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Dynamic Processes in the Copper-Catalyzed Substitution of Chiral Allylic Acetates Leading to Loss of Chiral Information

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Abstract: Copper-catalyzed α-substitution of enantiomerically pure secondary allylic esters with Grignard reagents was studied with the aim to find conditions that give racemic products. It was observed that the degree of chiral transfer is strongly dependent on the temperature. The loss of chiral information is consistent with an equilibration of the Cu^{III}(allyl) intermediates prior to product formation. Equilibration of the reaction intermediates is of importance for a possible development of a dynamic kinetic asymmetric transformation (DYKAT) process, in which a chiral catalyst is used to produce an optically active product from a racemic substrate, by means of a dynamic equilibrium of the diastereomeric reaction intermediates.

Keywords: allylic substitution · chirality · copper · dynamic processes · heterogeneous catalysis · racemization

Introduction

Asymmetric catalysis is currently a highly active area in synthetic organic chemistry involving transition metals, enzymes, and organocatalysts.[1] One of the most common approaches involves the use of a transition metal with a chiral ligand for the transformation of a prochiral substrate to an enantiomerically enrichced product. In copper(I) chemistry, this concept has been successfully exemplified in catalytic enantioselective 1,4-additions[2] and γ-substitution of allylic electrophiles.[2b,3,4] However, to the best of our knowledge no examples of dynamic kinetic asymmetric transformation (DYKAT) reactions based on copper catalysis have been reported.[5] We were interested in investigating the possibility to perform this type of asymmetric allylic alkylation, in which a racemic substrate is transformed to an optically active product (Scheme 1).

According to the Curtin–Hammet principle, two criteria must be fulfilled in order to obtain an optically active product from a racemic substrate through interconversion of the stereoisomeric intermediates (Scheme 1):[6]

1) There is a selective formation of product from one of the diastereomeric intermediates ($k_5 \gg k_{5'}$).
2) There is a fast equilibration of the reaction intermediates, to ensure restoration of the intermediate from which the desired product enantiomer is formed.

Since a dynamic equilibration of the allyl intermediates prior to product formation is a requirement for a successful DYKAT, we decided to study this process separately. Hence, the copper-catalyzed substitution of enantiopure **1** with an achiral catalyst was studied. With a full dynamic equilibrium prior to product formation a racemic product will be obtained from enantiopure **1**; in this case, **3** and **4** are enantiomers.[7]

As Cu^{III} intermediates in allylation reactions are short-lived, the rate of reductive elimination needs to be retarded. Previous studies in our group have shown that dialkylcuprate, compared to the relatively more electron-deficient monoalkylcopper species, provides kinetically more stable Cu^{III} intermediates from reaction with an allylic substrate.[8] For this reason a catalytic amount of copper in combination with a fast addition of the Grignard reagent to the reaction mixture was chosen to ensure formation of dialkylcuprate as the predominant catalytic species. To achieve reaction conditions that favor an equilibration of the allyl intermediates prior to product formation, different copper species, solvents, Grignard reagents, and temperatures were examined. It was found that the enantiomeric excess of the product varied with the reaction conditions, the reaction temperature being the most important parameter.

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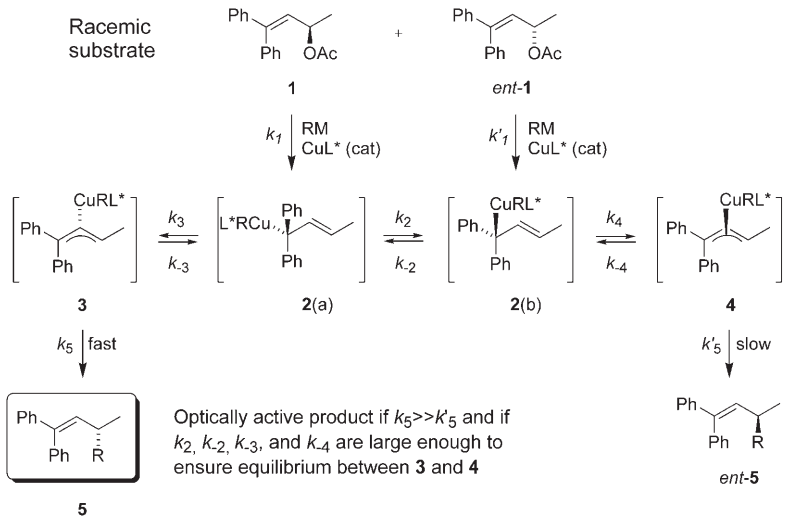
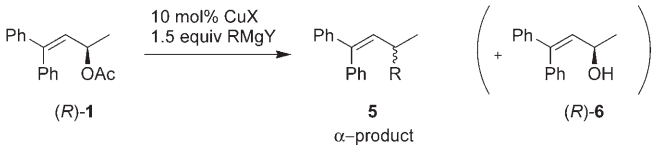


Scheme 1. Principle of copper(I)-catalyzed asymmetric allylic alkylation of a racemic substrate (L* = chiral ligand).

Results and Discussion

The allylic substitution reactions were performed by fast addition of Grignard reagent (within one minute) to a mixture of substrate (*R*)-**1** and a copper salt in the appropriate solvent (Scheme 2). The reaction is highly regioselective and α-



Scheme 2. Products formed in the in the allylation reaction.

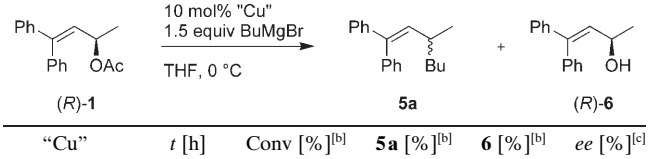
product **5** was the only regioisomer observed. The alcohol (*R*)-**6**, formed by alkyl anion attack at the carbonyl carbon atom, was observed in small amounts in most experiments.

Examination of copper sources: Different copper salts as catalysts were investigated. Copper halides and CuCN gave similar results concerning the conservation of chiral information (Table 1). However, CuCN and CuI appear to provide a less reactive cuprate, since they gave lower yield and more of alcohol **6** (Table 1, entries 2 and 3). Copper chloride was chosen as the catalyst for further studies, since it afforded a high yield of cross-coupling product **5a** in a short reaction time (Table 1, entry 4).

Influence of reaction temperature: The stereochemical outcome of the reaction was studied at different temperatures. It was found that the conservation of chiral information decreased with decreasing reaction temperature (Table 2 and Figure 1).

The linear relationship between temperature and loss of chiral information, as illustrated in Figure 1, is in accordance with a Cu^{III} intermediate in the copper-catalyzed allylic substitution reactions. Since Cu^{III} is a d^8 electron species, four ligands are required in order to form a 16-electron square-planar complex. It is likely that the Cu^{III} intermediate formed from oxidative addition is the 16-electron complex **7 L**(a) (Scheme 3). The ligand **L** may be a solvent molecule or another Lewis base moiety. In order to form product from 16-electron complex **7 L**(a) via π-allyl complex **8**, dissociation of ligand **L** is required. It is likely that the ligand L dissociates to give the σ-allyl transition state in which the copper starts to interact with the alkene π-system. Accordingly, the free energy of activation, $\Delta G^{\neq}$, for the conversion of **7 L**(a) to **8** will have a positive $\Delta S^{\neq}$ due to the loss of the ligand in the transition state. The com-

Table 1. Variation of copper catalyst.[a]



