JOC The Journal of Organic Chemistry

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Alcohol Cross-Coupling for the Kinetic Resolution of Diols via Oxidative Esterification

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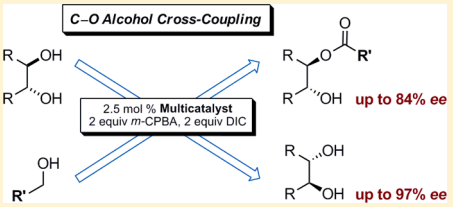
Supporting Information

ABSTRACT: We present an organocatalytic C−O-bond cross-coupling strategy to kinetically resolve racemic diols with aromatic and aliphatic alcohols, yielding enantioenriched esters. This one-pot protocol utilizes an oligopeptide multicatalyst, *m*-CPBA as the oxidant, and *N,N′*-diisopropylcarbodiimide as the activating agent. Racemic acyclic diols as well as *trans*-cycloalkane-1,2-diols were kinetically resolved, achieving high selectivities and good yields for the products and recovered diols.



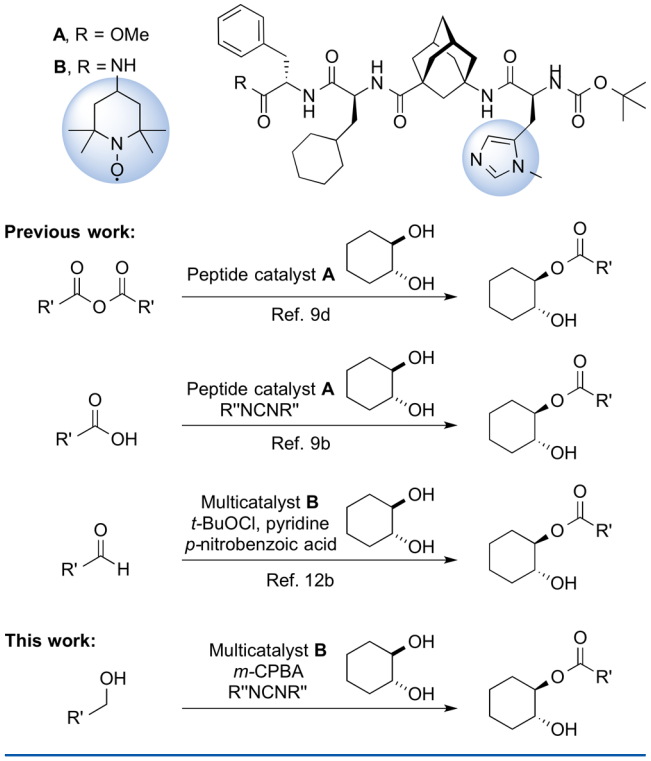
Cross-coupling reactions[1] describe C−C or C−heteroatom[2] σ-bond formation of two molecular fragments of intrinsically competing reactivities; such reactions are often catalyzed by transition metals. Replacing the metal catalyst by an organocatalyst is highly challenging, but this would enable the realization of novel C−X bond-forming strategies in organic synthesis.[3] A pertinent example is the oxidative cross-coupling of alcohols to esters,[4] which is of high practical relevance due to their synthetic versatility for the preparation of natural products, polymers, and pharmaceuticals. There are many procedures for the preparation of mixed esters starting from different alcohols using transitions metals,[2c,4,5] molecular iodine,[6] CBr_4 as bromine source,[7] or *N*-heterocyclic carbenes.[8] Scheidt and co-workers contributed also an enantioselective variant with moderate enantioselectivities.[8a] However, there is no report on a highly enantioselective organocatalytic oxidative esterification, combining two *different* alcohols. Here, we present the kinetic resolution of racemic diols starting from aliphatic or aromatic alcohols (Scheme 1).

Recently, we have shown that (±)-*trans*-cycloalkane-1,2-diols can be kinetically resolved using peptide catalyst **A**,[9] which is equipped with a nucleophilic *N*-π-methylhistidine[10] moiety for enantioselective acyl transfer employing anhydrides as the acyl source (Scheme 1).[9d] This approach also resulted in the first enantioselective Steglich esterification[11] starting from carboxylic acids as an acyl source.[9b] Most recently, we showed that aldehydes could be oxidized *in situ* and used to resolve diols with high enantioselectivities with multicatalyst **B**[12] (Scheme 1).

Alcohols would even be better acyl equivalents owing to their high stability and ubiquitous accessibility. We thus turned our attention to developing an organocatalytic enantioselective C−O alcohol cross-coupling protocol of diols using multicatalyst **B**, equipped with oxidation and acyl transfer active sites.[12] Our concept envisaged the oxidation of a mono alcohol, followed by conversion to the corresponding enantioenriched hydroxy ester in the presence of a diol in a one-pot fashion (Scheme 1).

Realizing this alcohol coupling strategy, we attempted to oxidize the alcohol to the corresponding aldehyde and transfer it *in situ* to a mixed anhydride with multicatalyst **B**, pyridine, *p*-nitrobenzoic acid (*p*-NBA), and *t*-BuOCl; mixed anhydrides generated from aldehydes can act as acyl synthons (Scheme 1).[12b,13] However, this procedure only provides unsatisfactory conversions and enantioselectivities for the product and the recovered diol.

Scheme 1. Various Acyl Sources for the Kinetic Resolution of *trans*-Cyclohexane-1,2-diol 4b Using Catalyst A or B

