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A Multicatalyst System for the One-Pot Desymmetrization/Oxidation of *meso*-1,2-Alkane Diols

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Stereoselective, homogeneously catalyzed cascade reactions are a key step toward resource-efficient transformations at the forefront of synthetic chemistry;[1–4] these types of reactions are well known and are labeled as domino, tandem, cascade, or zipper transformations.[2–4] Arguably, all catalyzed reactions to date can be classified with the principles 1–4 (Figure 1), but we are unaware of a concept that

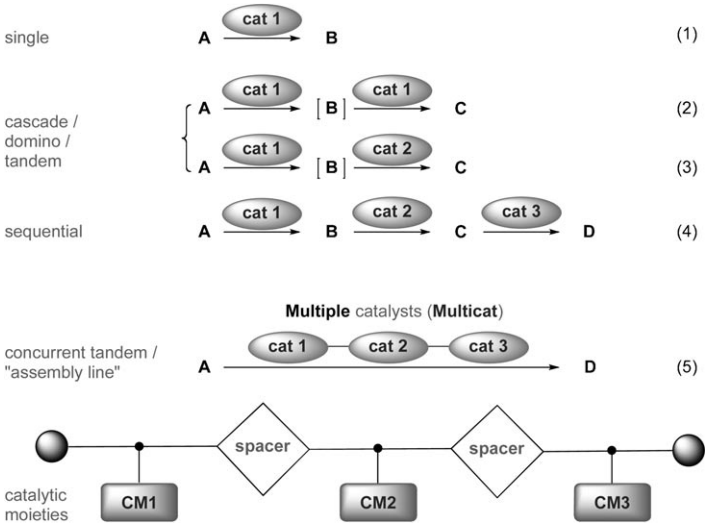

Figure 1. Prevalent catalytic principle reactions 1–4. Simplified depiction of the multicatalysis concept (reaction 5).

utilizes a multicatalyst system (principle 5), in which a variety of organocatalytic moieties is strung together on an arbitrary backbone. This concept is reminiscent of an assembly line, in which each interconnected station performs a particular function and only their proper sequence gives the desired product. It is also akin to many biological processes such as the protein biosynthesis.

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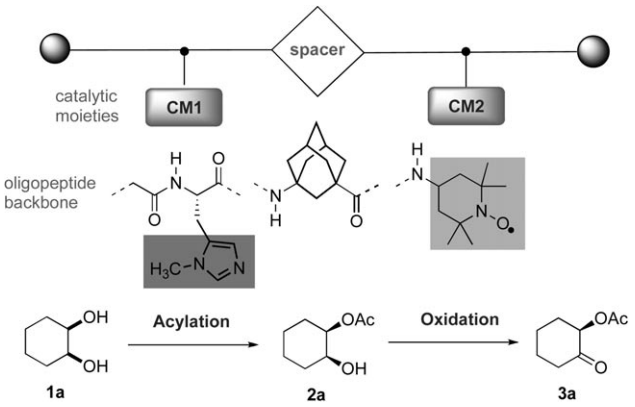
There are several (organo)catalytic approaches following principle 2 (Figure 1) by using a single catalyst and the same activation mode for each catalytic cycle.[1–4] Organocatalytic[3–6] as well as combined metal and organocatalytic (3, Figure 1)[4–7] cascade reactions are of contemporary interest. To the best of our knowledge there is only one example for a homogeneous (5, Figure 1) reaction using an achiral heterodimetallic catalyst.[8]

Here we present the first approach of an organocatalytic enantioselective concurrent tandem[1] ("assembly line") reaction by utilizing a multicatalyst with orthogonal (i.e., independent) catalytic moieties (CMs). Some of the obvious challenges with this concept are a) the selection of a proper backbone that is modular and compatible with all reaction conditions; b) compartmentalization of the catalytic moieties so that they do not interfere with each other (i.e., design of a spacer (Figure 1); c) the activities of the individual catalytic moieties (CMs) must be retained; d) the solubility of the multicatalyst in all the solvents required for the entire sequence; and e) the ease of preparation of the multicatalysts, ideally by automated synthesis. A far-fetched but not unreasonable goal would be the use of a library of CMs that can be assembled to serve the purpose of synthesizing a complex organic molecule in one pot by a programmed series of catalyzed reactions utilizing a retrosynthetic algorithm.

It is clear that our one-pot multicatalyst approach has some operational advantages (e.g., decreases solvent use, time, and enables a simpler workup) that become apparent as the number of catalyzed steps increases. The present work provides proof-of-principle studies of a new concept in catalysis.