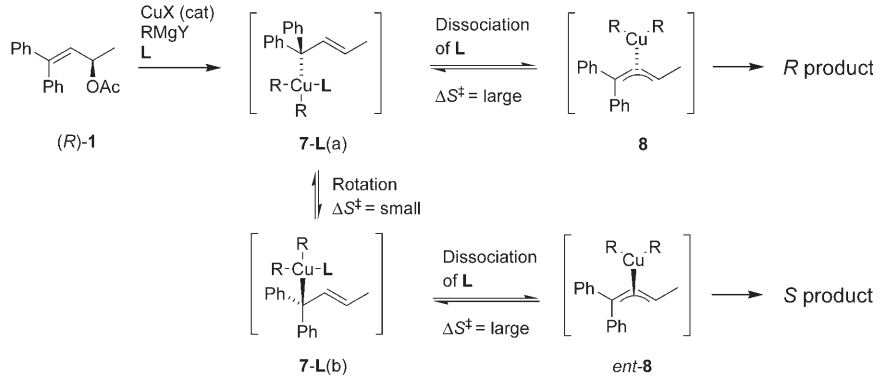
	"Cu"	t [h]	Conv [%][b]	**5a** [%][b]	**6** [%][b]	*ee* [%][c]
1	Li_2CuCl_4	3	90	72 (64)	<5	74
2	CuCN	o.n.[d]	60	42 (36)	22	70
3	CuI	o.n.[d]	>95	55	15	70
4	CuCl	1.75	>95	79 (67)	<5	69
5	$CuBr{\cdot}SMe_2$	3.75	>95	80 (72)	9	67

[a] Reaction conditions: Allylic acetate and "Cu" were mixed in THF. After the mixture was cooled to 0 °C, *n*BuMgBr was added. [b] Determined by ^{1}H NMR spectroscopy by using 2-decanol as internal standard. Yield of isolated product in parentheses. [c] Determined by chiral HPLC. [d] The reaction was run overnight.

Table 2. Effect of temperature.[a]

	T [°C]	t [h]	Conv [%][b]	**5a** [%][b]	**6** [%][b]	*ee* [%][c]
1	22	4	93	74 (62)	12	73
2	0	1.75	>95	79 (67)	<5	69
3	−20	13	>95	93 (70)	7	51
4	−30	12	>95	93 (67)	7	38
5	−40	16	>95	74 (67)	8	29
6	−60	16	47	25 (22)	6	15
7	−78	24	12	3 (2)	4	1

[a] Reaction conditions: Allylic acetate and CuCl (10 mol %) were mixed in THF. After the mixture was cooled to the appropriate temperature, *n*BuMgBr (1.5 equiv) was added within one minute. [b] Determined by ^{1}H NMR spectroscopy by using 2-decanol as internal standard. Yield of isolated product in parentheses. [c] Determined by chiral HPLC.



Scheme 3. Mechanistic explanation for the temperature-dependent loss of chiral information.

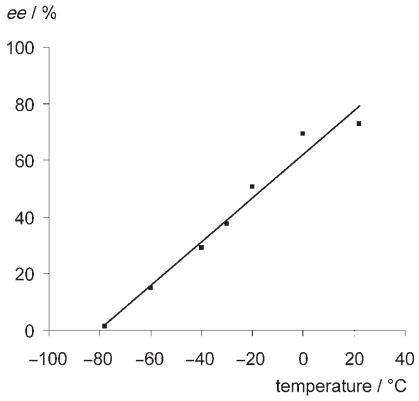


Figure 1. Product *ee* as a function of temperature.

peting transformation of **7 L**(a) to **7 L**(b) on the other hand has a $\Delta S^{\ddagger}$ close to zero, since it only involves a single bond rotation. Consequently, the formation of **8** from **7 L**(a) will be favored over formation of **7 L**(b) at high temperatures, whereas equilibration between rotamers **7 L**(a) and **7 L**(b) is favored over rearrangement to **8** at low temperatures. As a result conservation of chiral information is favored at high temperatures, whereas the degree of racemization will increase with decreased temperature.

To investigate if any other reaction mechanism may be the cause of the formation of racemic product, control experiments without the copper catalyst were performed. No cross-coupling products were formed, demonstrating that the alkylation of (*R*)-**1** is catalyzed by copper. In some of the experiments unreacted substrate (*R*)-**1** and the by-product alcohol **6** were recovered from the product mixture and their enantiomeric purity was analyzed. The *ee* of the recovered materials was identical to that of the starting material, confirming that the loss of chiral information does occur in the copper-mediated alkylation step of the allylic substrate.

Although a racemic product can be obtained at low temperature, the yields under these conditions are too low to be synthetically useful. Different solvents, organocopper reagents, Grignard reagents, additives, and substrates were therefore examined in order to find reaction conditions under which a racemic product could be obtained in synthetically useful yields.

Variation of solvents: A few solvents were tested in the copper-catalyzed allylic substitution of (*R*)-**1**. The best result, in terms of yield and racemic product, was obtained with THF as solvent (Table 3, entry 1). In contrast, Et_2O as solvent gave **5a** with high optical purity (Table 3, entry 2). The latter reaction was rather slow indicating that THF is a better coordinating solvent than Et_2O. Coordination by the solvent would provide a better stabilization of σ-allyl intermediate **7** and thereby facilitate the loss of chiral information. Acetonitrile has good coordinating abilities and thus was tested as the solvent. Unfortunately, this did not increase the loss of chiral information (Table 3, entry 3). Other solvents (CH_2Cl_2 and DMF) and solvent mixtures (THF/DMA, PhMe/THF and DMSO/THF) were tested over a range of reaction temperatures. These experiments were not successful; the reactions were often sluggish, gave low yields (0–74%) and the *ee* of the product was in the range of 24% to 51%.

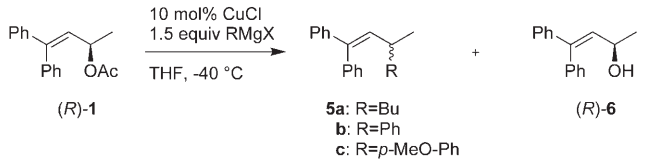
Table 3. Screening of solvents.[a]

	Solvent	*t* [h]	conv [%][b]	**5a** [%][b]	**6** [%][b]	*ee* [%][c]
1	THF	21	≥95	85	15	21
2[d]	Et_2O	18	43	34	9	93
3	CH_3CN	25	54	37	16	51

[a] Reaction conditions: Allylic acetate and CuCl (10 mol%) were mixed in the solvent stated in the Table. After the mixture was cooled to −40 °C, *n*BuMgCl (1.5 equiv) was added. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC. [d] As Grignard reagent *n*BuMgBr was used.

Examination of different Grignard reagents: The use of *n*BuMgCl gave more loss of chiral information than *n*BuMgBr in the copper-catalyzed reaction of (*R*)-**1** to **5** (Table 4, entries 1 and 2). Surprisingly, no loss of chiral information was observed when aryl Grignard reagents were used in place of *n*BuMgBr (Table 4, entries 3 and 4). The very high conservation of chiral information observed when employing aryl Grignard reagents could be due to the greater bulk of the aryl groups on copper. This would disfavor the coordination of a plausible ligand to the copper atom in σ-allyl intermediate **7 L**(a) and increase the rate of formation of **8**. The bulky phenyl groups would also increase the barrier for the single-bond rotation that interconverts rotamers **7 L**(a) and **7 L**(b). Both of these effects would ex-

Table 4. Variation of the Grignard reagents.[a]



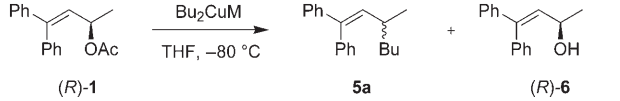
	RMgX	t [h]	Conv [%][b]	**5** [%][b]	**6** [%][b]	*ee* [%][c]
1	*n*BuMgBr	16	≥95	74	8	29
2	*n*BuMgCl	21	≥95	85	15	21
3	PhMgCl	23	57	42	9	≥99.5
4	*p*-MeOPhMgBr	15	44	31 (25)	13	≥99.5

[a] Reaction conditions: Allylic acetate and CuCl were mixed in THF. After the mixture was cooled to −40 °C, Grignard reagent was added. [b] Determined by ^{1}H NMR spectroscopy. 2-Decanol was used as internal standard for entries 1 and 3. Yield of isolated product in parentheses. [c] Determined by chiral HPLC.

plain why there is no loss of chiral information with aryl Grignard reagents.[9]

Stoichiometric amounts of cuprates: Stoichiometric amounts of organocuprate were tested in order to improve the rate of product formation at low temperatures. When one equivalent of $Bu_2CuMgCl$ was used at −80 °C, a low yield of product with 11 % *ee* was obtained (Table 5, entry 1). The use of Bu_2CuLi as nucleophile at −80 °C did produce a nearly racemic product, but the yield was low (Table 5, entry 2).