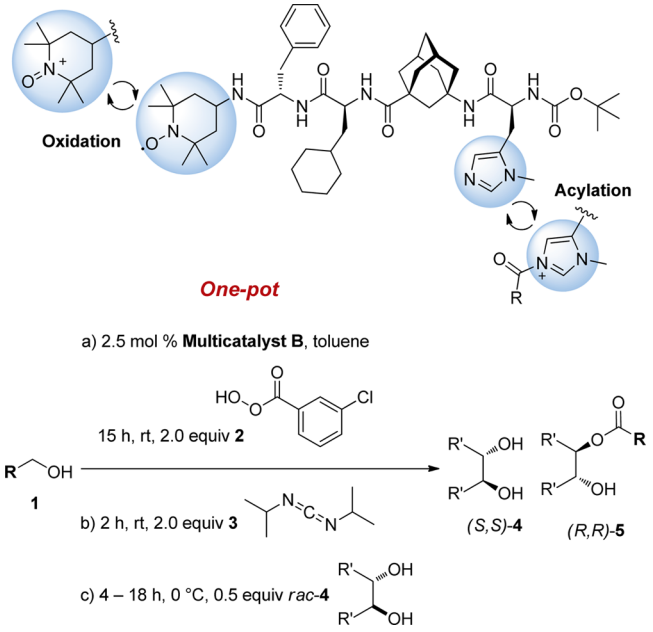


Received: November 23, 2014
Published: January 8, 2015

DOI: 10.1021/jo502670p
J. Org. Chem. 2015, 80, 1972−1978

Therefore, we decided to oxidize mono alcohols to the corresponding acids *in situ* with multicatalyst **B** and a terminal oxidant. The resulting acid was activated with dehydrating agent **3** (*N*,*N*′-diisopropylcarbodiimide, DIC), giving a mixed anhydride, whereby the less steric hindered acyl group (and more stable acyl moiety) of the anhydride was transferred enantioselectively onto the diol (Scheme 2).

Scheme 2. One-Pot Kinetic Resolution of *rac*-Diols Using Multicatalyst B



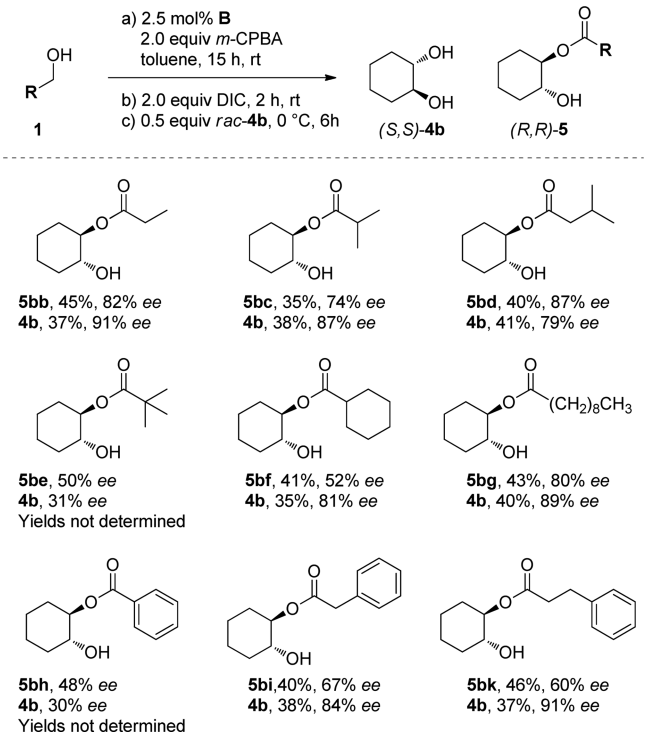
We optimized the reaction conditions for the oxidation of propanol (**1b**) to propionic acid with various oxidants. Toluene has proven to be the best solvent for the kinetic resolution of 1,2-diols with **A**, and therefore, we also used it for the oxidation step.[9a,b,d,13] Using stoichiometric amounts of trichloroisocyanuric acid (TCCA) and **B** resulted in full conversion to the acid, but in the subsequent esterification, no product formed, likely due to catalyst inhibition due to the hydrochloric acid generated in the oxidation step (addition of base did not improve this situation). *t*-BuOCl is not a suitable oxidation agent in this context because of its exothermic reaction with water. Use of 2.0 equiv of *m*-CPBA **2** as a stoichiometric oxidant gave nearly full conversion (90%, determined by GC) to propionic acid after 6 h at room temperature. We stirred the reaction for 15 h until the decomposition of the peracid was complete to avoid oxidation of the diol. The generated "waste" 3-chlorobenzoic acid (*m*-CBA) was used in the next step, generating a mixed anhydride with propionic acid using *N*,*N*′-diisopropylcarbodiimide **3** to remove water. We identified the ratio of the mixed and symmetric anhydrides of propionic acid and 3-chlorobenzoic acid formed during the reaction with NMR as described before.[12b,14] The anhydrides formed in a ratio of approximately 3:1 of mixed anhydride (3-chlorobenzoic propionic anhydride) relative to the symmetric anhydride of propionic acid (see the Supporting Information).

We recently showed that benzoic anhydrides generally react quite sluggishly with alcohols, owing to the increased stability of the intermediate acylium imidazolium ion.[9a,b] This is consistent with this "waste-re-use"-protocol. Despite use of an excess of *m*-CBA, we observed only 5% of aromatic byproduct (2-hydroxycyclohexyl 3-chlorobenzoate) under our optimized reaction conditions.

In an attempt to minimize the amount of the aromatic byproduct through use of sterically hindered peracids that would form Yamaguchi-type anhydrides,[15] we generated the peracids by treating the corresponding acyl chloride with 30% H_2O_2 in basic media.[16] Iodometric titration showed that smaller amounts of more sterically hindered peracids (compared to *m*-CPBA) formed, which are useless for our protocol. The aromatic byproduct was minimized by using 2.0 equiv of dehydrating agent **3** (with lower amounts, no product was obtained) with a reaction time of 2 h at room temperature and 0.5 equiv of **4b**. Relatively high dilution was required to achieve high enantioselectivities in the kinetic resolution for **4b**, but this is common for these types of reactions.[9d,17]

With these optimized reaction conditions, we generally obtained good yields and enantioselectivities for recovered diol **4b** and product **5bb** (**4b**: 37%, 91% *ee*; **5bb**: 45%, 82% *ee*, Scheme 3); as this is not a pseudo-first-order reaction, no *S*-

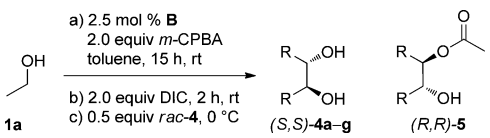
Scheme 3. Kinetic Resolution of *rac*-4b Using Various Alcohols as Acyl Synthons (Yields of Isolated Products Are Shown)