The challenges in a) and e) can be addressed by selecting, for example, an oligopeptide backbone that can be assembled readily. Oligopeptides with a secondary structure have shown to be highly versatile for the transfer of electrophiles to alcohols.[9] For the compartmentalization of the catalytic sites we chose a lipophilic admantane γ-amino acid (^{A}Gly in our shorthand notation),[10] which also enables the catalyst solubility in a broad variety of solvents. Such oligopeptides without apparent secondary structures[11] have proven to be particularly effective in stereoselective acyl-transfer reactions,[5,12] thus we have selected this type of catalyst for the present study.

We chose the enantioselective, catalytic acetylation and subsequent catalytic oxidation of *meso*-1,2-cycloalkane diol

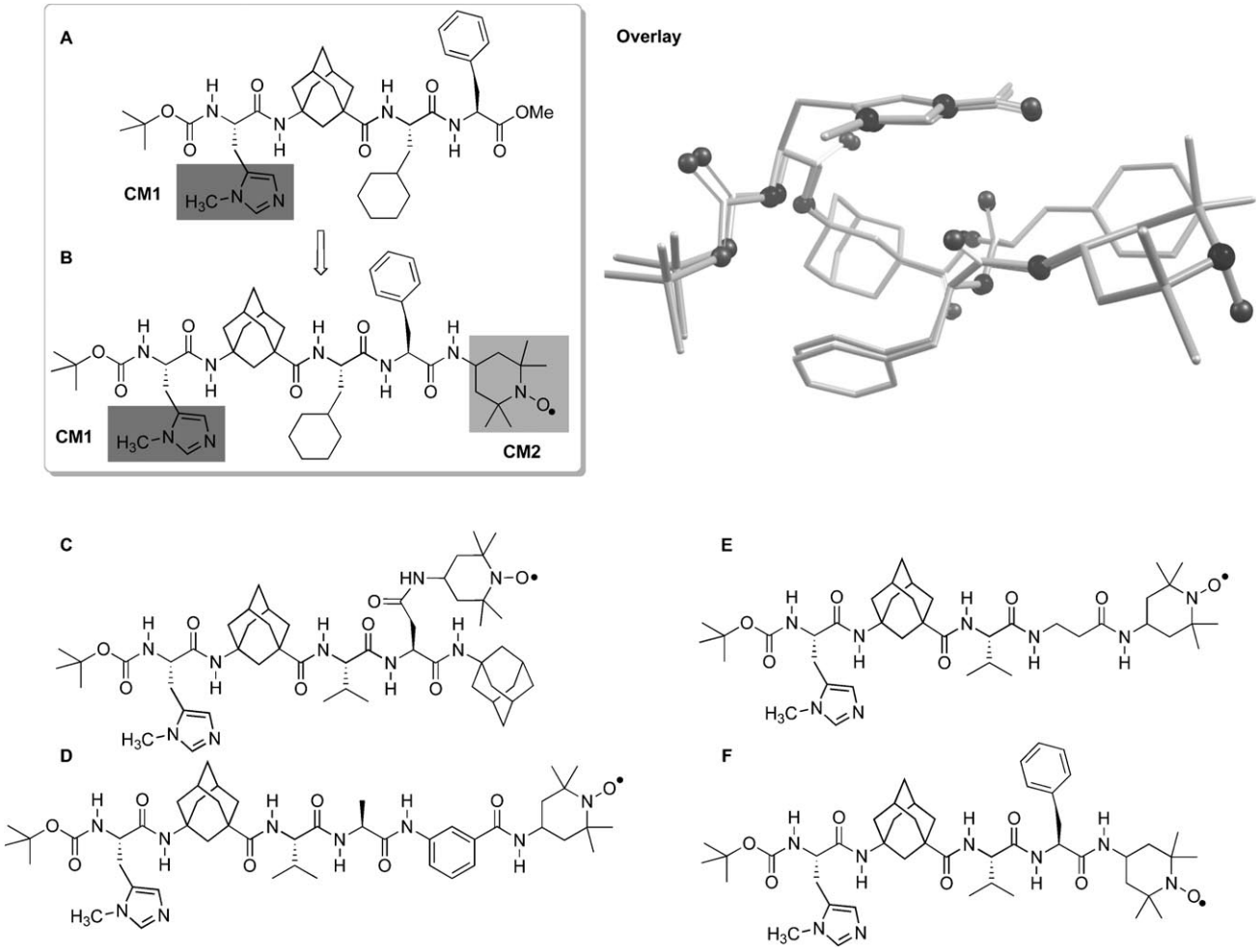


Scheme 1. Modular approach to build a multicatalyst in the organocatalytic sequence of **1a** to **3a**.