Table 5. Experiments using stoichiometric Bu_2CuM at low temperature.[a]

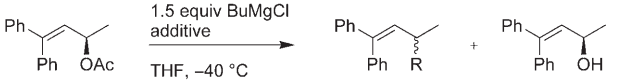


	M	t [h]	Conv [%][b]	**5a** [%][b]	**6** [%][b]	*ee* [%][c]
1	MgCl	84	32	16	16	11
2	Li	84	28	12	15	≤3

[a] Reaction conditions: Allylic acetate was added to a preformed solution of Bu_2CuM in THF. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC.

Effect of different additives: Changing from bromide to chloride in the butylmagnesium halide reagent increased the loss of chiral information (Table 4, entries 1 and 2). As this may be an effect of the halide interacting with the reaction intermediates, the influence of different salt additives was examined. The presence of magnesium bromide increased the conservation of chiral information (Table 6, entry 2), whereas the presence of lithium acetate was found to decrease it (Table 6, entry 3). A decreased reaction temperature (−60 °C) in combination with the presence of one equivalent of LiOAc gave after prolonged reaction time 59 % yield of **5a** with an *ee* of 11 % (Table 6, entry 4). Halide-free conditions were obtained by using copper acetate as catalyst and butylmagnesium acetate as nucleophile (Table 6, entry 5). This gave no significant change with respect to loss of chiral information (19 % *ee*) compared to the use of CuCl as catalyst and BuMgCl as nucleophile (21 % *ee*) (Table 4, entry 2).

Table 6. Effect of different additives.



	Equiv additive	Additive	t [h]	Conv [%][a]	**5a** [%][a]	**6** [%][a]	*ee* [%][b]
1[c]	–	–	10	≥95	83	13	29
2[c]	1.0	$MgBr_2$	23	75	66	10	40
3[c]	1.0	LiOAc	7	83	70	13	20
4[c,d]	1.0	LiOAc	72	74	59	15	11
5[e]	–	–	26	66	66 (48)	n.o.[f]	19
6	1.0	$P(OMe)_3$	22	20	7	13	85
7	0.22	$P(OMe)_3$	21	14	7	7	71
8	0.11	$P(OMe)_3$	16	32	21	10	39
9	0.11	NEt_3	16	72	60	12	22
10	0.11	DMAP	16	73	58	15	14
11	1.0	DMAP	22	76[g]	41[g]	10[g]	16
12	2.5	pyridine	20	33[g]	24[g]	11[g]	29

[a] Determined by ^{1}H NMR spectroscopy. Yield of isolated product in parentheses. [b] Determined by chiral HPLC. [c] *n*BuMgBr was used. [d] −60 °C. [e] Copper acetate was used as catalyst and butylmagnesium acetate as nucleophile. [f] Not observed. [g] 2-Decanol was used as internal standard.

A series of neutrally charged Lewis bases were investigated in order to find an appropriate ligand to stabilize σ-allyl intermediate **7** (see Scheme 3) and thereby perhaps increase the loss of chiral information. The rate of product formation as well as the loss of chiral information decreased when trimethyl phosphite was present in the reaction mixture (Table 6, entries 6–8). Monoalkylcopper reagents are known to be poor nucleophiles compared to dialkylcuprates, and reductive elimination is believed to occur faster from allyl Cu^{III} intermediates obtained from monoalkylcopper reagents compared to those obtained from dialkylcuprates.[8] Consequently, the decreased amount of cross-coupling product and the high conservation of chiral information observed in the presence of $P(OMe)_3$ suggests that the predominant nucleophile in the allylation reaction is $BuCu{\cdot}P(OMe)_3$ and not a dibutylcuprate. As the enantiomeric excess of the product was found to be a function of the amount trimethyl phosphite present in the reaction mixture (Table 6, entries 6–8), we believe that phosphite is reversibly coordinated to copper and that the relative amount of dibutylcuprate is reduced accordingly. Consequently, phosphites are not appropriate ligands for the purpose of obtaining racemic product. On the other hand 4-dimethylaminopyridine (DMAP) gave the opposite effect and the presence of 0.11 equivalents of DMAP, gave product **5a** with 14 % *ee* compared to 29 % *ee* in the absence of additives (Table 6, entry 10 versus entry 1). No further improvement with respect to the loss of chiral information was observed when the amount of DMAP was increased from 0.11 to 1.0 equivalents (Table 6, entry 11). This might be explained by the low solubility of DMAP in THF at −40 °C. Pyridine is more soluble in THF

than DMAP and consequently was tested as an analogue to DMAP. However, neither the yield nor the loss of chiral information was improved in the presence of pyridine compared to when no additive was used and **5a** was obtained in 29% *ee* (Table 6, entry 12).

Variation of leaving group: It is known from previous studies on copper-mediated alkylation of allylic esters that oxidative addition is the rate-determining step.[10] Consequently better leaving groups than acetate were studied in order to improve the product formation at low temperature. Attempts to prepare diethyl phosphate-, diphenylphosphinate-, and trifluoroacetate esters of alcohol **6** were unsuccessful and resulted in complex product mixtures in which elimination product and starting material was observed. Preparation of the corresponding chloride from enantiopure **6** led to a quantitative yield of apparently racemic product.[11] The trichloroacetate ester of **6** was successfully prepared, although this substrate did not give any cross-coupling product in the reaction with BuMgCl as nucleophile. The electron-deficient *p*-CF_3-benzoate ester (*R*)-**9** and perfluorobenzoate ester (*R*)-**10** were prepared from enantiopure alcohol **6**. These esters were more reactive than the original acetate (*R*)-**1**, although the conversion at low temperatures was still too low to give synthetically useful yields (Table 7).

Table 7. Effect of different leaving groups.[a]

(*R*)-**1**: R=Me
(*R*)-**9**: R=*p*-CF_3-Ph
(*R*)-**10**: R=C_6F_5

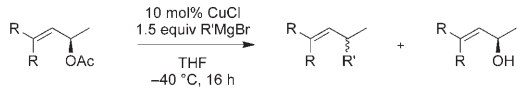
5a (*R*)-**6**

	Substrate	*T* [°C]	*t* [days]	conv [%][b]	**5a** [%][b]	**6** [%][b]	*ee* [%][c]
1[d]	(*R*)-**1**	−70	4	51[e]	34[e]	16[e]	10
2	(*R*)-**9**	−75	3	48	37	11	8
3	(*R*)-**10**	−75	3	45	45	n.o.[f]	6

[a] Reaction conditions: Allylic ester and CuCl were mixed in THF. After the mixture was cooled to the given temperature, *n*BuMgCl was added. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC. [d] 10 mol% of CuCl was used. [e] 2-Decanol was used as internal standard. [f] Not observed.

