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Chiral Chromium(III) Porphyrins as Highly Enantioselective Catalysts for Hetero-Diels–Alder Reactions Between Aldehydes and Dienes

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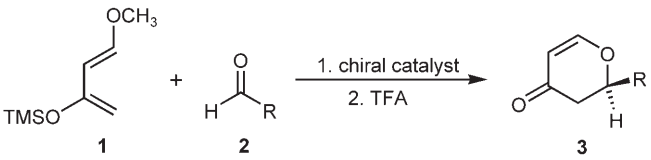
Abstract: Starting from enantiomerically pure 5,10,15,20-tetrakis[(1*S*,4*R*,5*R*,8*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene-9-yl]porphyrin, treatment with $CrCl_2$ and subsequent air oxidation afforded the corresponding Cr(III) complex, with chloride as counterion, in 96% yield. Anion exchange with $AgBF_4$ gave the corresponding tetrafluoroborate. These hitherto unknown chiral chromium porphyrins are efficient and highly enantioselective catalysts for the hetero-Diels–Alder reaction of aliphatic, aromatic, and heteroaromatic aldehydes with dienes of varying electron density. In the case of 1-methoxy-3-(trimethylsilyloxy)butadiene ("Danishefsky's diene"), enantiomeric excesses >90% were achieved in a number of cases, with furfural affording the highest ee (97%). Metal-coordinating aldehydes such as pyridine-2-carbaldehyde do not inactivate the Cr(III) porphyrin catalyst. The cycloaddition of less electron-rich dienes (such as 1-methoxybutadiene) is effected as well, affording diastereoselectivities up to >99:1, and enantiomeric excesses >80%.

Keywords: asymmetric catalysis; chromium; hetero-Diels–Alder reactions; Lewis acids; porphyrins

Introduction

The hetero-Diels–Alder reaction (HDA) between an electron-rich diene and an aldehyde provides pyran derivatives in one single step.[1] In 1982, Danishefsky et al. reported the seminal observation that the hetero-Diels–Alder reaction between an aldehyde **2** and 1-methoxy-3-(trimethylsilyloxy)butadiene (**1**; "Danishefsky's diene") is catalyzed by Lewis acids.[2] When chiral Lewis acids are employed, the dihydropyranones **3** can be obtained in enantiomerically enriched form (Scheme 1). Chiral pyran derivatives are synthetically most useful intermediates, and the HDA approach for their synthesis has been extended to numerous diene components other than **1**.[3] Various chiral Lewis acids have been developed for the highly enantioselective HDA of aldehydes with electron-rich dienes.[4] Recent developments in this field comprise the use of titanium in combination with BINOL derivatives by Ding et al.[4l,m] and of chromium-Schiff base complexes by Jacobsen et al.[4f,g,k,s] By the latter two approaches, enantioselectivies up to 99% were reported for the cycloaddition of benzaldehyde (**2**, R = Ph) to Danishefsky's diene **1** (Scheme 1).



1 2 3

Scheme 1. The HDA between Danishefsky's diene **1** and aldehydes **2**.

Organocatalysis is gaining more and more importance in asymmetric synthesis.[5a] Very recently, organocatalytic and highly enantioselective HDA reactions of aldehydes with Rawal's diene (1-dimethylamino-3-*tert*-butyldimethylsilyloxy-1,3-butadiene) through hydrogen bonding by TADDOL[5b] and by BAMOL[5c] (1,1′-biaryl-2,2′-dimethanol) for the synthesis of dihydropyranone derivatives were reported. Another extension of this approach for the synthesis of δ-lactones from aldehydes and Brassard's diene [1,3-dimethoxy-1-(trimethylsilyloxy)butadiene] was also reported using TADDOL.[5d] Certain metal complexes of porphyrins are well known to act as Lewis acid catalysts.[6] However, there appears to be no report on the use of chiral porphyrin complexes as catalysts for the asymmetric

HDA reaction. In this paper, we report that (i) Cr(III) porphyrins such as **4a**,**b** (Figure 1) are highly reactive catalysts that effect the HDA shown in Scheme 1 at low loading, that (ii) the chiral Cr(III) porphyrins **5a**,**b** effect the HDA between Danishefsky's diene **2** and a series of aldehydes with up to 97% ee, and that (iii) even less electron-rich dienes can be reacted with aldehydes in the presence of the chiral porphyrin catalyst **5b**.