1a as the test reaction (Scheme 1) because these two processes can be conducted in a one-pot approach by using two separate catalysts with good *ee* values and good overall yields (Scheme 1).[5] Here we will demonstrate not only that the two active catalysts (a π-Me-histidine residue on the oligopeptide and 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO) as the oxidizer) are still active and perform their independent functions when placed into one catalyst structure, but also that the oxidation step occurs under milder conditions than in the separate protocols. Whereas the operational advantages for the present reaction sequence are minor, our emphasis here is on the viability of this approach.

There are only a few enzymatic and chemical approaches using stereoselective acetyl transfer for the desymmetrization of, for example, **1a**.[13,14] The desymmetrization of *meso*-1,2-diols utilizing acetyl transfer is generally difficult, owing to facile intramolecular acetyl group migration of the monoprotected product **2**,[5,14,15] therefore immediate oxidation of the second OH group is an effective way to suppress racemization.[5] The obtained acylated α-acetoxy ketones (**3**, acetoins) are valuable chiral building blocks for which there are only a few selective syntheses (especially for cyclic ones).[5,16,17]

As we already had a very active acylation platform at hand (**A**, Scheme 2),[5,12] we first focused our attention to attaching a terminal TEMPO moiety to the oligopeptide back-

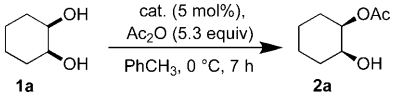


Scheme 2. Peptide-based multicatalysts and the schematic overlay of catalysts **A** and **B**.

bone (catalyst **B**, Scheme 2). This represents a logical extension of acylation catalyst **A** and is a test of the degree of the required orthogonality of the reactivity of the individual CMs.[5,12] Our initial proposal for **B** was to replace only the methyl ester group of catalyst **A** with the TEMPO-amide functionality, which would retain the selectivity of **A** in the acylative desymmetrization of **1a**, then to use the TEMPO moiety for the subsequent oxidation of intermediate **2a** (Scheme 1). A molecular force-field analysis of the acylated catalysts **A** and **B** reveals that the overall catalyst structures are very similar (see the overlay of the two structures in Scheme 2, top right) so that the acylation should not be affected negatively by the addition of the TEMPO moiety; both CMs are spatially well-separated.

Additionally, we varied the acylation–oxidation multicatalysis platform with respect to lipophilicity and the position of the TEMPO moiety (catalysts **C**–**F**). To check whether **B**–**F** indeed display the desired activity, we first examined their efficacy in the acylative desymmetrization of **1a** to **2a** (Table 1).

Table 1. Desymmetrization of *meso*-diol **1a** with catalysts **B**–**F**.



1a **2a**

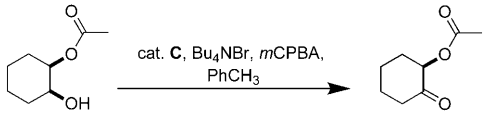
Entry	cat.	Yield **2a** [%][a,b]	e.r.[b] **2a**
1	**B**	76.5	88:12
2	**C**	54.6	74:26
3	**D**	20.3	49:51
4	**E**	49.6	67:33
5	**F**	50.5	69:31

[a] All reactions were performed with 0.03 mmol of substrate and were quenched with MeOH after the reaction. Without a catalyst, no conversion was observed. [b] Yields and enantiomer ratios were determined by GC analysis. See the Supporting Information for details.

We were pleased to observe that the (π-Me)-His moiety was active in the presence of the TEMPO moiety in all cases. Indeed, the best results were obtained for peptide **B** (88:12 e.r.) whose acylation CM in form of catalyst **A** was optimized earlier.[5,12] While **C** provided similar enantioselectivities, peptides **D**–**F** proved to be less effective. This important finding emphasizes that active CMs for one catalytic reaction can be transferred into a multicatalyst by combining them with other CMs without significant change, if any, in the individual CM selectivities.

With the good yields and selectivities for **B** in hand we investigated the TEMPO-moiety-catalyzed oxidation. We chose the oxidation of racemic **2a** in toluene (often the solvent of choice for peptide catalyzed selective acylations)[9] as the test reaction utilizing a variety of known TEMPO-catalyzed oxidation protocols.[18,19] Only the TEMPO/tetrabutyl ammonium bromide/*m*CPBA protocol led to significant conversions at room temperature. Our results and optimization studies with catalyst **C** (to demonstrate generality) in place of TEMPO are summarized in Table 2. Full conversions

Table 2. Optimization of the oxidation of **2a** with peptide catalyst **C**.