Variation of the substrate: When various substrates were tested it was found that the electron-deficient substrate (*R*)-**11** rendered the highest loss of chiral information and the electron-rich substrate (*R*)-**12** gave the lowest loss of chiral information (Table 8, entries 1–3). A plausible explanation of this observation is that electron-deficient substituents on the allyl terminus increase the activation energy for cross-coupling from Cu^{III} allyl complexes.[12] Consequently the rate of reductive elimination is decreased and the allyl intermediates have more time to equilibrate, prior to product formation. Substrate (*R*)-**13** was less reactive than substrates (*R*)-**1**, (*R*)-**11**, and (*R*)-**12** and no product was obtained at −40 °C. Allylic substitution of (*R*)-**13** at 0 °C gave 85% of α-product **16** with an *ee* exceeding 97%, (Table 8, entry 4). The α-product **16** was accompanied by a small amount (6%) of γ-product **17**.

Table 8. Effect of different substrates.[a]



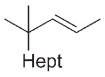
(*R*)-**1**: R=Ph
(*R*)-**11**: R=*p*-F-Ph
(*R*)-**12**: R=*p*-MeO-Ph
(*R*)-**13**: R=Me

5a: R=Ph, R'=Bu
14: R=*p*-F-Ph, R'=Bu
15: R=*p*-MeO-Ph, R'=Bu
16: R=Me, R'=Hept

(*R*)-**6**: R=Ph
18: R=*p*-F-Ph
19: R=*p*-MeO-Ph
20: R=Me

	Substrate	Product	Yield [%][b]	Alcohol [%][b]	Conv [%][b]	*ee* [%][c]
1	(*R*)-**1**	**5a**	74[d] (67)	8	≥95	29
2	(*R*)-**11**	**14**	58[d] (37)	15	≥95	20[e]
3	(*R*)-**12**	**15**	36	≥5	≥95	49
4[f]	(*R*)-**13**	**16**	85[d]	n.o.[g]	n.o.[g]	≥97[e]

[a] Reaction conditions: Unless otherwise noted allylic acetate and CuCl were mixed in THF. After the mixture was cooled to −40 °C, *n*BuMgBr was added within one minute. [b] Yield of isolated product unless otherwise noted. [c] Determined by chiral HPLC. [d] Determined by ^{1}H NMR spectroscopy, using 2-decanol as internal standard, except entry 4 which was determined by GC with decane as internal standard. [e] Determined by derivatization to the corresponding carboxylic acid (2-methylhexanoic acid (entry 2) and 2-methylnonanoic acid (entry 4)) via oxidative cleavage of the double bond using cat. $RuCl_3/NaIO_4$[14] whose enantiomers could be separated by GC. [f] The reaction was performed at 0 °C, using $CuBr{\cdot}SMe_2$ as catalyst and HeptMgBr as nucleophile. [g] Not observed.



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The higher reactivity in combination with the lower chirality transfer observed when using substrates (*R*)-**1**, (*R*)-**11**, and (*R*)-**12** compared to when using substrate (*R*)-**13** strongly indicates that aryl groups on the allyl terminus provide a stabilization of the allyl intermediates. This observation is also in accordance with recent theoretical studies.[12,13]

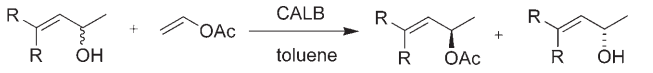
Preparation of starting materials: The alcohols **6** and **18**–**20** were obtained from reaction of the appropriate aldehydes with methylmagnesium chloride in THF. Kinetic resolution of the racemic alcohols by the use of *Candida antarctica* lipase B (CALB) and vinylacetate afforded (*R*)-**1** and (*R*)-**11**–**13** in high overall yields and with high *ee*'s (Table 9). The absolute configuration of the products were assigned according to Kazlauskas' rule.[15]

Aldehydes **21** and **22** were prepared from the corresponding benzophenone according to a literature procedure (Scheme 4).[16] The intermediate iminium salt in the preparation of **22** was resistant to hydrolysis and stirring over night in an aqueous solution of ammonium chloride was necessary to obtain aldehyde **22**.

Conclusion

The conservation of chiral information in the copper-catalyzed S_N2 substitution of γ-disubstituted allylic esters is

Table 9. Kinetic resolution of alcohols **6** and **18–20**.

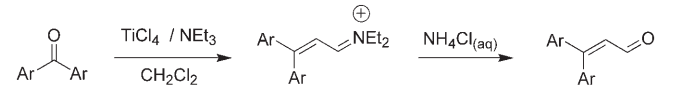


6: R=Ph
18: R=*p*-F-Ph
19: R=*p*-MeO-Ph
20: R=Me

(*R*)-**1**: R=Ph (*S*)-**6**, (*S*)-**18**-**20**
(*R*)-**11**: R=*p*-F-Ph
(*R*)-**12**: R=*p*-MeO-Ph
(*R*)-**13**: R=Me

	Product	*T* [°C]	*t* [h]	Conv [%][a]	CALB [mg mmol^{-1}]	*ee* [%][b]	Yield [%][e]
1	(*R*)-**1**	50	51	43	7.5	≥99.5	45.2
2	(*R*)-**11**	50	40	45	7.5	≥99.5	45.2
3[c]	(*R*)-**12**	RT	32	47	100	98.1	40.5
4[d]	(*R*)-**13**	RT	1.75	32	7.5	≥99.5	16.6

[a] Determined by ^{1}H NMR spectroscopy, except for entry 4, which was determined by GC. [b] Determined by chiral HPLC, except for entry 4, which was determined by chiral GC. [c] A large amount of enzyme and low temperature was used in order to suppress decomposition of starting material and product. [d] Diethyl ether was used as solvent. [e] Yield of isolated product.



Ar = *p*-F-Ph or *p*-MeO-Ph

21: Ar = *p*-F-Ph
22: Ar = *p*-MeO-Ph

Scheme 4. Preparation of aldehydes **21** and **22**.

strongly dependent on the reaction temperature. The temperature effect provides strong support for an equilibration of the transient allyl intermediates, prior to product formation and was rationalized by an entropy effect. This equilibration is a necessary condition for the development of a copper-catalyzed DYKAT process. The present study has established that one enantiomer of the allylic substrate can be transformed into both enantiomers of the product (racemate) by means of such a dynamic equilibrium, showing that a copper-catalyzed dynamic kinetic asymmetric transformation (DYKAT) is possible.

When a series of allylic substrates were examined, it was found that the electron-deficient substrates facilitate loss of chiral information. This observation is in accordance with that an electron-deficient allyl ligand on copper(III) is more reluctant to participate in reductive elimination.[13] Hence, the allyl intermediates will have more time to equilibrate and for this reason a greater loss of chiral information is observed.

It was observed that in the presence of DMAP or LiOAc the loss of chiral information increased, and the best overall result considering both yield and loss of chiral information was obtained at −60 °C in the presence of LiOAc as an additive (59 % yield, 11 % *ee*).

Experimental Section

General remarks: ^{1}H (400 or 300 MHz) and ^{13}C (100 or 75 MHz) NMR spectra were recorded on a Varian Mercury spectrometer. Chemical shifts (δ) are reported in ppm, with residual $CHCl_3$ ($\delta = 7.26$ and 77.16 ppm, respectively) as internal standard. Optical rotations were measured on a Perkins–Elmer 241 Polarimeter. Chiral chromatography analyses were performed by HPLC or GC. For HPLC, Chiralcel OD-H and Chiralcel AD columns (0.46 cm Ø * 25 cm) were used, flow rate 0.5 mL min^{-1}. For GC a CP-Chirasil-Dex CB column (25 m ∅ = 0.32 mm) was used, carrier gas; H_2, flow rate; 1.8 mL min^{-1}. GC program 1: Isothermal at 50 °C for 3 min, then increase 2 °C min^{-1} up to 90 °C, then increase 25 °C min^{-1} up to 200 °C and thereafter isothermal at 200 °C for 5 min. GC program 2: Isothermal at 100 °C for 5 min, then 4 °C min^{-1} up to 200 °C and thereafter isothermal at 200 °C for 5 min. Merck silica gel 60 (240–400 mesh) was used for flash chromatography and analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60-F_{254} plates. All experiments were performed by standard Schlenk techniques under an argon atmosphere. Unless otherwise noted, all materials were obtained from commercial sources and used without further purification. Grignard reagents were purchased from Aldrich or prepared by standard procedures. All Grignard reagents were titrated with 0.100 M $HCl_{(aq)}$, by using bromthymol blue as indicator, prior to use. Diethyl ether and THF were distilled from sodium benzophenone ketyl radical, toluene was distilled from sodium, and dichloromethane was distilled from calcium hydride prior to use. The absolute configurations of products obtained by kinetic resolution were assigned according to Kauzlauskas' rule.[15]