Results and Discussion

The Cr(III) porphyrin **4a** was prepared according to a procedure by Groves et al.[7] The chiral porphyrin present in the complexes **5a**,**b** was first introduced by Halterman et al. and is routinely produced in our laboratory on a multi-gram scale.[8] We achieved the insertion of chromium into the latter porphyrin by first reacting it with excess chromium(II) chloride ($CrCl_2$) in refluxing diglyme under argon, removal of excess chromium salt, and subsequent air oxidation to form the Cr(III) complex. By this route, the air-stable paramagnetic Cr(III) porphyrin **5a** was isolated in 96% yield (see Experimental Section). The complexation of Cr(III) results in a shift of the Soret band of the free ligand (λ_{max} = 421 nm) to λ_{max} = 453 nm. The tetrafluoroborates **4b** and **5b** were obtained from the corresponding chlorides **4a** and **5a** upon treatment with $AgBF_4$ in THF.

We first employed the achiral Cr(III) porphyrin **4a** to optimize the reaction conditions for the HDA between benzaldehyde (**2**, R = Ph) and Danishefsky's diene (**1**), because the catalytic activities of **4a** and **5a** as Lewis acids are similar to each other. Of the various solvents tried, methyl *tert.*-butyl ether (MTBE) afforded the highest catalytic activity. Effects of substrate concentration, catalyst loading and temperature are summarized in Table 1.

Optimal conditions were found at 2 M aldehyde concentration, where an almost quantitative yield of the product *rac*-**3** resulted when 3 mol % of the catalyst **4a** was applied at −18 °C for 18 h (Table 1, entry 3). Significantly longer reaction times were needed at lower substrate concentrations (entries 1, 2). Lower catalyst loading (2 mol %, entry 4) or further lowering of the temperature (entry 5) retard the cycloaddition, but still result in acceptable yields at reasonable reaction times.

The optimized reaction conditions of Table 1, entry 3 were applied to the asymmetric HDA using the catalyst **5a**. As shown in Table 2, entry 1, the HDA product **3a** was obtained in high yield (85%) and excellent enantiomeric purity (95% ee). This initial success prompted us to examine a number of other aldehydes in the asymmetric HDA with Danishefsky's diene **1**, catalyzed by the chiral Cr(III) porphyrins **5a**,**b**. The results are summarized in Table 2: Both aromatic (entries 1, 2, 5) and aliphatic (entries 3, 4) aldehydes could be reacted with the diene **1** to afford the expected dihydropyranones **3a**–**d** in good yields and enantiomeric purities. In particular, *n*-heptanal (**2c**) and furfural (**2d**) gave 92% and 97% ee, respectively (entries 4, 5).

trans-Cinnamic aldehyde (**2e**), an example for α,β-unsaturated aldehydes, underwent cycloaddition relatively sluggishly, and the reaction temperature had to be raised to 0 °C (entry 6). Most interestingly, pyridine-2-carbaldehyde (**2f**) could be reacted without any problem (entry 7). The latter result underpins the synthetic utility of our chiral porphyrin catalysts **5a**,**b** because transition metal catalysts tend to be inactivated by coordinating substrates (such as the pyridine derivative **2f**). In fact, this appears to be the first example of a successful Cr-catalyzed asymmetric HDA of a pyridinecarbaldehyde.[9] We attribute the pleasing catalytic activity of the Cr(III) porphyrin **5a** in the HDA of pyridine-2-carbaldehyde (**2f**) with Danishefsky's diene (**1**) to the fact that, in the porphyrin **5a**, access to the Lewis acidic

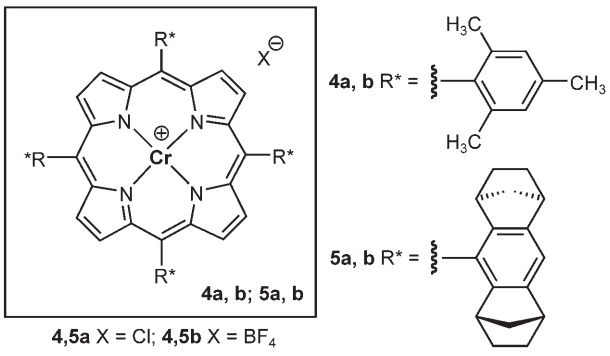


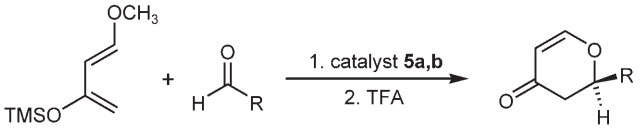
Figure 1. Chromium(III) porphyrins **4a**,**b** and **5a**,**b**.

