deprotonation of Alkyl-Substituted *O*-1,3-Butadien-2-yl Carbamates and Regioselective Asymmetric Homoaldol Reaction

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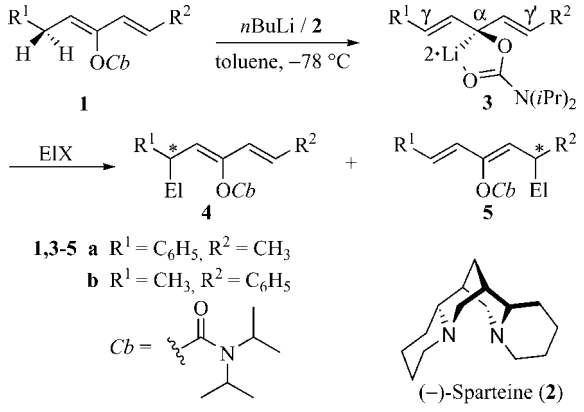
This work presents a facile method for the construction of geometrically defined 1,3-dien-2-yl carbamates. Their highly stereoselective asymmetric deprotonation with the chiral base pair *n*-butyllithium/(–)-sparteine (**2**) and substitution reactions allows the flexible synthesis of substituted stereohomogeneous 1,3-dienes. Diastereo- and enantioselective homoaldol reactions with aldehydes are possible after transmetallation of the lithium species with $ClTi(NEt_2)_3$. Intensive investigations for the interpretation of the stereochemical outcome of the reactions of each carbamate are also presented. Comparison of all results shows common properties of the allyllithium intermediates as well as surprising differences, which indicate a strong relationship between the structure of these intermediates and their reactivity.

Introduction

Recently we published the γ-deprotonation of phenyl-substituted 1,3-alkadien-2-yl *N*,*N*-diisopropyl carbamates,[1] such as **1a** or **1b**, and alk-1-en-3-yn-2-yl *N*,*N*-diisopropyl carbamates[2] by means of *n*-butyllithium/(–)-sparteine (**2**). The deprotonation occurs with high enantiotopic differentiation,[3,4] leading to almost diastereomerically pure lithium compounds **3a** or **3b**. Due to the stabilizing phenyl residue, the thermodynamic and kinetic acidity of **1a** and **1b** is high, leading to rapid proton removal. Upon trapping of **3a** or **3b** with different electrophiles, the major or even single product results from attack at the γ-position bearing the phenyl residue. Therefore the regioselectivity is determined by the electronic effects of the phenyl residue which stabilizes the electron density and the negative charge at the carbon atom adjacent to it (Scheme 1).[1]



Scheme 1. Lithiation of **1** and reaction with electrophiles.

The present work is an extension of this methodology on dienyl carbamates **11** and **15** which do not bear a phenyl substituent. The influence of steric effects on the regioselectivity of the reaction of the pentadienyllithium intermediates with electrophiles and their homoaldol reaction[5] was investigated. Intensive investigations for the interpretation of the stereochemical outcome of the reactions of each carbamate with electrophiles are also presented.

Results and Discussions

Synthesis of the Dienyl Carbamates 11 and 15

The dienyl carbamates **11** and **15** were prepared by a Negishi[6a] or Suzuki[6b] coupling reaction starting from the corresponding (*Z*)-alk-1-enyl carbamate **8a** or **8b**. After carbamoylation of the commercially available crotyl alcohol **6a** followed by complete isomerization of the allyl carbamate **7a** via lithiation, lithium-titanium exchange,[7] and protonation, the 1-butenyl carbamate **8a** was obtained in a total yield of 86% and a *Z*:*E* ratio > 98:2 (Scheme 2).[8] The allyl alcohol **6b** was synthesized starting from isobutyraldehyde by a Horner–Wittig–Emmons olefination and reduction of the resulting ester.[9] Carbamoylation of **6b** and isomerization according to the same procedure as described for **8a** afforded the 3-methylbut-1-enyl carbamate **8b** in 76% yield and a *Z*:*E* ratio > 98:2 (Scheme 2). The (*Z*)-enol carbamate **11** was obtained in 70% yield after vinylic lithiation of **8a**,[10] transmetallation to zinc (**9**), and palladium-catalyzed Negishi coupling[6a,10c] with 2-methylprop-1-enyl bromide (**10**) in a one-pot synthesis using $Pd(PPh_3)_4$

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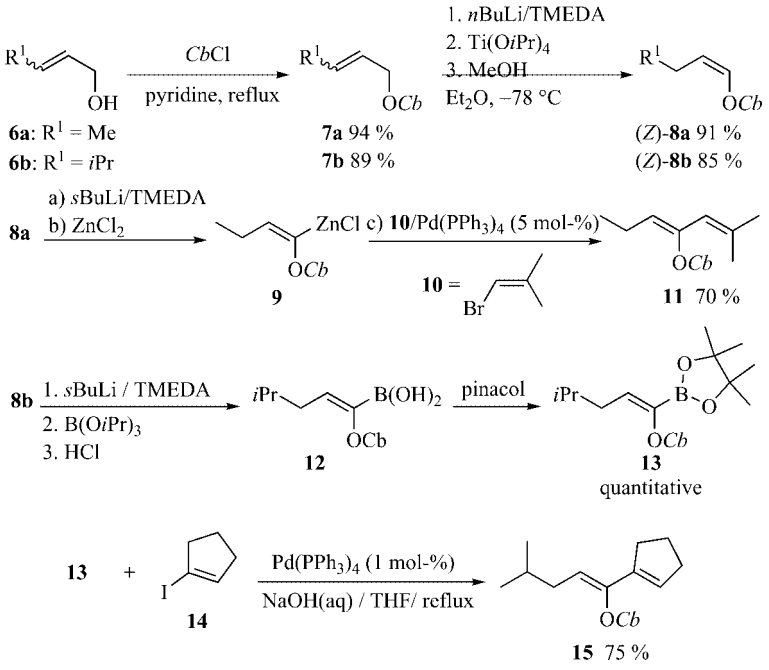
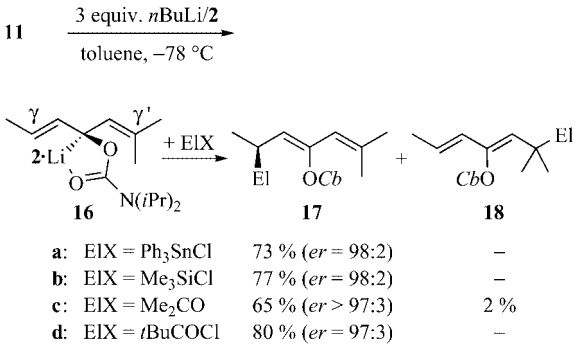


Scheme 2. Synthesis of the dienyl carbamates **11** and **15**.

(Scheme 2). In an alternative method, **8b** was lithiated, transmetallated to boron[11] and the resulting boronic acid (**12**) was esterified with pinacol quantitatively. The obtained (*Z*)-1-boron-substituted 1-alkenyl carbamate (**13**) can be purified chromatographically and was used in a Suzuki coupling with cyclopentenyl iodide (**14**)[12] and $Pd(PPh_3)_4$ as catalyst, affording the dienyl carbamate **15** in 75% yield.

Asymmetric Lithiation of 11 and Trapping with Electrophiles

As expected, the deprotonation of **11** by *n*-butyllithium/(–)-sparteine (**2**) proceeds under harsher conditions than those applied to the phenyl-substituted derivatives **1**.[1] Typically, 3 equiv. of the chiral base at –78 °C in toluene and 13 h reaction time are necessary for an efficient deprotonation (Scheme 3). Excess electrophile was then added and allowed to react for 3 to 5 hours at –78 °C depending on its reactivity. The use of stronger bases like *sec*-butyllithium or performing the deprotonation in polar solvents like Et_2O afforded slightly better yields upon trapping with electrophiles, but the enantiomeric ratio (*er*) of the products was considerably decreased. The results of the deprotonation and substitution experiments in Scheme 3 prove an efficient control of the regioselectivity by means of steric effects. Only one regioisomer could be isolated from each reaction with an electrophile. The two methyl groups at the γ′-position in **16** block that site against substitution. Even planar sp^2-hybridized carbonyl compounds avoid attack at that sterically demanding γ′-position affording only traces of the product **18**. The *Z*-configuration of the double bond in **11** is conserved in all products **17a**–**d**. This is proven by NOE experiments which show coupling through space between the carbamate group and the attached electrophile on one hand and between the two vinylic protons on the other hand. The stereochemistry of products **17** and the *anti*-S_E' mechanism of addition is discussed in the following sections.

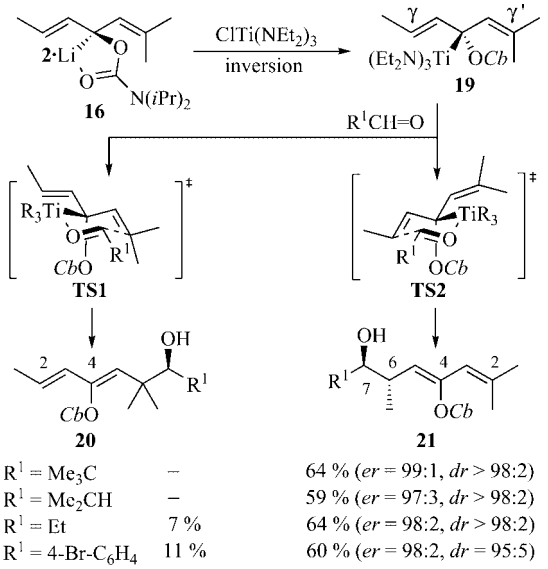


Scheme 3. Asymmetric deprotonation of **11** and trapping **16** with electrophiles.

Titanium-Mediated Homoaldol Reaction of 11

In another series of experiments, carbamate **11** was deprotonated and subjected to a metal exchange with $ClTi(NEt_2)_3$ for 1 hour (Scheme 4). The more covalently bound titanium compound now reacts through a close six-membered ring transition state[13] with aldehydes or ketones, providing excellent diastereoselectivities with complete 1,3-transfer of chirality.[5,14] The major product is in all cases the *anti*-homoaldol product **21** resulting from the transition state **TS2** where R^1 and the methyl group both occupy

pseudo-equatorial positions. **TS2** is also more energetically favored than the more sterically demanding transition state **TS1** where one methyl group at the γ′ position has to occupy an axial position. The *anti*-product is confirmed by a coupling constant $^3J_{H6–H7}$ of around 7.5 Hz between the protons on the two stereogenic centers. An exceptional case is the product **21a** resulting from the reaction with pivaldehyde which shows a coupling constant of $^3J_{H6–H7}$ = 3.5 Hz. This is however also the case of the *anti*-homoaldol products with pivaldehyde in other systems.[8a,15] The regioselectivity is excellent in case of bulkier R^1 groups such as in pivaldehyde and isobutyraldehyde. In case of unbranched aldehydes like propanal or aromatic aldehydes like 4-bromobenzaldehyde in addition 7% and 11% of the γ′-products **20c** and **20d** are obtained, respectively. The regioisomers are separable by column chromatography. The double bonds between C-2 and C-3 in the products **20** are (*E*)-configured, because of a typical coupling constant of $^3J_{H2–H3}$ = 15.2 Hz. NOE experiments secure the (*Z*)-configuration of the C4=C5 bond. In addition, an X-ray crystal structure of **21c** secures the relative configuration of the *anti*-product and the (*Z*)-configuration of the C4=C5 bond (Figure 1).



a:	$R^1 = Me_3C$	–	64 % (*er* = 99:1, *dr* > 98:2)
b:	$R^1 = Me_2CH$	–	59 % (*er* = 97:3, *dr* > 98:2)
c:	R^1 = Et	7 %	64 % (*er* = 98:2, *dr* > 98:2)
d:	R^1 = 4-Br-C_6H_4	11 %	60 % (*er* = 98:2, *dr* = 95:5)

Scheme 4. Titanium-mediated homoaldol reaction of **11** with aldehydes.

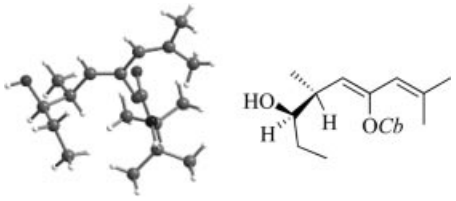


Figure 1. X-ray structure of **21c**.[16,17]

Single crystals of **21d** were studied by X-ray analysis with the anomalous dispersion technique. The absolute configuration was determined to be (*S*,*S*) (Figure 2).