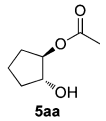
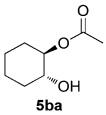
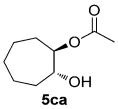
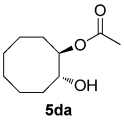
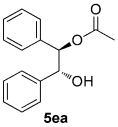
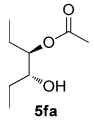
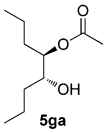


values can be given. We expanded the substrate scope and tested *trans*-cycloalkane-1,2-diols and racemic acyclic diols using ethanol **1a** as acyl source (Table 1). The best results were achieved for the kinetic resolution of *rac*-**4b** starting from ethanol **1a** (**4b**: 37%, 97% *ee*; **5ba**: 42%, 84% *ee*, Table 1). Diols **4c** and **4d** with larger ring sizes showed comparable results. Cyclic diol **4a** and acyclic aromatic diol **4e** react faster in the acylation sequence, but selectivities for the products (**5aa**, **5ea**) were only up to 44% *ee*. The successful conversion of aliphatic acyclic diols **4f** and **4g** demonstrates that this coupling protocol is not limited to cyclic diols (e.g., 73% *ee*, for both **4f** and **5fa**, respectively, Table 1). In all tested reactions, 3-chlorobenzoic byproduct formation is low (≤6%).

DOI: 10.1021/jo502670p
J. Org. Chem. 2015, 80, 1972–1978

Table 1. Substrate Scope Using Ethanol 1a as Acyl Source[a,b,c,d,e]



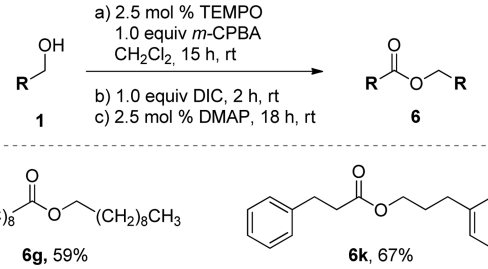
entry	product	t /h[a]	yield[b] (ee[c]) /% 4	5
1	 5aa	4	n.d.[e] (46)	n.d.[e] (44)
2	 5ba	6	37 (97)	42 (84)
3	 5ca	7	40 (92)	43 (84[d])
4	 5da	8	41 (92)	39 (81)
5	 5ea	4	n.d.[e] (75[d])	n.d.[e] (38[d])
6	 5fa	12	37 (73)	43 (73)
7	 5ga	18	40 (64)	23 (76)

[a]Reaction time for esterification. [b]Yield of isolated product and recovered diol. [c]Determined by chiral GC. [d]Determined by chiral HPLC. [e]n.d. = no data.

Various alcohols were employed to probe the generality and utility of this coupling protocol using *rac*-**4b**. Full conversion of the alcohol was determined by GC. Aliphatic alcohols **1b**−**1e** showed high enantioselectivities and high yields for the reisolated diol **4b** and products **5bb**−**5bd** and **5bg**. Using sterically more hindered alcohols resulted in increased formation of aromatic byproduct (4−7%; for details, see the Experimental Section). Alcohols **1e** and **1h** showed insufficient selectivities under these conditions. This procedure works well also with aromatic alcohols **1i** and **1k**, achieving a maximum *ee* of 91% for recovered diol **4b** (Scheme 3).

We also probed the "identity reaction", whereby the mono alcohol **1** serves as acyl *and* alcohol component at the same time. Indeed, an excess of alcohol **1** resulted in dimer **6** (Scheme 4). Such symmetric esters find multiple applications in the food and fragrance industries.[18] We oxidized alcohol **1** with 1.0 equiv of *m*-CPBA (for maximum conversion, 2.0 equiv of *m*-CPBA is necessary) and 2.5 mol % TEMPO as catalyst to the corresponding acid. With DIC, a mixed anhydride formed, and catalytic amounts of 4-dimethylaminopyridine (DMAP) transferred the acyl group of the anhydride onto the remaining alcohol **1**. Yields for **6g** and **6k** over three steps in one pot were good, and this protocol offers a novel access to symmetric esters.

Scheme 4. One-Pot Dimerization of Alcohols 1g and 1k



We have shown that aliphatic and aromatic alcohols can be coupled enantioselectively with racemic *trans*-cycloalkane-1,2-diols and racemic acyclic diols under oxidative conditions, achieving good yields and high enantioselectivities with multicatalyst **B**. Using the synthetically readily accessible alcohols as acyl sources, this coupling protocol extends the existing range of substrates that can serve as acyl synthons (anhydrides,[9d] acids,[9b] and aldehydes[12b]) to resolve racemic diols kinetically. Future challenges include an expansion of this protocol to racemic mono alcohols and recovery and immobilization of multicatalyst **B**.

EXPERIMENTAL SECTION

General Remarks. Unless otherwise noted, chemicals were purchased at the highest purity grade available and were used without further purifications. All solvents were distilled prior to use. Toluene was distilled from appropriate drying agents prior to use and stored under an argon atmosphere. Column chromatography and filtration was conducted using silica gel (0.040−0.063 mm). TLC R_f values are reported. ^{1}H and ^{13}C NMR spectra were recorded on 600, 400, or 200 MHz spectrometers, respectively, using TMS as the internal standard with chemical shifts given in ppm relative to TMS or the respective solvent residual peaks. ESI mass spectra were recorded using methanol solutions of the respective compounds. High-resolution ESI mass spectrometry was performed on an ESI-TOF mass spectrometer using methanol solutions of the respective compounds.

Synthesis of Multicatalyst B. Multicatalyst **B** was synthesized in solution using Boc-strategy and EDC/HOBt mediated couplings as described in the literature. Analytical data of the peptide were identical with those reported in the literature.[12]

Availability of the Alcohols and Racemic Starting Materials. The achiral alcohols were purchased at the highest purity grade available. Racemic *trans*-cyclopentane-1,2-diol (*rac*-**4a**), *trans*-cyclohexane-1,2-diol (*rac*-**4b**), and *rac*-hydrobenzoin (*rac*-**4e**) were purchased and used without further purification. *Trans*-cycloheptane-1,2-diol (*rac*-**4c**), *trans*-hexane-1,2-diol (*rac*-**4f**), and *trans*-octane-1,2-diol (*rac*-**4g**) were synthesized according to the method of the *Organikum*[19] using the freshly distilled (cyclo-) alkene, formic acid, and H_2O_2, followed by a saponification with aq. NaOH. *Trans*-cyclooctane-1,2-diol (*rac*-**4d**) was synthesized via epoxide opening of cyclooctaneoxide, in water with *p*-toluenesulfonic acid.[9d]

