Synthesis of Enantiopure Homoallylic Alcohols by a Highly Selective Asymmetric Allylation of Ketones

Lutz F. Tietze,* Kai Schiemann, Christoph Wegner, and Christian Wulff

Dedicated to Professor Klaus Kühlein on the occasion of his 60th birthday

Abstract: A highly selective asymmetric domino allylation of aliphatic ketones is described. When methyl ketones **1a–g**, the chiral trimethylsilyl ether **2**, and allylsilane **3** react in the presence of catalytic amounts of trifluoromethanesulfonic acid, the homoallylic ethers **4a–g** are produced with up to 24:1 diastereoselectivity and 89% yield. Cleavage of the obtained tertiary homoallylic ethers **4** using lithium or sodium in liquid ammonia gives the homoallylic alcohols **5** in 75 to 95% yield and up to 92% *ee*. Even ethyl methyl ketone **1a**, the most difficult example, showed a stereoselectivity of 9:1 at −78 °C and 24:1 at −109 °C. In addition, the allylation of protected hydroxyalkyl methyl ketones **7a–j** was investigated to give the corresponding homoallylic ethers **8a–j** with a diastereoselectivity of up to >24:1 and 98% yield. In contrast, ethyl alkyl ketones **1h–j** have a low selectivity.

Keywords: allylation · allyl alcohols · allylsilanes · asymmetric synthesis · domino reactions · ketones

Introduction

The allylation of a carbonyl moiety is an important transformation in organic chemistry,[1] since the resulting homoallylic alcohols are valuable intermediates in the synthesis of natural products and other complex structures. For the asymmetric allylation of aliphatic aldehydes, several highly selective methods have been developed that use allylsilanes in the presence of a chiral auxiliary, equimolar amounts of chiral allylboronic[2] and allyltitanic[3] reagents, or chiral acetals.[4] Recently also catalytic methods have been published.[5] However, the stereoselective allylation of aliphatic ketones was not possible until recently when we published a new procedure that gives good asymmetric induction even for the most difficult ketone, namely ethyl methyl ketone.[6] Thus, reaction of ethyl methyl ketone (**1a**), the chiral trimethylsilyl ether **2** derived from norpseudoephedrine, and allylsilane **3** in the presence of a catalytic amount of trifluoromethanesulfonic acid (TfOH) gives the homoallylic ether **4a** in high yield and a 9:1 diastereoselectivity. The transformation is performed in a domino-type process[7] by mixing all four components together. The tertiary homoallylic alcohols **5a** can easily be obtained from the ethers **4a** by treatment with sodium in liquid ammonia.

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In this paper we describe the details of the reaction with unfunctionalized and protected hydroxy ketones as well as the optimization of the reaction conditions.

Results and Discussion

Allylation of aliphatic, unfunctionalized ketones: Simple aliphatic methyl ketones were allylated by treatment of a mixture of two equivalents of the ketones **1a–g** with one equivalent of the trimethylsilyl ether of (1*R*,2*R*)-*N*-trifluoroacetylnorpseudoephedrine (**2**) and two equivalents of allylsilane **3** (Scheme 1) in the presence of a catalytic amount of trifluoromethanesulfonic acid (TfOH, 0.15 equiv) in dichloromethane at −78 °C for one to five hours (Table 1). Usually, the conversion is complete within one hour after addition of the catalyst and a longer reaction time does normally not improve the yield. The reaction is very clean and the formation of by-products is not observed. Thus, the ketones **1a–f** gave the homoallylic ethers **4a–f** with 59 to 87% isolated yield (87–91% yield based on conversion) and a good diastereoselectivity of 7.5:1 to 24:1. The reaction was quenched by addition of aqueous triethylamine and the products purified by column chromatography on silica gel. Increasing steric hindrance in the substrate, as in *tert*-butyl methyl ketone (**1g**), causes a significant decrease of the reaction rate; however, based on conversion the yield of the obtained ether **4g** is 88%. A similar observation was made for the reactions of ketones having longer alkyl side chains on both sides. Thus, only methyl ketones can be allylated at a reasonable rate; ethyl propyl ketone (**1h**) and hexyl propyl

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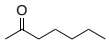
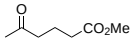
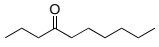
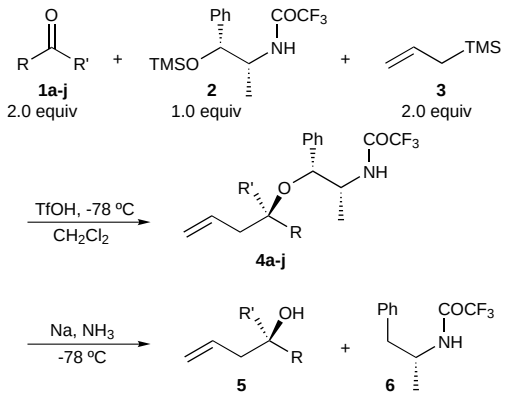
Table 1. Synthesis of homoallylic ethers **4a–j** from ketones **1a–j**.

1	R	4: Yield [%][a]	d.r.[b]	5: Yield [%]
a		87 (91)	9:1	76
b		63 (91)	10:1	92
c		73 (89)	10:1	–
d		79 (88)	7.5:1	–
e		58 (91)	7.5:1	–
f		59 (87)	24:1	85
g		22 (88)	10:1	–
h		21 (99)	1.5:1	–
i		22 (99)	1.4:1	–
j		< 1	–	–

[a] The yields are based on **2**. The yields in parentheses are based on conversion of **2**. [b] Diastereomeric ratio determined by ^{13}C NMR spectroscopy.

ketone (**1i**) gave only about 20% yield, and ethyl isopropyl ketone (**1j**) did not react at all. From this data it can be assumed that the substrate and the amino alcohol derivative form a pocket into which only a methyl group fits well but not an ethyl group. Therefore, not unexpectedly, the stereoselectivity in the reaction of **1h** and **1i** is rather low. The cleavage of the obtained ethers **4** to give the homoallylic alcohols **5** was performed by reductive removal of the benzyl moiety using 2.5 equiv of sodium or, even better, lithium in liquid ammonia at $-78\,^{\circ}C$. In addition to the alcohols **5** the amphetamine **6** was obtained, which could be removed by column chromatography. Reaction of **4a** under these conditions afforded **5a** in 76% isolated yield; **4b** and **4f** were transformed into the alcohols **5b** and **5f** in over 85% yield. The conversion was always quantitative, but the isolation of the alcohols **5** sometimes caused some problems due to their volatility. It should be kept in mind that the functionalized benzyl group in the tertiary homoallylic ethers **4** is a stable and useful protecting group. Thus, many transformations of the ethers **4** as the primary products, such as ozonolysis of the double bond to give an aldehyde moiety, can be performed before taking off the protecting group.

The absolute configuration of the obtained homoallylic ethers was determined by X-ray crystallographic analysis, performed for **4b** and **4f**. From this data it can be deduced that the allylation of the ketones **1** using the (*R*,*R*)-norpseudoephedrine derivative **2** occurs from the *Re* face; consequently, the enantiomeric homoallylic alcohols *ent*-**5** are obtained using the (*S*,*S*)-norpseudoephedrine derivative *ent*-**2** (Scheme 1).



Scheme 1. Allylation of aliphatic ketones **1**.

Allylation of functionalized ketones: For the use of the new procedure in the synthesis of natural products it was necessary to demonstrate that also functionalized ketones can be employed. As already shown, nonconjugated double bonds as in **1c** or ester moieties as in **1e** do not interfere with the reaction (Table 1). In addition, we have studied the transformation of hydroxyalkyl ketones (Table 2). First, the stability and usefulness of different protecting groups R for 4-hydroxy-2-butanone **7** were investigated, since free hydroxy ketones cannot be used in the allylation process. The

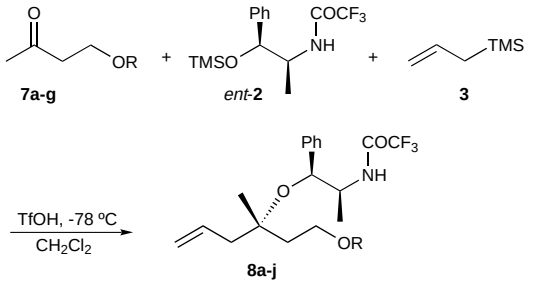
Table 2. Allylation of protected hydroxyalkyl ketones **7a–j**.