Preparation of aldehydes 21 and 22: Aldehydes **21** and **22** were prepared according to a literature procedure.[16]

3,3-Bis(*p*-methoxyphenyl)-2-propenal (22): A solution of $TiCl_4$ in CH_2Cl_2 (124 mL, 1.0 M) was added to a solution of 4,4′-dimethoxybenzophenone (7.5 g, 31 mmol) in CH_2Cl_2 (150 mL), cooled on a salt/ice bath. Subsequently triethylamine (12.6 g, 124 mmol) was added slowly. After stirring for 6 h, the reaction mixture was quenched by addition of saturated $NH_4Cl_{(aq)}$ and the resulting mixture was stirred over night. The two phases were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic phases were washed with brine and dried (Na_2SO_4). After evaporation of volatiles, a dark oil (4.52 g) was isolated which, according to ^{1}H NMR consisted of 93 % product and 7 % starting material. The crude product was used without further purification. The NMR-spectral data were in accordance with literature data.[17]

Synthesis of racemic alcohols 6, 18–19: Alcohols **6**, **18**, and **19** were prepared according to a literature procedure.[18]

4,4-Bis-(4-fluorophenyl)but-3-en-2-ol (18): The crude product was isolated in quantitative yield as colorless oil, which was used without further purification.

4,4-Bis-(4-methoxyphenyl)but-3-en-2-ol (19): The crude product was purified by flash chromatography on neutral alumina starting with 1:1 pentane/Et_2O and thereafter gradually changing to 100 % EtOAc. This gave 76 % yield of a yellow oil.

4-Methyl-3-penten-2-ol (20): Compound 20 was prepared according to a literature procedure.[19]

Synthesis of racemic esters 1 and 11–13: Racemic acetates **1** and **11–13** were prepared from alcohol **6** according to a literature procedure.[18]

3,3-Bis-(*p*-fluoro-phenyl)-1-methyl-allyl acetate (11): Colorless oil.

3,3-Bis-(*p*-methoxy-phenyl)-1-methyl-allyl acetate (12): White solid, m.p. below 50 °C.

4-Methyl-2-pent-3-enyl acetate (13): The crude product was a pale yellow oil.

Preparation of optically active esters (*R*)-1, (*R*)-11, (*R*)-12,and (*R*)-13

(*R*)-(+)-4,4-Diphenyl-2-acetoxy-but-3-ene ((*R*)-1): Racemic alcohol **6** (5.27 g, 23.5 mmol) and vinyl acetate (8.09 g, 94.0 mmol) were added to CALB (178 mg) in toluene (120 mL), and the mixture was stirred at 50 °C for 51 h. The reaction mixture was filtered and volatiles were evaporated in vacuo. The crude product was purified by flash chromatog-

raphy first using 9:1 pentane/Et_2O to give the acetate and then 7:3 pentane/Et_2O to elute the alcohol. The allylic acetate (*R*)-**1** was isolated as a colorless oil in 2.83 g (45.2%), ≥99.5% *ee* (OD-H column, hexane/*i*PrOH 99.9:0.1, $t_r(R)=27.7$, $t_r(S)=34.6$ min), $[\alpha]_D^{22}=+48.8$ ($c=1.67$ in $CHCl_3$). The NMR spectra were in accordance with the literature.[18]

(*S*)-(−)-4,4-Diphenyl-2-hydroxybut-3-ene ((*S*)-6): Alcohol (*S*)-**6** was isolated from the above experiment in 2.87 g (54.4%) as a colorless oil, 73.7% *ee* (OD-H column, hexane/*i*PrOH 90:10, $t_r(S)=12.7$, $t_r(R)=15.3$ min). A subsequent resolution of the residual alcohol under the same reaction conditions gave, after 93 h, 2.46 g of the alcohol as a colorless oil (99.5% *ee*), $[\alpha]_D^{22}=-62.6$ ($c=1.26$ in $CHCl_3$).

(*R*)-(+)-3,3-Bis-(*p*-fluorophenyl)-1-methylallyl acetate ((*R*)-11): Racemic **18** (6.51 g, 25.0 mmol) and vinyl acetate (8.61 g, 100 mmol) were added to CALB (188 mg) in toluene (125 mL), and the mixture was stirred at 50°C for 40 h. The reaction mixture was filtered and the volatiles were evaporated in vacuo. The crude product was purified by flash chromatography first with 9:1 pentane/Et_2O to give the acetate and then with 2:1 pentane/Et_2O to elute the alcohol. The allylic acetate (*R*)-**11** was isolated in 3.49 g (45.2%) as a colorless oil, ≥99.5% *ee* (AD column, *i*-hexane/*i*PrOH 99.9:0.1, $t_r(R)=23.8$ $t_r(S)=26.6$ min), $[\alpha]_D^{22}=+51.2$ ($c=1.98$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.23$–7.15 (m, 4H), 7.12–7.04 (m, 2H), 7.00–6.92 (m, 2H), 6.00 (d, $J=9.0$ Hz, 1H), 5.37 (dq, $J=9.0$, 6.4 Hz, 1H), 2.02 (s, 3H), 1.34 ppm (d, $J=6.4$ Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.0$, 162.6 (d, J(C,F)=247.8 Hz), 162.4 (d, J(C,F)=247.0 Hz), 141.8, 137.5 (d, J(C,F)=3.3 Hz), 134.7 (d, J(C,F)=3.4 Hz), 131.2 (d, J(C,F)=3.3 Hz), 129.1 (d, J(C,F)=7.9 Hz), 128.4, 115.5 (d, J(C,F)=21.6 Hz), 115.1 (d, J(C,F)=21.5 Hz), 69.3, 21.2, 21.0 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-114.6$ (m, 1F), −114.8 ppm (m, 1F); IR (KBr): $\tilde{\nu}=3047$, 2983, 2935, 1739, 1733, 1603, 1515, 1506, 1236, 834 cm^{-1}; HRMS: *m*/*z* calcd for $C_{18}H_{16}F_2O_2$ [M^+]: 302.1118; found: 302.1120.

(*S*)-(−)-4,4-Bis(4-fluorophenyl)but-3-en-2-ol ((*S*)-(−)-18): Alcohol (*S*)-**18** was isolated from the above experiment in 3.52 g (53.0%) as a colorless oil, 81.9% *ee* (AD column, *i*-hexane/*i*PrOH 95:5, $t_r(S)=21.1$, $t_r(R)=22.7$ min). A subsequent resolution gave 2.96 g of the alcohol in ≥99.5% *ee*, $[\alpha]_D^{22}=-35.0$ ($c=1.98$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.25$–6.90 (m, 8H), 6.01 (d, $J=9.1$ Hz, 1H), 4.34 (dq, $J=9.1$, 6.26 Hz, 1H), 1.87 (brs, 1H), 1.33 ppm (d, $J=6.3$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.6$ (d, J(C,F)=247.4 Hz), 162.4 (d, J(C,F)=247.0 Hz), 140.7, 137.9 (d, J(C,F)=3.3 Hz), 135.1 (d, J(C,F)=3.5 Hz), 132.6 (d, J(C,F)=1.6 Hz), 131.4 (d, J(C,F)=8.0 Hz), 129.2 (d, J(C,F)=8.1 Hz), 115.5 (d, J(C,F)=21.2 Hz), 115.2 (d, J(C,F)=21.5 Hz), 65.8, 23.9 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-114.7$ (m, 1F), −115.0 ppm (m, 1F); IR (KBr): $\tilde{\nu}=3394$, 2974, 2928, 1603, 1510, 1231, 835 cm^{-1}; HRMS: *m*/*z* calcd for $C_{16}H_{14}F_2O$ [M^+]: 260.1013; found: 260.1016.