Table 1. Optimization of the HDA of diene **1** with benzaldehyde (**2**, R = Ph) using the Cr(III) porphyrin **4a** as catalyst.[a]

Entry	Catalyst loading [mol %]	*T* [°C]	Substrate concentration [M]	Time [h]	Yield of **3** [%]
1	4	−18	1.0	42	91
2	3	−18	1.0	32	94
3	3	−18	2.0	18	97
4	2	−18	2.0	18	84
5	3	−25	2.0	19	82

[a] All reactions were performed in MTBE in the presence of dry 4 Å molecular sieves. Yields were determined by capillary GC.

Table 2. Asymmetric HDA of the aldehydes **2a – f** with the diene **1** using the Cr(III) porphyrins **5a**, **b** as catalysts.[a]



a: R = Ph; **b:** R = *c*-hexyl; **c:** R = *n*-hexyl;
d: R = 2-furyl; **e:** R = *trans*-β-styryl; **f:** R = 2-pyridyl

Entry	Aldehyde	Catalyst	T [°C]	Yield of **3a**–**f** [%][b]	ee of **3a**–**f** [%][c]
1	**2a**	**5a**	–18	85	95
2	**2a**	**5b**	–18	92	88
3	**2b**	**5a**	–18	76	88
4	**2c**	**5a**	–18	75	92
5	**2d**	**5a**	–18	70	97
6	**2e**	**5a**	0	55	74
7	**2f**	**5a**	–18	70	78

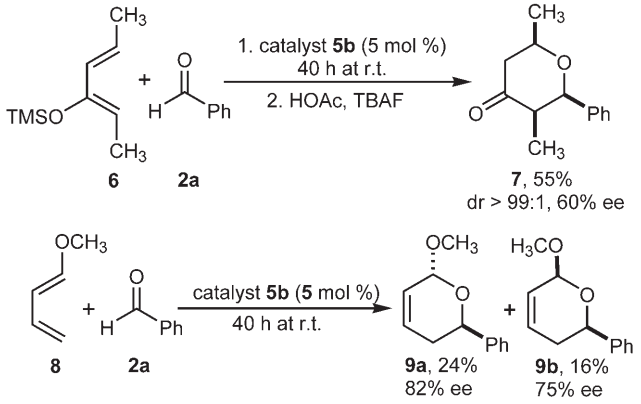
[a] The reactions were performed at 2.0 M substrate concentration in MTBE in the presence of 3 mol % of the catalysts **5a**,**b** and dry 4 Å molecular sieves for 24–40 h.
[b] Yield determined after isolation by column chromatography.
[c] Enantiomeric excess determined by capillary GC.

Cr(III) centre is sterically quite limited. Inspection of models suggests that the carbaldehyde function in the 2-position of the pyridine derivate **2f** prohibits binding *via* N. Instead, coordination *via* the aldehyde oxygen atom occurs, as with the other aldehydes examined.

Comparison of entries 1 and 2 of Table 2 reveals that the change from a (coordinating) chloride anion in catalyst **5a** to a (presumably non-coordinating) tetrafluoroborate anion in **5b** led to higher reactivity but somewhat decreased enantioselectivity. Unfortunately, tertiary aldehydes such as pivaldehyde showed very low reactivity towards the diene **1** even in the presence of the tetrafluoroborate catalyst **5b**.