7	R	8: Yield [%][a]	d.r.[b]
a	Ac	43	9:1
b	COO*t*Bu	25	10:1
c	Bz	30	10:1
d	3,5-NO_2-Bz	< 1	–
e	4-MeO–Bz	31	10:1
f	Et	64	6:1
g	4-MeO–Ph	45	10:1
h	Allyl	63	9:1
i	ThDMS	< 1	–
j	TBDPS	98	> 24:1

[a] The yields are based on **2**. [b] Determined by ^{13}C NMR spectroscopy.

Abstract in German: *Eine hochselektive asymmetrische domino-Allylierung von aliphatischen Ketonen wird beschrieben. Durch Reaktion der Methylketone **1a–g** mit dem chiralen Trimethylsilylether **2** und dem Allylsilan **3** in Gegenwart katalytischer Mengen Trifluormethansulfonsäure werden die Homoallylether **4a–g** mit einer Diastereoselektivität von bis zu 24:1 und Ausbeuten von 87–91% erhalten. Die Spaltung der entstandenen tertiären Homoallylether **4** mit Natrium oder Lithium in flüssigem Ammoniak ergibt die Homoallylalkohole **5** in 75–95% Ausbeute und bis zu 92% ee. Selbst Ethylmethylketon (**1a**) als das schwierigste Substrat zeigt eine Stereoselektivitääät von 9:1 bei $-78\,^{\circ}C$ und 24:1 bei $-109\,^{\circ}C$. Weiterhin wurde die Allylierung der geschützten Hydroxyalkylmethylketone **7a–j** untersucht, welche die entsprechenden Homoallylether **8a–j** mit Diastereoselektivitäten von bis zu >24:1 und bis zu 98% Ausbeute ergeben. Im Gegensatz dazu reagieren die Ethylalkylketone **1h–j** mit geringen Selektivitäten und Ausbeuten.*

application of the acylated substrates **7a–e** led to insufficient results with only low yields but good selectivity of the desired allylated products **8a–e** (Scheme 2). When β-alkoxy ketones such as β-ethoxy methyl ketone (**7f**) were employed the yields improved; however, the cleavage of an ethyl ether is rather difficult. Results similar to those for **7f** were obtained with **7h,** containing an allyl protecting group which can easily be removed by isomerisation with transition metal complexes like $[Rh(PPh)_3Cl]$ and hydrolysis of the vinyl ether thus formed. With the *p*-methoxyphenyl group again low yields of **8g** were obtained due to the acidic reaction conditions; in addition, the product is highly sensitive to oxygen. By far the best results, not only with regard to the yields but also the selectivity, were obtained with the *tert*-butyl diphenylsilyl protecting group. Thus, reaction of **7j** with **2** and **3** in the presence of TfOH gave the homoallylic ether **8j** nearly exclusively in 98% yield; only one diastereomer could be detected. Desilylation of **8j** was possible under mild conditions and with quantitative conversion by using TBAF in tetrahydrofuran (Scheme 2).



Scheme 2. Allylation of protected hydroxyalkyl ketones **7**.

Influence of the reaction conditions on the selectivity and the yields: For optimisation of the reaction conditions, the effect of the reaction time, temperature, catalyst, solvent, and additives was examined. The influence of the reaction time was checked with a mixture of one equivalents of **2**, two equivalents of the ketone **1a**, two equivalents of allylsilane **3** in dichloromethane and 0.2 equivalents of TfOH at $-78\,^{\circ}C$. After different time intervals the reaction was quenched by addition of triethylamine and the yields were determined (Figure 1). It could be seen that after 30 min the yield reached 70% and that after 1 h the conversion was complete (81%).

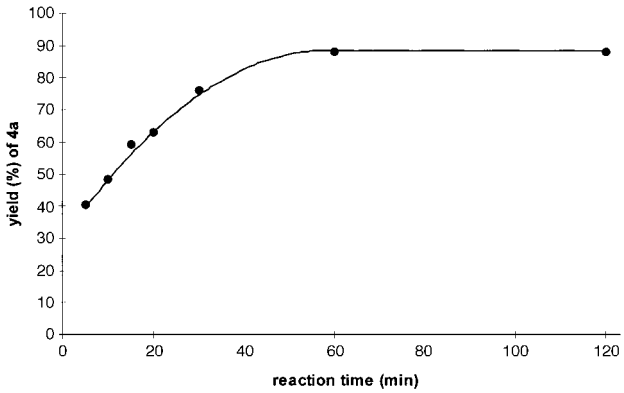


Figure 1. Allylation of **1a** with variation of the reaction time.

In the allylation of aldehydes with the described method TMSOTf was the most efficient catalyst; in contrast, TMSOTf is not suitable for the allylation of ketones. Thus, only 25% yield was obtained under these reaction conditions with ethyl methyl ketone (**1a**). Good results, however, are usually obtained with a 1:1 mixture of TMS-triflate and TfOH, but pure triflic acid gives the same results. Using other Brønsted acids such as sulfuric acid, oleum, trifluoroacetic acid, acetic acid, or perchloric acid no conversion was observed.

The necessary amount of the catalyst was determined by addition of varying quantities of TfOH to a mixture of one equivalent of **2**, two equivalents of ketone **1a** and two equivalents of allylsilane **3** dissolved in dichloromethane at $-78\,^{\circ}C$. After one hour the conversion was quenched with triethylamine and the yields were determined (Figure 2). In the presence of less than 10 mol% of the catalyst the conversion was rather slow but with more than 10 mol% the reaction rates were sufficient.

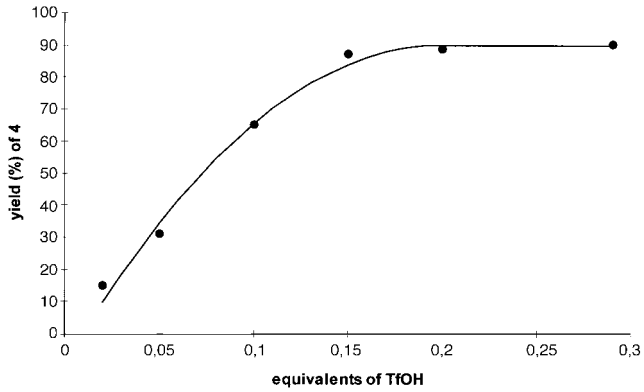


Figure 2. Allylation of **1a** with variation of the amount of TfOH.

Another interesting parameter of the described transformations is the influence of the temperature on the selectivity (Figure 3). Under the standard conditions, one equivalent of **2**, two equivalents of ketone **1a**, and two equivalents of

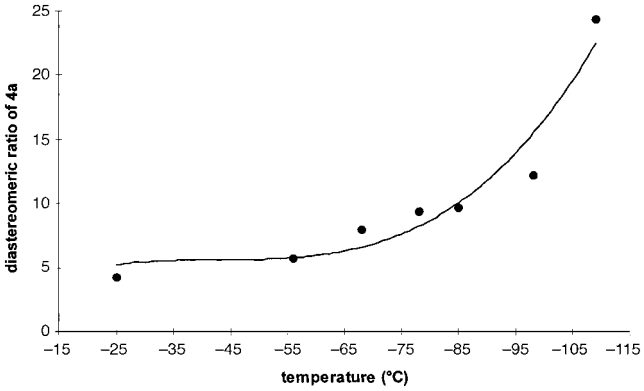


Figure 3. Allylation of **1a** with variation of the reaction temperature.

allylsilane **3** with 10 mol% of TfOH as catalyst for 1 h, a diastereoselectivity of only 4.2:1 was observed at $-25\,^{\circ}C$ whereas an excellent selectivity of 24:1 was found at $-109\,^{\circ}C$. Due to the low reaction rate at the latter temperature the

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yields of the homoallylic ether **4a** dropped to only 44%, but by using longer reaction times the yields can be improved. Since pure dichloromethane solidifies at −98 °C the reactions were performed in a 1:1 mixture of freon 1,1 and dichloromethane.

