Synthesis of Axially Chiral *N*-Hydroxyimides, Potential New Catalysts for Asymmetric Oxidations

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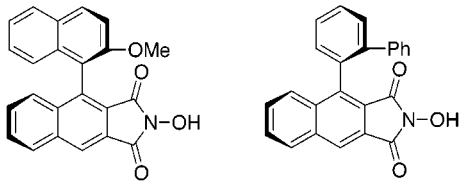
N-Hydroxyphthalimide (NHPI) has recently been recognized as a valuable catalyst for the oxidation of various organic compounds. It was first used by Masui et al. as an electrochemical oxidation mediator,[1] i.e., for the oxidation of secondary alcohols into ketones,[1a] of compounds having benzylic or allylic carbons into aryl or α,β-unsaturated ketones,[1b,c] of amides or lactams to imides,[1d] and of ethers to esters[1b] or for the oxidative deprotection of 4-phenyl-1,3-dioxolane protecting groups.[1e] More recently, various oxidations have been conducted in the presence of molecular oxygen and NHPI under nonelectrochemical conditions. Ishii et al. have used NHPI, generally in association with transition-metal complexes, for the aerobic oxidation of various organic substrates at atmospheric pressure and temperatures in the range 25−100 °C.[2]

We have reported the oxidation of organic substrates by molecular oxygen mediated by NHPI and acetaldehyde under normal pressure and temperature in the absence of any transition-metal catalyst.[3] Although the mechanisms involved in these reactions are not fully understood, a key intermediate in all NHPI-mediated oxidations appears to be phthalimide *N*-oxyl, a fairly stable but highly reactive free radical.[1c,f,2c,g,4]

Taking into account the unique properties of NHPI as an oxidation catalyst, it is likely that suitably designed chiral analogues should be of value for asymmetric catalysis. We report herein the synthesis of two new chiral *N*-hydroxyimides, **1a** and **1b**, and their first use as catalysts for a few representative asymmetric oxidations. Several structural requirements of NHPI chiral



1a **1b**

analogues may be anticipated for their optimal catalytic properties: Two previous reports[1g,2a] briefly indicated that lower efficiencies were observed when NHPI was replaced by other *N*-hydroxyimides such as *N*-hydroxysuccinimide, indicating that an *N*-hydroxyphthalimide subunit should be desirable. Also, owing to the strong oxidizing properties of NHPI-type catalysts, no oxidizable substituents, including aliphatic chains, should be present to avoid self-oxidation of the catalyst. *N*-Nydroxyimides **1a** and **1b** fulfill both requirements. We have first prepared their racemic form, by similar reaction sequences, as depicted in Scheme 1.

Bromo acetal **2** gave acetal alcohols **3a** and **3b** by standard procedures. Compounds **3a** and **3b** were next transformed into the corresponding isobenzofurans which, after in situ trapping by dimethylfumarate, furnished the Diels−Alder adducts **4a** and **4b**.[5] Both **4a** and **4b** were isolated as mixtures of diastereomers which were aromatized in the presence of methanesulfonic acid, furnishing diesters **5a** and **5b**. The formation of diacids **6a** and **6b**, followed by their transformation into *N*-hydroxyimides **1a** and **1b**, was straightforward. When NHPI was replaced by racemic **1a** or **1b** in some representative oxidation experiments,[3] very similar results were obtained as with NHPI itself, indicating that both **1a** and **1b** have the expected catalytic properties. To obtain **1a** and **1b** in their optically active form, resolution of the corresponding diacids **1a** and **1b** has been undertaken. In both cases, one of the diastereomeric salts formed with brucine crystallized preferentially from acetone. Optically pure **6a** and **6b** could thus be obtained readily.[6] Optically pure **6a** has been transformed into *N*-hydroxyimide **1a** by standard procedure without any loss of optical purity.[7] When the same transformation was effected with optically pure **6b**, the corresponding *N*-hydroxyimide **1b** has been obtained with an optical purity of only 80%,[8] indicating a lower rotational barrier around the biaryl axis when compared with the former case. Fortunately, ee of **1b** could be raised to nearly 100% after one

(1) (a) Masui, M.; Ueshima, T.; Ozaki, S. *J Chem. Soc., Chem. Commun.* **1983**, 479−480. (b) Masui, M.; Hara, S.; Ueshima, T.; Kawaguchi, T.; Ozaki, S. *Chem. Pharm. Bull.* **1983**, *31*, 4209−4211. (c) Masui, M.; Hosomi, K.; Tsuchida, K.; Ozaki, S. *Chem. Pharm. Bull.* **1985**, *33*, 4798−4802. (d) Masui, M.; Hara, S.; Ozaki, S. *Chem. Pharm. Bull.* **1986**, *34*, 975−979. (e) Masui, M.; Kawaguchi, T.; Ozaki, S. *J. Chem. Soc., Chem. Commun.* **1985**, 1484−1485. (f) Ueda, C.; Noyama, M.; Ohmori, H.; Masui, M. *Chem. Pharm. Bull.* **1987**, *35*, 1372−1377. (g) For a general review, see: Masui, M. *Stud. Org. Chem.* **1987**, *30*, 137−144.

