DOI: 10.1002/adsc.200505361

Palladium-Catalyzed *O*-Allylation of α-Hydroxy Carbonyl Compounds

Bernd Schmidt,[a,b,*] Stefan Nave[a]

[a] Universität Dortmund, Fachbereich Chemie, Organische Chemie, Otto-Hahn-Strasse 6, D-44227 Dortmund, Germany
Fax: (+49)-231-755-5363, e-mail: bernd.schmidt@uni-dortmund.de
[b] New address: Universität Potsdam, Institut für Chemie, Organische Chemie II, Karl-Liebknecht-Strasse 24–25, 14476 Golm, Germany
E-mail: berschmi@rz.uni-potsdam.de

Received: September 15, 2005; Accepted: December 16, 2005

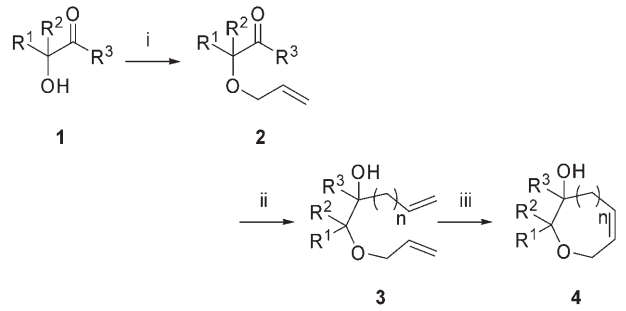
Supporting Information for this article is available on the WWW under http://asc.wiley-vch.de or from the author.

Abstract: α-Hydroxy carbonyl compounds undergo smooth *O*-allylation using allylic carbonates and Pd(0) catalysts. This method has significant advantages over other *O*-allylation methods as it provides a solution to several problems previously observed for this synthetic transformation.

Keywords: alcohols; allylation; allylic compounds; homogeneous catalysis; palladium

Introduction

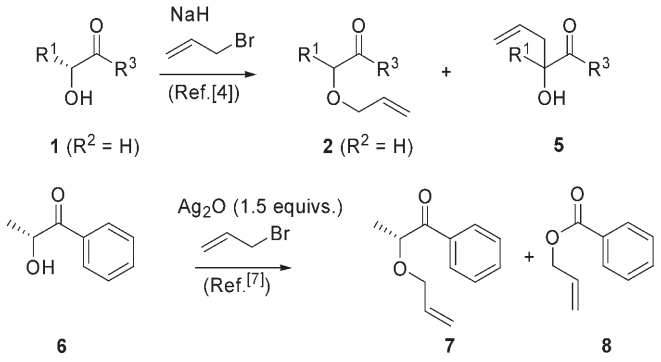
Over the past few years we have demonstrated that α-hydroxy carbonyl compounds[1] are versatile starting materials for the olefin metathesis-based synthesis of functionalized oxacycles.[2–7] Key features of our strategy are i) a selective *O*-allylation of the corresponding α-hydroxy carbonyl compound **1**, ii) the diastereoselective addition of vinyl- or allylmetal compounds to the resulting *O*-allyl ethers **2**, iii) the Ru-catalyzed ring closing metathesis of dienes **3**,[8,9] which yields dihydropyrans (n = 0) or oxepins (n = 1) **4**, respectively (Scheme 1). Oxacycles **4** have great potential in the *de novo* synthesis of carbohydrates or related compounds,[10,11] which has been demonstrated by us[5,12–14] and others.[15–19]



Scheme 1. Synthesis of functionalized oxacycles from α-hydroxy carbonyl compounds based on olefin metathesis.

Although apparently trivial, the first step of this sequence may cause significant problems. For instance, allylation of the corresponding sodium alkoxides with allyl bromide or iodide requires strongly basic conditions and leads to immediate racemization if, e.g., (*S*)-ethyl lactate is employed in the reaction.[2,20] In the case of mandelates not only racemization occurs, but a subsequent Wittig rearrangement of the primary *O*-allylation product is observed which gives a carbinol in preparatively useful yield (Scheme 2).[4] The same phenomenon was observed for α-hydroxy ketones such as benzoin.[7] Racemization and undesired Wittig rearrangements can be avoided by using trichloroacetimidates as allylating agent[21] or allyl bromide in the presence of excess silver oxide.[22,23] We have successfully used the latter method for α-hydroxy esters.[2,3,5] However, application of these conditions to aromatic α-hydroxy ketones[24] turned out to give less satisfactory results, because these substrates partially undergo an oxidative C–C bond cleavage under these conditions, resulting in the formation of allyl benzoate (**8**) as a by-product. For 3-hydroxypropiophenone (**6**) and substituted derivatives this side reaction becomes a serious limitation, as approximately 50% of the starting material are converted *via* this pathway (Scheme 2).[7]

This observation, together with the economical (overstoichiometric amounts of expensive Ag_2O are required) and ecological (generation of heavy metal-containing waste in large quantities) drawbacks of this



Scheme 2. Side reactions of established allylation procedures.