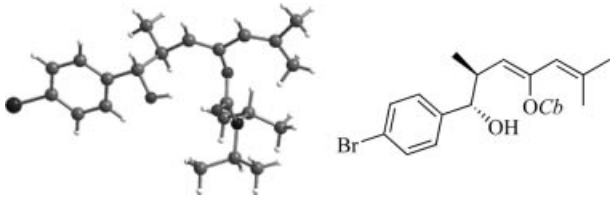
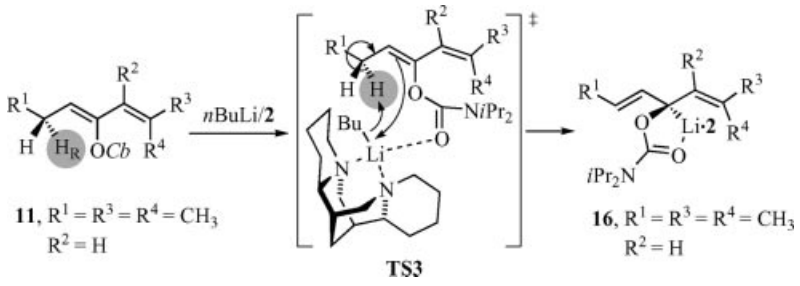


Figure 2. X-ray structure of (*S*,*S*,*Z*)-**21d**.[17,18]

The reaction of the aldehyde with the titanium species **19** through a Zimmerman–Traxler transition state[13] **TS2** determines the (*S*)-configuration of **19** (Scheme 4). Since the lithium/titanium exchange with $ClTi(NEt_2)_3$ in (–)-sparteine/allyllithium complexes[19] is known to occur under inversion of configuration,[14] the lithium intermediate **16** have to be assigned to the (*S*)-configuration. This lithium intermediate and its similar analogues **3** have proven to be configurationally stable at –78 °C.[1] This means that the chiral base pair *n*-butyllithium/(–)-sparteine (**2**) removes the *pro*-*R* proton from **11** through a nine-membered ring transition state **TS3** irrespective of the substituent at the γ-position (Scheme 5). This transition state has been suggested in a previous work, and agrees also with similar systems of 1,3-dien-2-yl carbamates (**1**).[1]

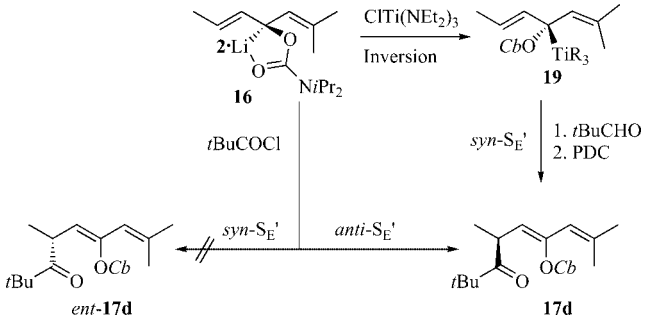
Stereochemistry of the Substitution Reactions of 16

The stannylation and silylation reactions of **11** are considered like most of similar reactions reported in the literature to proceed antarafacially.[20] Whether the reaction of the lithium intermediate **16** with pivaloyl chloride proceeds in an antara- or suprafacial way was determined as follows



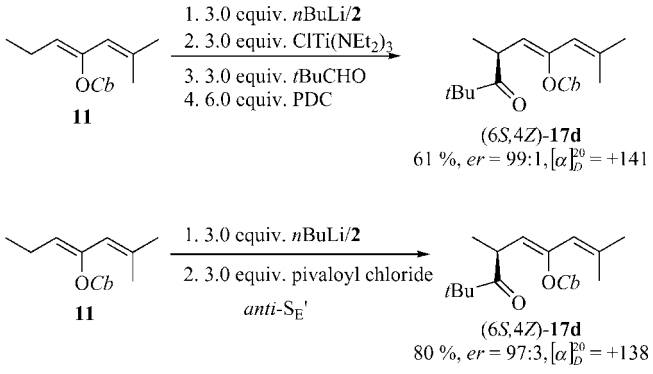
Scheme 5. Mechanism of deprotonation with *n*-butyllithium/(–)-sparteine (**2**).

(Scheme 6): The Li→Ti transmetallation occurs with inversion of configuration,[14,19,20] and carbonyl compounds add suprafacially to the allyltitanium intermediate **19** through a Zimmerman–Traxler transition state.[13] Oxidation of the product to the ketone **17d** provides a reference with which the corresponding adduct **17d** or *ent*-**17d**, obtained from the reaction of the lithium intermediate with the pivaloyl chloride, is compared.



Scheme 6. Determination of the reaction mechanisms for the lithium intermediates.

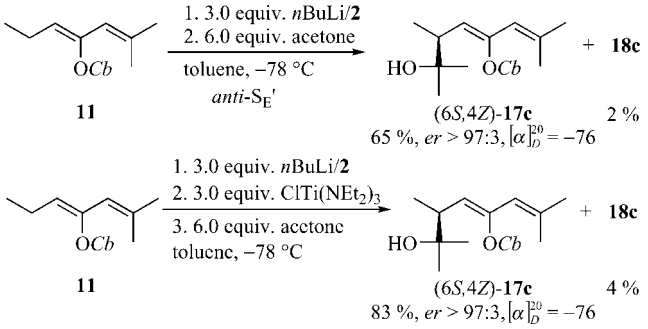
The titanium-mediated homoaldol reaction of **11** with pivaldehyde affords (6*S*,7*S*,4*Z*)-**21a** with an *er* value of 99:1 and *dr* > 98:2 (Scheme 4). Oxidation with excess PDC yields the ketone after 26 h and destroys the stereogenic center at C-7 without racemizing the other one at C-6. Thus (6*S*,4*Z*)-**17d** is obtained in 95% yield with an *er* value of 99:1 and $[\alpha]_D^{20}$ = +141 (Scheme 7).



Scheme 7. Determination of the *anti*-S_E' addition of pivaloyl chloride to **16**.

(6*S*,4*Z*)-**17d** is also produced ($[\alpha]_D^{20}$ = +138) by deprotonation of **11** and reaction of the lithiated intermediate with pivaloyl chloride (Scheme 7). Since the same enantiomer is obtained from both pathways, an inversion has to take place in the addition of pivaloyl chloride to the lithium intermediate **16**. This is achieved by an *anti*-S_E' mechanism.

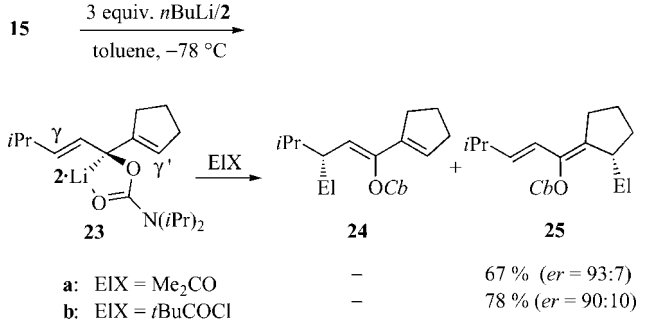
The same methodology presented in Scheme 6 was used to determine the reaction mechanism of **16** with acetone. The products of the lithium- and titanium-mediated reactions can be directly compared. The lithium- and the titanium-mediated reactions of **11** with acetone afford the same product (6*S*,4*Z*)-**17c** with the same specific optical rotation value, $[\alpha]_D^{20}$ = –76 (Scheme 8). This gives evidence for an *anti*-S_E' addition of the lithium intermediate **16** to ketones. The structure of the by-product **18c** which results from an addition at the γ′-position is presented in Scheme 3.



Scheme 8. Lithium- and titanium-mediated homoaldol reaction of **11** with acetone.

Asymmetric Lithiation of 15 and Trapping with Electrophiles

The dienyl carbamate **15** was also deprotonated with 3 equiv. of *n*-butyllithium/**2** in toluene for 16 h and trapped with carbonyl compounds (Scheme 9). Surprisingly, only one product, resulting from a substitution at the γ′-position in **23**, was obtained. The determination of the absolute configurations of the products and the *syn*-S_E' addition is described in the following sections. The (*Z*)-configuration of the *exo*-double bond in **25a** was confirmed through NOE experiments and for **25b** through a single-crystal X-ray analysis[21] (Figure 3). The (*E*)-configured disubstituted double bond is proven by a coupling constant of 16 Hz in both products **25a** and **25b**.



Scheme 9. Asymmetric deprotonation of **15** and trapping **23** with electrophiles.

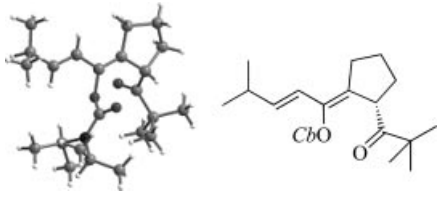
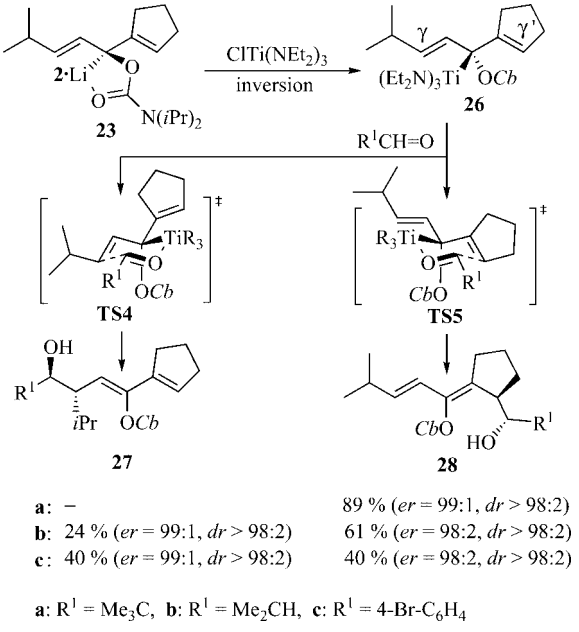


Figure 3. X-ray crystal structure of **25b**.[17,21]

Titanium-Mediated Homoaldol Reaction of 15

In another series of experiments, carbamate **15** was deprotonated, subjected to metal exchange with $ClTi(NEt_2)_3$

for 1 h, and allowed to react with excess aldehyde for 2 h (Scheme 10). Here the regioselectivity depends more on the R^1 group of the aldehyde. The difference in steric demand between the isopropyl group at the γ position and the cyclic group at the β′- and γ′-position in **26** is not large enough to induce excellent selectivity. In case of pivaldehyde, only one product **28a** was obtained, resulting from a substitution on the ring through **TS5**. However, from the reaction of **26** with isobutyraldehyde, both products **27b** and **28b** were isolated after column chromatography in a ratio of 28:72, respectively. More reactive aromatic aldehydes like 4-bromobenzaldehyde react equally at both positions and give a 50:50 mixture of the products **27c** and **28c**, which were separated by column chromatography. The configurations of the double bonds shown in Scheme 10 were determined by ^{1}H NMR and no other isomers could be isolated.



Scheme 10. Titanium-mediated homoaldol reaction of **15** with aldehydes.

Single crystals of **28c** were studied by X-ray analysis with the anomalous dispersion technique. The absolute configuration was determined to be (*R*,*R*) (Figure 4). This supports the proposed mechanism of deprotonation (Scheme 5) and the (*S*)-configuration of the lithium intermediate **23**.

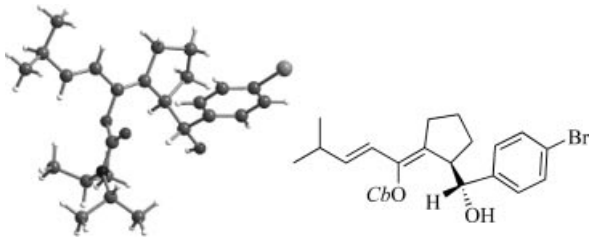
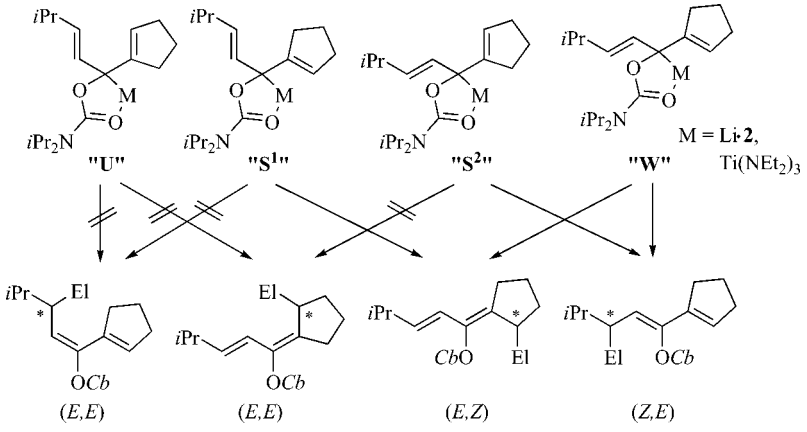


Figure 4. X-ray structure of (*R*,*R*,1*Z*,2*E*)-**28c**.[17,22]

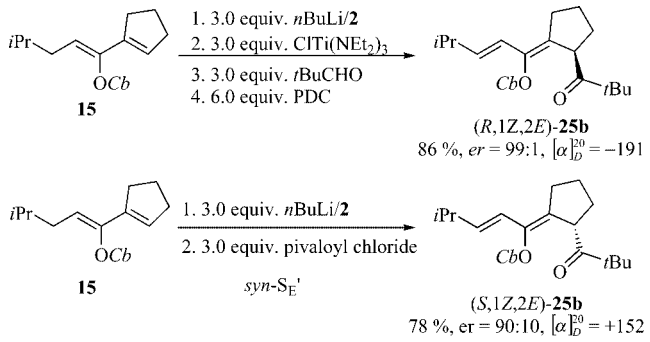
The fact that no other products resulting from isomerization of the double bonds were isolated is a pleasant feature of these lithium and titanium intermediates. This indicates that **23** and **26** react only through the "W"-conformer (zigzag-like shape). The other "U"- and "S"-conformers[23] – if present – exhibit much lower reactivities. Scheme 11 shows the four possible products which could be obtained through the different conformers of the lithium intermediate **23** or the titanium intermediate **26**. Only the "W"-conformer can give the observed products (*Z*,*E*) and (*E*,*Z*) by reacting at the γ- and the γ′-positions, respectively.