(*R*)-(+)-3,3-Bis(*p*-methoxyphenyl)-1-methylallyl acetate ((*R*)-12): Racemic alcohol **19** (3.67 g, 12.9 mmol) and vinyl acetate (4.44 g, 51.6 mmol) were added to CALB (1.29 g) in toluene (60 mL), and the mixture was stirred at RT for 30 h. The reaction mixture was filtered and the volatiles were evaporated in vacuo. The crude product was purified by flash chromatography on basic alumina using 4:1 pentane/EtOAc to give the acetate and thereafter the eluent was gradually changed to 100% EtOAc to elute the alcohol. The allylic acetate (*R*)-**12** was isolated in 1.70 g (40.5%) as a colorless oil, 98.1% *ee* (AD column, hexane/*i*PrOH 95:5, $t_r(R)=14.9$, $t_r(S)=17.5$ min). $[\alpha]_D^{22}=+40.8$ ($c=1.63$ in $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.13$ (dm, $J=8.6$ Hz, 2H), 7.10 (dm, $J=8.6$ Hz, 2H), 6.90 (dm, $J=8.8$ Hz, 2H), 6.80 (dm, $J=8.8$ Hz, 2H), 5.91 (d, $J=9.1$ Hz, 1H), 5.39 (dq, $J=9.1$, 6.3 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 2.01 (s, 3H), 1.32 ppm (d, $J=6.3$, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=170.2$, 159.5, 159.1, 143.2, 134.6, 131.6, 130.8, 128.8, 126.2, 113.8, 113.6, 69.9, 55.4, 55.3, 21.5, 21.3 ppm; IR (KBr): $\tilde{\nu}=2963$, 1730, 1606, 1511, 1237, 1048, 1033, 838 cm^{-1}; HRMS: *m*/*z* calcd for $C_{20}H_{22}O_4$ [M^+]: 326.1518; found: 326.1511.

(*S*)-4,4-Bis(4-methoxyphenyl)but-3-en-2-ol ((*S*)-19): The alcohol (*S*)-**19** was isolated from the above experiment in 1.51 g (42.0%) as a yellow oil, 56.7% *ee* (AD column, hexane/*i*PrOH 90:10, $t_r(S)=34.6$, $t_r(R)=39.8$ min). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.21$–7.15 (m, 2H), 7.14–7.08 (m, 2H), 6.94–6.88 (m, 2H), 6.85–6.78 (m, 2H), 5.95 (d, $J=9.0$ Hz, 1H), 4.40 (dq, $J=9.0$, 6.22 Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 1.65 (brs, 1H), 1.33 ppm (d, $J=6.2$, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=159.3$, 159.0, 141.9, 134.9, 132.0, 131.0, 130.6, 128.8, 113.7, 113.6, 65.9, 55.39, 55.37, 23.9 ppm; IR (KBr): $\tilde{\nu}=3379$, 2971, 1607, 1506, 1243, 1030 cm^{-1}; HRMS: *m*/*z* calcd for $C_{18}H_{20}O_3$ [M^+]; 284.1412; found: 284.1404.

(*R*)-(+)-4-Methyl-2-pent-3-enyl acetate ((*R*)-(+)-13): Racemic alcohol **20** (3.4 g, 34 mmol) and vinyl acetate (2.93 g, 34 mmol) were added to CALB (255 mg) in Et_2O (75 mL). The mixture was stirred at RT and the progress of the reaction was followed by GC. After 1.75 h (32% conversion), the reaction mixture was filtered and the mixture of volatile products was concentrated in vacuo. The crude product was purified by preparative HPLC, using a gradient eluent (pentane/Et_2O 10:1 to Et_2O 100%). The allylic acetate (*R*)-**13** was isolated in 0.817 g (16.6%) as a yellow oil, *ee* ≥99.5% (GC, $t_r(R)=24.0$, $t_r(S)=24.3$ min, GC Program 1), $[\alpha]_D^{22}=+31.5$ ($c=1.71$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.58$ (dq, $J=8.9$, 6.4 Hz, 1H), 5.16 (dhept, $J=8.9$, 1.4 Hz, 1H), 2.01 (s, 3H), 1.72 (d, $J=1.4$ Hz, 3H), 1.71 (d, $J=1.4$ Hz, 3H), 1.25 ppm (d, $J=6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=170.7$, 136.5, 125.1, 68.4, 25.9, 21.6, 21.1, 18.5 ppm; IR (KBr): $\tilde{\nu}=2978$, 1733, 1449, 1371, 1243 cm^{-1}; HRMS: *m*/*z* calcd for $C_8H_{14}O_2$ [M^+]: 142.0994; found: 142.0967. The alcohol (*S*)-**20** was isolated in 1.52 g (44.6%) as a yellow oil, *ee*=39.3% (GC, $t_r(R)=24.7$, $t_r(S)=25.2$ min, GC Program 1).

Preparation of allylic benzoates (*S*)-9 and (*S*)-10

(*S*)-(+)-3,3-Diphenyl-1-methyl-allyl *p*-CF_3-benzoate ((*S*)-(+)-9): Alcohol (*S*)-**6** (99.5% *ee*) (536 mg, 2.39 mmol) and pyridine (1.5 mL) were mixed in CH_2Cl_2 (3.5 mL). The reaction flask was put in a salt/ice bath and *p*-CF_3-benzoyl chloride (0.70 g, 3.4 mmol) was added. The cooling bath was removed and the reaction mixture was stirred for 5 h. Thereafter ≈1.5 mL of water was added followed by Et_2O. The organic phase was washed twice with brine. The combined aqueous phases were extracted with Et_2O and the combined organic phases were washed with 1 M $NaOH_{(aq)}$ (3×20 mL), followed by drying with Na_2SO_4 and evaporation of volatiles in vacuo. Purification through a short column of silica (pentane/Et_2O 4:1) afforded 958 mg (101%) of (*S*)-**9** as a yellow oil. An analytical sample was isolated by semipreparative HPLC (Kromasil 250×20 mm 100 SIL 5 μm column, 10 mL flow, pentane/Et_2O 40:1). $[\alpha]_D^{26}=+75.6$ ($c=1.19$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.14$ (dm, $J=8.4$ Hz, 2H), 7.69 (dm, $J=8.4$ Hz, 2H), 7.43–7.20 (m, 10H), 6.18 (d, $J=8.9$ Hz, 1H), 5.65 (dq, $J=8.9$, 6.3 Hz, 1H), 1.49 ppm (d, $J=6.3$, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=164.5$, 144.7, 141.4, 139.0, 134.4 (q, J(C,F)=33.0 Hz), 134.1, 130.1, 129.6, 128.6, 128.4, 128.0, 127.8, 127.6, 125.4, (q, J(C,F)=3.8 Hz), 123.8 (q, J(C,F)=272.3 Hz), 71.0, 21.3 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-63.4$ ppm (s, 3F); IR (KBr): $\tilde{\nu}=3059$, 2982, 1732, 1324, 1270, 1168, 863 ppm; HRMS: *m*/*z* calcd for $C_{24}H_{19}F_3O_2$ [M^+]: 396.1337; found: 396.1338.