Next, the suitability of the catalysts **5a**,**b** for the HDA between benzaldehyde (**2a**) and dienes of lower electron density [compared to Danishefsky's diene (**1**)] was addressed (Scheme 2). In fact, a slow reaction between (*Z*,*E*)-3-trimethylsilyloxy-2,4-hexadiene (**6**) and benzaldehyde (**2a**) was effected by the more active catalyst **5b**, whereas no substrate conversion occurred in the presence of **5a**. The *all*-cis diastereomer **7** shown in Scheme 2 (top) was formed exclusively, with an enantiomeric excess of 60%. Somewhat lower diastereoselectivity (>95% de) was reported by Jacobsen et al. for this transformation, at an enantiomeric excess of the *all*-cis product of up to 90%.[4g]

Even the less activated diene 1-methoxybutadiene (**8**) could be reacted with benzaldehyde (**2a**) (Scheme 2, bottom). In the presence of the catalyst **5b**, the HDA product was obtained as a *trans/cis* (**9a**/**9b**) mixture, the predominant *trans*-product **9a** showing an enantiomeric excess of 82%. The latter example appears to be the only reported asymmetric addition of an aromatic aldehyde to 1-methoxybutadiene (**8**). The yields stated in



Scheme 2. Asymmetric HDA of benzaldehyde (**2a**) with the less electron-rich dienes **6** and **8**, catalyzed by the Cr(III)-porphyrin **5b**.

Scheme 2 refer to 40 h reaction time at room temperature. At prolonged reaction times, or at increased catalyst loading, the cycloadditions shown proceed to completion (as do the ones with Danishefsky's diene **1**).

Conclusion

In summary, we could show that the readily available chiral Cr(III) porphyrins **5a**,**b** perform excellently in a number of HDA reactions, affording enantiomeric excesses >90% in a number of cases. It is particularly noteworthy that coordinating aldehydes such as pyridine-2-carbaldehyde (**2f**) can be reacted without any sign of catalyst inactivation. To the best of our knowl-

edge, this is the first report of a chiral metal porphyrin being used as catalyst in the HDA reaction. Our laboratory has shown previously that electronic tuning of porphyrin ligands can significantly enhance the performance of, e.g., their Ru complexes in epoxidation and cyclopropanation.[10] We expect similar advantageous effects for porphyrin-based Lewis acid catalysts.

Experimental Section

General Remarks

Catalysis experiments were performed under an argon atmosphere using standard Schlenk techniques. $CrCl_2$ (99.99%) was purchased from Aldrich. The solvents and aldehydes were first dried and freshly distilled prior to use, using standard techniques.[11] 1-Methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (Danishefsky's diene, **1**) and 1-methoxybutadiene (**8**) were purchased from Fluka or Aldrich. According to the NMR spectrum, the 1-methoxybutadiene purchased consisted exclusively of the *trans*-isomer. (*Z*,*E*)-3-Trimethylsilyloxy-2,4-hexadiene (**6**) was synthesized according to a literature procedure.[12] NMR spectra were taken on a Bruker AC 300 instrument. Chemical shifts δ (ppm) were referenced against the solvent signal; multiplicities are indicated as follows: br (broad signal), s (singlet), d (doublet), t (triplet), m (multiplet). The IR measurements were performed on a Perkin Elmer Paragon 1000 spectrometer. The band intensities are indicated as s (strong), m (medium) and w (weak). ESI mass spectra were recorded on a Finnigan MAT 900. EI mass spectra were measured on a Hewlett-Packard HP 6890 gas chromatograph equipped with an HP 5973 mass selective detector using a GC-MS standard method (Column HP-5; helium 1.0 mL min^{-1} (constant flow modus); inj.: 250 °C (split modus); det.: FID 250 °C; oven: 100 °C (5 min), 20 °C min^{-1}, 200 °C (15 min). The signs of the optical rotation for **3a**–**e** were determined on a Perkin Elmer polarimeter 343plus, and the CD spectra of **3a** and **3f** were measured on a Jasco J-810 spectropolarimeter. The absolute configuration of the pyranone products **3a**–**e** and **7** was determined by comparison of their sense of optical rotation with literature data.[4f,g] The absolute configuration of **3f** was assigned by comparison of its CD spectrum with that of **3a**. The *cis*/*trans*-assignment of the diastereomers **9a**/**9b** was done by NMR spectroscopy (NOE). Capillary GC data were obtained using a Hewlett-Packard HP 6890 GC system with flame ionization detector and HP-ChemStation software revised version A.05.01. A WCOT-FS, CP Chirasil-Dex CB column (25 m) was used for analytical chiral GLC separation with N_2 as carrier gas.