Stereochemistry of the Substitution Reactions of 23

The oxidation of (*R*,*R*,1*Z*,2*E*)-**28a**, which was obtained from the titanium-mediated homoaldol reaction of **15** with pivaldehyde with *er* = 99:1 (Scheme 12), with PDC at room temperature for 24 h afforded the ketone (*R*,1*Z*,2*E*)-**25b** in 97% yield with *er* = 99:1 and $[\alpha]_D^{20}$ = –191. Comparison of the optical rotation with that of the ketone obtained from the reaction of the lithium intermediate **23** with pivaloyl chloride ($[\alpha]_D^{20}$ = +152, Scheme 12) shows that the two products are enantiomers, and that the latter must be (*S*)-configured. This also means that the reaction of the acyl chloride with the lithium intermediate **23** proceeds via a *syn*-S_E' addition, contrary to the *anti*-S_E' addition to **16**.

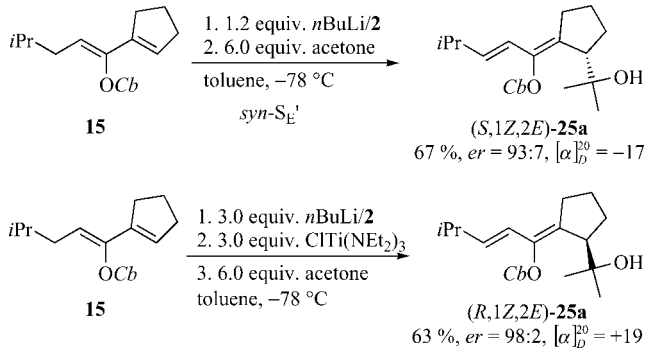


Scheme 11. Possible conformers of **23** and **26** and the double-bond configurations of the resulting dienes.



Scheme 12. Determination of the *syn*-S_E' addition of pivaloyl chloride to **23**.

The lithium-mediated reaction of **15** with acetone affords (*S*,1*Z*,2*E*)-**25a** with $[\alpha]_D^{20}$ = –17, while the opposite enantiomer (*R*,1*Z*,2*E*)-**25a** with $[\alpha]_D^{20}$ = +19 is obtained from the titanium-mediated reaction (Scheme 13). This is another proof of the fact that the lithium intermediate **23** adds in a *syn*-S_E' fashion to carbonyl compounds.



Scheme 13. Lithium- and titanium-mediated homoaldol reaction of **15** with acetone.

We assume that the steric bulk of the attached five-membered ring, which occupies the β′- and the γ′-position in the anion, affects the substitution in such a way that the coordination of the carbonyl compound with the lithium atom in **23** is necessary for a rapid reaction to take place. With one more substituent at the β′-position the direct *anti*-S_E' attack is impeded by steric effects, and the substitution of **23** with a ketone or an acyl chloride requires the electrophilic assistance of the lithium cation, inducing a *syn*-S_E' process.

Conclusions

Starting with 1-alkenyl carbamates, different Pd-catalyzed coupling reactions open facile access to diverse geometrically defined 1,3-dien-2-yl carbamates. The γ-deprotonation of these carbamates with the chiral base *n*-butyllithium/(–)-sparteine (**2**) proceeds with high enantiotopic differentiation concerning the *pro-R*-H in **11** and **15**. The mechanism of deprotonation, which is postulated to occur through a nine-membered ring transition state, holds true for these carbamates and many other examples presented in previous works. The lithium intermediates are configurationally stable with the lithium cation forming a stable five-membered chelate ring with the *Cb* group. They react stereoselectively and exclusively through the "W" conformer with electrophiles affording substituted stereohomogeneous 1,3-dienes. Substitution of lithium compound **16** with different electrophiles proceeds with a strict *anti*-S_E' mechanism at the less sterically hindered γ-position. However, the lithium intermediate **23** reacts in a *syn*-S_E' process with ketones and acyl chlorides at the γ′-position of the ring. Transmetallation of **16** and **23** with $ClTi(NEt_2)_3$ proceeds with inversion of configuration. *anti*-Homoaldol products are obtained from the reaction of the titanium species **19** and **26** with aldehydes in very good yields and with high enantio- and diastereomeric ratios. The regioselectivity is controlled by steric factors alone.

Experimental Section

General: Reactions with air- and moisture-sensitive compounds were performed under argon atmosphere. All solvents were refluxed over a suitable drying agent and distilled immediately before use. (–)-Sparteine was purchased from Aldrich and used without further purification. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was refluxed over CaH_2 and distilled under an argon atmosphere. *n*-BuLi was purchased from Acros (1.6 M hexane solution). $ClTi(NEt_2)_3$ was prepared following procedures described in literature[24] and stored under an argon atmosphere at room temperature. *N*,*N*-Diisopropylcarbamoyl chloride was prepared following a known procedure.[8a,25] Preparative liquid chromatography (flash chromatography) was performed under 1.4 bar argon pressure using silica gel, grade 40–63 μm, from Merck, Darmstadt (Germany). Solvents were distilled prior to use (PE = petroleum ether, *n*-pentane; EE = diethyl ether). Thin-layer chromatography was performed by using aluminum silica gel cards 60 F_{254} from Merck. The detection of the products was performed under UV light (λ = 254 nm) as well as with staining agents followed by heating. Gas chromatography was performed with an Agilent 6890 plus machine from Agilent, Böblingen (Germany) using the achiral HP-5 Quarz column (program: 50 °C start temperature for 0 min, 10 °C/min heating rate, 300 °C final temperature for 15 min) from Agilent. The retention times are given as t_R. High-performance liquid chromatography was carried out with an instrument from Waters GmbH, Eschborn (Germany). The apparatus consists of a 600 E Multisolvent Delivery System with In-Line Degasser, a Waters 717plus autosampler, and a Waters 996 photodiode array detector. The analysis of the data were done with the software program "Millenium Chromatography Manager", version 3.20, or Waters Empower 2. The following chiral columns were used: polystyrene-based columns CHIRA GROM 1 and CHIRA GROM 2 (length 50 mm or 250 mm, 2 mm inner diameter) from Grom, Herrenberg (Germany). *n*-Hexane and 2-propanol (HPLC grades) were used as eluents with a flow rate of 0.3 mL/min. The optical rotations were measured in a 10-cm cuvette with a polarimeter of the type Perkin–Elmer 341. Elemental analyses were performed with a Vario EL III from Elementar Analysen Systeme GmbH, Hanau (Germany). IR measurements were recorded with the spectrometers IFS 28 from Bruker Optik GmbH or 5 DXC from Nicolet, Offenbach/Main (Germany). Mass spectrometry was carried out by electron-spray ionization (ESI) on MicroTof from Bruker Daltonik, Bremen (Germany). The ^1H and ^{13}C NMR spectra were measured with the Bruker spectrometers ARX300, AMX400, or the Varian

spectrometer Unity Plus 600. TMS (δ = 0.0 ppm) or $CDCl_3$ (δ =7.24 ppm for remaining $CHCl_3$) was used as internal standard in ^1H NMR and $CDCl_3$ (δ = 77.0 ppm) in ^{13}C NMR spectra.

(4*Z*)-2-Methylhepta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (11): A solution of TMEDA (1.05 equiv., 15.75 mmol, 1.85 g) in THF (45 mL) was cooled to –78 °C and *s*BuLi (1.05 equiv., 15.75 mmol, 1.6 M in hexane, 9.9 mL) was added slowly. After stirring for 10 min, a solution of (*Z*)-**8a** (1.0 equiv., 15 mmol, 2.99 g) in THF (15 mL) was added dropwise and left stirring at –78 °C for 1 h. A solution of $ZnCl_2$ (1.05 equiv., 15.75 mmol, 0.5 M in THF, 31.5 mL) was added slowly at –78 °C and after 10 min the solution was warmed up to 0 °C for 45 min. The reaction mixture was transferred through a needle to a flask containing the 2-methyl-1-propenyl bromide (**10**) (1.05 equiv., 15.75 mmol, 2.15 g) and $Pd(PPh_3)_4$ (5 mol-%, 0.78 mmol, 0.89 g) in THF (25 mL), which were already mixed together and stirred at room temperature for 30 min. The reaction mixture was refluxed for 12 h then cooled down to room temperature before addition of 2 M HCl (45 mL). The organic phase was separated and the aqueous layer extracted three times with diethyl ether (60 mL each). The combined organic phase was washed with brine, dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (PE/DE, 12:1) affording the carbamate **11** as a colourless oil (2.66 g, 70%). t_R = 11.3 min; R_f = 0.41 (PE/DE, 4:1). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, 3 H, H-7); 1.26 (d, 12 H, CH_3-*Cb*); 1.77 (s, 3 H, H-1′); 1.83 (s, 3 H, H-1); 2.04 (dq, 2 H, H-6); 3.97 (b, 2 H, CH-*Cb*); 5.10 (t, 1 H, H-5); 5.26 (s, 1 H, H-3) ppm. $^3J_{Cb}$ = 6.8 Hz; $^3J_{5-6}$ = 7.6 Hz; $^3J_{6-7}$ = 7.7 Hz. NOE (500 MHz, $CDCl_3$): irradiation at δ = 5.26 ppm (H-3): NOE at δ = 5.10 ppm (H-5); 1.77 ppm (H-1′). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (C-7); 19.4 (C-6); 19.6 (C-1); 20.7 [21.0] (CH_3-*Cb*); 27.4 (C-1′); 46.5 (CH-*Cb*); 121.3 (C-5); 122.1 (C-3); 135.3 (C-2); 145.5 (C-4); 153.1 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 2968, 2934, 2875, 1714 (s, ν(C=O)), 1431, 1369, 1315, 1281, 1211, 1155, 1044, 1001, 927, 899, 859, 759 cm^{-1}. MS (ESI) (*m*/*z*): $[M + H^+]$ = 254.2105 (calcd. 254.2120); $[M + Na^+]$ = 276.1939 (calcd. 276.1939). $C_{15}H_{27}NO_2$ (253.38): calcd. C 71.10, H 10.74, N 5.53; found C 71.10, H 10.86, N 5.49.

(*Z*)-4-Methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-enyl *N*,*N*-Diisopropylcarbamate (13): TMEDA (1.1 equiv., 22 mmol, 2.56 g) was dissolved in DE (35 mL) and cooled down to –78 °C. *s*BuLi (1.1 equiv., 22 mmol, 1.38 M in hexane, 16 mL) was added dropwise. After 10 min, the carbamate (*Z*)-**34c** (20 mmol, 4.55 g), dissolved in DE (15 mL), was added slowly and stirred for 1 h. Triisopropyl borate (1.5 equiv., 30 mmol, 5.64 g, 7 mL) was added dropwise. The reaction was stirred further for 1 h. HCl (2 M, 20 mL) was added at –78 °C and the reaction mixture warmed up to room temperature. After separation of the phases, the organic phase was extracted 4 times with DE (20 mL each). The combined organic phases were dried with $MgSO_4$ and concentrated under vacuum. The crude product was dissolved in CH_2Cl_2 (20 mL) with pinacol (1.5 equiv., 30 mmol, 3.54 g). $MgSO_4$ (2 g) was added and the reaction mixture was stirred for 13 h. The crude product was filtered and concentrated under vacuum. After column chromatography (PE/DE, 6:1→1:1), (*Z*)-**41** (7.0 g, ca. 20 mmol, 99%, colourless liquid) was obtained. t_R = 14.2 min; R_f = 0.42 (PE/DE, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (d, 6 H, H-5); 1.23 (s, 12 H, H-2′); 1.27 (br. s, 12 H, CH_3-*Cb*); 1.65 (m, 1 H, H-4); 2.04 (dd, 2 H, H-3); 3.83 [4.18] (br. s, 1 H, CH-*Cb*); 5.03 (t, 1 H, H-2) ppm. $^3J_{2-3}$ = 7.3 Hz; $^3J_{3-4}$ = 7.3 Hz; $^3J_{4-5}$ = 6.7 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.2 [20.8] (CH_3-*Cb*); 22.4 (C-5); 25.0 (C-2′); 28.4 (C-4); 35.3 (C-3); 46.8 [48.4] (CH-*Cb*); 75.0 (C-2); 80.6 (C-1′); 114.0 (C-1); 152.8 (OCON) ppm. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 375.2672, 376.2638, 377.2671, 378.2695 (calcd. 375.2666, 376.2633, 377.2665, 378.2691). IR (neat): $\tilde{\nu}$ = = 2974, 2934, 2873, 1631 (s, ν(C=O)), 1452, 1355, 1153, 1123, 1035, 995, 949, 908, 763, 639 cm^{-1}.