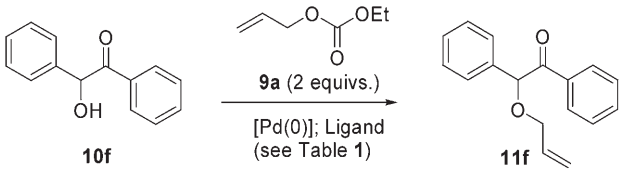
method led us to evaluate the potential of a Pd-catalyzed allylation process for this transformation. The Pd-catalyzed allylation has been widely applied to C-nucleophiles and is one of the most important C–C bond-forming reactions.[25] In this light it is somewhat surprising that many examples describing the Pd-catalyzed allylation of *O*-nucleophiles are limited to carboxylic acids and their salts,[26] phenols,[27–29] metal alkoxides[30–32] and intramolecular Pd-catalyzed decarboxylation of allyloxy carbonates.[33–35] Tsuji's statement that "alcohols are poor O-nucleophiles, and the Pd-catalyzed allylation of alcohols to form allyl alkyl ethers is somewhat sluggish"[36] might explain why this reaction has not been as thoroughly explored for aliphatic alcohols.[37–42] In this contribution conditions are described that allow the facile and selective allylation of several hydroxy carbonyl compounds using Pd catalysis, as well as some other substrates that have been found to be problematic under established conditions.

Results and Discussion

In their pioneering study, Sinou et al. described the use of allyl ethyl carbonate (**9a**) and a Pd(0) catalyst for the allylation of carbohydrates.[37] One important result of this work is that the allylation of anomeric hydroxy groups is much more facile, which has been attributed to their higher acidity. More recently, Haight et al. discovered, for primary, secondary and tertiary alcohols bearing no further functional groups, that the leaving group of the allyl carbonate exerts a strong influence on the efficiency of the reaction.[40] For instance, quantitative allylation of a secondary alcohol can be achieved with only 1.5 equivalents of allyl *tert*-butyl carbonate (**9c**), while more than 6.9 equivalents of the corresponding methyl derivative (**9b**) are required. As allyl ethyl carbonate (**9a**)[43] is more conveniently available than the corresponding *tert*-butyl derivative **9c**, we wanted to use this allylating agent for preparative purposes whenever possible, although it had to be assumed that the reactivity of **9a** is similar to the reactivity of allyl methyl carbonate (**9b**).

We started our investigation with a comparative study of various palladium catalysts. Under standardized conditions, benzoin (**10f**) and two equivalents of allyl ethyl carbonate (**9a**) were heated in refluxing THF in the presence of 2.5 mol % Pd precatalyst. In the case of dimeric precatalysts, 1.25 mol % were used. After one hour, the reaction was stopped and the crude reaction mixture was analyzed by NMR-spectroscopy (Scheme 3).

As can be seen from the results summarized in Table 1, less than 5% conversion is obtained with the catalyst/ligand combination $PdCl_2/PPh_3$. The two dimeric precatalysts $Pd_2(dba)_3 \cdot CHCl_3$ and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ give, in combination with PPh_3 as a ligand, better results, however, in the latter case unidentified by-products are observed in small amounts. It has previously been reported by Zumpe and Kazmaier that this precatalyst can be used for the selective *O*-allylation of Boc-protected serine methyl ester.[38] The modest activity of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in the allylation of **10f** might be explained by the fact that a sterically more hindered secondary rather than a primary alcohol is present. The best results for the allylation of **10f** were obtained with $Pd(OAc)_2$ in combination with PPh_3, or with $[Pd(PPh_3)_4]$ without additional ligand. In both cases, approximately 80% of **10f** were converted to **11f** after one hour, without noticeable formation of by-products.



Scheme 3. Pd-catalyzed allylation of benzoin with allyl ethyl carbonate.

Table 1. Evaluation of precatalysts for the allylation of benzoin (**10f**) with allyl ethyl carbonate (**9a**) (Scheme 3).

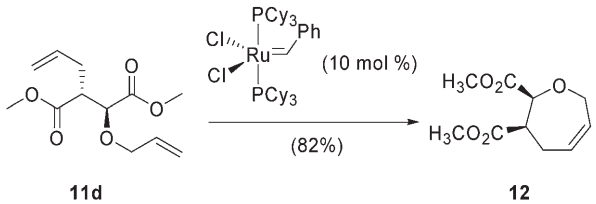
Entry	Precatalyst [mol %]	Ligand [mol %]	Ratio **11f**:**10f**[a]
1	$PdCl_2$ (2.5)	PPh_3 (12.5)	1:20
2	$Pd(OAc)_2$ (2.5)	PPh_3 (12.5)	4:1
3	$Pd_2(dba)_3 \cdot CHCl_3$ (1.25)	PPh_3 (3.1)	1:2
4	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.25)	PPh_3 (3.1)	1:1.2
5	$[Pd(PPh_3)_4]$ (2.5)	–	4:1

[a] Ratio was analyzed by ^1H NMR spectroscopy of the crude reaction mixture after one hour of reaction time (for details, see Experimental Section).