Description of Standard Conditions for Catalytic Runs with Diols 4a−g (Table 1). The conditions for the kinetic resolutions of *trans*-cyclopentane-1,2-diol (*rac*-**4a**), *trans*-cyclohexane-1,2-diol (*rac*-**4b**), *trans*-cycloheptane-1,2-diol (*rac*-**4c**), *trans*-cyclooctane-1,2-diol (*rac*-**4d**), *rac*-hydrobenzoin (**4e**), *trans*-hexane-3,4-diol (*rac*-**4f**), and *trans*-octane-4,5-diol (*rac*-**4g**) with ethanol **1a** are given exemplarily by the following experimental protocol. Ethanol (59 μL, 1.0 mmol) and

DOI: 10.1021/jo502670p
J. Org. Chem. 2015, 80, 1972−1978

multicatalyst **B** (23 mg, 25 μmol, 2.5 mol %) were dissolved in 5 mL of toluene. Oxidizing agent, *m*-CPBA (430 mg, 2.0 mmol), was added at room temperature, and the reaction mixture was stirred for 15 h. After oxidation, the reaction was diluted with 200 mL of toluene and *N*,*N*′-diisopropylcarbodiimide (DIC, 310 μL, 2.0 mmol) was added to generate the mixed anhydride. After 2 h reaction time, the reaction mixture was cooled to 0 °C and the diol (0.5 mmol) was added. The reaction mixture was quenched with 10 mL of methanol and then filtered through 60 g of silica gel washed with EtOAc to remove the catalyst. Purification methods were different for each synthesis and can be found in the corresponding paragraph (see below).

Data for the Preparative Kinetic Resolution of *rac*-4b with 1a. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc:Et_3N 99.9:0.1 afforded 22 mg (0.19 mmol, 37%, R_f = 0.20) of diol **4b**, 33 mg (0.21 mmol, 42%, R_f = 0.64) of monoacetate **5ba**, and 5 mg (0.02 mmol, 4%, R_f = 0.84) of aromatic byproduct (2-hydroxycyclohexyl 3-chlorobezoate, **7b**). The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (97% *ee*) and **5ba** (84% *ee*) was determined by chiral GC analysis.

Enantiomers of diol **4b** were separated by chiral GC employing a 30 m FS-Hydrodex γ-DiMOM column (Machery-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−240 °C, 10 °C/min. Retention Times: R_1 (*S*,*S*) = 29.2 min; R_2 (*R*,*R*) = 29.6 min. Racemic **5ba** was synthesized as described in the literature to proof GC retention times.[9d] Enantiomers of monoacetate **5ba** were separated by chiral GC employing a 30 m FS-Hydrodex γ-DiMOM column (Machery-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−240 °C, 10 °C/min. Retention Times: R_1 (*S*,*S*) = 40.0 min; R_2 (*R*,*R*) = 40.8 min. Analytical data of the product (*rac*-**5ba**) were identical with those reported in the literature.[20] Analytical data for **7b**: ^{1}H NMR (200 MHz, CDCl3): δ/ppm =8.04−8.00 (s, 1 H); 7.97−7.88 (d, *J* = 7.8 Hz; 1 H); 7.57−7.46 (d, *J* = 7.8 Hz; 1 H); 7.44−7.32 (t, *J* = 7.8 Hz; 1 H); 4.93−4.76 (m, 1 H); 3.82−3.60 (m, 1 H); 2.17−1.92 (m, 3 H); 1.83−1.68 (m, 2 H); 1.49−1.29 (m, 4 H). ^{13}C NMR (50 MHz, CDCl3): δ/ppm = 165.5; 134.5; 133.1; 132.1; 129.7; 127.8; 79.2; 72.8; 33.1; 30.0; 23.9; 23.8. IR (KBr): ∼ν /cm^{-1} = 3448; 2931; 2862; 1717; 1573; 1287; 1256; 1124; 1072; 1014; 744. HR-MS (ESI): *m*/*z* = 277.0608 [M + Na]$^+$ (calc. *m*/*z* = 277.0607). Anal. Calcd for $C_{13}H_{15}ClO_3$: C 61.30, H 5.94; found: C 61.22, H 5.91.

Data for the Preparative Kinetic Resolution of *rac*-4a with 1a. Enantiomeric excess for **5aa** (44% *ee*) and **4a** (46% *ee*) was determined without a further purification step. Enantiomers of diol **4a** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDAc column (Machery-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−180 °C, 2 °C/min. Retention Times: R_1 (*S*,*S*) = 26.7 min; R_2 (*R*,*R*) = 27.2 min. Racemic **5aa** was synthesized as described in the literature to proof retention times.[9d] Enantiomers of monoacetate **5aa** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDAc column (Machery-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−180 °C, 2 °C/min. Retention Times: R_1 (*S*,*S*) = 19.0 min; R_2 (*R*,*R*) = 18.6 min. Analytical data of the product (*rac*-**5aa**) were identical with those reported in the literature.[20]

Data for the Preparative Kinetic Resolution of *rac*-4c with 1a. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with Hexane:EtOAc:Et_3N (3:7:0.01) afforded 26 mg (0.20 mmol, 40%, R_f = 0.21) of diol **4c**. Monoacetate **5ca** and byproduct **7c** were separated by a further column chromatography (7:3 Hexane:EtOAc), resulting in 37 mg (0.22 mmol, 43%, R_f = 0.19) of monoacetate **5ca** and 6 mg (0.02 mmol, 5%, R_f = 0.21) of aromatic byproduct **7c**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4c** (92% *ee*) and **5ca** (84% *ee*) was determined by chiral GC analysis.