Chloro-{5,10,15,20-tetrakis[(1*S*,4*R*,5*R*,8*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene-9-yl]porphyrinato}chromium(III) (5a)

The porphyrin ligand[8] (200 mg, 0.175 mmol) was suspended in diglyme (200 mL) and heated to reflux under argon. $CrCl_2$ (215 mg, 1.75 mmol) was added in two portions over a 10 min period. After *ca.* 15 min, the mixture turned into a homogeneous deep-green solution and was refluxed for another 6 h. The solution was then allowed to cool to room temperature, brine (150 mL) was added, and the mixture was stirred under air during 12 h. The mixture was then extracted with dichloromethane (2 × 150 mL). The organic phase was washed with H_2O (2 × 150 mL), dried over Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by column chromatography on neutral alumina (Fluka, Brockmann activity I) using gradient elution, from dichloromethane to 3% methanol-dichloromethane. The fractions containing the product were combined and stirred with saturated aqueous NH_4Cl (150 mL) overnight. The organic phase was separated, washed successively with aqueous $NaHCO_3$ (150 mL), brine (3 × 150 mL) and dried over Na_2SO_4. After filtration and evaporation under reduced pressure, a deep-green solid was obtained which was dried overnight under vacuum (5×10^{-2} mbar); yield: 207 mg (96%); mp > 250 °C; HR-ESI-MS (CH_2Cl_2–MeOH): calcd. for $C_{87}H_{76}{}^{52}CrN_4$ = 1192.5475 ($M^+ - Cl$); found = 1192.547 ($M^+ - Cl$); ESI-MS (CH_2Cl_2 – MeOH): *m*/*z* [%] = 1192.53 [Por*^{52}Cr, 20.3], 1224.54 [Por*^{52}Cr(MeOH), 16.4], 1256.61 [Por*^{52}Cr(MeOH)$_2$, 100], 1257.6 [Por*^{53}Cr(MeOH)$_2$, 98.6], 1258.6 [Por*^{54}Cr(MeOH)$_2$, 54.3], 1259.6 [Por*^{54}Cr(MeOH)$_2$, 19.9]; IR (film): $\tilde{\nu}$ = 2956 [s, ν(C–H) alkyl], 2917 [m, ν(C–H) alkyl], 2865 [m, ν(C–H) alkyl], 1575, 1525, and 1497 [w, ν(C=C) aryl], 1470 and 1445 [w, δ(C–H) alkyl],1325 [w], 1290 [m], 1261 [w], 1203 and 1194 [w], 1105 [s], 1071 and 1063 [m], 1008 [s], 960 and 947 [m], 861 [m, δ(C–H) aryl], 797 [s, δ(C–H) aryl], 753, 733, and 710 [m] cm^{-1}; UV-VIS: λ_{max} = 453 nm (CH_2Cl_2).

{5,10,15,20-Tetrakis[(1*S*,4*R*,5*R*,8*S*)-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene-9-yl]porphyrinato}chromium(III) Tetrafluoroborate (5b)

To a solution of the chloride **5a** (100 mg, 0.081 mmol) in THF (3 mL) was added $AgBF_4$ (17.4 mg, 0.089 mmol) at room temperature. The reaction mixture was refluxed for 2 h under argon. It was then allowed to cool to room temperature and filtered through a plug of celite. Evaporation of the solvent under reduced pressure afforded a deep green solid; yield: 96 mg (92%); ^{19}F NMR ($CDCl_3$, 470.51 MHz): δ = −146.4 (brs) [reference: δ (CF_3CO_2H) = −77.5].

The same protocol was applied for anion exchange of the chloride **4a**, affording 94% of tetrafluoroborate **4b**.

General Procedure for the Hetero-Diels–Alder Reaction of Aldehydes with Danishesky's Diene (1)

The chromium porphyrin **4a** or **5a** and the aldehyde (**2a**–**f**, 0.50 mmol) were dissolved in MTBE (0.25 mL), and 4 Å molecular sieves (200 mg) were added under argon. The reaction was started by the addition of Danishefsky's diene (**1**, 0.53 mmol, 1.06 equivs.) at the temperature stated in the Table 2. After stirring for 24–40 h under argon, the reaction mixture was diluted with 3 mL of dichloromethane, and two drops of TFA were added. The solution was then evaporated under reduced pressure to afford a deep green oil. The crude residue was purified by column chromatography as described individually below.