(*Z*)-1-Cyclopent-1-enyl-4-methylpent-1-en-1-yl *N*,*N*-Diisopropylcarbamate (15): 1-Iodocyclopent-1-ene (**14**) (1.0 equiv., 5 mmol, 0.35 g) and $Pd(PPh_3)_4$ (1 mol-%, 0.1 mmol, 116 mg) in THF (10 mL) were stirred at room temperature for 30 min until the solution (A) became clear. During this time, a mixture (B) of (*Z*)-**13** (1.0 equiv., 5 mmol, 1.77 g), THF (5 mL), and NaOH (2.0 equiv., 10 mmol, 2 M, 5 mL) was prepared and added while stirring rapidly, through a cannula to (A). The reaction mixture was refluxed for 13 h. Subsequently, the reaction was cooled down to room temperature. NaOH (3 M, 2.5 mL) was added followed by H_2O_2 (30%, 2.5 mL) dropwise over 30 min. The phases were separated and the aqueous phase was extracted 3 times with PE. The combined organic phases were dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash chromatography on silica gel (PE/DE, 25:1→9:1) affording the product **15** (3.8 mmol, 1.10 g, 75%, brown oil). t_R = 14.2 min; R_f = 0.39 (PE/DE, 4:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (d, 6 H, H-5); 1.25 [1.32] (d, 6 H, CH_3-*Cb*); 1.67 (m, 1 H, H-4); 1.94 (m, 4 H, H-3, H-4′); 2.43 (m, 2 H, H-5′); 2.50 (br. s, 2 H, H-3′); 3.92 [4.07] (b, 1 H, CH-*Cb*); 5.25 (t, 1 H, H-2); 5.64 (br. s, 1 H, H-2′) ppm. $^3J_{Cb}$ = 6.8 Hz; $^3J_{2-3}$ = 7.5 Hz; $^3J_{4-5}$ = 6.7 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4 [21.5] (CH_3-*Cb*); 22.4 (C-5); 23.1 (C-3); 28.3 (C-4); 32.0 (C-4′); 32.9 (C-3′); 34.9 (C-5′); 45.8 [46.5] (CH-*Cb*); 117.4 (C-2′); 125.9 (C-2); 138.9 (C-1′); 145.1 (C-1); 153.0 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 2966, 2954, 2934, 2898, 2870, 2847, 1711 (s, ν(C=O)), 1655, 1459, 1430, 1366, 1319, 1293, 1266, 1221, 1184, 1158, 1136, 1044, 1011, 952, 896, 779, 755, 621, 587 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na^+]$ = 316.2249 (calcd. 316.2252). $C_{18}H_{31}NO_2$ (293.44): calcd. C 73.67, H 10.65, N 4.77; found C 73.53, H 10.82, N 4.65.

Deprotonation of 11 and Substitution with Electrophiles

Reaction with Ph_3SnCl. (6*S*,4*Z*)-2-Methyl-6-(triphenylstannyl)-hepta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (17a): A solution of (–)-sparteine (3.0 equiv., 0.90 mmol, 212 mg) in toluene (1.5 mL) was cooled to –78 °C. *n*-BuLi (3.0 equiv., 1.6 M in hexane, 0.90 mmol, 0.56 mL) was added slowly. After 10 min a solution of the carbamate **11** (1.0 equiv., 0.3 mmol, 76 mg) in toluene (1 mL) was added. After 13 h, a solution of the corresponding electrophile (Ph_3SnCl, 3 equiv., 0.9 mmol, 347 mg) in toluene (1 mL) was added dropwise within 5 min. The solution was stirred for 2 h and the reaction was stopped by addition of MeOH (0.4 mL) at –78 °C. The flask was removed from the acetone/dry ice bath, and 1 mL of 2 M HCl were added. After warming to room temperature, the organic phase was separated and the aqueous phase washed three times with DE (5 mL each). The combined organic phases were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (PE/DE, 20:1) afforded (*S*,*Z*)-**17a** (132 mg, 73%, white solid).

The racemic version of the reaction is done the same way with TMEDA (3.0 equiv., 0.90 mmol, 105 mg) as ligand instead of (–)-sparteine. *rac*-(*Z*)-**17a** was obtained in 27% yield. The racemic products were used as reference for the separation of the enantiomers on chiral HPLC. t_R = 21.7 min; R_f = 0.48 (PE/DE, 4:1); decomposes at 180 °C. $[\alpha]_D^{20}$ = –4.5 (*c* = 0.98 in $CHCl_3$; *er* = 98:2; (*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm), 50 × 2 mm; *i*PrOH/*n*-hexane, 1:3000; $t_{R(6S)}$ = 7 min, $t_{R(6R)}$ = 11 min. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 [1.16] (br. s, 6 H, CH_3-*Cb*); 1.43 (d, 3 H, H-7); 1.59 (s, 3 H, H-1); 1.68 (s, 3 H, H-8); 2.92 (dq, 1 H, H-6); 3.59 (br. s, 2 H, CH-*Cb*); 5.25 (d, 1 H, H-5); 5.54 (s, 1 H, H-3); 7.26 (m, 9 H, H-Ph); 7.46 (m, 6 H, H-Ph) ppm. $^3J_{5-6}$ = 11.5 Hz; $^3J_{6-7}$ = 7.5 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.3 (C-6); 19.1

(C-7); 20.4 [20.9] (CH_3-*Cb*), 21.9 (C-8); 27.2 (C-1); 45.6 [46.3] (CH-*Cb*); 120.7 (C-5); 124.5 (C-3); 138.8 (C-2); 142.3 (C-4); 152.2 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3064, 3044, 2962, 2921, 2862, 1958, 1877, 1818, 1715 (s, ν(C=O)), 1697, 1591, 1480, 1429, 1369, 1299, 1276, 1211, 1137, 1074, 1043, 1022, 901, 867, 731, 699, 446 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 626.2062 (calcd. 626.2057).

Reaction with TMSCl. (6*S*,4*Z*)-2-Methyl-6-(trimethylsilyl)hepta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (17b): Following the protocol given above, using TMSCl (3 equiv., 0.9 mmol, 98 mg) for 5 h and purification by column chromatography (PE/DE, 20:1) afforded (*S*,*Z*)-**17b** (75 mg, 77%, yellowish oil). *rac*-(*Z*)-**17b** was obtained in 22% yield. t_R = 13.3 min; R_f = 0.63 (PE/DE, 4:1) $[\alpha]_D^{20}$ = –1.1 (*c* = 1.53 in $CHCl_3$; *er* = 98:2). Chiral HPLC: CHIRA GROM 2 (8 μm), 50 × 2 mm; *i*PrOH/*n*-hexane, 1:3000; $t_{R(6S)}$ = 2 min; $t_{R(6R)}$ = 4 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.03 (s, 9 H, TMS); 1.05 (d, 3 H, H-7); 1.26 (br. s, 12 H, CH_3-*Cb*); 1.77 (s, 1 H, H-1); 1.81 (s, 1 H, H-8); 3.83 [4.10] (br. s, 1 H, CH-*Cb*); 4.12 (m, 1 H, H-6); 4.91 (d, 1 H, H-5); 5.65 (s, 1 H, H-3) ppm; $^3J_{5-6}$ = 10.9 Hz; $^3J_{6-7}$ = 7.2 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –3.3 (TMS); 14.7 (C-7); 19.3 (C-8); 20.5 (CH_3-*Cb*); 27.0 (C-1); 45.8 (CH-*Cb*); 65.6 (C-6); 121.3 (C-5); 123.6 (C-3); 133.6 (C-2); 143.2 (C-4); 152.7 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 2965, 2925, 2868, 1715 (s, ν(C=O)), 1432, 1369, 1295 (s, δ(Si–CH_3), 1248, 1217, 1145, 1045, 1005, 853 (m, γ(Si–CH_3), 837, 759 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 348.2330 (calcd. 348.2335). $C_{18}H_{35}NO_2Si$ (325.56): calcd. C 66.41, H 10.84, N 4.30; found C 66.27, H 10.98, N 4.17.

Reaction with Acetone. (6*S*,4*Z*)-7-Hydroxy-2,6,7-trimethylocta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (17c) and (2*E*,4*Z*)-7-Hydroxy-6,6,7-trimethylocta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (18c): Using acetone (6 equiv., 1.8 mmol, 104 mg) for 3 h afforded (*S*,*Z*)-**17c** (61 mg, 65%, colourless oil) and (2*E*,4*Z*)-**18c** (2 mg, 2%, colourless oil) (PE/DE, 2:1). *rac*-(*Z*)-**17c** and (2*E*,4*Z*)-**18c** were obtained in yields of 15 and 4%, respectively.

17c: t_R = 14.1 min; R_f = 0.35 (PE/DE, 1:2) $[\alpha]_D^{20}$ = –76.0 (*c* = 0.72 in $CHCl_3$; *er* > 97:3; (6*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 250 × 2 mm; *i*PrOH/*n*-hexane, 1:200; $t_{R(6R)}$ = 28 min; $t_{R(6S)}$ = 31 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, 3 H, H-10); 1.08 [1.11] (s, 3 H, H-8); 1.19 (d, 12 H, CH_3-*Cb*); 1.72 (s, 3 H, H-1); 1.77 (s, 3 H, H-9); 2.41 (dq, 1 H, H-6); 3.82 [3.92] (br. s, 1 H, CH-*Cb*); 5.05 (d, 1 H, H-5); 5.63 (s, 1 H, H-3) ppm. $^3J_{Cb}$ = 7.1 Hz; $^3J_{5-6}$ = 10.6 Hz; $^3J_{6-10}$ = 7.0 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 (C-10); 19.8 (C-9); 21.0 [21.7] (CH_3-*Cb*); 25.8 (C-1); 27.4 [28.5] (C-8); 42.3 (C-6); 46.8 (CH-*Cb*); 72.8 (C-7); 121.2 (C-3); 122.5 (C-5); 136.7 (C-2); 146.4 (C-4); 153.8 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3469 (m, ν(OH)), 2970, 2934, 2877, 1692 (s, ν(C=O)), 1461, 1435, 1371, 1342, 1306, 1279, 1215, 1187, 1138, 1045, 1011, 953, 903, 870, 758, 653, 584 cm^{-1}. MS (ESI) (*m*/*z*): $[M + H]^+$ = 312.2495 (calcd. 312.2539); $[M + Na]^+$ = 334.2319 (calcd. 334.2358). $C_{18}H_{33}NO_3$ (311.46): calcd. C 69.41, H 10.68, N 4.50; found C 69.00, H 10.68, N 4.34.

18c: t_R = 14.7 min; R_f = 0.42 (PE/DE, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (s, 6 H, H-8); 1.19 (s, 6 H, H-9); 1.25 [1.32] (d, 6 H, CH_3-*Cb*); 1.75 (d, 3 H, H-1); 2.60 (br. s, 1 H, OH); 3.67 [4.29] (sept, 1 H, CH-*Cb*); 5.18 (s, 1 H, H-5); 5.54 (dq, 1 H, H-2); 5.95 (d, 1 H, H-3) ppm. $^3J_{Cb}$ = 6.6 Hz; $^3J_{1-2}$ = 6.6 Hz; $^3J_{2-3}$ = 15.9 Hz. IR (neat): $\tilde{\nu}$ = 3459 (m, ν(OH)), 2973, 2935, 2877, 1699 (s, ν(C=O)), 1472, 1436, 1370, 1308, 1282, 1215, 1155, 1045, 1021, 955, 903, 873, 760 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 334.2351 (calcd. 334.2358).

Reaction with Pivaloyl Chloride. (6*S*,4*Z*)-2,6,8,8-Tetramethyl-7-oxonona-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (17d): Using pivaloyl chloride (3 equiv., 0.9 mmol, 109 mg) for 2 h afforded (*S*,*Z*)-**17d** (81 mg, 80%, colourless oil) (PE/DE, 20:1). *rac*-(*Z*)-**59** was obtained in 37% yield. t_R = 15.0 min; R_f = 0.52 (PE/DE, 4:1); $[\alpha]_D^{20}$ = +137.7 (*c* = 1.10 in $CHCl_3$; *er* = 97:3; (*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 50 × 2 mm; *i*PrOH/*n*-hexane, 1:3000; $t_{R(6S)}$ = 4 min; $t_{R(6R)}$ = 6 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.14 (s, 9 H, H-9); 1.17 (d, 3 H, H-11); 1.30 (d, 12 H, CH_3-*Cb*); 1.77 (s, 3 H, H-1); 1.80 (s, 3 H, H-10); 3.83 (br. s, 2 H, CH-*Cb*); 3.94 (dq, 1 H, H-6); 5.12 (d, 1 H, H-5); 5.59 (s, 1 H, H-3); $^3J_{Cb}$ = 6.8 Hz; $^3J_{5-6}$ = 9.9 Hz; $^3J_{6-11}$ = 6.7 Hz. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8 (C-11); 19.4 (C-10); 20.6 [21.4] (CH_3-*Cb*), 26.2 (C-9); 27.1 (C-1); 37.8 (C-6); 44.8 (C-8); 46.2 [46.6] (CH-*Cb*); 120.5 (C-5); 120.6 (C-3); 136.8 (C-2); 145.3 (C-4); 152.2 (OCON); 216.8 (C-7) ppm. IR (neat): $\tilde{\nu}$ = 2972, 2937, 2873, 1716 (s, ν(C=O)), 1477, 1433, 1369, 1294, 1214, 1154, 1044, 987, 924, 900, 757 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 360.20 (calcd. 360.25). $C_{20}H_{35}NO_3$ (337.50): calcd. C 71.18, H 10.45, N 4.15; found C 71.54, H 10.48, N 4.57.