Enantiomers of diol **4c** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Machery-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 140 °C isotherm. Retention Times: R_1 (*S*,*S*) = 9.5 min; R_2 (*R*,*R*) = 9.8 min. Racemic **5ca** was synthesized as described in the literature to proof retention times.[9d] Enantiomers of monoacetate **5ca** were separated by chiral HPLC employing a Chiralpak IA column (Daciel). Eluent: Hexane/2-Propanol 90:10. Flow: 1.00 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 7.6 min; R_2 (*R*,*R*) = 8.6 min. Analytical data of the product (*rac*-**5ca**) were identical with those reported in the literature.[20b] Analytical data for **7c**: ^{1}H NMR (200 MHz, CDCl3): δ/ppm = 8.04−7.98 (s, 1 H); 7.97−7.90 (d, *J* = 7.8 Hz; 1 H); 7.57−7.50 (d, *J* = 7.8 Hz; 1 H); 7.43−7.35 (t, *J* = 7.8 Hz; 1 H); 5.03−4.93 (m, 1 H); 3.96−3.86 (m, 1 H); 2.58−2.39 (s, 1 H); 1.96−1.85 (m, 2 H); 1.83−1.70 (m, 4 H); 1.66−1.51 (m, 4 H). ^{13}C NMR (50 MHz, CDCl3): δ/ppm = 165.7; 134.6; 133.1; 132.1; 129.7; 129.7; 127.8; 83.1; 75.9; 32.8; 30.4; 28.2; 23.0; 22.9. IR (KBr): ∼ν /cm^{-1} = 3494; 2934; 2854; 1701; 1572; 1340; 1324; 1290; 1258; 1140; 1036; 754; 741. HR-MS (ESI): *m*/*z* = 291.0760 [M + Na]$^+$ (calc. *m*/*z* = 291.0758). Anal. Calcd for $C_{14}H_{17}ClO_3$: C 62.52, H 6.38; found: C 62.57, H 6.38.

Data for the Preparative Kinetic Resolution of *rac*-4d with 1a. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with Hexane:EtOAc:Et_3N (3:7:0.01) afforded 30 mg (0.21 mmol, 41%, R_f = 0.26) of diol **4d**. Monoacetate **5da** and byproduct **7d** were separated by a further column chromatography (7:3 Hexane:EtOAc), resulting in 36 mg (0.20 mmol, 39%, R_f = 0.24) of monoacetate **5da** and byproduct **7d** 8 mg (0.02 mmol, 5%, R_f = 0.25). The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4d** (92% *ee*) and **5da** (81% *ee*) was determined by chiral GC analysis.

Enantiomers of diol **4d** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Machery Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 80−130 °C, 0.4 °C/min. Retention Times: R_1 (*S*,*S*) = 100.8 min; R_2 (*R*,*R*) = 102.9 min. Racemic **5da** was synthesized as described in the literature to proof retention times.[9d] Enantiomers of monoacetate **5da** were separated by chiral GC employing a 30 m FS-Hydrodex β-6TBDM column (Machery Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 80−130 °C, 0.4 °C/min. Retention Times: R_1 (*S*,*S*) = 93.8 min; R_2 (*R*,*R*) = 94.7 min. Analytical data of the product (*rac*-**5ca**) were identical with those reported in the literature.[20b,21] Analytical data for **7d** were identical with those reported in the literature.[22]

Data for the Preparative Kinetic Resolution of *rac*-4e with 1a. Enantiomeric excess for **5ea** (38% *ee*) and **4e** (75% *ee*) was determined without a further purification step. Enantiomers of diol **4e** were separated by chiral HPLC employing a Chiralpack IA column (Daciel) Eluent: Hexane/2-Propanol 95:5. Flow: 1 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 23.1 min; R_2 (*R*,*R*) = 26.7 min. Racemic **5ea** was synthesized as described in the literature to proof retention times.[23] Enantiomers of diol **5ea** were separated by chiral HPLC employing a Chiralpack IA column (Daciel). Eluent: Hexane/2-Propanol 90:10. Flow: 1 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 12.9 min; R_2 (*R*,*R*) = 9.5 min. Analytical data of the product (*rac*-**5ea**) were identical with those reported in the literature.[23]

Data for the Preparative Kinetic Resolution of *rac*-4f with 1a. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with Hexane:EtOAc:Et_3N (3:7:0.01) afforded 22 mg (0.19 mmol, 37%, R_f = 0.38) of diol **4f**, 34 mg (0.21 mmol, 43%, R_f = 0.64)

DOI: 10.1021/jo502670p
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of monoacetate **5fa**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4f** (73% *ee*) and **5fa** (73% *ee*) was determined by chiral GC analysis.

Enantiomers of diol **4f** were separated by chiral GC employing a 30 m FS-Hydrodex *β*-6-TBDM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−150 °C, 2 °C/min. Retention Times: R_1 (*S*,*S*) = 25.1 min; R_2 (*R*,*R*) = 24.7 min. Racemic **5fa** was synthesized as described in the literature to proof retention times.[13] Enantiomers of diol **5fa** were separated by chiral GC employing a 30 m FS-Hydrodex *β*-6-TBDM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−150 °C, 2 °C/min. Retention Times: R_1 (*S*,*S*) = 19.2 min; R_2 (*R*,*R*) = 22.5 min. Analytical data of the product (*rac*-**5fa**) were identical with those reported in the literature.[13]

Data for the Preparative Kinetic Resolution of *rac*-4g with 1a. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with hexane:EtOAc:Et_3N (2:1:0.01) afforded 29 mg (0.20 mmol, 40%, R_f = 0.34) of diol **4g**, 22 mg (0.12 mmol, 23%, R_f = 0.53) of monoacetate **5ga**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4g** (64% *ee*) and **5ga** (76% *ee*) was determined by chiral GC analysis.

Enantiomers of diol **4g** were separated by chiral GC employing a 30 m FS-Hydrodex *γ*-DIMOM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−150 °C, 2 °C/min. Retention Times: R_1 (*S*,*S*) = 15.6 min; R_2 (*R*,*R*) = 15.8 min. Racemic **5ga** was synthesized as described in the literature to proof retention times.[13] Enantiomers of diol **5ga** were separated by chiral GC employing a 30 m FS-Hydrodex *γ*-DIMOM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−150 °C, 2 °C/min. Retention Times: R_1 (*S*,*S*) = 17.0 min; R_2 (*R*,*R*) = 17.2 min. Analytical data of the product (*rac*-**5ga**) were identical with those reported in the literature.[13]

Description of the Preparative Experiments with *trans*-Cyclohexane-1,2-diol Using the Alcohols 1b−k (Scheme 3). The conditions for the kinetic resolutions of *trans*-cyclohexane-1,2-diol (*rac*-**4b**) with the alcohols **1b−1k** as acyl source are given exemplarily by the following experimental protocol. 1.0 mmol alcohol and multicatalyst **B** (23 mg, 25 *μ*mol, 2.5 mol %) were dissolved in 5 mL of toluene. Oxidizing agent, *m*-CPBA (430 mg, 2.0 mmol), was added at room temperature, and the reaction mixture was stirred for 15 h. After oxidation, the reaction was diluted with 200 mL of toluene and *N*,*N*′-diisopropylcarbodiimide (DIC, 310 *μ*L, 2 mmol) was added to generate the mixed anhydride. After 2 h reaction time, the reaction mixture was cooled to 0 °C and *rac*-**4b** (58 mg, 0.5 mmol) was added. The reaction mixture was quenched with 10 mL of methanol and then filtered through 60 g of silica gel washed with EtOAc to remove the catalyst. Purification methods were different for each synthesis and can be found in the corresponding paragraph (see below).