(*S*)-3,3-Diphenyl-1-methyl-allyl perfluorobenzoate ((*S*)-10): Alcohol (*S*)-**6** (99.5% *ee*) (528 mg, 2.35 mmol), pyridine (0.305 mL, 3.77 mmol), and DMAP (36 mg, 0.29 mmol) were mixed in CH_2Cl_2 (19 mL). At −60°C perfluorobenzoyl chloride (0.42 mL, 2.9 mmol) was added. The reaction mixture was stirred for 7 h, while the temperature was allowed to reach 0°C. While still kept in cooling bath, water was added. The aqueous phase was extracted with Et_2O (2×10 mL). The combined organic phases were washed twice with $NaHCO_{3(aq)}$ and subsequently twice with water. After drying over Na_2SO_4, volatiles were evaporated in vacou, which gave 899 mg (91%) of crude product as a pale yellow solid. The crude product was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.45$–7.33 (m, 3H), 7.32–7.18 (m, 7H), 6.11 (d, $J=9.1$ Hz, 1H), 5.64 (dq, $J=9.1$, 6.4 Hz, 1H), 1.49 ppm (d, $J=6.4$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=158.2$, 145.6, 145.4 (dm, J(C,F)=256.0 Hz), 143.2 (dm, J(C,F)=258.7 Hz), 141.3, 138.9, 137.9 (dm, J(C,F)=254.7 Hz), 129.7, 128.7, 128.5, 128.3, 128.1, 127.7, 126.7, 109.1 (m), 73.0, 21.2 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-139.2$ (m, 2F), −149.8 (tt $J=20.8$, 4.2 Hz, 1F), −161.0 ppm (m, 2F); IR (KBr): $\tilde{\nu}=3084$, 2992, 1737, 1505, 1233, 992, 766, 702 cm^{-1}; HRMS: *m*/*z* calcd for $C_{23}H_{15}F_5O_2$ [M^+]: 418.0992; found: 418.1001.

General procedure for the copper(I)-catalyzed allylic substitution reactions: The allylic acetate (*R*)-**1** (123.8 mg 0.465 mmol, >99.5% *ee*) and CuCl (4.6 mg, 0.046 mmol) were mixed in THF (4 mL) and cooled to

−40 °C. A solution of *n*BuMgBr in THF (1.06 mL, 0.66 M) was added over a period of one minute and the reaction mixture was stirred at the appropriate temperature. After 16 h the reaction mixture was quenched by addition of $HCl_{(aq)}$ (2 M, 10 mL) followed by addition of 2-decanol (51.3 mg, 0.324 mmol) as internal standard. The aqueous phase was extracted with Et_2O (3×10 mL) and the combined organic phases were washed with H_2O (10 mL), followed by drying with Na_2SO_4 and evaporation of volatiles in vacuo. The formation of **5a** was determined to be 74%, together with 8% of alcohol **6**, and the conversion to >95%, according ^{1}H NMR analysis of the crude product. Column chromatography (100% pentane) afforded 82.5 mg (74%) of **5a** as a colorless oil, 29.3% *ee* (OD-H column, 100% *i*-hexane, $t_r(R)=9.9$, $t_r(S)=10.5$ min).

Preparation of BuMgOAc: A solution of nBu_2Mg in heptane (1.88 mL, 1.0 M) was added to a solution of acetic acid (113 mg, 1.88 mmol) in THF (3 mL) at −40 °C. The reaction mixture was stirred for 25 min at −40 °C and used immediately thereafter.

Allylic substitution of (*R*)-1 mediated by stoichiometric amounts of $Bu_2CuMgCl$: *n*BuMgCl in THF (0.87 mL 2.3 M) added to a suspension of CuCl (49.5 mg 0.500 mmol) in THF (25 mL) at −20 °C was. The mixture was stirred at the given temperature for a half an hour. After cooling the reaction mixture to −80 °C, the allylic acetate (*R*)-**1** (133 mg 0.500 mmol, >99.5% *ee*) in THF (5 mL) was added. After 3.5 days $HCl_{(aq)}$ (2 M, 3 mL) was added slowly to the reaction mixture, while still in the cooling bath. Subsequently, most of the THF was evaporated and the aqueous phase was extracted with Et_2O (3×10 mL) and subsequently the combined organic phases were washed with H_2O (10 mL), followed by drying with Na_2SO_4 and evaporation of volatiles in vacuo. The formation of **5a** was determined to 16% together with 16% of alcohol (*R*)-**6** according to ^{1}H NMR analysis of the crude product. The optical purity of **5a** (11% *ee*) was determined by chiral HPLC.

Allylic substitution of (*R*)-1 mediated by stoichiometric amounts of Bu_2CuLi: *n*BuLi in hexanes (1.25 mL 1.6 M) was added to a suspension of CuCl (99.0 mg 1.00 mmol) in THF (6 mL) at −20 °C. The mixture was stirred at the given temperature for 15 min. After cooling the reaction mixture to −80 °C, the allylic acetate (*R*)-**1** (133 mg 0.500 mmol, >99.5% *ee*) in THF (2 mL) was added. After 3.5 days $HCl_{(aq)}$ (2 M, 3 mL) was added slowly to the reaction mixture, while still in the cooling bath. Thereafter ≈10 mL of water was added and the aqueous phase was extracted with Et_2O (3×10 mL) and the combined organic phases were washed with H_2O (10 mL), followed by drying with Na_2SO_4 and evaporation of volatiles in vacuo. The formation of **5a** was determined to be 12% together with 15% of alcohol (*R*)-**6** according to ^{1}H NMR analysis of the crude product. The optical purity of **5a** (≤ 3% *ee*) was determined by chiral HPLC.

Cross-coupling products 5a–c and 14–16: As reference compounds for chiral chromatography racemic **5a**, **5b** (colorless oils), **5c** (colorless solid), **14**, **15** (colorless oils) and **16** were prepared from the appropriate racemic allylic acetates.

(*R*)-(−)-1,1-Diphenyl-3-methylheptene ((*R*)-5a): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.41$–7.15 (m, 10H), 5.87 (d, $J=10.3$ Hz, 1H), 2.36–2.20 (m, 1H), 1.39–1.10 (m, 6H) 1.01 (d, $J=6.6$ Hz, 3H) 0.84 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=142.9$, 140.8, 140.2 (2 C), 136.6, 130.0, 128.3, 128.2, 127.2, 126.9, 37.5, 33.9, 29.9, 22.9, 21.6, 14.2 ppm; optical rotation was estimated for a sample of **5a** with an *ee* of 92.5%; $[\alpha]_D^{24}=-85.2$ ($c=1.03$ in $CHCl_3$); IR (KBr): $\tilde{\nu}=2957$, 2924, 1599, 1495, 1445, 762, 701 cm^{-1}; HRMS: *m*/*z* calcd for $C_{20}H_{24}$ [M^+]: 264.1878; found: 264.1873.

(*S*)-(+)-1,1,3-Triphenylbutene ((*S*)-5b): Column chromatography (100% pentane) gave a colorless oil, which formed a colorless solid on standing (m.p. = 59.8–63.9 °C). The optical purity (≥99.5% *ee*) was determined by chiral HPLC (OD-H column, 100% *i*-hexane $t_r(R)=21.7$, $t_r(S)=23.7$ min), $[\alpha]_D^{22}=+80.6$ ($c=1.83$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.43$–7.13 (m, 15H), 6.21 (d, $J=10.4$ Hz, 1H), 3.60 (dq, $J=10.4$, 6.8 Hz, 1H), 1.38 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=146.3$, 142.5, 140.3, 140.2, 134.3, 130.0, 128.6, 128.4, 128.2, 127.4, 127.2, 127.13, 127.08, 126.1, 39.4, 22.5 ppm: IR (KBr): $\tilde{\nu}=2960$, 2920, 1493, 1443, 767, 754, 699 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{20}$ [M^+]: 284.1565; found: 284.1562.