Titanium-Mediated Homoaldol Reaction of 11

Reaction with Pivaldehyde. (6*S*,7*S*,4*Z*)-7-Hydroxy-2,6,8,8-tetramethylnona-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (21a): The deprotonation was performed as described previously for **11** (1.0 equiv., 0.3 mmol, 76 mg). After 13 h a solution of $ClTi(NEt_2)_3$ (3.0 equiv., 0.90 mmol, 270 mg) in toluene (1 mL) was added dropwise within 3 min. After another 1 h, the corresponding ketone or aldehyde (pivaldehyde (3 equiv., 0.9 mmol, 78 mg) in toluene (1 mL) was added dropwise within 5 min. The solution was stirred for additional 2 h and then the reaction was stopped and worked up as described above. After column chromatography (PE/DE, 6:1→4:1), (*S*,*S*,*Z*)-**21a** (65 mg, 64%, colourless oil) was obtained. The racemate was synthesized according to the same procedure by applying TMEDA (3.0 equiv., 0.90 mmol, 105 mg) as ligand. *rac*-(*Z*)-**21a** was obtained in 40% yield and with a *dr* > 98:2. t_R = 15.2 min; R_f = 0.18 (PE/DE = 2:1); $[\alpha]_D^{20}$ = –56.1 (*c* = 0.98 in $CHCl_3$; *er* = 99:1; *dr* > 98:2; (*S*,*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 50 × 2 mm; *i*PrOH/*n*-hexane, 1/200; $t_{R(6S,7S)}$ = 2 min; $t_{R(6R,7R)}$ = 5 min. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (s, 9 H, H-9); 1.11 (d, 3 H, H-11); 1.26 (d, 12 H, CH_3-*Cb*); 1.77 (s, 1 H, H-1); 1.84 (s, 1 H, H-10); 2.18 (br. s, 1 H, OH); 2.71 (m, 1 H, H-6); 3.11 (d, 1 H, H-7); 3.89 [4.07] (br. s, 1 H, CH-*Cb*); 5.24 (d, 1 H, H-5); 5.59 (s, 1 H, H-3) ppm. $^3J_{Cb}$ = 7.1 Hz; $^3J_{6-7}$ = 3.5 Hz; $^3J_{5-6}$ = 10.6 Hz; $^3J_{6-11}$ = 7.1 Hz ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4 (C-11); 21.0 (C-10); 20.6 [21.3] (CH_3-*Cb*); 26.6 (C-1); 27.1 (C-8); 32.7 (C-9); 35.9 (C-6); 46.3 (CH-*Cb*); 83.1 (C-7); 120.9 (C-5); 122.8 (C-3); 135.7 (C-2); 144.4 (C-4); 153.1 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3493 (m, ν(OH)), 2967, 2870, 1693 (s, ν(C=O)), 1480, 1462, 1433, 1369, 1275, 1215, 1190, 1147, 1095, 1045, 992, 874, 762, 651, 584 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 362.2669 (calcd. 362.2671). $C_{20}H_{37}NO_3$ (339.51): calcd. C 70.75, H 10.98, N 4.13; found C 70.74, H 11.17, N 3.88.

Reaction with 2-Methylpropanal. (6*S*,7*R*,4*Z*)-7-Hydroxy-2,6,8-trimethylnona-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (21b): Using 2-methylpropanal (3 equiv., 0.9 mmol, 65 mg), (6*S*,7*R*,*Z*)-**21b** (58 mg, 59%, yellow oil) (PE/DE, 6:1→4:1) was obtained. *rac*-(*Z*)-**21b** was obtained in 31% yield and with a *dr* > 98:2. t_R = 14.7 min; R_f = 0.32 (PE/DE, 2:1) $[\alpha]_D^{20}$ = –96 (*c* = 0.98 in $CHCl_3$; *er* = 97:3; *dr* > 98:2; (6*S*,7*R*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 50 × 2 mm; *i*PrOH/*n*-hexane, 1/200; $t_{R(6S,7R)}$ = 2 min; $t_{R(6R,7S)}$ = 3 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (d, 3 H, H-11); 0.96 [0.99] (d, 3 H, H-9); 1.26 (d, 12 H, CH_3-*Cb*); 1.75 (m, 1 H, H-8); 1.78 (s, 1 H, H-1); 1.85 (s, 1 H, H-10); 2.47 (m, 1 H, H-6); 2.83 (br. s, 1 H, OH); 3.14 (dd, 1 H, H-7); 3.98 (br. s, 2 H, CH-*Cb*); 5.07 (d, 1 H, H-5); 5.59 (s, 1 H, H-3) ppm. $^3J_{Cb}$ = 7.1 Hz; $^3J_{5-6}$ = 10.4 Hz; $^3J_{6-7}$ = 3.2 Hz; $^3J_{7-8}$ = 8.4 Hz; $^3J_{6-11}$ = 7.1 Hz; $^3J_{8-9}$ = 7.1 Hz ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.6 (C-11); 17.4 (C-9); 19.5 (C-10); 20.3

(C-1); 21.3 (CH_3-*Cb*); 27.0 (C-1); 29.9 (C-8); 34.8 (C-6); 46.4 (CH-*Cb*); 79.3 (C-7); 120.5 (C-5); 123.7 (C-3); 136.6 (C-2); 145.8 (C-4); 153.8 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3461 (m, ν(OH)), 2968, 2933, 2873, 1691 (s, ν(C=O)), 1471, 1435, 1370, 1317, 1305, 1279, 1215, 1193, 1148, 1044, 998, 975, 869, 761, 585 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 348.2509 (calcd. 348.2515). $C_{19}H_{35}NO_3$ (325.49): calcd. C 70.11, H 10.84, N 4.30; found C 70.00, H 10.95, N 4.27.

Reaction with *n*-Propanal. (6*S*,7*R*,4*Z*)-7-Hydroxy-2,6-dimethylnona-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (20c) and (7*S*,2*E*,4*Z*)-7-Hydroxy-6,6-dimethylnona-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (21c): Using *n*-propanal (3 equiv., 0.9 mmol, 52 mg), (6*S*,7*R*,*Z*)-**21c** (60 mg, 64%, white solid) and (*S*,2*E*,4*Z*)-**20c** (7 mg, 7%, colourless oil) were separated (PE/DE, 6:1→4:1). *rac*-(*Z*)-**21c** was obtained in 27% yield and with a *dr* > 98:2. The other regioisomer **20c** could not be detected.

(6*S*,7*R*,*Z*)-21c: t_R = 14.3 min; R_f = 0.21 (PE/DE, 2:1); m.p. 67–68 °C; $[\alpha]_D^{20}$ = –95 (*c* = 0.98 in $CHCl_3$; *er* = 98:2; *dr* > 98:2; (6*S*,7*R*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 250×2 mm; *i*PrOH/*n*-hexane, 1:200; $t_{R(6S,7R)}$ = 12 min; $t_{R(6R,7S)}$ = 14 min. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, 3 H, H-9); 0.98 (d, 3 H, H-11); 1.26 (d, 12 H, CH_3-*Cb*); 1.37 (m, 2 H, H-8); 1.78 (s, 3 H, H-1); 1.85 (s, 3 H, H-10); 2.40 (m, 1 H, H-6); 2.73 (br. s, 1 H, OH); 3.31 (m, 1 H, H-7); 3.91 [4.04] (br. s, 1 H, CH-*Cb*); 5.05 (d, 1 H, H-5); 5.61 (s, 1 H, H-3) ppm. $^3J_{Cb}$ = 7.1 Hz; $^3J_{5-6}$ = 10.9 Hz; $^3J_{6-11}$ = 7.1 Hz; $^3J_{8-9}$ = 7.6 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.9 (C-9); 17.3 (C-11); 19.4 (C-10); 20.5 [21.3] (CH_3-*Cb*); 27.0 (C-1); 27.4 (C-8); 36.3 (C-6); 46.4 (CH-*Cb*); 76.1 (C-7); 120.6 (C-3); 123.2 (C-5); 136.4 (C-2); 146.0 (C-4); 153.6 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3463 (m, ν(OH)), 2970, 2927, 2878, 1690 (s, ν(C=O)), 1660, 1460, 1438, 1373, 1343, 1330, 1278, 1216, 1188, 1157, 1139, 1108, 1046, 1013, 992, 902, 869, 756, 711, 652, 582 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 334.2366 (calcd. 334.2358). $C_{18}H_{33}NO_3$ (311.46): calcd. C 69.41, H 10.68, N 4.50; found C 69.31, H 10.67, N 4.65. Single crystals of (*S*,*S*,*Z*)-**21c** were obtained from PE and DE;[16] see Figure 1.

20c: t_R = 14.5 min; R_f = 0.25 (PE/DE, 2:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.99 (t, 3 H, H-9); 1.06 (s, 3 H, H-10); 1.12 (s, 3 H, H-10′); 1.26 [1.27, 1.31, 1.32] (d, 3 H, CH_3-*Cb*); 1.56 (m, 2 H, H-8); 1.75 (d, 3 H, H-1); 2.71 (br. s, 1 H, OH); 3.73 [4.27] (sept, 1 H, CH-*Cb*); 3.24 (t, 1 H, H-7); 5.05 (s, 1 H, H-5); 5.54 (dq, 1 H, H-2); 5.93 (d, 1 H, H-3) ppm. $^3J_{Cb}$ = 6.9 Hz; $^3J_{1-2}$ = 6.8 Hz; $^3J_{2-3}$ = 15.8 Hz; $^3J_{7-8}$ = 10.4 Hz; $^3J_{8-9}$ = 7.1 Hz ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.8 (C-9); 17.8 (C-1); 20.5 [20.6, 21.2, 21.3] (CH_3-*Cb*); 24.2 (C-10); 24.3 (C-10′); 24.8 (C-8); 41.1 (C-6); 46.0 [47.2] (CH-*Cb*); 80.3 (C-7); 123.8 (C-5); 126.7 (C-3); 128.4 (C-2); 145.4 (C-4); 153.1 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3471 (m, ν(OH)), 2969, 2934, 2875, 1700 (s, ν(C=O)), 1436, 1371, 1312, 1280, 1216, 1145, 1045, 1020, 976, 956, 903, 854, 759 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 334.2366 (calcd. 334.2358).

Reaction with 4-Bromobenzaldehyde. (6*S*,7*S*,*Z*)-7-(4-Bromophenyl)-7-hydroxy-2,6-dimethylhepta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (20d) and (7*S*,2*E*,4*Z*)-7-(4-Bromophenyl)-7-hydroxy-6,6-dimethylhepta-2,4-dien-4-yl *N*,*N*-Diisopropylcarbamate (21d): Using 4-bromobenzaldehyde (3 equiv., 0.9 mmol, 156 mg), (*S*,*S*,*Z*)-**21d** (78 mg, 60%, white solid) and (*S*,2*E*,4*Z*)-**20d** (14 mg, 11%, colourless oil) were obtained (PE/DE, 15:1→9:1). *rac*-(*Z*)-**21d** was obtained in 32% yield and with a *dr* > 98:2. *rac*-(2*E*,4*Z*)-**20d** could not be detected.