(*R*)-2-Phenyl-2,3-dihydropyran-4-one [(*R*)-3a]

After purification by flash chromatography on silica gel (cyclohexane/ethyl acetate, 7:3), the product (*R*)-**3a** was obtained as a clear oil; yield: 73 mg (0.42 mmol, 84%); 95% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 170 °C (16 min)], τ_R(minor) = 11.46 min (*S*), τ_R(major) = 11.89 min (*R*).

(*R*)-2-Cyclohexyl-2,3-dihydropyran-4-one [(*R*)-3b]

After purification by flash chromatography on silica gel (cyclohexane/ethyl acetate, 7:3), the product (*R*)-**3b** was obtained as a clear oil; yield: 68 mg (0.38 mmol, 76%); 88% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 160 °C (20 min), 15 °C min^{-1}, 170 °C (2 min)], τ_R(minor) = 15.19 min (*S*), τ_R(major) = 15.84 min (*R*).

(*S*)-2-(*n*-Hexyl)-2,3-dihydropyran-4-one [(*S*)-3c]

After purification by flash chromatography on silica gel (cyclohexane/ethyl acetate, 8:2), the product (*S*)-**3c** was obtained as a clear oil; yield: 68 mg (0.375 mmol, 75%); 92% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 150 °C (17.5 min), 15 °C min^{-1}, 180 °C (2 min)], τ_R(minor) = 14.61 min (*R*), τ_R(major) = 15.13 min (*S*).

(*R*)-2-(2-Furyl)-2,3-dihydropyran-4-one [(*R*)-3d]

After purification by flash chromatography on silica gel (cyclohexane/ethyl acetate, 7:3), the product (*R*)-**3d** was obtained as a clear oil; yield: 58 mg (0.35 mmol, 70%); 97% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 150 °C (17.5 min), 15 °C min^{-1}, 180 °C (2 min)], τ_R(minor) = 12.49 min (*S*), τ_R(major) = 12.79 min (*R*).

(*R*)-2-(*trans*-β-Styryl)-2,3-dihydropyran-4-one [(*R*)-3e]

After purification by flash chromatography on silica gel (cyclohexane/ethyl acetate, 7:3), the product (*R*)-**3e** was obtained as a clear oil; yield: 55 mg (0.275 mmol, 55%); 74% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 160 °C (80 min), 15 °C min^{-1}, 180 °C (2 min)], τ_R(minor) = 59.71 min (*S*), τ_R(major) = 61.87 min (*R*).

(*R*)-2-(2-Pyridyl)-2,3-dihydropyran-4-one [(*R*)-3f]

After purification by column chromatography on neutral alumina (cyclohexane/ethyl acetate, 1:1), the product (*R*)-**3f** was obtained as a clear oil; yield: 61.3 mg (0.35 mmol, 70%); 78% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 160 °C (25 min), 15 °C min^{-1}, 180 °C (2 min)], τ_R(minor) = 18.91 min (*S*), τ_R(major) = 20.59 min (*R*).

(2*R*,3*R*,6*R*)-2-Phenyl-3,6-dimethyltetrahydropyran-4-one [(2*R*,3*R*,6*R*)-7]