Data for the Preparative Kinetic Resolution of *rac*-4b with 1b. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 22 mg (0.19 mmol, 37%, R_f = 0.20) of diol **4b**. Monopropionate **5bb** and byproduct **7b** were separated by a further column chromatography (1:1 hexane:EtOAc), resulting in 26 mg (0.23 mmol, 45%, R_f = 0.25) of **5bb** and 6 mg (0.03 mmol, 5%, R_f = 0.36) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (91% *ee*) and **5bb** (82% *ee*) was determined by chiral GC analysis.

Racemic **5bb** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monopropionate **5bb** were separated by chiral GC employing a 30 m FS-Hydrodex *γ*-DiMOM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−240 °C, 10 °C/min. Retention Times: R_1 (*S*,*S*) = 36.7 min; R_2 (*R*,*R*) = 36.9 min. Analytical data of the product (*rac*-**5bb**) were identical with those reported in the literature.[24]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1c. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 23 mg (0.19 mmol, 38%, R_f = 0.20) of diol **4b**. Monoisobutyrate **5bc** and byproduct **7b** were separated by a further column chromatography (7:3 hexane:EtOAc), resulting in 33 mg (0.18 mmol, 35%, R_f = 0.28) of monoisobutyrate **5bc** and 9 mg (0.03 mmol, 7%, R_f = 0.36) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (87% *ee*) and **5bc** (74% *ee*) was determined by chiral GC analysis.

Racemic **5bc** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of diol **5bc** were separated by chiral GC employing a 30 m FS-Hydrodex *γ*-DiMOM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−240 °C, 10 °C/min. Retention Times: R_1 (*S*,*S*) = 37.1 min; R_2 (*R*,*R*) = 37.2 min. Analytical data of the monoacylated product (*rac*-**5bc**) were identical with those reported in the literature.[25]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1d. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 23 mg (0.19 mmol, 38%, R_f = 0.20) of diol **4b**. Monoisovalerate **5bd** and byproduct **7b** were separated by HPLC (Diol-Phase, 0.48 CV/min., 15% TBME, 85% hexane), resulting in 40 mg (0.20 mmol, 40%) of monoisovalerate **5bd** and 6 mg (0.02 mmol, 5%) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (87% *ee*) and **5bd** (79% *ee*) was determined by chiral CG/HPLC analysis.

Racemic **5bc** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monoprotected diol **5bd** were separated by chiral HPLC employing a Chiralpack IC column (Daicel). Eluent: Hexane/2-Propanol 90:10. Flow: 1 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 7.8 min; R_2 (*R*,*R*) = 8.4 min. Analytical data of the monoisovalerate (*rac*-**5bd**) were identical with those reported in the literature.[12b]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1e. Enantiomeric excess for **5be** (50% *ee*) and **4b** (31% *ee*) was determined without a further purification step. Enantiomers of monopivalate **5be** were separated by chiral GC employing a 30 m FS-Hydrodex *γ*-DiMOM column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100 °C, 30 min; 100−240 °C, 5 °C/min. Retention Times: R_1 (*S*,*S*) = 40.3 min; R_2 (*R*,*R*) = 40.4 min. Analytical data of the monoacylated product (*rac*-**5be**) were identical with those reported in the literature.[9b]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1f. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 20 mg (0.18 mmol, 35%, R_f = 0.20) of diol **4b**. Monocyclohexanecarboxylate **5bd** and byproduct **7b** were separated by HPLC (Diol-Phase, 0.48 CV/min., 15% TBME, 85% hexane), resulting in 46 mg (0.21 mmol, 41%) of monocyclohexanecarboxylate **5bf** and 7 mg (0.03 mmol, 5%) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (87% *ee*) and **5bf** (79% *ee*) was determined by chiral CG/HPLC analysis.

Racemic **5bf** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monoprotected diol **5bf** were separated by chiral HPLC employing a Chiralpack IC column

DOI: 10.1021/jo502670p
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(Daicel). Eluent: Hexane/2-Propanol 90:10. Flow: 1 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 9.2 min; R_2 (*R*,*R*) = 9.8 min. Analytical data of the monoisovalerate (*rac*-**5bf**) were identical with those reported in the literature.[12b]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1g. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 23 mg (0.20 mmol, 40%, R_f = 0.20) of diol **4b**. Monodecanoate **5bg** and byproduct **7b** were separated by a further column chromatography (7:3 hexane:EtOAc), resulting in 58 mg (0.23 mmol, 46%, R_f = 0.61) of monodecanoate **5bg** and 6 mg (0.02 mmol, 5%, R_f = 0.52) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (89% *ee*) and **5bg** (80% *ee*) was determined by chiral CG/HPLC analysis.

Racemic **5bg** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monoprotected diol **5bg** were separated by chiral HPLC employing a Chiralpack IC column (Daicel). Eluent: Hexane/2-Propanol 95:5. Flow: 1 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 12.8 min; R_2 (*R*,*R*) = 13.5 min. Analytical data of the monoisovalerate (*rac*-**5bd**) were identical with those reported in the literature.[12b]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1h. Enantiomeric excess for **5bh** (48% *ee*) and **4b** (30% *ee*) was determined without a further purification step. Racemic **5bh** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monoprotected diol **5bh** were separated by chiral GC employing a 30 m FS-Hydrodex β-TBDAc column (Macherey-Nagel). *T* (Injector + Detector) = 250 °C. Splitflow = 80 mL/min. Precolumn pressure = 0.8 bar. Conditions: 100−200 °C, 1.4 °C/min. Retention Times: R_1 (*S*,*S*) = 70.3 min; R_2 (*R*,*R*) = 70.5 min. Analytical data of the monoacylated product (*rac*-**5bh**) were identical with those reported in the literature.[26]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1i. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 22 mg (0.19 mmol, 38%, R_f = 0.20) of diol **4b**. Monophenylacetate **5bi** and byproduct **7b** were separated by HPLC (Chiralpak IB, 0.24 CV/min., 10% Isopropanol, 90% hexane), resulting in 54 mg (0.20 mmol, 40%) of monophenylacetate **5bi** and 5 mg (0.02 mmol, 4%) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (84% *ee*) and **5bi** (67% *ee*) was determined by chiral HPLC/GC analysis.