(2) (a) Ishii, Y.; Nakayama, K.; Takeno, M.; Sakaguchi, S.; Iwahama, T.; Nishiyama, Y. *J. Org. Chem.* **1995**, *60*, 3934−3935. (b) Iwahama, T.; Sakaguchi, S.; Nishiyama, Y.; Ishii, Y. *Tetrahedron Lett.* **1995**, *36*, 6923−6926. (c) Ishii, Y.; Iwahama, T.; Sakaguchi, S.; Nakayama, K.; Nishiyama, Y. *J. Org. Chem.* **1996**, *61*, 4520−4526. (d) Ishii, Y.; Kato, S.; Iwahama, T.; Sakaguchi, S. *Tetrahedron Lett.* **1996**, *37*, 4993−4996. (e) Ishii, Y. *J. Mol. Catal. A: Chem.* **1997**, *117*, 123−137. (f) Sakaguchi, S.; Eikawa, M.; Ishii, Y. *Tetrahedron Lett.* **1997**, *37*, 7075−7078. (g) Yoshino, Y.; Hayashi, Y.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1997**, *62*, 6810−6813. (h) Kato, S.; Iwahama, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 222−223. (i) Sakaguchi, S.; Takase, T.; Iwahama, T.; Ishii, Y. *Chem. Commun.* **1998**, 2037−2038. (j) Iwahama, T.; Sakaguchi, S.; Ishii, Y. *Tetrahedron Lett.* **1998**, *39*, 9059−9062.

(3) Einhorn, C.; Einhorn, J.; Marcadal, C.; Pierre, J. L. *Chem. Commun.* **1997**, 447−448.

(4) Lemaire, H.; Rassat, A. *J. Chem. Phys.* **1964**, *61*, 1580−1588.

(5) For reviews on the chemistry of isobenzofurans, see: (a) Friedrichsen, W. *Adv. Heterocycl. Chem.* **1980**, *26*, 135−241. (b) Rodrigo, R. *Tetrahedron* **1988**, *44*, 2093−2135.

(6) Enantiomeric purity of **6a** and **6b** has been estimated by ^{1}H NMR at 200 MHz. Mixing racemic **6a** with 1 equiv optically pure α-methylbenzylamine led to an efficient splitting of the sharp singlet at 8.68 ppm. The same effect was observed with **6b** on the 8.50 ppm singlet. Levorotatory diacid **6a**, obtained from the crystalline salt formed with brucine, has been isolated with a 24% yield (theoretical yield 50%); ee > 99%. $[\alpha]^{20.7}_D$ −43.7° (c = 2, MeOH). Levorotatory diacid **6b** has been obtained with a 45% yield from the crystalline salt formed with brucine; ee > 99%. $[\alpha]^{21.7}_D$ −3.35° (c = 0.4, MeOH). Dextrorotatoty **6b** has been isolated from the mother liquors; ee = 97%. $[\alpha]^{21.7}_D$ +3.25° (c = 0.4, MeOH).

(7) Splitting of the OMe singlet at 3.71 ppm was observed in the ^{1}H NMR spectrum of racemic **1a** when 1 equiv of optically pure α-methylbenzylamine was added.