(*R*)-1,1-Diphenyl-3-(*p*-methoxyphenyl)butene ((*R*)-5c): The yield of (*R*)-**5c** was determined to 31% and the amount of **6** to 13%, by ^{1}H NMR analysis of the crude product. Column chromatography (pentane/Et_2O 50:1) gave 54.5 mg (25%) of (*R*)-**5c** as a colorless solid (m.p. = 106.4–108.1 °C) in ≥99.5% *ee* (AD column, *i*-hexane:*i*PrOH 99.9:0.1, $t_r(S)=15.7$, $t_r(R)=18.8$ min), $[\alpha]_D^{25}=+107$ ($c=1.29$ in $CHCl_3$); ^{1}H NMR (100 MHz, $CDCl_3$): $\delta=7.45$–7.32 (m, 3H), $\delta=7.30$–7.19 (m, 7H), 7.15 (dm, $J=8.9$ Hz, 2H), 6.86 (dm, $J=8.9$ Hz, 2H), 6.21 (d, $J=10.4$ Hz, 1H), 3.81 (s, 3H), 3.58 (dq, $J=10.4$, 6.9 Hz, 1H) 1.39 ppm (d, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=158.0$, 142.6, 140.3, 140.0, 138.5, 134.6, 130.0, 128.4, 128.2, 128.0, 127.4, 127.2, 127.1, 114.1, 55.4, 38.6, 22.6 ppm; IR (KBr): $\tilde{\nu}=2957$, 1609, 1511, 1249, 1233, 1177, 1035, 833 cm^{-1}; HRMS: *m*/*z* calcd for $C_{23}H_{22}O$ [M^+]; 314.1671; found: 314.1672.

(*R*)-1,1-Di(*p*-fluorophenyl)-3-methylheptene ((*R*)-14): The conversion was determined to be >95%, the yield of (*R*)-**14** to be 58%, and the amount of alcohol **18** to be 15%, by ^{1}H NMR analysis of the crude product. Column chromatography (pentane 100%) gave 112.1 mg (37%) of (*R*)-**14** as a colorless oil. The optical purity was analyzed by GC of the 2-methyl-hexanoic acid (20% *ee*), obtained by oxidative cleavage of the olefin.[14] ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.22$–7.01 (m, 6H), 7.00–6.89 (m, 2H), 5.80 (d, $J=10.2$ Hz, 1H), 2.34–2.14 (m, 1H), 1.42–1.08 (m, 6H), 1.01 (d, $J=6.6$ Hz, 3H), 0.85 ppm (t, $J=7.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=162.2$ (d, J(C,F) = 246.0 Hz), 162.0 (d, J(C,F) = 245.4 Hz), 138.9 (m), 138.3, 136.9, 136.2 (d, J(C,F) = 3.5 Hz), 130.1 (d, J(C,F) = 205.3 Hz), 130.0 (d, J(C,F) = 205.6 Hz), 115.3 (d, J(C,F) = 21.3 Hz), 115.0 (d, J(C,F) = 21.3 Hz), 37.5, 33.9, 29.9, 22.9, 21.5, 14.2 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-116.0$ (m, 1F), −116.5 ppm (m, 1F); IR (KBr): $\tilde{\nu}=2959$, 2927, 2871, 2856, 1603, 1512, 1506, 1232, 1157, 835 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{20}F_2$ [M^+]: 300.1690; found: 300.1688.

(*R*)-1,1-Di(*p*-methoxyphenyl)-3-methylheptene ((*R*)-15): Column chromatography (pentane/Et_2O 19:1) gave 54.5 mg (36%) of (*R*)-**15** as a colorless oil in 49% *ee* (AD column, hexane:*i*PrOH 99.9:0.1, $t_r(R)=15.0$, $t_r(S)=16.3$ min). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.15$ (dm, $J=8.9$ Hz, 2 H), 7.08 (dm, $J=8.9$ Hz, 2 H), 6.89 (dm, $J=9.0$ Hz, 2 H), 6.79 (dm, $J=9.0$ Hz, 2 H), 5.72 (d, $J=10.2$ Hz, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.34–2.20 (m, 1H), 1.36–1.09 (m, 6H), 0.99 (d, $J=6.5$ Hz, 3H), 0.84 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=158.7$, 158.5, 139.2, 136.0, 134.9, 133.3, 131.0, 128.3, 113.6, 113.5, 55.4, 55.3, 37.6, 33.8, 29.9, 22.9, 21.7, 14.2 ppm; IR (KBr): $\tilde{\nu}=2956$, 2926, 1607, 1286, 1243, 1037, 830, 806 cm^{-1}; HRMS: *m*/*z* calcd for $C_{22}H_{28}O_2$ [M^+]: 324.2089; found: 324.2078.

(*R*)-2,4-Dimethyl-2-undecene ((*R*)-16): According to GC, using decane as internal standard, 85% of α-product (*R*)-**16** was obtained together with 6% of the corresponding γ-product (**17**). The optical purity of (*R*)-**16** was determined by transformation to 2-methyl-nonanoic acid (≥97% *ee*), obtained by oxidative cleavage of olefin,[14] and subsequent analysis by chiral GC. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.87$ (d, $J=9.3$ Hz, 1 H), 2.34–2.23 (m, 1 H), 1.68 (d, $J=1.4$ Hz, 3 H), 1.60 (d, $J=1.4$ Hz, 3 H), 1.35–1.10 (m, 12 H), 0.89 (d, $J=6.7$ Hz, 3 H), 0.88 ppm (t, $J=6.9$ Hz, 3 H).

4,4-Dimethyl-2-undecene (17): Only those peaks that could be distinguished in a ^{1}H NMR spectrum of a mixture of **16** and **17** are reported. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=5.37$ (d, $J=15.5$ Hz, 1 H), 5.29 (dq, $J=15.3$, 5.9 Hz, 1 H), 1.65 (d, $J=5.9$ Hz, 3 H), 0.94 ppm (s, 6 H).

Determination of optical purity by oxidation to the corresponding carboxylic acids: Racemic 2-methylhexanoic acid and 2-methylnonanoic acid were prepared for GC-references. The characterization of 2-methylnonanoic acid will be reported elsewhere.[20]

2-Methylhexanoic acid: The Sharpless procedure[14] was followed: cross-coupling product **14** (38.1 mg, 0.127 mmol) and $NaIO_4$ (128 mg, 0.598 mmol) were mixed in a 1:1 mixture of CCl_4 and CH_3CN (2 mL). A solution of $RuCl_3{\cdot}H_2O$ (2.6 mg, 12.5 μmol) in H_2O (1.5 mL) was added to the flask and the reaction mixture was vigorously stirred. The reaction was completed within 3 h, according to TLC. Thereafter, Et_2O (10 mL) and $NaHCO_{3(aq)}$ (10 mL) were added. The organic phase was subsequently extracted with $NaHCO_{3(aq)}$ (3×10 mL). The aqueous phases were combined and concentrated $HCl_{(aq)}$ was carefully added until the pH reached 2. The product was extracted from the aqueous phase with CH_2Cl_2 (3×

10 mL). The combined organic phases were dried over Na_2SO_4 and the product was concentrated in vacuo, giving 14.6 mg (88%) of crude product as a colorless oil, 20% *ee* (GC, $t_r(S)=10.1$, $t_r(R)=10.6$ min, GC program 2). The ^{1}H NMR and ^{13}C NMR spectral data were in accordance with literature data.[21]

2-Methylnonanoic acid: An analytical sample of a 93:7 mixture of α-product (*R*)-**16** and γ-product **17** were oxidised, according to the Sharpless procedure.[14] The optical purity (≥97% *ee*) of the (*R*)-2-methylnonanoic acid obtained from (*R*)-**16** was determined by chiral GC ($t_r(S)=$ 23.1, $t_r(R)=23.5$ min, GC program 2).

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