With these results in hand, we started to evaluate the substrate scope of this allylation procedure for several other α-hydroxy carbonyl compounds. Application of the conditions found for the allylation of benzoin to enantiomerically pure *S*-ethyl lactate (**10a**) and *S*-methyl mandelate (**10b**) gave the allyl ethers *S*-**11a** and *S*-**11b**, respectively, in enantiomerically pure form. Confirmation of the stereochemical integrity of this allylation protocol was achieved for **10a** by comparison of the $[\alpha]_D$ values with data from the literature.[44] Allyl ether **11b** had previously only been described in racemic form, which made it necessary to determine the enantiomeric excess of *S*-**11b** using HPLC on a chiral stationary phase. After comparison with racemic **11b**, the ee was determined to be $>98\%$, indicating that no racemization occurred. Examples **11c**, **d**, **e** illustrate that the rapid assembly of substrates for ring closing metathesis reactions is possible using the Pd-catalyzed allylation reaction. Precursors **10c**[45] and **10e**[46] have been prepared in one step by addition of allyl- or allenylmetal compounds to ethyl glyoxalate. Ester **10d** is available in one step from dimethyl malate *via* a highly diastereoselective enolate allylation, using a method described by Seebach et al.[47] The ratio of diastereomers observed for **10d** is not altered during the *O*-allylation. The relative configuration assigned to **11d** was confirmed by conversion of this diene to oxepine **12** using a ring closing metathesis reaction catalyzed by $[RuCl_2(PCy_3)_2{=}CHPh]$.[48] Indicative for the *cis*-configuration of both ester substituents is a small value for the coupling constant $^3J_{H\text{-}2,H\text{-}3}$ of 3.6 Hz (Scheme 4).

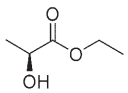
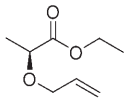
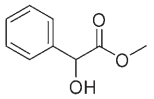
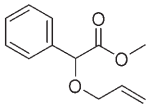
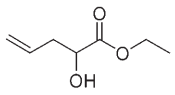
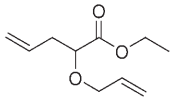
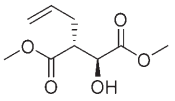
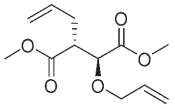
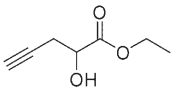
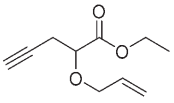
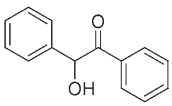
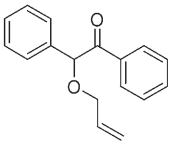
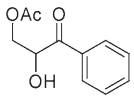
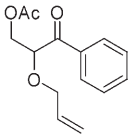
Compounds **11f** and **11g** are examples for the allylation of aromatic α-hydroxy ketones. Ketone **10g** was obtained from cinnamyl acetate together with the regioisomeric by-product using Plietker's ketohydroxylation protocol.[49] Removal of the by-product was not possible at this stage, but was achieved after allylation by careful column chromatography. This might explain why **11g** was obtained in only mediocre yield. Neither **10f** nor **10g** undergo any C–C bond cleavage or other undesired side reactions during the allylation process, which is, as discussed in the introduction, a serious problem if the silver oxide-allyl bromide method is applied to these substrates. The results obtained for the allylation of α-hydroxy carbonyl compounds are summarized in Table 2.

With these results in hand, we evaluated the Pd-catalyzed allylation of other substrates that have caused problems with established allylation protocols. Results are summarized in Table 3.



Scheme 4. RCM of diene **11d** to oxepine **13**.

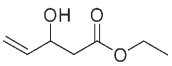
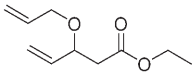
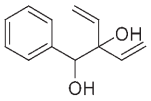
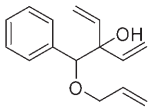
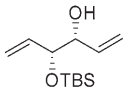
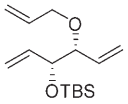
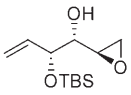
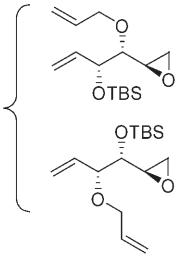
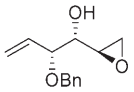
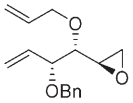
Table 2. Pd-catalyzed allylation of α-hydroxy carbonyl compounds.[a]

α-Hydroxy carbonyl compound		Allylation product		Yield
	**10a**		**11a**	86%
	**10b**		**11b**	83%
	**10c**		**11c**	84%
	**10d**		**11d**	99%
	**10e**		**11e**	89%
	**10f**		**11f**	88%
	**10g**		**11g**	52%

[a] *Conditions:* **9a** (2.0 equivs.), THF, $Pd(PPh_3)_4$ (2.5 mol %), 65 °C.