The chromium porphyrin **5b** (32 mg, 25 μmol, 5 mol %) and benzaldehyde (**2a**, 52.2 mg, 0.50 mmol) were dissolved in MTBE (0.25 mL), and 4 Å molecular sieves (200 mg) were added at room temperature under argon. The reaction was started by the addition of (*Z*,*E*)-3-(trimethylsilyloxy)-hexa-2,4-diene (**6**, 90 mg, 0.53 mmol, 1.06 equivs.). After stirring for 40 h at room temperature, the reaction mixture was diluted with 2 mL of THF. The temperature was lowered to 0 °C, and acetic acid (57 μL, 1 mmol) and a solution of 1 M tetrabutylammonium fluoride in THF (735 μL, 0.75 mmol) were added. Stirring was continued for another 0.5 h. The resulting mixture was extracted with hexane : diethyl ether (2:1, 30 mL). The organic phase was washed successively with H_2O (2 × 15 mL), saturated aqueous $NaHCO_3$ (15 mL), brine (15 mL), and dried over $MgSO_4$. After filtration, the solution was evaporated under reduced pressure. Purification of the residue by flash chromatography (silica gel, cyclohexane/EtOAc, 7:3) afforded the product (2*R*,3*R*,6*R*)-**7** as a pale yellow oil; yield: 56 mg (0.275 mmol, 55%); 60% ee determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 170 °C (16 min)], τ_R(minor) = 7.80 min (2*S*,3*S*,6*S*), τ_R(major) = 8.80 min (2*R*,3*R*,6*R*); GC-MS (EI): τ_R = 10.50 min, *m*/*z* (%) = 204 (M^+, 66), 117 (73), 98 (49), 77 (29), 56 (100); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.20 (m, 6H), 4.70 (d, ^3J = 2.8 Hz, 1H), 3.81 (m, ^3J = 6.0 Hz, ^3J = 2.8 Hz, 1H), 2.55 (ddd, ^3J = 7.2 Hz, ^3J = 2.8 Hz, *J* = 1.2 Hz, 1H), 2.47 (dd, ^2J = 14.6 Hz, ^3J = 11.5 Hz, 1H), 2.25 (ddd, ^2J = 14.6 Hz, ^3J = 2.8 Hz, ^4J = 1.3 Hz, 1H), 1.36 (dt, ^2J_t = 19.9 Hz, ^3J_d = 6.1 Hz, 3H), 0.82 (dt, ^2J_t = 19.9 Hz, ^3J_d = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 211.6, 138.7, 128.3, 127.3, 125.5, 80.0, 73.7, 50.7, 45.6, 22.2, 11.4.

6-Methoxy-2-Phenyl-3,6-dihydro-*2H*-pyran [9a, b]

The chromium porphyrin **5b** (32 mg, 25 μmol, 5 mol %) and benzaldehyde (**2a**, 52.2 mg, 0.50 mmol) were dissolved in MTBE (0.25 mL), and 4 Å molecular sieves (200 mg) were added at room temperature under argon. The reaction was started by the addition of 1-methoxybutadiene (**8**, 44.1 mg, 0.52 mmol, 1.06 equivs.). After stirring for 40 h at room temperature, the reaction mixture was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, cyclohexane:EtOAc, 7:3) to afford a pale yellow oil; yield: 37 mg [0.2 mmol, 40% which contained both the *trans*- and *cis*-diastereomers **9a** and **9b** (**9a**/**9b** = 60:40)], 83% ee for *trans*-diastereomer (**9a**) and 75% ee for *cis*-diastereomer (**9b**) determined by chiral GC analysis [CP Chirasil-Dex CB; N_2 0.9 mL min^{-1} (constant flow modus); inj.: 180 °C (split modus); det.: FID 180 °C; oven: 170 °C (16 min)], τ_R(**9a**-minor) = 6.87 min, τ_R(**9a**-major) = 7.06 min, τ_R(**9b**-minor) = 7.99 min, τ_R(**9b**-major) = 8.21 min); GC-MS (EI): τ_R(**9a**) = 9.64 min, τ_R(**9b**) = 9.89 min, *m*/*z* (%) = 159 (M^+-31, 14), 129 (13), 115 (13), 91 (25), 84 (100); **9a** (*trans*): ^{1}H NMR (300 MHz,

$CDCl_3$): δ = 7.40 – 7.17 (m, 5H), 6.08 – 5.98 (m, 1H), 5.77 (dtd, J_d = 10.5 Hz, J_t = 2.8 Hz, J_d = 1.5 Hz, 1H), 4.96 – 4.94 (m, 1H), 4.84 (dd, ^3J = 11.0 Hz, ^4J = 4.2 Hz, 1H) 3.38 (s, 3H), 2.36 – 2.12 (m, 2H), ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 142.3, 129.1, 128.5, 127.6, 126.2, 125.5, 96.4, 68.4, 55.3, 32.2; **9b** (*cis*): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40 – 7.17 (m, 5H), 6.08 – 5.98 (m, 1H), 5.67 (dqt, J_d = 10.2 Hz, J_{qt} = 1.3 Hz, 1H), 5.24 – 5.19 (m, 1H), 4.72 (dd, ^3J = 9.9 Hz, ^4J = 4.0 Hz, 1H), 3.47 (s, 3H), 2.36 – 2.12 (m, 2H), ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 137.5, 129.6, 128.4, 128.3, 127.5, 125.7, 99.2, 74.0, 55.2, 32.9.

Supporting Information

Further characterization data for compounds **3a**–**f**, **7** and **9a**, **b** are given in the Supporting Information.

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