In addition to the temperature also the nature of the solvent has a great influence on the diastereoselectivity (Table 3).

Table 3. Allylation of **1a** in different solvents.

Solvent	**4a**: Yield [%][a]	d.r.[b]
CH_2Cl_2	91	9.0:1
$CHCl_3$	90	6.5:1
freon 1,1	95	8.4:1
CH_2Cl_2/freon 1,1	97	9.9:1
toluene	90	5.3:1
THF	20	8.3:1

[a] The yields are based on **2**. [b] Determined by ^{13}C NMR spectroscopy.

Again under the standard conditions described in the previous paragraph, the reaction was performed in different solvents. Chloroform was as suitable as dichloromethane giving 90% of the homoallylic ether **4a**; however, due to the relatively high melting point of chloroform (−63 °C) the reaction had to be performed at −60 °C with a consequent decrease of the diastereoselectivity to 6.5:1. In pure freon 1,1 at −78 °C the homoallylic ether **4a** was obtained with 95% yield and in a 8.4:1 ratio, whereas in a one-to-one mixture of dichloromethane and freon 1,1 a nearly quantitative conversion to give **4a** in a 10:1 ratio was observed. Nonpolar solvents like toluene could also be used with good yields (>90%), but the selectivity was disappointingly low at 5:1. In contrast, in polar solvents like tetrahydrofuran a good selectivity was observed, but the yields were unacceptable with only 20% after a reaction time of two days.

One clear disadvantage of the described allylation is the requirement for two equivalents of the ketone **1** in relation to the chiral trimethylsilyl ether **2**. To investigate the influence of the amount of ketone we varied the number of equivalents of **1a** stepwise from 0.7 to 3.0 in the standard system (Figure 4). The optimum of conversion with nearly 90% yield was observed using two equivalents of **1a**. Using more than two equivalents the yields stayed constant whereas the yield dropped to 30% employing only one equivalent of **1a**.

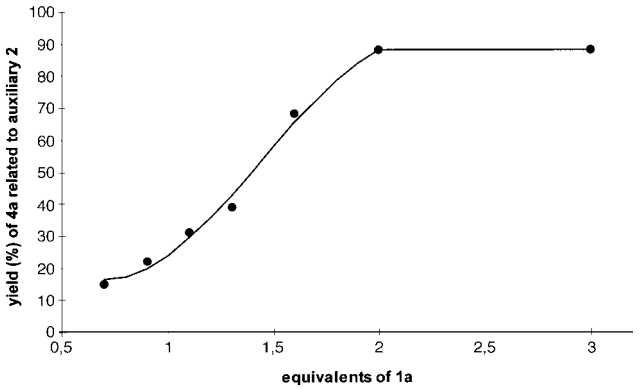


Figure 4. Allylation of **1a** with variation of the amount of **1a**.

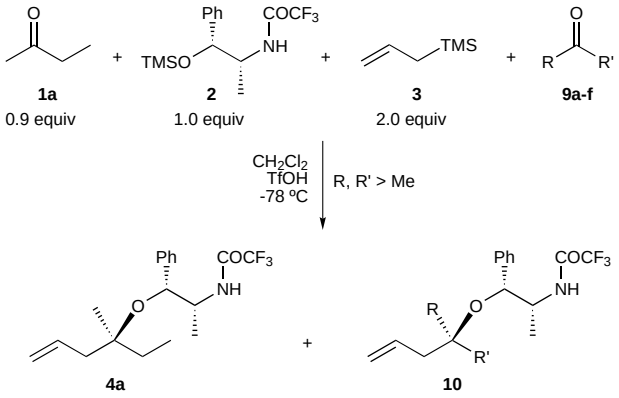
The problem of using a twofold excess of the ketone being clearly unacceptable for ketones which are expensive or difficult to synthesize can be overcome by adding sterically hindered ketones. As already shown, these ketones react very slowly or not at all to give the corresponding homoallylic ethers (Table 1). However, very bulky ketones were not useful, but diethyl ketone (**9a**), ethyl propyl ketone (**9b**), ethyl isopropyl ketone (**9c**), propyl hexyl ketone (**9d**), propyl octyl ketone (**9e**) and diisopropyl ketone (**9f**) were suitable additives (Table 4). The best results were obtained with the

Table 4. Allylation of **1a** in the presence of ketones **9**.[a]

9	R	R′	equiv	*ent*-**4a**: Yield [%][b]	**10**: Yield [%][c]
a	ethyl	ethyl	1.0	33	7
b	ethyl	propyl	1.0	46	8
			2.0	60	13
			5.0	69	25
c	ethyl	isopropyl	1.0	48	–
			2.0	76	1
			5.0	88	2
d	propyl	hexyl	2.0	58	12
e	propyl	octyl	2.0	52	2
f	isopropyl	isopropyl	1.0	28	–
			5.0	65	–
			17	99	–

[a] Reaction conditions: 0.9 equiv of **1a**, 1.0 equiv of **2**, 2.0 equiv of **3**. [b] The yields are based on **1a**. [c] The yields are based on **2**.

ketones **9c** and **9f** containing at least one isopropyl group (Scheme 3). With the other ketones considerable amounts of the allylated products **10** were formed. Thus, in the presence of 5 equiv of **9c**, the allylation of 0.9 equiv of **1a**, 1.0 equiv of



Scheme 3. Allylation of **1a** in the presence of bulky ketones **9**.

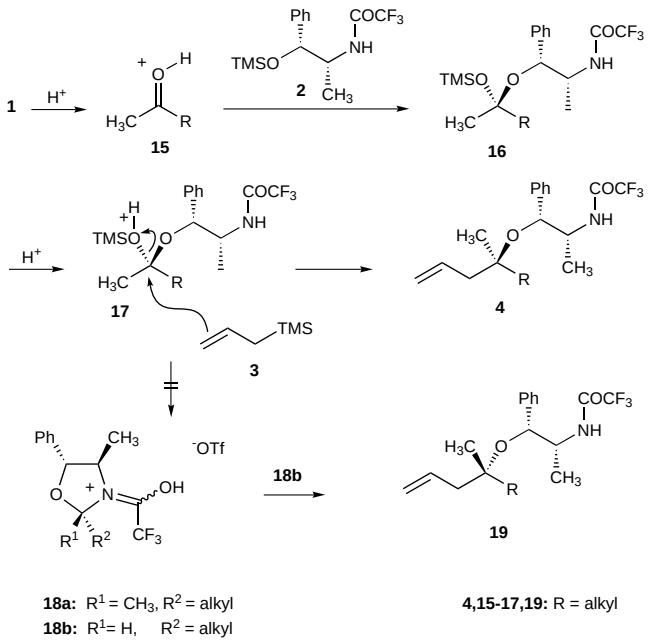
ent-**2**, and 2.0 equiv of **3** furnished the homoallylic ether *ent*-**4a** in 88% yield with only traces of the allylated **9c**; when 17 equiv of the additive **9f** were used, a quantitative conversion to give *ent*-**4a** was observed. In contrast, without the additive *ent*-**4a** was formed in only 24% yield, if 0.9 equiv of **1a** are used. In all transformation the diastereoselectivity was as high as for the reactions without any additive (9:1).

Structure elucidation of the homoallylic ethers and homoallylic alcohols: The constitution of the obtained homoallylic

ethers **4** and homoallylic alcohols **5** could easily be determined by ^{1}H NMR spectroscopy as discussed for the examples **4a** and **5a**. The hydrogens at the vinyl group of **4a** resonate at $\delta = 5.04 - 5.17$ and $\delta = 5.73 - 5.95$ as multiplets, for the methyl group at the newly formed stereogenic centre a singlet at $\delta =$ 1.00 is observed, and the norpseudoephedrine moiety gives signals at $\delta = 4.57$ as a doublet with $J = 4.0$ Hz and at $\delta =$ $4.00 - 4.14$ as a multiplet. The signals for the phenyl group are found at $\delta = 7.20 - 7.37$ and the signal for the NH group at $\delta =$ 6.48 as a broad doublet with $J = 7.5$ Hz. The two diastereotopic protons 3-H resonate at $\delta = 2.27 - 2.38$ as a multiplet. In the ^{1}H NMR spectrum of the corresponding homoallylic alcohol **5a** the signals for the ephedrine moiety are missing and the hydrogen of the newly formed hydroxyl group resonates at $\delta = 1.60$ as a broad singlet.