Racemic **5bi** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monoprotected diol **5bi** were separated by chiral HPLC employing a Chiralpack IB column (Daicel). Eluent: Hexane/2-Propanol 90:10. Flow: 0.7 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 14.0 min; R_2 (*R*,*R*) = 10.7 min. Analytical data of the monoacylated product (*rac*-**5bi**) were identical with those reported in the literature.[12b]

Data for the Preparative Kinetic Resolution of *rac*-4b with 1k. After the filtration, the solvents were removed under reduced pressure. The residue was with cold CH_2Cl_2 suspended and filtrated to remove insoluble 3-chlorobenzoic acid. CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with EtOAc and 0.1% Et_3N afforded 22 mg (0.19 mmol, 37%, R_f = 0.20) of diol **4b**. Monophenylpropionate **5bk** and byproduct **7b** were separated by a further column chromatography (7:3 hexane:EtOAc), resulting in 57 mg (0.23 mmol, 46%, R_f = 0.27) of monophenylpropionate **5bi** and 5 mg (0.02 mmol, 5%, R_f = 0.37) of byproduct **7b**. The isolated compounds were then directly characterized by NMR, and the enantiomeric excess for **4b** (91% *ee*) and **5bk** (60% *ee*) was determined by chiral HPLC/GC analysis.

Racemic **5bk** was synthesized as described in the literature to proof retention times.[12b] Enantiomers of monoprotected diol **5bk** were separated by chiral HPLC employing a Chiralpack IB column (Daicel). Eluent: Hexane/2-Propanol 90:10. Flow: 0.7 mL/min. UV-detector λ = 220 nm and refractometer. Retention Times: R_1 (*S*,*S*) = 11.1 min; R_2 (*R*,*R*) = 9.4 min. Analytical data of the monoisovalerate (*rac*-**5bk**) were identical with those reported in the literature.[12b]

Identification of 3-Chlorobenzoic Propionic Anhydride and Propionic Anhydride by NMR. Propionic acid (7.4 μL, 0.1 mmol) and 3-chlorobenzoic acid (31.3 mg, 0.2 mmol) were dissolved in 5 mL of toluene-d_8, and *N*,*N*′-diisopropylcarbodiimide (DIC, 31.0 μL, 0.2 mmol) was added to generate the mixed anhydride. After 2 h at room temperature, 0.7 mL was filtered into a NMR tube and subjected to ^{1}H and ^{13}C NMR spectroscopy. NMR data: see the Supporting Information.

Description of the Experiments Synthesizing Symmetric Esters 6g and 6k. 2.0 mmol alcohol and 2.5 mol % TEMPO (7.8 mg, 5 μmol) were dissolved in 5 mL of CH_2Cl_2. Oxidizing agent, *m*-CPBA (430 mg, 2.0 mmol), was added at room temperature, and the reaction mixture was stirred for 15 h. After oxidation, *N*,*N*′-diisopropylcarbodiimide (DIC, 310 μL, 2 mmol) was added to generate the mixed anhydride. After 2 h reaction time, 4-dimethylaminopyridine (6.1 mg, 2.5 mol %, 5 μmol) was added and the reaction mixture was stirred for 18 h at room temperature. The reaction mixture was washed three times with saturated $NaHCO_3$ solution, with water and brine, and the organic phase was dried over $MgSO_4$.

Purification of **6g**: CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with 9:1 cyclohexane:EtOAc afforded 185 mg (0.59 mmol, 59%, R_f = 0.70) of dimer **6g**. Analytical data of the product (**6g**) were identical with those reported in the literature.[18]

Purification of **6k**: CH_2Cl_2 was removed, and the crude product was purified by silica gel column chromatography. Eluting with 97:3 hexane:EtOAc afforded 180 mg (0.67 mmol, 67%, R_f = 0.38) of dimer **6k**. Analytical data of the product (**6k**) were identical with those reported in the literature.[18]

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Dr. Erwin Röcker and Anika Bernhardt for excellent analytical support, and the COST − ORCA action (CM0905) and the Liebig-College for creating networking and exchange opportunities. Stimulating discussions with Prof. Michael Harmata (Univ. of Missouri at Columbia) are gratefully acknowledged.

■ REFERENCES

(1) Meijere, A. d.; Diederich, F. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2004.

(2) (a) Wang, Q.; Zheng, H.; Chai, W.; Chen, D.; Zeng, X.; Fu, R.; Yuan, R. *Org. Biomol. Chem.* **2014**, *12*, 6549. (b) Vorogushin, A. V.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 8146. (c) Rout, S. K.; Guin, S.; Ghara, K. K.; Banerjee, A.; Patel, B. K. *Org. Lett.* **2012**, *14*, 3982. (d) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (e) Lee, C.-F.; Liu, Y.-C.; Badsara, S. S. *Chem.—Asian J.* **2014**, *9*, 706. (f) Bariwal, J.; Van der Eycken, E. *Chem. Soc. Rev.* **2013**, *42*, 9283.

(3) (a) Zhang, G.; Ma, Y.; Wang, S.; Kong, W.; Wang, R. *Chem. Sci.* **2013**, *4*, 2645. (b) Wu, H.; He, Y.-P.; Xu, L.; Zhang, D.-Y.; Gong, L.-Z.