(*S*,*S*,*Z*)-21d: t_R = 20.6 min; R_f = 0.52 (PE/DE, 1:2); m.p. 90–91.5 °C $[\alpha]_D^{20}$ = –133 (*c* = 0.98 in $CHCl_3$; *er* = 98:2; *dr* = 95:5; (*S*,*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 50×2 mm; *i*PrOH/*n*-hexane, 1:200; $t_{R(6R,7R)}$ = 9 min; $t_{R(6S,7S)}$ = 12 min. ^1H NMR (300 MHz, $CDCl_3$): δ = 0.78 (d, 3 H, H-9); 1.30 (br. s, 12 H, CH_3-*Cb*); 1.81 (s, 1 H, H-1); 1.87 (s, 1 H, H-8); 2.49 (ddq, 1 H, H-6); 3.96 (br. s, 2 H, CH-*Cb*); 4.07 (br. s, 1 H, OH); 4.21 (d, 1 H, H-7); 5.10 (d, 1 H, H-5); 5.64 (s, 1 H, H-3); 7.18 (d, 2 H, H-Ph); 7.42 (d, 2 H, H-Ph) ppm. $^3J_{6-9}$ = 6.7 Hz; $^3J_{5-6}$ = 10.6 Hz; $^3J_{6-7}$ = 9.3 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (C-9); 19.6 (C-8); 20.6 [21.3] (CH_3-*Cb*); 27.1 (C-1); 29.7 (C-6); 46.6 (CH-*Cb*); 78.2 (C-7); 120.4 (C-5)*; 121.1 (C-3)*; 123.1 (C-Br); 128.7, 131.2 (CH-Ph); 137.4 (C_q-Ph); 143.0 (C-2); 146.8 (C-4); 154.0 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3428 (m, ν(OH)), 2998, 2968, 2931, 2872, 1694 (s, ν(C=O)), 1483, 1435, 1381, 1368, 1310, 1284, 1215, 1139, 1043, 1010, 838, 824, 765, 557 cm^{-1}. MS (ESI) (*m*/*z*):$[M + H]^+$ = 438.2, 440.2 (calcd. 438.2, 440.2); $[M + Na]^+$ = 460.1, 462.1 (calcd. 460.1, 462.1). $C_{22}H_{32}BrNO_3$ (438.40): calcd. C 60.27, H 7.36, N 3.19; found C 59.99, H 7.16, N 3.16. Single crystals of (*S*,*S*,*Z*)-**21d** were obtained from PE and DE;[18] see Figure 2.

(*S*,2*E*,4*Z*)-20d: t_R = 20.8 min; R_f = 0.58 (PE/DE = 1:2). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.97 (s, 3 H, H-8); 1.13 (s, 3 H, H-8′); 1.29 [1.34, 1.35] (d, 12 H, CH_3-*Cb*); 1.77 (d, 3 H, H-1); 3.76 [4.29] (sept, 1 H, CH-*Cb*); 3.90 (br. s, 1 H, OH); 4.44 (s, 1 H, H-7); 4.92 (s, 1 H, H-5); 5.61 (dq, 1 H, H-2); 5.93 (d, 1 H, H-3); 7.20 (d, 2 H, H-Ph); 7.42 (d, 2 H, H-Ph) ppm. $^3J_{Cb}$ = 6.8 Hz; $^3J_{1-2}$ = 6.8 Hz; $^3J_{2-3}$ = 15.2 Hz. NOE (500 MHz, $CDCl_3$): irradiation at δ = 5.93 ppm (H-3): NOE at δ = 4.92 ppm (H-5), 1.77 ppm (H-1); irradiation at δ = 4.92 ppm (H-5): NOE at δ = 5.93 ppm (H-3), 4.44 ppm (H-7), 1.13 ppm (H-8), 0.97 ppm (H-8′). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 17.9 (C-8); 20.5 (C-8′); 20.6 [21.2] (CH_3-*Cb*); 26.0 (C-1); 41.8 (C-6); 46.1 [47.3] (CH-*Cb*); 80.9 (C-7); 120.9, 124.5, 125.4, 128.3, 129.6, 130.4 (C-2, C-3, C-5, CH-Ph, C-Br); 140.2 (C_q-Ph); 146.2 (C-4); 153.8 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3405 (m, ν(OH)), 2971, 2934, 2864, 1697 (s, ν(C=O)), 1635, 1484, 1436, 1379, 1307, 1277, 1214, 1140, 1067, 1044, 1020, 956, 903, 883, 844, 830, 776, 761, 573 cm^{-1}. MS (ESI) (*m*/*z*): $[M + Na]^+$ = 460.1473, 462.1459 (calcd. 460.1464, 462.1446).

Reaction with Acetone. Synthesis of (*S*)-17c and 18c: Using acetone (6.0 equiv., 1.8 mmol, 104 mg), (*S*,*Z*)-**17c** (78 mg, 83%, colourless oil) and (2*E*,4*Z*)-**18c** (4 mg, 4%, colourless oil) were separated (PE/DE, 2:1).

(*S*,*Z*)-17c: $[\alpha]_D^{20}$ = –76.0 (*c* = 0.89 in $CHCl_3$; *er* > 97:3; (*S*)).

Oxidation of (*S*,*S*,*Z*)-21a: (*S*,*S*,*Z*)-**21a** (1.0 equiv., 0.15 mmol, 51 mg), obtained from the titanium-mediated homoaldol reaction of **11** with pivaldehyde, was treated with excess PDC (6 equiv., 0.9 mmol, 350 mg) and molecular sieves in CH_2Cl_2 (5 mL) at room temperature for 26 h. The reaction mixture was filtered through a short silica gel column and concentrated under vacuum. Purification by column chromatography (PE/DE, 20:1) afforded (*S*,*Z*)-**17d** (48 mg, 95%, colourless oil); $[\alpha]_D^{20}$ = +141 (*c* = 0.95 in $CHCl_3$; *er* = 99:1; (*S*)).

Deprotonation of 15 and Substitution with Electrophiles

Reaction with Acetone. (2′*S*,1*Z*,2*E*)-1-[2-(2-Hydroxyprop-2-yl)cyclopentylidene]-4-methylpent-2-enyl *N*,*N*-Diisopropylcarbamate (25a): A solution of (–)-sparteine (3.0 equiv., 0.90 mmol, 212 mg) in toluene (1.5 mL) was cooled to –78 °C. *n*-BuLi (3.0 equiv., 1.6 M in hexane, 0.90 mmol, 0.56 mL) was added slowly. After 10 min a solution of the carbamate **15** (1.0 equiv., 0.3 mmol, 88 mg) in toluene (1 mL) was added. After 16 h, a solution of the corresponding electrophile (acetone, 6 equiv., 1.8 mmol, 104 mg) in toluene (1 mL) was added dropwise within 5 min. The solution was stirred for 3 h and the reaction was stopped by addition of MeOH (0.4 mL) at –78 °C. The flask was removed from the acetone/dry ice bath, and 1 mL of 2 M HCl were added. After warming to room temperature, the organic phase was separated and the aqueous phase washed

three times with DE (5 mL each). The combined organic phases were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (PE/DE, 3:1) afforded (*S*,1*Z*,2*E*)-**25a** (70 mg, 67%, yellow oil).

The racemic version of the reaction was done the same way with TMEDA (3.0 equiv., 0.90 mmol, 105 mg) as ligand instead of (–)-sparteine. *rac*-(1*Z*,2*E*)-**25a** was obtained in 80% yield. t_R = 14.4 min; R_f = 0.39 (PE/DE, 1:1) $[a]_D^{20}$ = –17.5 (*c* = 0.55 in $CHCl_3$; *er* = 93:7; (*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm) 250 × 2 mm; *i*PrOH/*n*-hexane, 1:600; $t_{R(R)}$ = 14 min; $t_{R(S)}$ = 16 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, 6 H, H-5); 1.08 (s, 3 H, H-22′); 1.15 (s, 3 H, H-22′′); 1.24 [1.28] (d, 6 H, CH_3-*Cb*); 1.58, 1.81 (m, 4 H, H-3′, H-4′); 2.34, 2.57 (m, 3 H, H-4, H-5′); 2.80 (br. s, 1 H, OH); 2.86 (m, 1 H, H-2′); 3.65 [4.26] (br. s, 1 H, CH-*Cb*); 5.49 (dd, 1 H, H-3); 6.10 (d, 1 H, H-2) ppm. $^3J_{Cb}$ = 6.8 Hz; $^3J_{2-3}$ = 15.9 Hz, $^3J_{3-4}$ = 7.0 Hz; $^3J_{4-5}$ = 6.6 Hz. NOE (500 MHz, $CDCl_3$): irradiation at δ = 6.13 ppm (H-2): NOE at δ = 2.34, 2.57 ppm (H-4, H-5′). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4 [21.0] (CH_3-*Cb*); 22.2 (C-5); 24.1 (C-3′)*; 26.2, 28.4 (C-22′, $C_2$2′′); 28.9 (C-4′)*; 30.1 (C-5′)*; 30.9 (C-4); 45.7 [47.1] (CH-*Cb*); 52.3 (C-2′); 74.0 (C-21′); 120.4 (C-3); 133.9 (C-1′); 136.7 (C-2); 140.0 (C-1); 152.5 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3412 (m, ν(OH)), 2974, 2934, 2902, 2872, 1706 (s, ν(C=O)), 1632, 1490, 1452, 1370, 1355, 1294, 1236, 1194, 1153, 1123, 1065, 1046, 1035, 995, 949, 908, 878, 851, 823, 763, 710, 639, 580, 528 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 374.2676 (374.2671). $C_{21}H_{37}NO_3$ (351.28): calcd. C 71.75, H 10.61, N 3.98; found C 71.68, H 10.86, N 3.91.

Reaction with Pivaloyl Chloride. (2′*S*,1*Z*,2*E*)-4-Methyl-1-(2-pivaloylcyclopentylidene)pent-2-enyl *N*,*N*-Diisopropylcarbamate (25b): Using pivaloyl chloride (6 equiv., 1.8 mmol, 217 mg) for 2 h afforded (*S*,1*Z*,2*E*)-**25b** (88 mg, 78%, white solid) (PE/DE, 6:1). *rac*-(1*Z*,2*E*)-**25b** was obtained in 67% yield. t_R = 16.0 min; R_f = 0.29 (PE/DE, 4:1); m.p. 117–118 °C. $[a]_D^{20}$ = +152.4 (*c* = 1.12 in $CHCl_3$; *er* = 90:10; (*S*)). Chiral HPLC: CHIRA GROM 2 (8 μm); 250 × 2 mm; *i*PrOH/*n*-hexane, 1:600; $t_{R(S)}$ = 9 min; $t_{R(R)}$ = 15 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (d, 6 H, H-5); 1.22 [1.26, 1.44, 1.41] (d, 3 H, CH_3-*Cb*); 1.25 (s, 9 H, H-23′); 1.73, 1.81, 1.93, 2.12, 2.42, 2.64 (m, 7 H, H-3′, H-4′, H-5′, H-4); 3.52 [4.52] (sept, 1 H, CH-*Cb*); 4.14 (dd, 1 H, H-2′); 5.55 (dd, 1 H, H-3); 6.11 (d, 1 H, H-2) ppm. $^3J_{Cb}$ = 6.8 Hz; $^3J_{2-3}$ = 16.0 Hz; $^3J_{3-4}$ = 6.7 Hz; $^3J_{4-5}$ = 7.1 Hz; $^3J_{2'-3'(cis)}$ = 4.6 Hz; $^3J_{2'-3'(trans)}$ = 9.0 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4 [20.5, 20.6, 21.0] (CH_3-*Cb*); 22.3 (C-5); 25.1 (C-23′), 27.0, 30.4, 31.0 (C-3′, C-4′, C-5′); 32.8 (C-4); 44.5 [45.0] (CH-*Cb*); 47.5 (C-2′); 48.1 (C-22′); 120.6 (C-3); 134.0 (C-1′); 135.9 (C-2); 138.4 (C-1); 151.6 (OCON); 216.6 (C-21′) ppm. IR (neat): $\tilde{\nu}$ = 2967, 2904, 2872, 1702 (s, ν(C=O)), 1466, 1430, 1371, 1322, 1241, 1217, 1158, 1137, 1045, 999, 959, 751, 655, 599, 522 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 400.2825 (calcd. 400.2828). $C_{23}H_{39}NO_3$ (377.56): calcd. C 73.17, H 10.41, N 3.71; found C 73.11, H 10.43, N 3.53. Single crystals of (*S*,1*Z*,2*E*)-**25b** were obtained from PE and DE;[21] see Figure 3.