As expected, the absolute configuration of the newly formed stereogenic centers in the homoallylic ethers **4** could not be determined by NMR spectroscopy. For this purpose an X-ray crystallographic analysis was performed for the homoallylic ethers **4b** and **4f**.

Mechanistic considerations for the allylation of ketones: The excellent diastereoselectivity in the allylation of aliphatic ketones by the described procedure is surprising since all other published methods which gave excellent results in the allylation of aldehydes failed for ketones. In considering the mechanism it should be emphasized that the allylation of ketones and the allylation of aldehydes lead to opposite absolute configurations of the newly formed stereogenic center; therefore, it was assumed that the hydrogen of the aldehydes corresponds to the methyl group of the alkyl methyl ketones.[9] Thus, different reaction mechanisms must be considered for the two transformations. In the first step we assume the formation of an oxenium ion **15** by reaction of **1** under proton catalysis with TfOH (Scheme 4), which on reaction with the trimethylsilyl ether **2** gives the mixed acetal **16**.[10] An allylation of the protonated mixed acetal **17** by the allylsilane **3** in a S_N2 type fashion might then give the homoallylic ethers **4** directly. The formation of an oxazolidinium ion **18a** as assumed in the reaction of aldehydes (**18b**) seems to be less likely due to the steric hindrance of the ketones; thus, oxazolidines were not observed as by-products in the transformations of ketones. The assumption of a direct attack of **3** on the protonated mixed acetal **17** would explain the opposite facial selectivity in the reaction of aldehydes and ketones since for aldehydes an inversion should take place by opening of the intermediate *N*,*O*-acetal **18b** to give **19**, as observed. However, there are many open questions, and so far we are neither able to explain the astounding high selectivity in the formation of **4** nor the influence of the N–$COCF_3$ group in **2** which is necessary for the reaction.



Scheme 4. Proposed mechanism of the allylation of ketones **1**.

Conclusion

The described facially selective allylation of aliphatic methyl ketones using norpseudoephedrine (**2**) and allylsilane **3** is a highly powerful method for the synthesis of enantiopure homoallylic ethers and alcohols. For nearly all examined ketones a diastereoselectivity of at least 9:1 was found; this is a distinct enhancement compared with all other allylation methods. In addition, protected hydroxyalkyl ketones could also be employed with a diastereoselectivity up to >24:1 and 98% yield. Optimization of the reaction conditions allowed the reduction of the reaction time and the amount of the employed ketone as well as an increase in selectivity. Thus, transformation of ethyl methyl ketone gave the corresponding homoallylic ether in a 24:1 ratio at $-109\,^\circ$C. The differentiation of a methyl and an ethyl group makes this method one of the strongest known asymmetric principles, shaping this procedure into a new, very useful instrument in the toolbox of the synthetic chemist.

Experimental Section

General aspects: All reactions were performed in oven-dried glassware in an atmosphere of nitrogen unless otherwise noted. Melting points were determined on a Mettler FP61 and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 digital polarimeter in a 1-dm cell. IR spectra were recorded on a Bruker IFS 25 FT-IR instrument, and ^{1}H NMR and ^{13}C NMR spectra with a Bruker AM-300 and a Varian VXR-200. Chemical shifts were reported on the δ scale relative to $CDCl_3$ as an internal standard. Mass spectra were measured at 70 eV with a Varian MAT 311A. GC analysis was carried out with hydrogen as carrier gas on a DB 1701 column (J&W Scientific, 0.25 mm × 50 m). HPLC analysis was carried out on Nucleosil 5C18 (250 mm, 5 μm). TLC chromatography was performed on precoated silica gel SIL G/UV_{254} plates (Macherey Nagel), and silica gel 32–63 (0.032–0.064 mm) (Macherey Nagel) was used for column chromatography. Microanalyses were carried out by the Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Göttingen.

General procedure 1: Preparation of homoallylic ethers 4a–d, f–i, *ent*-4e, and 8a–c, e–k, i from 1, 2 or *ent*-2, and 3: A 1:1 mixture of TfOH (0.1 mmol) and TMSOTf (0.1 mmol) or pure TfOH (0.2 mmol) was added at $-78\,^\circ$C with stirring to a solution of a ketone **1a–j** (2.00 mmol) or **7a–j** (2.00 mmol), (*R*,*R*)- and (*S*,*S*)-2-trifluoroacetylamino-1-trimethylsiloxy-1-phenylpropane (**2** and *ent*-**2**, 319 mg, 1.00 mmol), respectively, and allyl-

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trimethylsilane (**3**, 228 mg, 2.00 mmol) in CH_2Cl_2 (4 mL), and stirring was continued at −78 °C. After quenching the reaction by addition of triethylamine (160 μL) the mixture was poured into water (10 mL), the organic phase separated and the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by column chromatography on silica gel with *tert*-butyl methyl ether/petroleum ether (20/1) gave the appropriate homoallylic ethers **4a–j** and **8a–j**, respectively.

(4*S*,1′*R*,2′*R*)-4-Methyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-hex-1-ene (**4a**): Reaction of ketone **1a** (144 mg, 180 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 1 h gave the homoallylic ether **4a** (282 mg, 0.82 mmol, 82 %) as colorless needles; 32 mg of **2** were recovered (0.10 mmol, 10 %). M.p. 67 °C; $[\alpha]_D^{20} = +11.0°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.81$ (t, $J = 7.0$ Hz, 3H), 1.00 (s, 3H), 1.21 (d, $J = 7.0$, 3H), 1.41 (q, $J = 7.0$ Hz, 2H), 2.27–2.38 (m, 2H), 4.07 (m, 1H), 4.57 (d, $J = 4.0$ Hz, 1H), 5.04–5.17 (m, 2H), 5.73–5.95 (m, 1H), 6.48 (br d, $J = 7.5$ Hz, 1H), 7.20–7.37 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.47$, 17.15, 23.09, 32.23, 43.25, 52.12, 74.37, 79.32, 116.02 (q, $^1J_{CF} = 285$ Hz), 117.91, 126.73, 127.81, 128.32, 134.44, 141.82, 156.51 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3308$ cm^{-1}, 3110, 3088, 3032, 2978, 2938, 2884, 1726, 1704, 1566, 1208, 1186, 1164, 1082, 912, 762, 726, 702; MS (70 eV, EI): *m*/*z* (%) = 302 (1), 230 (100), 107 (35), 97 (16), 69 (3); $C_{18}H_{24}F_3NO_2$ (343.4): calcd C 62.96, H 7.04; found C 63.10, H 7.08.

(4*S*,1′*R*,2′*R*)-4-Methyl-5-phenyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-hex-1-ene (**4b**): Reaction of ketone **1b** (293 mg, 290 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 48 h gave the homoallylic ether **4b** (264 mg, 0.63 mmol, 63 %) as colorless needles; 99 mg of **2** were recovered (0.31 mmol, 31 %). M.p. 100 °C; $[\alpha]_D^{20} = +31.0°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.08$ (s, 3H), 1.21 (d, $J = 7.0$, 3H), 1.70 (t, $J = 7.0$ Hz, 2H), 2.41 (d, $J = 7.5$ Hz, 2H), 2.51 (m, 2H), 4.12 (m, 1H), 4.63 (d, $J = 4.0$ Hz, 1H), 5.14 (d, $J = 12$ Hz, 1H), 5.16 (d, $J = 17$ Hz, 1H), 5.62–5.97 (m, 1H), 6.35 (br d, $J = 7.5$ Hz, 1H), 6.93 (d, $J = 6.0$ Hz, 2H), 7.07–7.43 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.66$, 23.70, 30.11, 41.58, 43.55, 51.72, 74.24, 78.68, 115.81, 115.83 (q, $^1J_{CF} = 285$ Hz), 118.21, 126.71, 127.94, 128.09, 128.32, 133.89, 141.13, 142.31, 156.38 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3428$ cm^{-1}, 3294, 3084, 3028, 2980, 2968, 1724, 1704, 1566, 1206, 1188, 1164, 912, 752, 722, 702; MS (70 eV, EI): *m*/*z* (%) = 378 (1), 279 (9), 230 (100), 173 (45), 131 (26), 117 (27), 107 (18), 91 (44); $C_{24}H_{28}F_3NO_2$ (419.5): calcd C 68.72, H 6.73; found C 68.68, H 6.73.