DOI: 10.1021/jo502670p
J. Org. Chem. 2015, 80, 1972−1978

Angew. Chem., Int. Ed. **2014**, *53*, 3466. (c) Tan, B.; Toda, N.; Barbas, C. F., III *Angew. Chem., Int. Ed.* **2012**, *51*, 12538. (d) Song, X.; Song, A.; Zhang, F.; Li, H.-X.; Wang, W. *Nat. Commun.* **2011**, *2*, 524. (e) Padmanaban, M.; Biju, A. T.; Glorius, F. *Org. Lett.* **2010**, *13*, 98. (f) Northrup, A. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 6798. (g) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.; Kwong, F. Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 16737. (h) He, L.; Guo, H.; Li, Y.-Z.; Du, G.-F.; Dai, B. *Chem. Commun.* **2014**, *50*, 3719.

(4) (a) Xu, B.; Madix, R. J.; Friend, C. M. *J. Am. Chem. Soc.* **2010**, *132*, 16571. (b) Wang, L.; Li, J.; Dai, W.; Lv, Y.; Zhang, Y.; Gao, S. *Green Chem.* **2014**, *16*, 2164. (c) Powell, A. B.; Stahl, S. S. *Org. Lett.* **2013**, *15*, 5072. (d) Jagadeesh, R. V.; Junge, H.; Pohl, M.-M.; Radnik, J.; Brückner, A.; Beller, M. *J. Am. Chem. Soc.* **2013**, *135*, 10776.

(5) Yamamoto, N.; Obora, Y.; Ishii, Y. *J. Org. Chem.* **2011**, *76*, 2937.

(6) Mori, N.; Togo, H. *Tetrahedron* **2005**, *61*, 5915.

(7) Dohi, T.; Fukushima, K.-i.; Kamitanaka, T.; Morimoto, K.; Takenaga, N.; Kita, Y. *Green Chem.* **2012**, *14*, 1493.

(8) (a) Maki, B. E.; Chan, A.; Phillips, E. M.; Scheidt, K. A. *Tetrahedron* **2009**, *65*, 3102. (b) Maki, B. E.; Chan, A.; Phillips, E. M.; Scheidt, K. A. *Org. Lett.* **2007**, *9*, 371.

(9) (a) Müller, C. E.; Zell, D.; Hrdina, R.; Wende, R. C.; Wanka, L.; Schuler, S. M. M.; Schreiner, P. R. *J. Org. Chem.* **2013**, *78*, 8465. (b) Hrdina, R.; Müller, C. E.; Schreiner, P. R. *Chem. Commun.* **2010**, *46*, 2689. (c) Müller, C. E.; Zell, D.; Schreiner, P. R. *Chem.—Eur. J.* **2009**, *15*, 9647. (d) Müller, C. E.; Wanka, L.; Jewell, K.; Schreiner, P. R. *Angew. Chem., Int. Ed.* **2008**, *47*, 6180.

(10) Davie, E. A. C.; Mennen, S. M.; Xu, Y.; Miller, S. J. *Chem. Rev.* **2007**, *107*, 5759.

(11) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.

(12) (a) Müller, C. E.; Hrdina, R.; Wende, R. C.; Schreiner, P. R. *Chem.—Eur. J.* **2011**, *17*, 6309. (b) Hofmann, C.; Schuler, S. M. M.; Wende, R. C.; Schreiner, P. R. *Chem. Commun.* **2014**, *50*, 1221.

(13) Hrdina, R.; Müller, C. E.; Wende, R. C.; Wanka, L.; Schreiner, P. R. *Chem. Commun.* **2012**, *48*, 2498.

(14) Toledo, H.; Pisarevsky, E.; Abramovich, A.; Szpilman, A. M. *Chem. Commun.* **2013**, *49*, 4367.

(15) (a) Suzuki, K.; Yamaguchi, T.; Matsushita, K.; Iitsuka, C.; Miura, J.; Akaogi, T.; Ishida, H. *ACS Catal.* **2013**, *3*, 1845. (b) Dhimitruka, I.; SantaLucia, J. *Org. Lett.* **2005**, *8*, 47. (c) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989.

(16) (a) Ogata, Y.; Sawaki, Y. *Tetrahedron* **1967**, *23*, 3327. (b) Herbst, R. M.; Wilson, K. R. *J. Org. Chem.* **1957**, *22*, 1142.

(17) (a) Jarvo, E. R.; Copeland, G. T.; Papaioannou, N.; Bonitatebus, P. J.; Miller, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 11638. (b) Jarvo, E. R.; Miller, S. J. *Tetrahedron* **2002**, *58*, 2481.

(18) Abramovich, A.; Toledo, H.; Pisarevsky, E.; Szpilman, A. M. *Synlett* **2012**, *23*, 2261.

(19) Autorenkollektiv; *Organikum: Organisch-chemisches Grundpraktikum*, 19th ed.; Deutscher Verlag der Wissenschaften: Leipzig, Germany, 1993.

(20) (a) Fang, C.; Ogawa, T.; Suemune, H.; Sakai, K. *Tetrahedron: Asymmetry* **1991**, *2*, 389. (b) Bódai, V.; Orovecz, O.; Szakács, G.; Novák, L.; Poppe, L. *Tetrahedron: Asymmetry* **2003**, *14*, 2605. (c) Sevin, A.; Cense, J.-M. *Bull. Soc. Chim. Fr.* **1974**, 918.

(21) Posner, G. H.; Rogers, D. Z. *J. Am. Chem. Soc.* **1977**, *99*, 8208.

(22) Muramatsu, W.; William, J. M.; Onomura, O. *J. Org. Chem.* **2011**, *77*, 754.

(23) (a) Wallace, T. W.; Wardell, I.; Li, K.-D.; Leeming, P.; Redhouse, A. D.; Challand, S. R. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2293. (b) Oikawa, M.; Wada, A.; Okazaki, F.; Kusumoto, S. *J. Org. Chem.* **1996**, *61*, 4469. (c) Brugidou, J.; Christol, H.; Sales, R. *Bull. Soc. Chim. Fr.* **1974**, 2027.

(24) Iranpoor, N.; Firouzabadi, H.; Safavi, A.; Shekarriz, M. *Synth. Commun.* **2002**, *32*, 2287.

(25) Kawabata, T.; Nagato, M.; Takasu, K.; Fuji, K. *J. Am. Chem. Soc.* **1997**, *119*, 3169.

(26) Matsumura, Y.; Maki, T.; Murakami, S.; Onomura, O. *J. Am. Chem. Soc.* **2003**, *125*, 2052.

DOI: 10.1021/jo502670p
J. Org. Chem. 2015, 80, 1972−1978