Compound **10h**, for instance, undergoes a retro-aldol reaction upon attempted deprotonation of the OH group with NaH. On the other hand, no conversion is observed with the silver oxide/allyl bromide method. Under the conditions described here, allyl ether **11h** is obtained in good yield. The same observations as for **10h** have also been made for diol **10i**: decomposition occurs under basic conditions, whereas silver oxide/allyl bromide has no effect at all. Using Pd-catalysis, selective mono-allylation to **11i** was observed in excellent yield. Triene **11j** was required for a parallel study dealing with selectivity aspects of RCM reactions. We suspected that conversion of **10j** into the sodium alkoxide under strongly basic conditions might lead to inter- or intramolecular scrambling of the silyl group, an effect that has previously been observed by us in other cases.[50] Under the conditions described here, **11j** was obtained exclusively in good yield. However, allylation of epoxide **10k** (obtained as a single diastereomer from **10j** under the conditions of a Sharpless epoxidation) results in

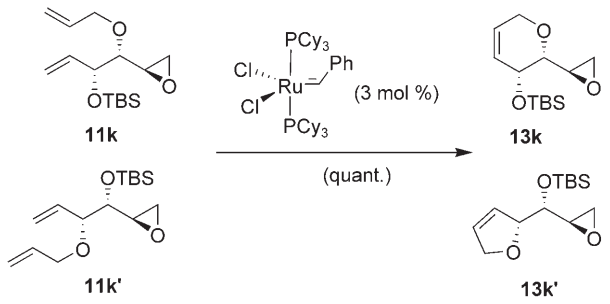
Table 3. Pd-catalyzed allylation of other secondary alcohols.[a]

Secondary alcohol		Allylation product		Yield
	**10h**		**11h**	76%
	**10i**		**11i**	93%
	**10j**		**11j**	74%
	**10k**		**11k** **11k'**	96%
	**10l**		**11l**	49%

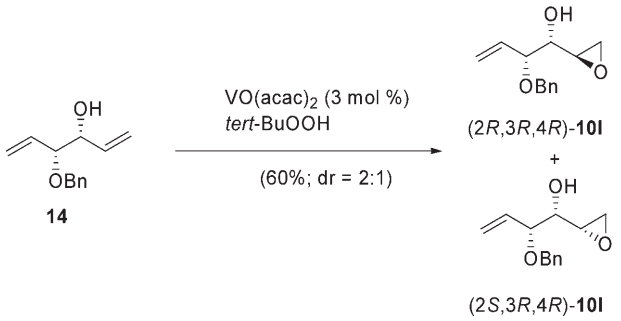
[a] *Conditions:* **9a** (2.0 equivs.), THF, $Pd(PPh_3)_4$ (2.5 mol %), 65 °C.

the formation of two isomers **11k** and **11k′** in a 2:1 ratio. It was not possible to decide on the basis of routine NMR spectra whether **11k** and **11k′** are diastereomers or regioisomers, resulting from a scrambling of the TBS group prior to allylation. To answer this question, the 2:1 mixture of **11k** and **11k′** was subjected to ring closing metathesis. The products were identified as dihydropyran **13k** and dihydrofuran **13k′**, which leads to the assignment of the structures depicted in Table 3 and Scheme 5 to **11k** and **11k′**.

This result suggests that scrambling of the silyl group also occurs during the allylation of **10j**, however, due to the C_2-symmetry of the parent diol this effect is not



Scheme 5. RCM of the mixture of **11k** and **11k′**.



Scheme 6. V-catalyzed epoxidation of **14**.

visible. Pd-catalyzed allylic substitutions involving silyl ethers as pronuclecophiles have precedence in the literature.[51,52] However, such reactions normally involve the presence of nucleophiles such as fluorides or chlorides which induce desilylation, leading to an alkoxide which is the actual nucleophile in the allylation reaction. In the present case, ethoxide liberated from the allyl carbonate might be the nucleophile responsible for desilylation. Alternatively, ethoxide might act as a base which deprotonates the secondary alcohol in **10k** and induces intramolecular transfer of the silyl group. Although it is likely that other silyl ethers show a lower tendency towards migration, we did not investigate this issue further but chose a benzyl ether as OH protecting group. The required precursor **10l** was prepared from the mono-benzyl ether of 1,5-hexadiene-3,4-diol (**14**)[53] using a vanadium-catalyzed epoxidation. Under these conditions, **10l** was obtained as a 2:1 mixture of diastereomers (Scheme 6).

It has previously been reported that **10l** can be obtained from **14** in diastereomerically pure form under Sharpless conditions.[54,55] Submitting **10l** as a 2:1 mixture of diastereomers to the conditions of the Pd-catalyzed allylation gives, as expected, the allyl ether **11l** in good yield and an unaltered ratio of diastereomers.

Conclusion

The results presented in this contribution clearly demonstrate that Pd-catalyzed *O*-allylation has a strong potential beyond the more acidic O-nucleophiles such as carboxylates and phenols. We have applied this reaction successfully to a variety of α-hydroxy carbonyl compounds, which normally require expensive reagents in over-stoichiometric amounts. An extension to some other substrates that are difficult to allylate under established conditions is also described. Application of this method to the solution of synthetic problems associated with the metathesis-based synthesis of oxacycles is currently underway in our laboratory.