(4*S*,1′*R*,2′*R*)-4-Methyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-oct-1,7-diene (**4c**): Reaction of ketone **1c** (196 mg, 230 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 48 h gave the homoallylic ether **4c** (270 mg, 0.73 mmol, 73 %) as colorless needles; 57 mg of **2** were recovered (0.18 mmol, 18 %). M.p. 62 °C; $[\alpha]_D^{20} = +22.7°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.02$ (s, 3H), 1.22 (d, $J = 7.0$, 3H), 1.41–1.67 (m, 2H), 1.86–2.20 (m, 2H), 2.33 (d, $J = 7.0$ Hz, 2H), 4.09 (m, 1H), 4.59 (d, $J = 4.0$ Hz, 1H), 4.80–4.93 (m, 2H), 5.04–5.18 (m, 2H), 5.54–5.94 (m, 2H), 6.41 (br d, $J = 7.5$ Hz, 1H), 7.19–7.38 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.86$, 23.54, 28.15, 38.63, 43.46, 51.79, 74.29, 78.68, 114.08, 115.82 (q, $^1J_{CF} = 285$ Hz), 118.00, 126.61, 127.70, 128.19, 134.03, 141.20, 156.41 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3310$ cm^{-1}, 3108, 3080, 3030, 2980, 2940, 2920, 1722, 1702, 1564, 1208, 1184, 1168, 912, 758, 722, 704; MS (70 eV, EI): *m*/*z* (%) = 328 (1), 230 (100), 123 (51), 117 (32), 107 (30), 91 (7), 81 (30), 55 (7), 41 (9); $C_{20}H_{26}F_3NO_2$ (369.4): calcd C 65.02, H 7.09; found C 64.86, H 7.03.

(4*S*,1′*R*,2′*R*)-4-Methyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-non-1-ene (**4d**): Reaction of ketone **1d** (228 mg, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 48 h gave the homoallylic ether **4d** (304 mg, 0.79 mmol, 79 %) as colorless needles; 35 mg of **2** were recovered (0.11 mmol, 11 %). M.p. 67 °C; $[\alpha]_D^{20} = +17.7°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.82$ (t, $J = 7.0$ Hz, 3H), 1.00 (s, 3H), 1.00–1.60 (m, 8H), 1.22 (d, $J = 7.0$, 3H), 2.31 (d, $J = 7.0$ Hz, 2H), 4.06 (m, 1H), 4.55 (d, $J = 4.0$ Hz, 1H), 5.10 (dd, $J = 9.0$, 1.0 Hz, 2H), 5.61–5.94 (m, 1H), 6.46 (br d, $J = 7.5$ Hz, 1H), 7.18–7.41 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 13.96$, 17.06, 22.53, 23.46, 23.66, 32.21, 39.49, 43.46, 51.96, 74.30, 79.01, 115.81 (q, $^1J_{CF} = 285$ Hz), 117.81, 126.60, 127.74, 128.21, 134.32, 141.47, 156.39 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3318$ cm^{-1}, 3104, 3082, 3028, 2966, 2936, 2874, 1722, 1702, 1564, 1210, 1182, 1166, 1058, 914, 758, 724, 704; MS (70 eV, EI): *m*/*z* (%) = 344 (1), 279 (9), 230 (75), 179 (32), 139 (100), 117 (27), 107 (33), 83 (27), 69 (18), 55 (25), 41 (12); $C_{21}H_{30}F_3NO_2$ (385.5): calcd C 65.43, H 7.84; found C 65.40, H 7.94.

(5*R*,1′*S*,2′*S*)-Methyl-5-methyl-5-(2′-trifluoroacetamido-1′-phenylpropoxy)-oct-7-enoate (***ent*-4e**): Reaction of ketone **1e** (288 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 48 h gave the homoallylic ether *ent*-**4e** (241 mg, 0.58 mmol, 58 %) as colorless oil; 115 mg of **2** were recovered (0.36 mmol, 36 %). $[\alpha]_D^{20} = -12.5°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.94$ (s, 3H), 1.12 (d, $J = 7.0$, 3H), 1.20–1.67 (m, 4H), 2.05 (t, $J = 7.0$ Hz, 2H), 2.23 (d, $J = 7.0$ Hz, 2H), 3.57 (s, 3H), 4.01 (m, 1H), 4.50 (d, $J = 4.0$ Hz, 1H), 5.03 (dd, $J = 13$, 2.0 Hz, 2H), 5.58–5.85 (m, 1H), 6.46 (br d, $J = 7.5$ Hz, 1H), 7.18–7.41 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.86$, 19.12, 23.56, 33.97, 38.63, 43.37, 51.42, 51.76, 74.43, 78.62, 115.77 (q, $^1J_{CF} = 285$ Hz), 118.10, 126.59, 127.73, 128.16, 133.94, 141.25, 156.35 (q, $^2J_{CF} = 35$ Hz), 173.90; IR (film): $\tilde{\nu} = 3320$ cm^{-1}, 3078, 3028, 2976, 2952, 1720, 1552, 1304, 1210, 1182, 1166, 1056, 916, 758, 726, 704; MS (70 eV, EI): *m*/*z* (%) = 374 (1), 230 (100), 169 (58), 137 (23), 117 (25), 107 (10), 95 (18), 91 (18); $C_{21}H_{28}F_3NO_4$ (415.5): calcd C 60.71, H 6.79; found C 60.93, H 6.91.

(4*S*,1′*R*,2′*R*)-4,5-Dimethyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-hex-1-ene (**4f**): Reaction of ketone **1f** (176 mg, 220 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 48 h gave the homoallylic ether **4f** (190 mg, 0.53 mmol, 53 %) as colorless needles; 125 mg of **2** were recovered (0.39 mmol, 39 %). M.p. 113 °C; $[\alpha]_D^{20} = -4.5°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.82$ (s, 3H), 0.86 (d, $J = 7.0$ Hz, 3H), 0.96 (d, $J = 7.0$ Hz, 3H), 1.19 (d, $J = 7.0$ Hz, 3H), 1.79 (quint, $J = 7.0$, 1H), 2.31–2.49 (m, 2H), 4.09 (m, 1H), 4.60 (d, $J = 4.0$ Hz, 1H), 5.08–5.21 (m, 2H), 5.72–5.97 (m, 1H), 6.39 (br d, $J = 7.5$ Hz, 1H), 7.19–7.41 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.57$, 17.16, 17.28, 21.31, 35.08, 40.62, 51.76, 74.09, 80.85, 115.75 (q, $^1J_{CF} = 285$ Hz), 117.86, 126.77, 127.74, 128.20, 134.09, 141.31, 156.42 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3312$ cm^{-1}, 3106, 3066, 3028, 2942, 1720, 1704, 1564, 1208, 1184, 1164, 1070, 912, 762, 722, 702; MS (70 eV, EI): *m*/*z* (%) = 230 (100), 117 (42), 111 (35), 107 (15), 91 (9), 69 (24), 55 (13), 41 (7); $C_{19}H_{26}F_3NO_2$ (357.4): calcd C 63.85, H 7.33; found C 63.74, H 7.28.