Titanium-Mediated Homoaldol Reaction of 15

Reaction with Pivaldehyde. (1*Z*,2*E*)-1-[(2*R*)-2-((1*R*)-1-Hydroxy-2,2-dimethylpropyl)cyclopentylidene]-4-methylpent-2-enyl *N*,*N*-Diisopropylcarbamate (28a): The deprotonation was performed as described previously for **15** (1.0 equiv., 0.3 mmol, 88 mg). After 16 h a solution of $ClTi(NEt_2)_3$ (3.0 equiv., 0.90 mmol, 270 mg) in toluene (1 mL) was added dropwise within 3 min. After another 1 h, the corresponding ketone or aldehyde (pivaldehyde, 3 equiv., 0.9 mmol, 78 mg) in toluene (1 mL) was added dropwise within 5 min. The solution was stirred for additional 2 h and then the reaction was stopped and worked up as described above. After column chromatography (PE/DE, 6:1→4:1), (*R*,*R*,1*Z*,2*E*)-**28a** (101 mg, 89%, colourless oil) was obtained. The racemate was synthesized by deprotonation of **15** with *s*BuLi (3.0 equiv., 1.2 M in hexane, 0.90 mmol, 0.75 mL) in presence of TMEDA (3.0 equiv., 0.90 mmol, 105 mg) for 8 h, followed by transmetallation and reaction with pivaldehyde as described before. *rac*-(1*Z*,2*E*)-**28a** was obtained in 67% yield and with a *dr* > 98:2. t_R = 16.3 min; R_f = 0.55 (PE/DE, 1:1) $[a]_D^{20}$ = +79.7 (*c* = 1.11 in $CHCl_3$; *er* = 99:1; *dr* > 98:2; (*R*,*R*)) Chiral HPLC: CHIRA GROM 1 (8 μm), 250 × 2 mm; *i*PrOH/*n*-hexane, 1:1000; t_R = 17 min (major enantiomer) and 22 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (d, 9 H, H-23′); 1.00 [1.01] (d, 3 H, H-5); 1.28 (br. s, 12 H, CH_3-*Cb*); 1.59, 1.69, 1.78, 1.92 (m, 1 H, H-3′, H-4′); 2.37, 2.43, 2.54 (m, 1 H, H-4, H-5′); 3.00 (m, 2 H, H-2′, H-21′); 3.14 (br. s, 1 H, OH); 3.82 [4.23] (br. s, 1 H, C-*Cb*); 5.51 (dd, 1 H, H-3); 6.06 (d, 1 H, H-2) ppm. $^3J_{Cb}$ = 6.8 Hz; $^3J_{2-3}$ = 15.9 Hz, $^3J_{3-4}$ = 6.8 Hz; $^3J_{4-5}$ = 6.9 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3 [20.5, 21.0, 21.3] (CH_3-*Cb*); 22.4, 22.5 (C-5); 26.1, 28.2, 30.9, 33.9 (C-3′, C-4′, C-5′, C-4); 36.6 (C-2′); 43.1 (C-22′); 46.1 [46.9] (CH-*Cb*); 81.0 (C-21′); 120.2 (C-3); 135.8 (C-1′); 136.1 (C-2); 139.0 (C-1); 154.1 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3407 (m, ν(OH)), 2960, 2871, 1677 (s, ν(C=O)), 1466, 1436, 1369, 1330, 1300, 1249, 1211, 1154, 1132, 1081, 1043, 1015, 960, 902, 765, 647, 602, 580 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 402.2980 (calcd. 402.2984). $C_{23}H_{41}NO_3$ (379.58): calcd. C 72.78, H 10.89, N 3.69; found C 72.72, H 10.78, N 3.51.

Reaction with 2-Methylpropanal. (3*S*,4*R*,1*Z*)-1-Cyclopent-1-enyl-4-hydroxy-3-isopropyl-5-methylhex-1-enyl *N*,*N*-Diisopropylcarbamate (27b) and (1*Z*,2*E*)-1-[(2*R*)-2-((1*S*)-1-Hydroxy-2-methylpropyl)cyclopentylidene]-4-methylpent-2-enyl *N*,*N*-Diisopropylcarbamate (28b): Using 2-methylpropanal (3 equiv., 0.9 mmol, 65 mg), (2′*R*,21′*S*,1*Z*,2*E*)-**28b** (67 mg, 61%, yellowish oil) and (3*S*,4*R*,*Z*)-**27b** (26 mg, 24%, oily solid) were separated (PE/DE, 6:1). *rac*-**27b** and *rac*-**28b** were obtained in yields of 17% and 50%, respectively. The *dr* of both products was > 98:2.

(2′*R*,21′*S*,1*Z*,2*E*)-28b: t_R = 15.5 min; R_f = 0.51 (PE/DE, 1:1); $[a]_D^{20}$ = +38.7 (*c* = 1.24 in $CHCl_3$; *er* > 98:2; *dr* > 98:2; (*R*,*S*)) Chiral HPLC: CHIRA GROM 2 (8 μm) 250 × 2 mm; *i*PrOH/*n*-hexane, 1:1000; t_R = 18 min (major enantiomer) and 19 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 [1.00] (d, 3 H, H-23′); 0.98 [1.01] (d, 3 H, H-5); 1.29 (m, 12 H, CH_3-*Cb*); 1.53–1.85 (m, 5 H, H-3′, H-4′, H-4); 2.48 (dd, 1 H, H-21′); 2.47 (br. s, 1 H, OH); 2.37 (m, 1 H, H-22′); 2.89 (m, 2 H, H-5′); 3.14 (m, 1 H, H-2′); 3.87 [4.14] (sept, 1 H, CH-*Cb*); 5.52 (dd, 1 H, H-3); 6.08 (d, 1 H, H-2) ppm. $^3J_{2-3}$ = 15.8 Hz; $^3J_{3-4}$ = 7.0 Hz; $^3J_{4-5}$ = 7.1 Hz; $^3J_{2'-21'}$ = 7.8 Hz; $^3J_{21'-22'}$ = 7.1 Hz; $^3J_{22'-23'}$ = 6.7 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.3 [20.4] (C-23′); 20.6 [21.3] (CH_3-*Cb*); 22.2, 22.3 (C-5); 23.2 (C-4′); 28.1, 30.5 (C-3′, C-5′); 30.9, 31.7 (C-4, C-22′); 45.7 (C-2′); 46.1 [46.9] (CH-*Cb*); 77.3 (C-21′); 120.1 (C-3); 134.7 (C-1′); 136.5 (C-2); 139.4 (C-1); 153.8 (OCON) ppm. IR (neat): $\tilde{\nu}$ = 3426 (m, ν(OH)), 2960, 2872, 1691 (s, ν(C=O)), 1463, 1433, 1369, 1330, 1304, 1250, 1215, 1061, 1069, 1044, 1010, 959, 895, 762, 602, 517, 502 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 388.2820 (calcd. 388.2828). $C_{22}H_{39}NO_3$ (365.55): calcd. C 72.28, H 10.75, N 3.83; found C 72.10, H 10.77, N 3.77.

(3*S*,4*R*,*Z*)-27b: t_R = 15.5 min; R_f = 0.42 (PE/DE, 1:1); $[a]_D^{20}$ = –56.6 (*c* = 0.77 in $CHCl_3$; *er* = 99:1; *dr* > 98:2; (3*S*,4*R*)) Chiral HPLC: CHIRA GROM 2 (8 μm) 250 × 2 mm; *i*PrOH/*n*-hexane, 1:600; $t_{R(3S,4R)}$ = 16 min; $t_{R(3R,4S)}$ = 30 min. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 [0.84] (d, 3 H, H-6); 0.87 [1.00] (d, 3 H, H-8); 1.24 [1.26, 1.32] (d, 3 H, CH_3-*Cb*); 1.73–1.99 (m, 4 H, H-4′, H-5, H-7); 2.28–2.61 (m, 5 H, H-3, H-3′, H-5′); 3.12 (br. s, 1 H, OH); 3.41 (bd, 1 H, H-4); 4.02 (br. s, 2 H, CH-*Cb*); 5.24 (d, 1 H, H-2); 5.66 (br. s, 1 H,

H-2′) ppm. $^3J_{Cb}$ = 6.9 Hz; $^3J_{2-3}$ = 11.3 Hz; $^3J_{5-6}$ = $^3J_{7-8}$ = 6.9 Hz. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3 [16.9] (C-8); 20.4 [20.5, 20.6] (CH_3-*Cb*); 21.6 [22.2] (C-6); 23.1 (C-4′); 28.1 (C-7); 29.9 (C-5); 32.2, 33.0 (C-3′, C-5′); 45.6 (C-3); 46.3 [46.7] (CH-*Cb*); 75.8 (C-4); 117.4 (C-2); 126.7 (C-2′); 138.9 (C-1′); 147.1 (C-1); 154.1 (OCON) ppm. IR (neat): ṽ = 3424 (m, ν(OH)), 2959, 2932, 2872, 1686 (s, ν(C=O)), 1464, 1436, 1369, 1292, 1272, 1214, 1155, 1138, 1044, 1003, 759, 590 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 388.2823 (calcd. 388.2828). $C_{22}H_{39}NO_3$ (365.55): calcd. C 72.28, H 10.75, N 3.83; found C 72.18, H 10.81, N 3.71.

Reaction with 4-Bromobenzaldehyde. [3*S*,3(1*S*),1*Z*]-3-[(4-Bromophenyl)(hydroxy)methyl]-1-cyclopent-1-enyl-4-methylpent-1-enyl *N*,*N*-Diisopropylcarbamate (27c) and [2′*R*,2′(1*R*),1*Z*,2*E*]-1-{2-[(4-Bromophenyl)(hydroxy)methyl]cyclopentylidene}-4-methylpent-2-enyl *N*,*N*-Diisopropylcarbamate (28c): Using 4-bromobenzaldehyde (3 equiv., 0.9 mmol, 167 mg), (*R*,*R*,1*Z*,2*E*)-**28c** (58 mg, 40%, white solid) and (*S*,*S*,*Z*)-**27c** (57 mg, 40%, colourless oil) were separated (PE/DE, 6:1→4:1). *rac*-(1*Z*,2*E*)-**28c** and *rac*-(*Z*)-**27c** were obtained in yields of 25 and 26%, respectively. The *dr* of both products was > 98:2.

(*S*,*S*,*Z*)-27c: t_R = 22.1 min; R_f = 0.44 (PE/DE, 1:1) $[\alpha]_D^{20}$ = –36.3 (*c* = 0.57 in $CHCl_3$; *er* = 99:1; *dr* > 98:2; (*S*,*S*)) Chiral HPLC: CHIRA GROM 2 (8 μm) 250 × 2 mm; *i*PrOH/*n*-hexane, 1:500; t_R = 58 min and 64 min (major enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.66 [0.81] (d, 3 H, H-5); 1.25 [1.26, 1.27, 1.30] (d, 3 H, CH_3-*Cb*); 1.72 (m, 1 H, H-4); 1.92 (m, 2 H, H-4′); 2.28–2.60 (m, 5 H, H-3, H-3′, H-5′); 4.00 (br. s, 2 H, CH-*Cb*); 4.38 (d, 1 H, H-6); 4.52 (br. s, 1 H, OH); 5.25 (d, 1 H, H-2); 5.67 (br. s, 1 H, H-2′); 7.09 (d, 2 H, H-Ph); 7.36 (d, 2 H, H-Ph) ppm. $^3J_{Cb}$ = 6.9 Hz; $^3J_{2-3}$ = 11.3 Hz; $^3J_{3-6}$ = 10.2 Hz; $^3J_{4-5}$ = 6.6 Hz. NOE (500 MHz, $CDCl_3$): irradiation at δ = 5.67 ppm (H-2′): NOE at δ = 4.00 ppm (CH-*Cb*), 2.43 ppm (H-3′), 1.27 (CH_3-*Cb*); irradiation at δ = 5.25 ppm (H-2): NOE at δ = 4.38 ppm (H-6), 2.28–2.60 ppm (H-3, H-5′), 0.81 ppm (H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.4 [22.3] (C-6); 20.5 [20.7, 21.5, 21.6] (CH-*Cb*); 23.1 (C-4′); 28.1 (C-4); 32.2, 33.0 (C-3′, C-5′); 46.6 [46.9] (CH-*Cb*); 51.1 (C-3); 75.0 (C-6); 116.1 (C-2); 121.0 (C–Br); 127.6 (C-2′); 128.6, 131.3 (CH-Ph); 138.7 (C-1′); 144.0 (C_q-Ph); 147.9 (C-1); 154.2 (OCON) ppm. IR (neat): ṽ = 3420 (m, ν(OH)), 2963, 2930, 2872, 1680 (s, ν(C=O)), 1484, 1467, 1435, 1370, 1325, 1293, 1274, 1212, 1155, 1137, 1070, 1045, 1010, 909, 822, 760, 730, 647, 519 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 500.1768, 502.1753 (calcd. 500.1776, 502.1756). $C_{25}H_{36}BrNO_3$ (478.46): calcd. C 62.76, H 7.58, N 2.93; found C 62.58, H 7.56, N 2.76.