2a **3a**

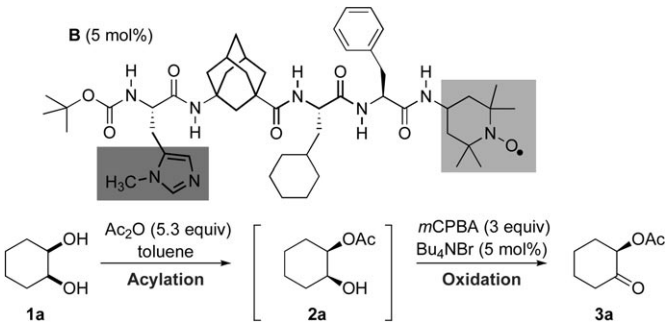
Entry	**C** [mol%]	*m*CPBA [equiv]	Bu_4NBr [mol%]	*T* [°C]	*t*[h]	Yield [%][a]
1	10	3	10	RT	1	73.8
2	10	3	10	RT	3	70.8
3	0	3	10	RT	4	0
4	5	3	5	RT	1	48.7
5	5	3	5	RT	3	21.2
6	5	1.5	5	RT	1	65.5
7	5	1.5	5	RT	3	65.0
8	5	1	5	RT	1	55.1
9	5	1	5	RT	3	58.9
10	5	3	5	−20	1	52.9
11	5	3	5	−20	3	88.7
12	5	3	5	0	1	>99
13	5	3	0	0	1	25.4
15	0	3	5	0	1	0
16	5	1.5	5	0	1	86.8
17	5	1.5	5	0	3	94.2
18	3.5	3	3.5	0	1	89.3
19	3.5	3	3.5	0	3	95.8
20	2	3	2	0	1	40.3
21	2	3	2	0	3	55.9
22	1	3	1	0	1	9.7
23	1	3	1	0	3	10.1
24[b]	5	3	5	0	1	63.1
25[b]	5	3	5	0	3	>99
26[c]	5	3	5	0	1	7.8
27[c]	5	3	5	0	3	20.4

[a] All reactions were performed with 0.03 mmol of substrate. Yields were determined by GC analysis. [b] TEMPO was used as the catalyst. [c] TEMPO amine was used as the catalyst; see the Supporting Information for details.

could be obtained with **C** (5 mol%), *m*CPBA (3 equiv), and Bu_4NBr (5 mol%) at 0°C (Table 2, entry 12) in a fast reaction (1 h), a condition necessary to avoid racemization of **2a**. Decreasing the amount of *m*CPBA also suppressed the undesired Baeyer–Villiger oxidation of **3a**; without **C** no reaction takes place (Table 2, entries 3 and 15). The enanatiomeric ratio (e.r.) values of the product were determined for all peptide-**C**-catalyzed oxidations of Table 2; only marginal selectivities were observed (the same is true for catalyst **B**). More importantly, **B** and **C** are *more* active than TEMPO (Table 2, entry 24), whose yield was only 63.1% after 1 h using the same conditions as for entry 12. TEMPO amine (the precursor for the synthesis of the TEMPO peptides) only gave the product in 7.8% yield after 1 h (Table 2, entry 26). That is, although the short peptide is not capable of an enantioselective oxidation, it does aid in the oxidation step, most likely through a binding event and a resulting proximity effect as suggested for the preceding acylation step.[11]

Multicatalysts **B** and **C** were then employed for a one-pot acylation/oxidation reaction sequence employing acetic anhydride in toluene, followed by addition of *meta*-chloroperbenzoic acid (*m*CPBA) and Bu_4NBr (results shown for **B** in

Table 3. Desymmetrization of *meso*-diol **1a** and subsequent oxidation of **2a** to **3a** with catalyst **B** at various temperatures.



		Acylation			Oxidation	
T [°C]	t [h]	Conversion [%][a,c]	Yield **2a** [%][a,c]	e.r.[b] **2a**	Conversion to **3a** [%][a,c]	e.r.[b] **3a**
RT	6	89.1	70.6	85:15	51.6	84:16
10	6	80.6	72.1	87:13	91.0	87:13
0	7	87.1	76.5	88:12	>99	88:12
−10	22	87.5	67.7	83:17	>99	84:16
−20	20	77.2	67.1	80:20	57.2	82:18
−20	20	79.5[d]	69.0[d]	80:20[d]	77.1[d]	79:21[d]

[a] All reactions were performed with 0.03 mmol of substrate. [b] Enantiomeric ratios were determined by chiral GC analysis. [c] Conversions and yields were determined by GC analysis. [d] 10 mol% of catalyst **B** was used; see Supporting Information for details.