(4*S*,1′*R*,2′*R*)-4,5,5-Trimethyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-hex-1-ene (**4g**): Reaction of ketone **1g** (201 mg, 250 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 72 h gave the homoallylic ether **4g** (82 mg, 0.22 mmol, 22 %) as colorless needles; 240 mg of **2** were recovered (0.75 mmol, 75 %). M.p. 156 °C; $[\alpha]_D^{20} = -4.7°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.85$ (s, 3H), 0.99 (s, 9H), 1.20 (d, $J = 7.0$ Hz, 3H), 2.51 (d, $J = 7.5$ Hz, 2H), 4.10 (m, 1H), 4.73 (d, $J = 4.0$ Hz, 1H), 5.05–5.20 (m, 2H), 5.82–6.07 (m, 1H), 6.37 (br d, $J = 7.5$ Hz, 1H), 7.19–7.49 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.66$, 19.03, 26.10, 38.89, 40.79, 51.81, 74.82, 82.78, 115.80 (q, $^1J_{CF} = 285$ Hz), 117.28, 126.77, 127.72, 128.21, 136.25, 141.51, 156.44 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3432$ cm^{-1}, 3114, 3066, 3028, 2976, 2962, 2926, 1726, 1704, 1568, 1210, 1186, 1164, 1048, 916, 760, 726, 702; MS (70 eV, EI): *m*/*z* (%) = 330 (1), 230 (100), 125 (21), 117 (44), 115 (12), 111 (4), 107 (10), 91 (14), 69 (26), 55 (12), 43 (18), 41 (23); $C_{20}H_{28}F_3NO_2$ (371.5): calcd C 64.67, H 7.60; found C 64.76, H 7.55.

(4*S*,1′*R*,2′*R*)-4-Ethyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-hept-1-ene (**4h**): Reaction of ketone **1h** (200 mg, 246 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 2 h gave the homoallylic ether **4h** (78 mg, 0.21 mmol, 21 %) as colorless needles. M.p. 97 °C; $[\alpha]_D^{20} = +17.7°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.65–0.90$ (m, 6H), 1.14 (d, $J = 7.0$ Hz, 3H), 1.19–1.63 (m, 6H), 2.22 (ddd, $J = 7.0$, 2.0, 1.0 Hz, 2H), 4.12 (ddq, $J = 7.0$, 6.5, 5.0 Hz, 1H), 4.62 (d, $J = 5.0$ Hz, 1H), 4.94–5.14 (m, 2H), 5.60–5.91 (m, 1H), 6.32 (br d, $J = 6.5$ Hz, 1H), 7.15–7.23 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 9.56$, 15.81, 17.21, 18.09, 30.16, 39.48, 42.03, 52.72, 74.84, 82.88, 117.20 (q, $^1J_{CF} = 288$ Hz), 118.85, 128.54, 129.21, 129.49, 135.70, 142.01, 157.82 (q, $^2J_{CF} = 36$ Hz); IR (KBr): $\tilde{\nu} = 3312$ cm^{-1}, 3108, 3078, 3030, 2964, 2940, 2876, 1726, 1704, 1564, 1210, 1184, 1168, 1072, 914, 758, 702; MS (70 eV, CI(NH_3)): *m*/*z* (%) = 389 (100); $C_{20}H_{28}F_3NO_2$ (371.5): calcd C 64.67, H 7.60; found C 64.47, H 7.73.

(4*S*,1′*R*,2′*R*)-4-Propyl-4-(2′-trifluoroacetamido-1′-phenylpropoxy)-dec-1-ene (**4i**): Reaction of ketone **1i** (312 mg, 379 μL, 2.00 mmol) with **2** (319 mg, 1.00 mmol) according to general procedure 1 for 2 h gave the homoallylic ether **4i** (93 mg, 0.22 mmol, 22 %) as colorless needles. M.p. 56 °C; $[\alpha]_D^{20} = +15.2°$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.78$ (t, $J = 7.5$ Hz, 3H), 0.87 (t, $J = 6.5$ Hz, 3H), 0.98–1.69 (m, 14H), 1.16 (d, $J = 7.0$ Hz, 3H), 2.25 (ddd, $J = 7.0$, 1.0, 1.0 Hz, 2H), 4.14 (ddq, $J = 8.0$, 7.0, 5.0 Hz, 1H), 4.62 (d, $J = 5.0$ Hz, 1H), 4.96–5.16 (m, 2H), 5.64–5.91 (m, 1H), 6.34 (br d, $J = 8.0$ Hz, 1H), 7.20–7.44 (m, 5H); ^{13}C NMR (50 MHz,

$CDCl_3$): $\delta = 14.06, 14.49, 15.99, 16.82, 22.59, 23.57, 29.75, 31.75, 36.44, 38.58, 41.11, 51.41, 73.63, 81.28, 115.90$ (q, $^1J_{CF} = 288$ Hz), 117.57, 127.24, 127.83, 128.21, 134.35, 140.68, 156.52 (q, $^2J_{CF} = 36$ Hz); IR (KBr): $\tilde{\nu} = 3312$ cm^{-1}, 3108, 3078, 3032, 2960, 2934, 2872, 1726, 1704, 1566, 1210, 1184, 1166, 1050, 914, 760, 702; MS (70 eV, CI(NH_3)): *m/z* (%) = 445 (100); $C_{24}H_{36}F_3NO_2$ (427.6): calcd C 67.40, H 8.49; found C 67.46, H 8.38.

General procedure 2: Synthesis of the homoallylic alcohols 5 from 4 by reductive removal of the chiral auxiliary: Condensed ammonia (40 mL) and afterwards solid sodium (2.5 equiv) was added at $-78\,^\circ$C to a solution of the homoallylic ether **4** (0.5 mmol) in THF (1 mL) with vigorous stirring. When the solution turned deep blue, the reaction was quenched by adding methanol (5 mL). The mixture was concentrated, the residue dissolved in Et_2O (20 mL), and the obtained solution washed with brine and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue purified by column chromatography on silica gel with ethyl ether/pentane (1/10) as the eluent to give the homoallylic alcohol **5**.

(3*S*)-3-Methylhex-5-en-3-ol (**5a**): Reaction of **4a** (172 mg, 0.50 mmol) with sodium (29 mg, 1.25 mmol) according to general procedure 2 gave **5a** (49 mg, 0.38 mmol, 76%). $[\alpha]_D^{20} = +8.7^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.0$ Hz, 3H), 1.15 (s, 3H), 1.49 (q, $J = 7.0$ Hz, 2H), 1.60 (br s, 1H), 2.22 (d, $J = 7.0$ Hz, 2H), 5.05–5.20 (m, 2H), 5.77–5.99 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 8.16$, 26.14, 34.23, 45.75, 72.33, 118.50, 134.11; IR (film): $\tilde{\nu} = 3382$ cm^{-1}, 3076, 2932, 2862, 1462, 1378, 1262, 1126, 1056, 1032, 1000, 912, 734; $C_7H_{14}O$ (114.2): calcd C 73.63, H 12.36; found C 73.55, H 12.21.

(3*S*)-3-Methyl-1-phenylhex-5-en-3-ol (**5b**): Reaction of **4b** (210 mg, 0.50 mmol) with sodium (29 mg, 1.25 mmol) according to general procedure 2 gave **5b** (88 mg, 0.46 mmol, 92%). $[\alpha]_D^{20} = -58.0^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.16$ (s, 3H), 1.58 (br s, 1H), 1.55–1.79 (m, 2H), 2.30 (d, $J = 7.0$ Hz, 2H), 2.60–2.82 (m, 2H), 5.07–5.22 (m, 2H), 5.89 (ddd, $J = 16$, 10, 7.0 Hz, 1H), 7.12–7.38 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 26.73$, 30.25, 43.70, 46.43, 72.03, 119.03, 125.65, 128.34, 128.40, 133.77, 142.51; IR (film): $\tilde{\nu} = 3344$ cm^{-1}, 3080, 3066, 3028, 2958, 2928, 2872, 1458, 1380, 1216, 1180, 1116, 1062, 1030, 994, 912, 730, 694; MS (70 eV, EI): *m/z* (%) = 191 (2), 149 (39), 131 (16), 105 (8), 91 (100), 43 (20); $C_7H_{14}O$ (190.3): calcd C 82.06, H 9.53; found C 82.00, H 9.45.