(*R*,*R*,1*Z*,2*E*)-28c: t_R = 22.2 min; R_f = 0.37 (PE/DE, 1:1); m.p. 87–89 °C. $[\alpha]_D^{20}$ = +109.9 (*c* = 1.42 in $CHCl_3$; *er* = 99:1; *dr* > 98:2; (*R*,*R*)) Chiral HPLC: CHIRA GROM 2 (8 μm) 250 × 2 mm; *i*PrOH/*n*-hexane, 1:600; t_R = 15 min and 37 min (major enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (d, 6 H, H-5); 1.30 [1.31, 1.35, 1.36] (d, 3 H, CH_3-*Cb*); 1.39–1.72 (m, 4 H, H-3′, H-4′); 2.41 (m, 1 H, H-4); 2.51 (m, 2 H, H-5′); 3.04 (m, 2 H, H-2′); 3.47 (br. s, 1 H, OH); 3.91 [4.19] (sept, 1 H, CH-*Cb*); 4.45 (d, 1 H, H-21′); 5.59 (dd, 1 H, H-3); 6.09 (d, 1 H, H-2) ppm. $^3J_{Cb}$ = 6.7 Hz; $^3J_{2-3}$ = 16.0 Hz; $^3J_{3-4}$ = 6.7 Hz; $^3J_{4-5}$ = 7.4 Hz; $^3J_{2'-21'}$ = 9.3 Hz NOE (500 MHz, $CDCl_3$): irradiation at δ = 6.11 ppm (H-2): NOE at δ = 5.59 ppm (H-3), 2.52 ppm (H-5′); 2.41 ppm (H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5 [20.6, 21.4, 21.5] (CH_3-*Cb*); 22.2 (C-5); 23.0 (C-4′); 27.9, 28.7 (C-3′, C-5′); 31.0 (C-4); 46.5 [46.8] (CH-*Cb*); 50.2 (C-2′); 74.8 (C-21′); 120.0 (C-3); 121.1 (C-Br); 128.7, 131.2 (CH-Ph); 133.1 (C-1′); 137.4 (C-2); 140.5 (C-1); 142.5 (C_q-Ph); 154.1 (OCON) ppm. IR (neat): ṽ = 3470 (m, ν(OH)), 3000, 2964, 2933, 2873, 1690 (s, ν(C=O)), 1592, 1484, 1463, 1435, 1371, 1328, 1307, 1246, 1214, 1153, 1137, 1069, 1044, 1011, 960, 824, 754, 664, 617, 602 cm^{-1}. MS (ESI) (*m*/*z*): [M + Na]$^+$ = 500.1775, 502.1758 (calcd. 500.1776, 502.1756). $C_{25}H_{36}BrNO_3$ (478.46): calcd. C 62.76, H 7.58, N 2.93; found C 62.70, H 5.57, N 2.75. Single crystals of (*R*,*R*,1*Z*,2*E*)-**28c** were obtained from PE and DE;[22] see Figure 4.

Reaction with Acetone. Synthesis of (*R*)-25a: Using acetone (6 equiv., 1.8 mmol, 104 mg), (*R*,1*Z*,2*E*)-**25a** (66 mg, 63%, yellow oil) was obtained (PE/DE, 3:1). $[\alpha]_D^{20}$ = +19.3 (*c* = 0.95 in $CHCl_3$; *er* = 98:2; (*R*)).

Oxidation of (*R*,*R*,1*Z*,2*E*)-28a: (*R*,*R*,1*Z*,2*E*)-**28a** (1.0 equiv., 0.20 mmol, 76 mg), obtained from the titanium-mediated homoaldol reaction of **15** with pivaldehyde, was treated with excess PDC (6 equiv., 1.2 mmol, 460 mg) and molecular sieves in CH_2Cl_2 (10 mL) at room temperature for 24 h. The reaction mixture was filtered and concentrated under vacuum. Purification by column chromatography (PE/DE, 6:1) afforded pure (*R*,*R*,1*Z*,2*E*)-**28a** (73 mg, 97%, white solid); $[\alpha]_D^{20}$ = –191 (*c* = 0.97 in $CHCl_3$; *er* = 99:1; (*R*)); m.p. 119.5–121 °C.

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[1] D. Hoppe, R. Bou Chedid, R. Fröhlich, *Org. Lett.* **2006**, *8*, 3061.
[2] D. Hoppe, R. Bou Chedid, M. Brümmer, R. Fröhlich, B. Wibbeling, *Angew. Chem.* **2007**, *119*, 3192; *Angew. Chem. Int. Ed.* **2007**, *46*, 3131.
[3] D. Hoppe, O. Zschage, *Angew. Chem.* **1989**, *101*, 67; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 69.
[4] Reviews: a) D. Hoppe, T. Hense, *Angew. Chem.* **1997**, *109*, 2376; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2282; b) D. Hoppe, F. Marr, M. Brüggemann, in *Organolithiums in Enantioselective Synthesis* (Ed.: D. M. Hodgson); Topics in Organometallic Chemistry; Springer-Verlag: Berlin, **2003**; vol. 5, p. 61; c) P. Beak, T. A. Johnson, D. D. Kim, S. H. Lim, in *Organolithiums in Enantioselective Synthesis* (Ed.: D. M. Hodgson); Topics in Organometallic Chemistry; Springer-Verlag: Berlin, **2003**; vol. 5, p. 134; d) D. Hoppe, G. Christoph, in *Chemistry of Organolithium Compounds* (Eds.: Z. Rappoport, I. Marek); John Wiley & Sons Ltd. Chichester, UK, **2004**; vol. 2, p. 1055; e) H. Ahlbrecht, U. Beyer, *Synthesis* **1999**, 365.
[5] a) D. Hoppe, *Angew. Chem.* **1984**, *96*, 930; *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 931; b) D. Hoppe, in *Methoden der Org. Chem.*, 4th ed. (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann); Thieme: Stuttgart, New York, **1995**; vol. 21b.
[6] a) E. Negishi, X. Zeng, Z. Tan, M. Qian, Q. Hu, Z. Huang, in *Metal-Catalyzed Cross-Coupling Reactions,* 2nd ed.; A. de Meijere, F. Diedrich, Eds.; VCH: Weinheim, **2004**; vol. 2, p. 815; b) A. Suzuki, *Handbook of Organopalladium Chemistry for Organic Synthesis* (Ed.: E. Negishi.); John Wiley & Sons Inc. **2002**, vol. 1, p. 249.
[7] Reviews: a) M. T. Reetz, *Organotitanium Reagents in Organic Synthesis*, 1st ed.; Springer-Verlag: Berlin, **1986**; b) B. Weidmann, D. Seebach, *Angew. Chem.* **1983**, *95*, 12; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 32; c) M. T. Reetz, Organotitanium Chemistry, in *Organometallics in Synthesis*, 2nd ed.; Schlosser, M., Ed.; Wiley: Chichester, **2002**; p. 817.
[8] a) D. Hoppe, R. Hanko, A. Brönneke, F. Lichtenberg, E. van Hülsen, *Chem. Ber.* **1985**, *118*, 2822; b) D. Hoppe, K. Behrens, R. Fröhlich, O. Meyer, *Eur. J. Org. Chem.* **1998**, 2397.

[9] a) X. J. Wang, Y. Li, C. X. Zhang, *J. Chin. Chem. Soc.* **2003**, *50*, 1183; b) A. K. Ghosh, H. Y. Lee, W. J. Thompson, C. Culberson, M. K. Holloway, S. P. McKee, P. M. Munson, T. T. Duong, A. M. Smith, P. L. Darke, J. A. Zugay, E. A. Emini, W. A. Schleif, J. R. Huff, P. S. Anderson, *J. Med. Chem.* **1994**, *37*, 1177.

[10] a) D. Hoppe, H. Paulsen, *Tetrahedron* **1992**, *48*, 5667; b) D. Hoppe, B. Peschke, J. Lüßmann, M. Dyrbusch, *Chem. Ber.* **1992**, *125*, 1421; c) S. Sengupta, V. Snieckus, *J. Org. Chem.* **1990**, *55*, 5680; d) P. Kocienski, N. J. Dixon, *Synlett* **1989**, 52.

[11] a) D. Hoppe, E. Beckmann, *Synthesis* **2005**, 217; b) D. Hoppe, E. Beckmann, V. Desai, *Synlett* **2004**, 2275.

[12] a) D. H. R. Barton, G. Bashiardes, J.-L. Fourrey, *Tetrahedron Lett.* **1983**, *24*, 1605; b) J. M. MacDougall, V. J. Santora, S. K. Verma, P. Turnbull, C. R. Hernandez, H. W. Moore, *J. Org. Chem.* **1998**, *63*, 6905; c) X. J. Wang, S. A. Hart, B. Xu, M. D. Mason, F. A. Etzkorn, *J. Org. Chem.* **2003**, *68*, 2343.

[13] H. E. Zimmerman, D. M. Traxler, *J. Am. Chem. Soc.* **1957**, *79*, 1920.

[14] D. Hoppe, M. Seppi, R. Kalkofen, J. Reupohl, R. Fröhlich, *Angew. Chem.* **2004**, *116*, 1447; *Angew. Chem. Int. Ed.* **2004**, *43*, 1423.

[15] J. Reuber, Dissertation, University of Münster, **2004**; R. Kalkofen, *Dissertation*, University of Münster, **2005**.

[16] X-ray crystal structure analysis for **21c**: formula $C_{18}H_{33}NO_3$, M = 311.45, colorless crystal 0.35 × 0.30 × 0.25 mm, a = 9.378(1), b = 11.460(1), c = 18.439(1) Å, V = 1981.7(3) Å^3, ρ_{calc} = 1.044 g cm^{-3}, μ = 0.550 mm^{-1}, empirical absorption correction (0.831 ≤ T ≤ 0.875), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, T = 223 K, ω and φ scans, 9108 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.60 Å^{-1}, 3287 independent (R_{int} = 0.030) and 3210 observed reflections [$I \geq 2\sigma(I)$], 208 refined parameters, R = 0.032, wR_2 = 0.087, Flack parameter –0.1(2), max. residual electron density 0.11 (–0.11) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

[17] Data sets were collected with Nonius KappaCCD diffractometers, in case of Mo-radiation equipped with a rotating anode generator. Programs used: COLLECT (Nonius B. V., 1998) for data collection, Denzo-SMN (Z. Otwinowski, W. Minor, *Methods Enzymol.* **1997**, *276*, 307–326) for data reduction, SORTAV (R. H. Blessing, *Acta Crystallogr., Sect. A* **1995**, *51*, 33–37; R. H. Blessing, *J. Appl. Crystallogr.* **1997**, *30*, 421–426) and Denzo (Z. Otwinowski, D. Borek, W. Majewski, W. Minor, *Acta Crystallogr., Sect. A* **2003**, *59*, 228–234) for absorption correction, SHELXS-97 (G. M. Sheldrick, *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473) for structure solution, SHELXL-97 (G. M. Sheldrick, University of Göttingen, 1997) for structure refinement, SCHAKAL (E. Keller, University of Freiburg, **1997**) for graphics. CCDC-636950 to -636953 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.

[18] X-ray crystal structure analysis for (*S*,*S*,*Z*)-**21d**: formula $C_{22}H_{32}BrNO_3$, M = 438.40, colorless crystal 0.60 × 0.15 × 0.10 mm, a = 8.426(1), b = 9.016(1), c = 15.375(1) Å, β = 94.57(1), V = 1164.3(2) Å^3, ρ_{calc} = 1.250 g cm^{-3}, μ = 2.557 mm^{-1}, empirical absorption correction (0.309 ≤ T ≤ 0.784), Z = 2, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, T = 223 K, ω and φ scans, 6367 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.58 Å^{-1}, 2631 independent (R_{int} = 0.043) and 2584 observed reflections [$I \geq 2\sigma(I)$], 253 refined parameters, R = 0.042, wR_2 = 0.116, Flack parameter 0.05(3), max. residual electron density 0.43 (–0.37) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

[19] D. Hoppe, R. Hanko, *Angew. Chem.* **1982**, *94*, 378; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 372.

[20] H. Paulsen, C. Graeve, D. Hoppe, *Synthesis* **1996**, 141.

[21] X-ray crystal structure analysis for (*S*,1*Z*,2*E*)-**25b**: formula $C_{23}H_{39}NO_3$, M = 377.55, colorless crystal 0.45 × 0.35 × 0.20 mm, a = 11.110(1), b = 11.204(1), c = 18.863(1) Å, V = 2348.0(3) Å^3, ρ_{calc} = 1.068 g cm^{-3}, μ = 0.069 mm^{-1}, empirical absorption correction (0.970 ≤ T ≤ 0.986), Z = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 0.71073 Å, T = 198 K, ω and φ scans, 18301 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.67 Å^{-1}, 5671 independent (R_{int} = 0.079) and 3142 observed reflections [$I \geq 2\sigma(I)$], 253 refined parameters, R = 0.075, wR_2 = 0.229, Flack parameter –1(2), max. residual electron density 0.83 (–0.31) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

[22] X-ray crystal structure analysis for (*R*,*R*,1*Z*,2*E*)-**28c**: formula $C_{25}H_{36}BrNO_3$, M = 478.46, colorless crystal 0.30 × 0.15 × 0.15 mm, a = 6.522(1), b = 12.719(1), c = 15.109(1) Å, β = 97.46(1), V = 1242.7(2) Å^3, ρ_{calc} = 1.279 g cm^{-3}, μ = 1.678 mm^{-1}, empirical absorption correction (0.633 ≤ T ≤ 0.787), Z = 2, monoclinic, space group $P2_1$ (No. 4), λ = 0.71073 Å, T = 198 K, ω and φ scans, 10810 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.67 Å^{-1}, 5368 independent (R_{int} = 0.061) and 3590 observed reflections [$I \geq 2\sigma(I)$], 278 refined parameters, R = 0.053, wR_2 = 0.113, Flack parameter 0.02(1), max. residual electron density 0.56 (–0.42) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

[23] a) M. Schlosser, G. Rauchschwalbe, *J. Am. Chem. Soc.* **1978**, *100*, 3258; b) A. Nakamura, H. Yasuda, M. Yamauchi, Y. Ohnuma, *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1481.

[24] a) M. T. Reetz, R. Urz, T. Schuster, *Synthesis* **1985**, 540; b) E. P. Benzing, W. A. Kornicker, *Chem. Ber.* **1961**, *94*, 2263.

[25] T. Krämer, Dissertation, University of Kiel, **1989**.

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