Table 3). The best results were achieved with **B**, which gave a one-pot synthesis of **3a** from **1a** in 76% overall yield and with an e.r. of 88:12 at 0°C. The often employed use of an amine as a base did not markedly improve the selectivity of the desymmetrization at 0°C[5] but instead hampered the oxidation step.

Although catalysts **D**–**F** are somewhat less selective in the desymmetrization of **1a** we decided to compare all catalysts in the concurrent tandem reaction using the optimized conditions of Table 3. The tested multicatalysts not only differ in their activities and selectivities in the desymmetrization step, they also behave differently in the oxidation. Whereas the more lipophilic catalysts **B**, **C**, and **F** were active in the oxidation of **2a**, **D** and **E** proved to be much less effective (Table 4). The peptide sequence and structure clearly affects the ability of the TEMPO moiety in the oxidation step.

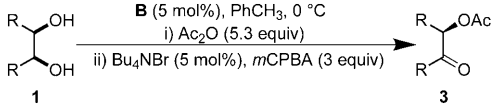
Table 4. Desymmetrization of *meso*-diol **1a** and subsequent oxidation of **2a** to **3a** with catalysts **B**–**F**. Conditions are the same as in Table 3; T = 0°C.

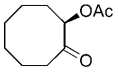
		Acylation			Oxidation	
Cat.	t [h]	Conversion [%][a,c]	Yield **2a** [%][a,c]	e.r.[b] **2a**	Conversion of **2a** to **3a** [%][a,c]	e.r.[b] **3a**
B	7	87.1	76.5	88:12	>99	88:12
C	22	89.4	63.5	74:26	96	74:26
D	25	50.7	43.7	48:52	31	47:53
E	23	87.1	65.5	65:35	65	67:13
F	23	84.9	59.3	66:34	94	66:34

[a] All reactions were performed with 0.03 mmol of substrate. [b] Enantiomeric ratios were determined by chiral GC analysis. [c] Conversions and yields were determined by GC analysis. See the Supporting Information for details.

Our multicatalyst acylation/oxidation protocol is also applicable to other vicinal *meso*-diols (Table 5). The yields and selectivities are generally good; the best result could be obtained for *cis*-cyclooctane-1,2-diol **1c** (e.r. 91:9, 83% isolated product yield). The slightly lower yields for **3b** and **3d** are due to a fast Baeyer–Villiger oxidation of the products (Table 5).

Table 5. Concurrent tandem desymmetrization/oxidation of *meso*-diols **1** under optimized conditions with multicatalyst **B**.



	Product[c]	t [h] desym.	t [h] ox.	Yield **3** [%][a]	e.r.[b] **3**
3b		2	0.5	60	87:13
3a		6	1	70	88:12
3c		3	1	83	91:9
3d		5	0.5	49	83:17

[a] All reactions were performed in toluene with 0.5 mmol of **1**; there is no conversion without catalyst. The yields are the isolated product yields of the purified products. [b] Enantiomeric ratios were determined by chiral GC analysis; see the Supporting Information for details. [c] The absolute configurations of enantiomerically pure (+)-**3a** and (−)-**3b** obtained with **B** is *R* in both cases, as determined by comparison with literature data;[17] this gives 1-acetoxy-2-hydroxycyclohexane **2a** and 1-acetoxy-2-hydroxycyclopentane **2b** as (1*R*,2*S*).

In our proof-of-principle studies, we have identified the first organocatalytic multicatalyst reaction by utilizing a short oligopeptide with two orthogonal catalytic moieties (CMs). This one-pot reaction sequence results in enantioenriched products in good overall yields. Remarkably, the incorporation of a TEMPO moiety in an oligopeptide sequence increases the oxidation activity compared to using TEMPO itself, either in the same sequence of reactions or in a separate reaction. Multicatalyst **B** is the logical advancement of acylation peptide **A**,[5,12] which emphasizes the modular nature of the CMs.

The C-terminal exchange of the methyl ester by the TEMPO amide has only very little effect on the selectivity of the desymmetrization reaction. This observed orthogonality in reactivity is probably achieved through the lipophilic, bulky, and inert ^{A}Gly spacer, which keeps the CMs apart and prevents the formation of a secondary structure.[11] The next step is to expand on the number of catalytic steps in complex reaction sequences to develop one-pot, multicatalyst synthetic protocols that give valuable, enantiomerically enriched functional organic molecules from simple precursors.