(3*R*)-2,3-Dimethylhex-5-en-3-ol (**5f**): Reaction of **4f** (179 mg, 0.50 mmol) with sodium (29 mg, 1.25 mmol) according to general procedure 2 gave **5f** (54 mg, 0.42 mmol, 85%). $[\alpha]_D^{20} = +14.2^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.90$ (d, $J = 7.0$ Hz, 3H), 0.94 (d, $J = 7.0$ Hz, 3H), 1.08 (s, 3H), 1.40 (br s, 1H), 1.69 (sept, $J = 7.0$ Hz, 1H), 2.23 (d, $J = 7.0$ Hz, 2H), 5.07–5.22 (m, 2H), 5.78–5.99 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.90$, 17.53, 22.83, 36.84, 44.12, 74.25, 118.60, 134.09; IR (film): $\tilde{\nu} = 3380$ cm^{-1}, 3314, 3082, 2976, 2936, 2882, 1448, 1418, 1380, 1276, 1192, 1088, 1052, 912, 882; MS (70 eV, EI): *m/z* (%) = 87 (84), 69 (34), 43 (100); $C_8H_{16}O$ (128.2): calcd C 74.94, H 12.58; found C 75.12, H 12.52.

(3*S*,1′*S*,2′*S*)-1-*O*-Acetyl-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-en-1-ol (**8a**): Reaction of ketone **7a** (260 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 4 h gave the homoallylic ether **8a** (172 mg, 0.43 mmol, 43%) as colorless needles. M.p. 93 °C; $[\alpha]_D^{20} = -17.8^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.02$ (s, 3H), 1.18 (d, $J = 7.0$ Hz, 3H), 1.76 (dd, $J = 7.5$, 7.5 Hz, 1H), 1.79 (dd, $J = 7.5$, 7.5 Hz, 1H), 2.00 (s, 3H), 2.35 (d, $J = 7.5$ Hz, 2H), 4.00–4.25 (m, 3H), 4.61 (d, $J = 4.5$ Hz, 1H), 5.12 (d, $J = 15.5$ Hz, 1H), 5.13 (d, $J = 12.0$ Hz, 1H), 5.82 (ddd, $J = 16$, 12, 7.5 Hz, 1H), 6.41 (br d, $J = 8.0$ Hz, 1H), 7.19–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.54$, 20.98, 23.81, 37.92, 43.83, 51.57, 60.65, 74.33, 77.82, 115.65 (q, $^1J_{CF} = 288$ Hz), 118.64, 126.64, 127.92, 128.36, 133.46, 140.75, 156.46 (q, $^2J_{CF} = 37$ Hz), 171.03; IR (KBr): $\tilde{\nu} = 3412$ cm^{-1}, 3330, 3094, 3034, 2976, 2938, 2926, 1714, 1558, 1454, 1376, 1266, 1212, 1178, 1158, 1046, 916, 758, 724, 702; MS (70 eV, EI): *m/z* (%) = 400 (1), 386 (1), 360 (13), 71 (18), 43 (100); $C_{20}H_{26}F_3NO_4$ (401.4): calcd C 59.84, H 6.53; found C 59.93, H 6.82.

(3*S*,1′*S*,2′*S*)-*O*-Pivaloyl-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-en-1-ol (**8b**): Reaction of ketone **7b** (344 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 4 d gave the homoallylic ether **8b** (111 mg, 0.25 mmol, 25%) as colorless oil. $[\alpha]_D^{20} = -16.8^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.15$ (s, 9H), 1.17 (d, $J = 7.5$ Hz, 3H), 1.43 (s, 3H), 1.62–1.91 (m, 2H), 2.35 (d, $J = 7.5$ Hz, 2H), 3.99–4.25 (m, 3H), 4.62 (d, $J = 3.5$ Hz, 1H), 5.12 (d, $J = 12$ Hz, 1H), 5.13 (d, $J = 16$ Hz, 1H), 5.83 (ddd, $J = 16$, 12, 7.5 Hz, 1H), 6.41 (br d, $J = 8.0$ Hz, 1H), 7.19–7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.44$, 17.29, 27.02, 38.60, 43.91, 46.12, 51.59, 60.59, 75.53, 77.81, 115.77 (q, $^1J_{CF} = 290$ Hz), 118.48, 125.88, 126.68, 127.81, 133.54, 140.77, 156.37 (q, $^2J_{CF} = 37$ Hz); IR (film): $\tilde{\nu} = 3318$ cm^{-1}, 3080, 2978, 2938, 2876, 1724, 1712, 1554, 1456, 1286, 1210, 1166, 1056, 704; MS (70 eV, FD): *m/z* (%) = 402 (2), 303 (4), 230 (100), 197 (83), 107 (61), 95 (95), 57 (45), 41 (17).

(3*S*,1′*S*,2′*S*)-*O*-Benzoyl-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-en-1-ol (**8c**): Reaction of ketone **7c** (384 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 4 d gave the homoallylic ether **8c** (130 mg, 0.28 mmol, 28%) as a colorless oil. $[\alpha]_D^{20} = -20.8^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.08$ (s, 3H), 1.19 (d, $J = 6.5$ Hz, 3H), 1.78–2.08 (m, 2H), 2.41 (d, $J = 7.5$ Hz, 2H), 4.03–4.23 (m, 1H), 4.26–4.54 (m, 2H), 4.65 (d, $J = 4.0$ Hz, 1H), 5.14 (d, $J = 11$ Hz, 1H), 5.16 (d, $J = 16$ Hz, 1H), 5.86 (ddd, $J = 16$, 11, 7.5 Hz, 1H), 6.43 (d, $J = 8.0$ Hz, 1H), 7.44 (dd, $J = 7.5$, 7.5 Hz, 2H), 7.56 (t, $J = 7.5$ Hz, 1H), 8.02 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.54$, 23.96, 38.13, 43.90, 51.59, 61.15, 74.41, 77.89, 115.81 (q, $^1J_{CF} = 288$ Hz), 118.69, 126.66, 127.92, 128.30, 128.35, 129.46, 132.89, 133.46, 140.74, 156.47 (q, $^2J_{CF} = 37$ Hz, C=O), 166.49; IR (film): $\tilde{\nu} = 3318$ cm^{-1}, 3072, 2978, 2936, 1720, 1706, 1552, 1454, 1276, 1208, 1178, 1070, 712; MS (70 eV, FD): *m/z* (%) = 422 (2), 323 (4), 230 (100), 217 (83), 105 (80), 95 (97), 77 (47); $C_{25}H_{28}F_3NO_4$ (463.5): calcd C 64.78, H 6.09; found C 64.88, H 6.26.

(3*S*,1′*S*,2′*S*)-*O*-*p*-Methoxybenzoyl-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-en-1-ol (**8e**): Reaction of ketone **7e** (444 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 4 d gave the homoallylic ether **8e** (155 mg, 0.31 mmol, 31%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.06$ (s, 3H), 1.18 (d, $J = 6.5$ Hz, 3H), 1.77–2.04 (m_c, 2H), 2.39 (d, $J = 7.5$ Hz, 2H), 3.85 (s, 3H), 4.02–4.22 (m, 1H), 4.22–4.50 (m, 2H), 4.65 (d, $J = 4.5$ Hz, 1H), 5.14 (d, $J = 12$ Hz, 1H), 5.16 (d, $J = 16$ Hz, 1H), 5.85 (ddd, $J = 16$, 12, 7.5 Hz, 1H), 6.53 (br d, $J = 8.0$ Hz, 1H), 6.90 (d, $J = 8.5$ Hz, 2H), 7.19–7.43 (m, 5H), 7.94 (d, $J = 8.5$ Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.52$, 23.93, 38.14, 43.87, 51.60, 55.35, 60.82, 74.40, 77.87, 113.53, 115.84 (q, $^1J_{CF} = 288$ Hz), 118.61, 122.57, 126.66, 127.89, 128.32, 131.49, 133.52, 140.81, 156.47 (q, $^2J_{CF} = 37$ Hz), 166.26; $C_{26}H_{30}F_3NO_5$ (493.5): calcd C 63.28, H 6.13; found C 62.75, H 6.27.