Experimental Section

General Remarks

Experiments were conducted in dry reaction vessels under an atmosphere of dry argon. Solvents were purified by standard procedures. ^{1}H NMR spectra were recorded on a Bruker Avance DRX 400, Bruker Avance DRX 500, or Varian Inova 600 in $CDCl_3$ or benzene-d_6. Chemical shifts (δ) are reported in ppm relative to TMS with $CHCl_3$ ($\delta_H = 7.24$ ppm, $\delta_C = 77.0$ ppm) or C_6D_5H ($\delta_H = 7.18$ ppm, $\delta_C = 128.0$ ppm) as internal standard. Coupling constants (*J*) are given in Hertz. In ^{13}C NMR spectra the number of coupled protons was analyzed by APT or DEPT experiments and is denoted by a number in parentheses following the δ_C value. IR spectra were recorded as films on NaCl or KBr plates. The peak intensities are defined as strong (s), medium (m) or weak (w). Mass spectra were obtained at 70 eV. Optical purities were determined by HPLC using a HP-LC-1050 system equipped with a Daicel Chiralcel OD column. The following compounds were prepared according to procedures described in the literature: **10c**,[45] **10d**,[47] **10e**,[46] **10g**,[49] **10h**,[56] **10i**,[3] **10j**,[57] $Pd_2(dba)_3 \cdot CHCl_3$,[58] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$,[59] and $[Pd(PPh_3)_4]$.[58]

Screening Experiments for Different Pd-Precatalysts

Compound **10f** (0.2 mmol) and carbonate **9a** (0.4 mmol) were dissolved in THF (2.0 mL). The appropriate Pd-precatalyst and the ligand were added, and all samples were simultaneously heated in closed vials in a stainless steel heating block for one hour. After this time, the reactions were quenched by filtration through a short pad of silica, followed by elution with ether. After evaporation of all volatiles, the ratio **11f**:**10f** was determined from the ^{1}H NMR-spectrum by comparison of the integrals of the *ortho* protons of the C(=O)C_6H_5 moiety, which are baseline-separated at 500 MHz. Alternatively, the integral of the singlet observed for the proton C*H*(Oallyl) of **11f** can be compared with the integral of the OH signal of **10f**. In both cases comparable values for the **11f**:**10f** ratio are obtained. GC analysis turned out to be unreliable due to partial decomposition of pure **11f** under GC conditions.

General Procedure for the Pd-Catalyzed Allylation

In a flame-dried Schlenk tube, the alcohol (1 mmol) was dissolved in 5 mL of dry THF. In a second Schlenk tube, a solution of allyl ethyl carbonate (260 mg, 2.0 mmol) and $Pd(PPh_3)_4$ (28.8 mg, 2.5 mol %) in dry THF (5 mL) was prepared and added to the substrate solution *via* a Teflon cannula. The reaction mixture was heated to reflux until TLC indicated complete consumption of the starting material (approximately 3 to 4 hours). The reaction mixture was allowed to cool to ambient temperature and then filtered through a short pad of silica, followed by washing with MTBE. After evaporation of the solvents, the crude product was purified by flash chromatography.

***S*-(−)-*O*-Allyl ethyl lactate (11a):** Obtained from *S*-(−)-ethyl lactate (**10a**) (591 mg, 5 mmol) as a colorless liquid; yield: 681 mg (86%). Spectroscopic data are identical to those reported in the literature.[3] Optical rotation compares well to the value reported in the literature: $[\alpha]_D^{25}$: −77.7° (*c* 2.21, MeOH); ref.[44] $[\alpha]_D^{25}$: −70.7° (*c* 2.68, MeOH).

***S*-(+)-*O*-Allyl methyl mandelate (11b):** Obtained from *S*-(+)-methyl mandelate (**10b**) (415 mg, 2.5 mmol) as a colorless liquid; yield: 430 mg (83%). Spectroscopic data are identical to those reported in the literature.[3] $[\alpha]_D^{25}$: +95.3° (*c* 1.59, MeOH). The enantiomeric excess of **11b** was determined by HPLC analysis (Daicel Chiralcel OD, eluent: heptane/2-propanol, 98:2, flow 0.7 mL/min, 20 °C) to be > 98% after comparison with racemic **11b**.

***Rac*-2-Allyloxypent-4-enoic acid ethyl ester (11c):** Obtained from **10c**[45] (144 mg, 1.0 mmol) as a colorless liquid; yield: 158 mg (84%).

***(2R,3S)*-2-Allyl-3-allyloxysuccinic acid dimethyl ester (11d):** Obtained from **10d**[47] (101 mg, 0.5 mmol) as a colorless liquid; yield: 120 mg (99%).

***Rac*-2-Allyloxypent-4-ynoic acid ethyl ester (11e):** Obtained from **10e**[46] (3.43 g, 24.1 mmol) as a colorless liquid; yield: 3.91 g (89%).