Experimental Section

General: Catalysts **A**–**F** were synthesized in solution using a Boc-protection strategy and EDC/HOBt couplings. The generalized peptide synthesis for **B** is given below. For ^{1}H NMR (400 MHz, $CDCl_3$): see the Supporting Information; the NMR signals are broad because of the unpaired electron on TEMPO.

Procedure for EDC/HOBt coupling in solution: An equimolar ratio of the *N*-Boc-protected amino acid and the peptide fragment, EDC (1.1 equiv) and HOBt (1.1 equiv) were dissolved in dry dichloromethane. Then, triethylamine (2.2 equiv) was added and the solution was stirred overnight. To the reaction mixture was then added ethyl acetate (200 mL) and then the solution was extracted with citric acid solution (0.5 M, 4×25 mL), saturated $NaHCO_3$ solution (4×25 mL), water (3×25 mL), and brine (2×25 mL). The organic phase was dried over Na_2SO_4 and filtered and the solvent was evaporated to give the product. The same strategy was used for the esterification of Boc-L-Phe-OH (1.33 g, 5 mmol) with benzyl alcohol to prepare Boc-L-Phe-OBzl. The Boc-L-(π-Me)-His-OH couplings were performed using an equimolar ratio of Boc-L-(π-Me)-His-OH and NH_3Cl-^{A}Gly-L-Cha-L-Phe-OBzl, EDC (2.2 equiv), HOBt (2.2 equiv), and Et_3N (4.4 equiv) in dry dichloromethane overnight. All peptide fragments were used in the next coupling step without further purification.

Cleavage of the Boc-protecting group: The peptide was dissolved in a solution of HCl (4 N) in 1,4-dioxane (10 mL) and stirred for 45 min. Excess HCl was removed by flushing the reaction mixture with argon for 45 min. After evaporation of the solvent in vacuo the deprotected peptides were used for peptide coupling without purification.

After the last coupling step, the crude peptide was purified by column chromatography (eluting with $CHCl_3$/MeOH 9:1) to afford 1.51 g (1.8 mmol, 36%) of colorless tetrapeptide Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OBzl (R_f = 0.33).

Reductive benzyl ester-deprotection: The deprotection of the benzyl ester Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OH (0.5 mmol, 418.6 mg) was performed by using 10% Pd/C (73.6 mg) in MeOH under hydrogen atmosphere. The crude product was purified by column chromatography (eluting with CH_2Cl_2/MeOH 8:2) to afford 226.5 mg (0.3 mmol, 61%) of colorless tetrapeptide Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OH (R_f = 0.3).

Coupling of TEMPO amine with Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OH: An equimolar ratio of Boc-L-(π-Me)-His-^{A}Gly-L-Cha-L-Phe-OH (186.7 mg, 0.25 mmol) and TEMPO amine (42.8 mg, 0.25 mmol), EDC (2.2 equiv), HOBt (2.2 equiv) and *N*,*N*-diisopropylethylamine, (DiPEA, 4.4 equiv) in dry dichloromethane was stirred overnight. The reaction mixture was added to ethyl acetate (200 mL) and extracted with water (3×50 mL) and brine (2×25 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent evaporated. The crude product was then purified by column chromatography (eluting with CH_2Cl_2/MeOH 8:2) to afford 156.5 mg (0.17 mmol, 70%) of a slightly orange product (R_f = 0.82). The peptide was characterized by ESI-MS, HR-ESI-MS, NMR, IR, EPR, EA and by its specific optical rotation. $[\alpha]_D^{28} = -23.4°$ (c = 0.647 g 100 mL^{-1}; $CHCl_3$). For ^{1}H NMR see the Supporting Information.^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.2 (C=O); 170.7 (C=O); 168.8 (C=O); 168.6 (C=O); 154.4 (C=O); 137.4, 135.3, 128.1, 127.5, 127.3, 126.0, 125.9, 79.3, 53.4, 50.9, 41.2, 39.2, 39.1, 37.8, 37.3, 37.0, 36.2, 33.9, 33.1, 32.3, 31.2, 27.7, 27.2, 26.3, 25.1, 25.0, 24.8 ppm. IR (KBr): $\tilde{\nu}$ = 3309, 3063, 2975, 2923, 2853, 1654, 1510, 1454, 1392, 1366, 1280, 1243, 1168 cm^{-1}; MS: (ESI): m/z: calcd for: 900.6 $[M+H]^+$; found: 900.7; 922.6 $[M+Na]^+$; found: 922.5; 938.5 $[M+K]^+$; found: 938.5; 1822.1 $[2M+Na]^+$; found: 1822.3; HR-ESI: m/z: calcd for: 900.5832 $[M+H]^+$; found 900.5833.