(3*S*,1′*S*,2′*S*)-1-Ethoxy-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-ene (**8f**): Reaction of ketone **7f** (232 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 4 d gave the homoallylic ether **8f** (248 mg, 0.64 mmol, 64%) as colorless needles. M.p. 60 °C; $[\alpha]_D^{20} = -15.0^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.03$ (s, 3H), 1.16 (t, $J = 7.0$ Hz, 3H), 1.18 (d, $J = 7.0$ Hz, 3H), 1.74 (td, $J = 7.0$, 4.0 Hz, 2H), 2.32 (d, $J = 7.0$ Hz, 2H), 3.40 (qd, $J = 5.0$, 1.0 Hz, 2H), 3.40–3.58 (m, 2H), 4.01–4.15 (m, 1H), 4.59 (d, $J = 4.0$ Hz, 1H), 5.10 (dd, $J = 10$, 2.0 Hz, 2H), 5.70–5.95 (m, 1H), 6.53 (br d, $J = 7.5$ Hz, 1H), 7.19–7.43 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 15.05$, 16.81, 23.92, 39.04, 44.02, 51.81, 66.11, 66.40, 74.46, 78.10, 115.79 (q, $^1J_{CF} = 286$ Hz), 118.11, 126.63, 127.80, 128.15, 133.87, 141.32, 156.84 (q, $^2J_{CF} = 35$ Hz); IR (KBr): $\tilde{\nu} = 3308$ cm^{-1}, 3110, 3086, 3028, 2976, 2936, 2874, 1722, 1700, 1566, 1382, 1210, 1182, 1168, 1118, 1106, 1054, 916, 760, 724, 704; MS (70 eV, FD): *m/z* (%) = 388 (1), 346 (1), 230 (100), 141 (23), 117 (23), 59 (15), 55 (41); $C_{20}H_{28}F_3NO_3$ (387.5): calcd C 62.00, H 7.28; found C 62.19, H 7.51.

1-*p*-Methoxyphenoxy-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-ene (**8g**): Reaction of ketone **7g** (388 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 3 d gave the homoallylic ether **8g** (210 mg, 0.45 mmol, 45%) as colorless oil. $[\alpha]_D^{20} = -29.3^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.08$ (s, 3H), 1.17 (d, $J = 7.0$ Hz, 3H), 1.78–2.04 (m, 2H), 2.40 (d, $J = 7.0$ Hz, 2H), 3.76 (s, 3H), 3.82–4.06 (m, 2H), 4.04–4.19 (m, 1H), 4.62 (d, $J = 4.5$ Hz, 1H), 5.13 (d, $J = 12$ Hz, 1H), 5.15 (d, $J = 16$ Hz, 1H), 5.87 (ddd, $J = 16$, 12, 7.0 Hz, 1H), 6.41 (br d, $J = 8.0$ Hz, 1H), 6.66–6.87 (m, 4H), 7.19–7.37 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.63$, 23.96, 38.70, 44.10, 51.67, 55.70, 64.53, 74.41, 78.16, 114.59, 115.30, 115.93 (q, $^1J_{CF} = 288$ Hz), 118.46, 126.67, 127.91, 128.33, 133.77, 140.89, 152.83, 153.73, 156.41 (q, $^2J_{CF} = 37$ Hz); IR (film): $\tilde{\nu} = 3316$ cm^{-1}, 3074, 2976, 2938, 1712, 1510, 1456, 1230, 1212, 1180, 1042, 826, 704; MS (70 eV, FD): *m/z* (%) = 465 (38), 352 (52), 230 (100), 124 (57), 107 (49), 95 (27); $C_{25}H_{30}F_3NO_4$ (465.5): calcd C 64.50, H 6.50; found C 65.05, H 6.82; HRMS (M^+): calcd 465.2127; found 465.2126.

(3*S*,1′*S*,2′*S*)-1-Allyloxy-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-ene (**8h**): Reaction of ketone **7h** (256 mg, 2.00 mmol) with *ent*-

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2 (319 mg, 1.00 mmol) according to general procedure 1 for 3 d gave the homoallylic ether **8h** (252 mg, 0.63 mmol, 63 %) as a colorless, air-sensitive oil. $[\alpha]_D^{20} = -14.3^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.03$ (s, 3H), 1.18 (d, $J = 7.0$ Hz, 3H), 1.73 (dd, $J = 7.0$, 7.0 Hz, 1H), 1.75 (dd, $J = 7.0$, 7.0 Hz, 1H), 2.32 (d, $J = 7.5$ Hz, 2H), 3.37–3.56 (m, 2H), 3.88 (d, $J = 6.0$ Hz, 2H), 4.01–4.14 (m, 1H), 4.57 (d, $J = 4.0$ Hz, 1H), 5.05–5.27 (m, 4H), 5.75–5.92 (m, 2H), 6.52 (br d, $J = 8.0$ Hz, 1H), 7.21–7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 17.06$, 24.08, 39.15, 44.18, 51.93, 72.01, 74.53, 78.25, 115.85 (q, $^1J_{CF} = 288$ Hz), 117.09, 118.38, 126.72, 127.96, 128.41, 134.04, 134.83, 141.32, 156.78 (q, $^2J_{CF} = 37$ Hz); IR (film): $\tilde{\nu} = 3312$ cm^{-1}, 3078, 2976, 1708, 1554, 1454, 1210, 1162, 758, 702; MS (70 eV, CI (NH_3)): m/z (%) = 417 (100).

(3*S*,1′*S*,2′*S*)-1-(*tert*-Butyldiphenylsiloxy)-3-methyl-3-(1′-phenyl-2′-trifluoroacetamido-1′-propoxy)-hex-5-ene (**8j**): Reaction of ketone **7j** (653 mg, 2.00 mmol) with *ent*-**2** (319 mg, 1.00 mmol) according to general procedure 1 for 5 h gave the homoallylic ether **8j** (586 mg, 0.98 mmol, 98 %) as a colorless oil. $[\alpha]_D^{20} = -20.6^\circ$ ($c = 1$, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.96$ (s, 3H), 1.01 (s, 9H), 1.12 (d, $J = 7.0$ Hz, 3H), 1.71 (t, $J = 7.0$ Hz, 2H), 2.27 (dd, $J = 7.0$, 7.0 Hz, 2H), 3.58–3.78 (m, 2H), 3.92–4.12 (m, 1H), 4.52 (d, $J = 4.5$ Hz, 1H), 5.03 (d, $J = 18$ Hz, 1H), 5.06 (d, $J = 10$ Hz, 1H), 5.76 (ddd, $J = 18$, 10, 7.0 Hz, 1H), 6.32 (br d, $J = 8.0$ Hz, 1H), 7.11–7.66 (m, 15H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 16.77$, 19.06, 23.83, 26.81, 42.06, 44.10, 51.74, 60.12, 74.19, 78.11, 115.81 (q, $^1J_{CF} = 288$ Hz), 118.06, 126.55, 127.61, 127.69, 127.75, 134.00, 135.52, 141.13, 156.37 (q, $^2J_{CF} = 37$ Hz); IR (film): $\tilde{\nu} = 3428$ cm^{-1}, 3320, 3134, 3072, 3052, 3030, 2958, 2932, 2890, 1720, 1710, 1548, 1428, 1380, 1210, 1168, 1110, 1090, 1028, 916, 756, 740, 728, 704; MS (70 eV, FD): m/z (%) = 540 (1), 500 (1), 269 (38), 239 (20), 230 (17), 199 (100), 141 (3), 117 (13); $C_{34}H_{42}F_3NO_3Si$ (597.8): calcd C 68.31, H 7.08; found C 67.83, H 7.24.

General procedure 3: Preparation of homoallylic ether *ent*-4a from 1, *ent*-2, and 3: TfOH (0.2 mmol) was added at $-78\,^\circ$C with stirring to a solution of ketone **1a** (2.00 mmol), (*S*,*S*)-2-trifluoroacetylamino-1-trimethylsiloxy-1-phenylpropane (*ent*-**2**, 319 mg, 1.00 mmol), allyltrimethylsilane (**3**, 228 mg, 2.00 mmol), and ketones **9** (1–17 equiv) in CH_2Cl_2 (4 mL), and stirring was continued at $-78\,^\circ$C. After the reaction had been quenched by addition of triethylamine (160 μL) the mixture was poured into water (10 mL), the organic phase separated and the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by column chromatography on silica gel with *tert*-butyl methyl ether/petroleum ether (20/1) gave the homoallylic ether **4a**.

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