***rac*-Benzoin allyl ether (11f):** Obtained from *rac*-benzoin (**10f**) (424 mg, 2.0 mmol) as a colorless liquid; yield: 444 mg (88%). Spectroscopic data are identical to those reported in the literature.[7]

***rac*-Acetic acid 2-allyloxy-3-oxo-3-phenyl-propyl ester (11g):** Obtained from **10g**[49] (104 mg, 0.5 mmol) as a colorless liquid; yield: 65 mg (52%).

***Rac*-3-Allyloxypent-4-enoic acid ethyl ester (11h):** Obtained from **10h**[56] (72 mg, 0.50 mmol) as a colorless liquid; yield: 70 mg (76%).

3-(Allyloxyphenylmethyl)-penta-1,4-dien-3-ol (11i): Obtained from **10i**[3] (380 mg, 2.0 mmol) as a colorless liquid; yield: 430 mg (93%). Spectroscopic data are identical to those reported in the literature.[3]

(3*R*,4*R*)-3-Allyloxy-4-(*tert*-butyldimethylsilanyloxy)-1,5-hexadiene (11j): Obtained from **10j**[57] (228 mg, 1 mmol) as a colorless liquid; yield: 200 mg (74%).

(2*R*,3*R*,4*R*)-1,2-Epoxy-4-(*tert*-Butyldimethylsilanyloxy)-hex-5-en-3-ol (10k)

The title compound was prepared in analogy to a literature procedure:[60] To a solution of Ti(O-*i*-Pr)$_4$ (2.81 mL, 9.5 mmol) in DCM (45 mL) in a Schlenk tube was added L-(+)-diethyl tartrate (1.89 mL, 11.0 mmol) at −30 °C. After 15 min of stirring, a solution of **10j**[57] (1.80 g, 7.9 mmol) in DCM (5 mL), followed by a solution of *tert*-butyl hydroperoxide in toluene (2.85 M, 14.2 mmol, 5.0 mL) was added. The reaction mixture was then stored in a freezer at −30 °C for 15 days, after which another 10.0 mL of *tert*-butyl hydroperoxide in toluene (2.85 M, 28.4 mmol) were added. After 3 more days at −30 °C, $FeSO_4$ (5.0 g) was dissolved in an aqueous solution of tartaric acid (15 wt %, 47 mL) and added to the reaction mixture. The mixture was allowed to warm to room temperature and filtered through a pad of celite, extracted twice with dichloromethane, and washed with brine. After drying over $MgSO_4$, filtration, evaporation of the solvents and flash chromatography (silica, cyclohexane:MTBE 5:1) **10k** (yield: 1.38 g, 72%) was obtained as a colorless liquid in diastereomerically pure form (NMR), along with unreacted starting material (135 mg, 8%).

Alternatively, to a solution of **10j**[57] (460 mg, 2.0 mmol) in toluene (10 mL) was added vanadyl acetylacetonate (11 mg,

2 mol %) and *tert*-butyl hydroperoxide (0.45 mL, 5.5 M in decane, 2.5 mmol). After heating the mixture to reflux for 3 hours, additional *tert*-butyl hydroperoxide (0.2 mL, 5.5 M in decane, 1.1 mmol) was added and heating was continued for 0.5 hours. After cooling to ambient temperature, 10 mL of water were added, and the mixture was extracted three times with ethyl acetate. The combined organic phases were washed with saturated Na_2CO_3 solution, dried over $MgSO_4$, filtered and the solvents removed under vacuum. After column chromatography, **10k** was obtained as a colorless oil as a 4:1 ratio of diastereomers (NMR); yield: 250 mg (52%).

Attempted Synthesis of [1-(Allyloxyoxiranylmethyl)-allyloxy]-*tert*-butyl(dimethyl)silane (11k)

Following the general procedure, **10k** (489 mg, 2.0 mmol) was converted to an inseparable 2:1 mixture of the title compound **11k** and its isomer **11k′**; combined yield: 547 mg (96%).

Characteristic NMR data for major isomer **11k:** ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 79.5 (1), 74.2 (1), 72.5 (2), 51.0 (1), 44.6 (2).

Characteristic NMR-data for major isomer **11k′**: ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 82.5 (1), 72.3 (1), 69.8 (2), 51.8 (1), 44.0 (2).

Subjecting the mixture to the conditions of ring closing metathesis reaction gives a mixture of dihydropyran 13k and dihydrofuran **13k′**: To a solution of the inseparable mixture of **11k** and **11k′** (284 mg, 1.0 mmol) in CH_2Cl_2 was added $[RuCl_2(PCy_3)_2{=}CHPh]$[48] (25 mg, 3.0 mol %). After complete conversion of the starting materials, the solvent was removed under vacuum to give **13k** and **13k′** as an inseparable mixture which was analyzed by NMR spectroscopy without further purification. Mass of crude product: 260 mg, approximately 100%.