The conditions for the desymmetrization and direct one-pot oxidation of the non-acylated OH group are given exemplarily: catalyst **B** (22.5 mg, 0.025 mmol, 5 mol%) and diol **1a** (58.1 mg, 0.5 mmol) were dissolved in dry toluene (90 mL) under an argon atmosphere. The reaction mixture was cooled to 0°C and Ac_2O (250 μL, 2.65 mmol, 5.3 equiv) was added and the mixture was stirred for 6 h. For the oxidation of the non-acylated OH group, Bu_4NBr (8.1 mg, 0.025 mmol, 5 mol%) and *m*CPBA (70%, 370 mg, 1.5 mmol, 3 equiv) were added and the reaction mixture was stirred at 0°C for 1 h and then filtered using silica gel (25 g) suspended with EtOAc to remove the catalyst. The organic solution was washed four times with $NaHCO_3$ (8%, 25 mL). The aqueous phases were extracted twice with ethyl acetate (30 mL) and the combined organic phases were washed three times with water (30 mL) and twice with brine (30 mL). After drying over Na_2SO_4 and filtering off the drying reagent the solvents were removed in vacuo. The crude product was purified by silica gel column chromatography. Eluting with EtOAc/hexane (1:1) afforded 54.7 mg (0.35 mmol, 70.0%) of colorless α-acetoxy ketone **3a** (R_f = 0.31). The product was characterized by NMR and chiral GC analyses.

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Keywords: alcohols · desymmetrization · one-pot synthesis · organocatalysis · peptides

[1] J.-C. Wasilke, S. J. Obrey, R. T. Baker, G. C. Bazan, *Chem. Rev.* **2005**, *105*, 1001–1020.
[2] D. E. Fogg, E. N. dos Santos, *Coord. Chem. Rev.* **2004**, *248*, 2365–2379; J. M. Lee, Y. Na, H. Han, S. Chang, *Chem. Soc. Rev.* **2004**, *33*, 302–312; A. Ajamian, J. L. Gleason, *Angew. Chem.* **2004**, *116*, 3842–3848; *Angew. Chem. Int. Ed.* **2004**, *43*, 3754–3760; T. A. Cernak, T. H. Lambert, *J. Am. Chem. Soc.* **2009**, *131*, 3124–3125.
[3] a) A. N. Alba, X. Companyo, M. Viciano, R. Rios, *Curr. Org. Chem.* **2009**, *13*, 1432–1474.
[4] C. Grondal, M. Jeanty, D. Enders, *Nat. Chem.* **2010**, *2*, 167–178.
[5] C. E. Müller, D. Zell, P. R. Schreiner, *Chem. Eur. J.* **2009**, *15*, 9647–9650.
[6] J. L. García Ruano, V. Marcos, J. A. Suanzes, L. Marzo, J. Alemán, *Chem. Eur. J.* **2009**, *15*, 6576–6580; I. Ibrahem, G.-L. Zhao, R. Rios, J. Vesely, H. Sundén, P. Dziedzic, A. Córdova, *Chem. Eur. J.* **2008**, *14*, 7867–7879; L.-Q. Lu, Y.-J. Cao, X.-P. Liu, J. An, C.-J. Yao, Z.-H. Ming, W.-J. Xiao, *J. Am. Chem. Soc.* **2008**, *130*, 6946–6948; G.-L. Zhao, W.-W. Liao, A. Córdova, *Tetrahedron Lett.* **2006**, *47*, 4929–4932; S. P. Lathrop, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 13628–13630.
[7] C. Zhong, X. Shi, *Eur. J. Org. Chem.* **2010**, 2999–3025; M. Rueping, R. M. Koenigs, I. Atodiresei, *Chem. Eur. J.* **2010**, *16*, 9350–9365; D. Monge, K. L. Jensen, P. T. Franke, L. Lykke, K. A. Jørgensen, *Chem. Eur. J.* **2010**, *16*, 9478–9484; S. Chercheja, S. K. Nadakudity, P. Eilbracht, *Adv. Synth. Catal.* **2010**, *352*, 637–643; K. L. Jensen, P. T. Franke, C. Arróniz, S. Kobbelgaard, K. A. Jørgensen, *Chem. Eur. J.* **2010**, *16*, 1750–1753; M. I. Hall, S. J. Pridmore, J. M. J. Williams, *Adv. Synth. Catal.* **2008**, *350*, 1975–1978; B.-C. Hong, R. Y. Nimje, M.-F. Wu, A. A. Sadani, *Eur. J. Org. Chem.* **2008**, 1449–1457; S. Chercheja, P. Eilbracht, *Adv. Synth. Catal.* **2007**, *349*, 1897–1905; K. Sorimachi, M. Terada, *J. Am. Chem. Soc.* **2008**, *130*, 14452–14453.
[8] A. Zanardi, R. Corberán, J. A. Mata, E. Peris, *Organometallics* **2008**, *27*, 3570–3576; A. Zanardi, J. A. Mata, E. Peris, *J. Am. Chem. Soc.* **2009**, *131*, 14531–14537.
[9] E. A. Colby Davie, S. M. Mennen, Y. Xu, S. J. Miller, *Chem. Rev.* **2007**, *107*, 5759–5812.
[10] L. Wanka, C. Cabrele, M. Vanejews, P. R. Schreiner, *Eur. J. Org. Chem.* **2007**, 1474–1490.
[11] C. B. Shinisha, R. B. Sunoj, *Org. Lett.* **2009**, *11*, 3242–3245.
[12] C. E. Müller, L. Wanka, K. Jewell, P. R. Schreiner, *Angew. Chem.* **2008**, *120*, 6275–6278; *Angew. Chem. Int. Ed.* **2008**, *47*, 6180–6183;

R. Hrdina, C. E. Müller, P. R. Schreiner, *Chem. Commun.* **2010**, *46*, 2689–2690.
[13] K. Naemura, R. Fukuda, M. Murata, M. Konishi, K. Hirose, Y. Tobe, *Tetrahedron: Asymmetry* **1995**, *6*, 2385–2394; T. Kawabata, R. Stragies, T. Fukaya, Y. Nagaoka, H. Schedel, K. Fuji, *Tetrahedron Lett.* **2003**, *44*, 1545–1548; A. C. Spivey, F. Zhu, M. B. Mitchell, S. G. Davey, R. L. Jarvest, *J. Org. Chem.* **2003**, *68*, 7379–7385.
[14] H. Hemmerle, H.-J. Gais, *Tetrahedron Lett.* **1987**, *28*, 3471–3474; E. Vedejs, O. Daugulis, S. T. Diver, *J. Org. Chem.* **1996**, *61*, 430–431.
[15] Z.-F. Xie, I. Nakamura, H. Suemune, K. Sakai, *J. Chem. Soc. Chem. Commun.* **1988**, 966–967; K. Laumen, R. Seemayer, M. P. Schneider, *J. Chem. Soc. Chem. Commun.* **1990**, 49–51.
[16] T. Harada, I. Wada, A. Oku, *J. Org. Chem.* **1989**, *54*, 2599–2605; Y. Zhu, L. Shu, Y. Tu, Y. Shi, *J. Org. Chem.* **2001**, *66*, 1818–1826; X. Feng, L. Shu, Y. Shi, *J. Am. Chem. Soc.* **1999**, *121*, 11002–11003; X. Feng, L. Shu, Y. Shi, *J. Org. Chem.* **2002**, *67*, 2831–2836; S. Gravil, H. Veschambre, R. Chênevert, J. Bolte, *Tetrahedron Lett.* **2006**, *47*, 6153–6157; K. Bogár, P. H. Vidal, A. R. Alcántara León, J.-E. Bäckvall, *Org. Lett.* **2007**, *9*, 3401–3404; Y. Zhao, J. Rodrigo, A. H. Hoveyda, M. L. Snapper, *Nature* **2006**, *443*, 67–70; Y. Zhao, A. W. Mitra, A. H. Hoveyda, M. L. Snapper, *Angew. Chem.* **2007**, *119*, 8623–8626; *Angew. Chem. Int. Ed.* **2007**, *46*, 8471–8474.
[17] T. Sugimura, H. Iguchi, R. Tsuchida, A. Tai, N. Nishiyama, T. Hakushi, *Tetrahedron: Asymmetry* **1998**, *9*, 1007–1013; C. Tanyeli, E. Turkut, I. M. Akhmedov, *Tetrahedron: Asymmetry* **2004**, *15*, 1729–1733.
[18] TEMPO/NaOCl/KBr, TEMPO/$Ca(OCl)_2$/KBr, TEMPO/$PhI(OAc)_2$, TEMPO/trichlorocyanuric acid (TCCA)/$NaHCO_3$, TEMPO/Bu_4NBr/*m*CPBA were used.
[19] W. Adam, C. R. Saha-Möller, P. A. Ganeshpure, *Chem. Rev.* **2001**, *101*, 3499–3548; M. Tomizawa, M. Shibuya, Y. Iwabuchi, *Org. Lett.* **2009**, *11*, 1829–1831.

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