(2*R*,3*R*,4*R*)-1,2-Epoxy-4-(benzyloxy)-hex-5-en-3-ol [(2*R*,3*R*,4*R*)-10 l] and (2*S*,3*R*,4*R*)-1,2-Epoxy-4-(benzyloxy)-hex-5-en-3-ol [(2*S*,3*R*,4*R*)-10l][54]

To a solution of **14**[53] (1021 mg, 5.0 mmol) in toluene (25 mL) was added vanadyl acetylacetonate (53 mg, 4 mol %) and *tert*-butyl hydroperoxide (2.6 mL, 2.85 M in toluene, 7.5 mmol). The mixture was heated to reflux for 2 hours. After cooling to ambient temperature, 10 mL of water were added, and the mixture was extracted three times with ethyl acetate. The combined organic phases were washed with saturated Na_2CO_3 solution, dried over $MgSO_4$, filtered and the solvents removed under vacuum. After column chromatography, **10l** was obtained as a colorless oil in a 2:1 ratio of diastereomers (NMR); yield: 665 mg (60%).

2-(1-Allyloxy-2-benzyloxybut-3-enyl)-oxirane (11l): Obtained from **10l** (694 mg, 3.2 mmol) as a colorless liquid in a 2:1 ratio of diastereoisomers; yield: 402 mg (49%).

(2*S*,3*R*)-2,3,4,7-Tetrahydrooxepine-2,3-dicarboxylic acid Dimethyl Ester (12)

To a solution of **11d** (484 mg, 2.0 mmol) in toluene (100 mL) was added $[RuCl_2(PCy_3)_2{=}CHPh]$ (168 mg, 10 mol %). The mixture was stirred at ambient temperature until the starting material was fully consumed (2.5 h), as indicated by TLC. The reaction mixture was filtered over a short pad of silica and washed with ether. The solvent was evaporated, and the residue was purified by flash chromatography on silica using cyclohexane/MTBE (5:1) as eluent; yield: 353 mg (82%).

Acknowledgements

Generous financial support by the Deutsche Forschungsgemeinschaft and the Chemistry department of the University of Dortmund is gratefully acknowledged. We thank Nina Mészaros and Christa Nettelbeck for excellent technical assistance.

References

[1] G. M. Coppola, H. F. Schuster, α-*Hydroxy acids in enantioselective synthesis*, Wiley-VCH, Weinheim, **1997**.
[2] B. Schmidt, H. Wildemann, *Synlett* **1999**, 1591–1593.
[3] B. Schmidt, H. Wildemann, *J. Org. Chem.* **2000**, *65*, 5817–5822.
[4] B. Schmidt, H. Wildemann, *J. Chem. Soc. Perkin Trans. 1* **2000**, 2916–2925.
[5] B. Schmidt, H. Wildemann, *Eur. J. Org. Chem.* **2000**, 3145–3163.
[6] B. Schmidt, H. Wildemann, *J. Chem. Soc. Perkin Trans. 1* **2002**, 1050–1060.
[7] H. Wildemann, P. Dünkelmann, M. Müller, B. Schmidt, *J. Org. Chem.* **2003**, *68*, 799–804.
[8] B. Schmidt, J. Hermanns, *Top. Organomet. Chem.* **2004**, *13*, 223–267.
[9] S. J. Connon, S. Blechert, *Top. Organomet. Chem.* **2004**, *11*, 93–124.
[10] A. Kirschning, M. Jesberger, K.-U. Schöning, *Synthesis* **2001**, 507–540.
[11] R. Roy, S. K. Das, *Chem. Commun.* **2000**, 519–529.
[12] B. Schmidt, *J. Chem. Soc. Perkin Trans. 1* **1999**, 2627–2637.
[13] B. Schmidt, *Org. Lett.* **2000**, *2*, 791–794.
[14] B. Schmidt, T. Sattelkau, *Tetrahedron* **1997**, *53*, 12991–13000.
[15] B.-C. Hong, Z.-Y. Chen, A. Nagarajan, K. Rudresha, V. Chavan, W.-H. Chen, Y.-F. Jiang, S.-C. Zhang, G.-H. Lee, S. Sarshar, *Tetrahedron Lett.* **2005**, *46*, 1281–1285.
[16] I. Izzo, P. Del Gaudio, C. Della Monica, M. Squitieri, F. De Riccardis, *Heterocycles* **2003**, *60*, 2057–2063.
[17] S. Aragonès, F. Bravo, Y. Díaz, M. I. Matheu, S. Castillón, *Tetrahedron: Asymmetry* **2003**, *14*, 1847–1856.
[18] J. A. Marco, M. Carda, S. Rodríguez, E. Castillo, M. N. Kneeteman, *Tetrahedron* **2003**, *59*, 4085–4101.
[19] M. Carda, S. Rodríguez, F. González, E. Castillo, A. Villanueva, J. A. Marco, *Eur. J. Org. Chem.* **2002**, 2649–2655.
[20] J. Roos, F. Effenberger, *Tetrahedron: Asymmetry* **1999**, *10*, 2817–2828.
[21] J. Christoffers, U. Rößler, *J. Prakt. Chem.* **2000**, **342**, 654–658.

[22] H. G. Aurich, F. Biesemeier, M. Boutahar, *Chem. Ber.* **1991**, *124*, 2329–2334.
[23] M. Lautens, J.-F. Paquin, S. Piguel, *J. Org. Chem.* **2002**, *67*, 3972–3974.
[24] A. S. Demir, Ö. Sesenoglu, E. Eren, B. Hosrik, M. Pohl, E. Janzen, D. Kolter, R. Feldmann, P. Dünkelmann, M. Müller, *Adv. Synth. Catal.* **2002**, *344*, 96–103.
[25] K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4442–4489.
[26] D. R. Deardorff, D. C. Myles, K. D. MacFerrin, *Tetrahedron Lett.* **1985**, *26*, 5615–5618.
[27] B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1998**, *120*, 815–816.
[28] M. Massacret, P. Lhoste, R. Lakhmiri, T. Parella, D. Sinou, *Eur. J. Org. Chem.* **1999**, 2665–2673.
[29] B. Nay, J.-F. Peyrat, J. Vercauteren, *Eur. J. Org. Chem.* **1999**, 2231–2234.
[30] E. Keinan, M. Sahai, Z. Roth, *J. Org. Chem.* **1985**, *50*, 3558–3566.
[31] B. M. Trost, E. J. McEachern, F. D. Toste, *J. Am. Chem. Soc.* **1998**, *120*, 12702–12703.
[32] H. Kim, C. Lee, *Org. Lett.* **2002**, *4*, 4369–4371.
[33] F. Guibé, Y. Saint M'leux, *Tetrahedron Lett.* **1981**, *22*, 3591–3594.
[34] F. Guibé, *Tetrahedron* **1997**, *53*, 13509–13556.
[35] F. Guibé, *Tetrahedron* **1998**, *54*, 2967–3042.
[36] J. Tsuji, *Palladium reagents and catalysts*, Wiley, Chichester, **1995**, p. 335.
[37] R. Lakhmiri, P. Lhoste, D. Sinou, *Tetrahedron Lett.* **1989**, *30*, 4669–4672.
[38] F. L. Zumpe, U. Kazmaier, *Synthesis* **1999**, 1785–1791.
[39] C. Morin, L. Ogier, *J. Carbohydr. Chem.* **2000**, *19*, 111–118.
[40] A. R. Haight, E. J. Stoner, M. J. Peterson, V. K. Grover, *J. Org. Chem.* **2003**, *68*, 8092–8096.
[41] F. P. Marmsäter, J. A. Vanecko, F. G. West, *Tetrahedron* **2002**, *58*, 2027–2040.
[42] T. Honda, H. Namiki, M. Watanabe, H. Mizutani, *Tetrahedron Lett.* **2004**, *45*, 5211–5213.
[43] A. Qureshi, D. H. Solomon, D. P. Kelly, *Eur. Polymer Journal* **1995**, *31*, 809–818.
[44] G. Broggini, G. Molteni, T. Pilati, *Tetrahedron: Asymmetry* **2000**, *11*, 1975–1983.
[45] F. P. J. T. Rutjes, M. Kooistra, H. Hiemstra, H. E. Schoemaker, *Synlett* **1998**, 192–194.
[46] F. Bohlmann, P. Herbst, H. Gleinig, *Chem. Ber.* **1961**, *94*, 948–957.
[47] D. Seebach, J. Aebi, D. Wasmuth, *Org. Synth. Coll. Vol.* VII, 153–159, **1990**.
[48] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100–110.
[49] B. Plietker, *J. Org. Chem.* **2004**, *69*, 8287–8296.
[50] B. Schmidt, M. Pohler, B. Costisella, *Tetrahedron* **2002**, *58*, 7951–7958.
[51] S. A. Stanton, S. W. Felman, C. S. Parkhurst, S. A. Godleski, *J. Am. Chem. Soc.* **1983**, *105*, 1964–1969.
[52] T. Suzuki, O. Sato, M. Hirama, Y. Yamamoto, M. Murata, T. Yasumoto, N. Harada, *Tetrahedron Lett.* **1991**, *32*, 4505–4508.
[53] K. J. Quinn, A. K. Isaacs, R. A. Arvary, *Org. Lett.* **2004**, *6*, 4143–4145.
[54] U. Küfner, R. R. Schmidt, *Liebigs Ann. Chem.* **1986**, 1600–1609.
[55] S. Takano, Y. Iwabuchi, K. Ogasawara, *J. Am. Chem. Soc.* **1991**, *113*, 2786–2787.
[56] M. T. Crimmins, B. W. King, P. S. Watson, L. E. Guise, *Tetrahedron* **1997**, *53*, 8963–8974.
[57] K. J. Quinn, A. K. Isaacs, B. A. DeChristopher, S. C. Szklarz, R. A. Arvary, *Org. Lett.* **2005**, *7*, 1243–1245.
[58] M. Schlosser, *Organometallics in Synthesis – A Manual*, Wiley, Chichester, **2002**.
[59] S. Komiya, *Synthesis of Organometallic compounds – a practical guide*, Wiley, Chichester, **1997**.
[60] V. S. Martin, in: *Asymmetric oxidation reactions*, (Ed.: T. Katsuki), Oxford University Press, Oxford, **2001**, pp. 50–69.