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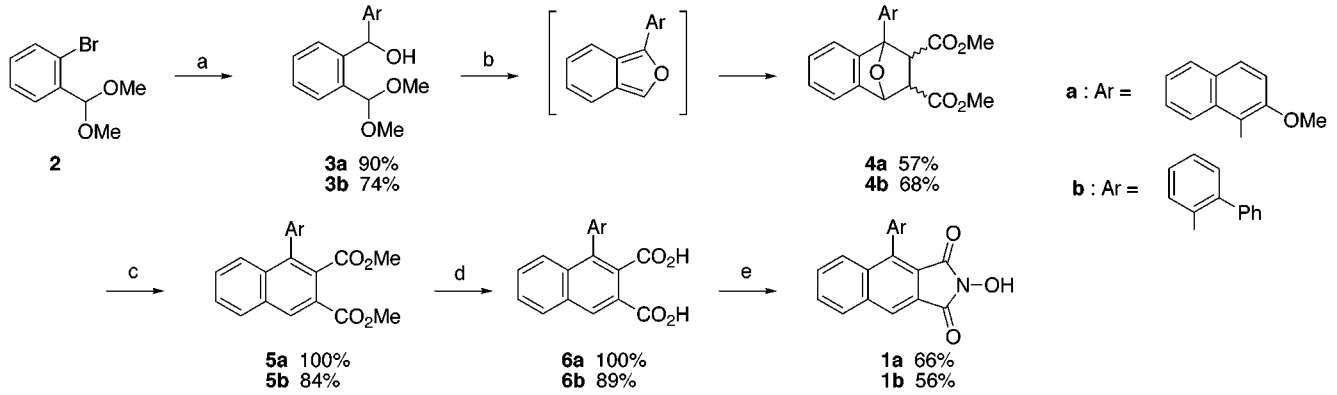
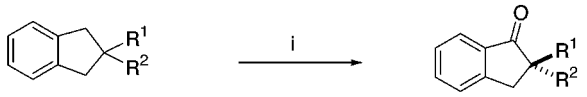
Scheme 1[a]



[a] Reagents: (a) (i) *n*-BuLi, THF, -78°C ' 0°C; (ii) ArCHO, 0°C ' rt; (b) for **3a**: dimethylfumarate, PTSA,toluene, reflux; for **3b**: dimethylfumarate, PTSA, xylenes, reflux; (c) 2eq $MeSO_3H$, CH_2Cl_2, 0°C; (d) KOH, MeOH, reflux; (e) (i) Ac_2O, reflux; (ii) $NH_2OH.HCl$, pyridine, rt ' 95°C.

Scheme 2[a]

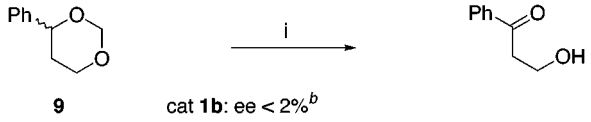


7a : R^1 = H, R^2 = Me — **8a** 63%, 2% ee with **1a**; 50%, 4% ee with **1b**

7b : R^1 = OMe, R^2 = Ph — **8b** 41%, 2% ee with **1a**; 42%, 8% ee with **1b**

[a] Reagents: (i) 10 mol% **1a** or **1b**, MeCHO, O_2, acetonitrile

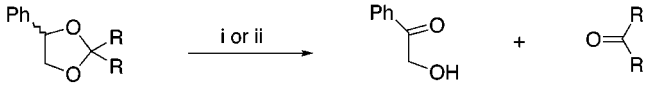
Scheme 3[a]



9 — cat **1b**: ee < 2%[b]

[a] Reagents: (i) 10 mol% **1b**, MeCHO, O_2, acetonitrile. [b]ee of remaining **9** at half completion:

Scheme 4[a]



10a : R = Me — i, cat **1b:** ee 7%[b]

10b : R = Ph — i, cat **1a**: ee 8%[b]; ii, cat **1a**: ee 12%[b]; i, cat **1b**: ee 18%[b]; ii, cat **1b**: ee 24%[b]

[a] Reagents: (i) 10 mol% **1a** or **1b**, MeCHO, O_2, acetonitrile; (ii) 10 mol% **1a** or **1b**, 10 mol% CuCl, O_2, acetonitrile. [b]ee of remaining **10** at half completion:

recrystallization from ethanol. No loss of optical purity was observed after storage for several weeks at room temperature.

With optical pure **1a** and **1b** in hand, we have attempted to catalyze some asymmetric oxidations. Indane is readily oxidized into 1-indanone in good yields by NHPI-mediated oxidations.[2a,3] Indanes bearing two different substituents on carbon 2 are interesting substrates for asymmetric oxidations, as they have two enantiotopic benzylic carbons (Scheme 2). 2-Methylindane **7a**, when oxidized by molecular oxygen/acetaldehyde[3] catalyzed by optically pure **1a** or **1b**, gave as expected 2-methylindan-1-one **8a** in good yields but with only negligible asymmetric inductions (2% and 4% ee).[9] Likewise, 2-methoxy-2-phenylindane **7b** gave ketone **8b**; in this case, the difference of induction between catalyst **1a** and **1b** was more pronounced: 2% and 8% ee.[10] When the same transformation (**7b** into **8b**) was performed at −20 °C, ee has been raised to 12% with catalyst **1b**. A lower temperature (−78 °C) led to an exceedingly slow reaction.

As NHPI is able to effect oxidative deprotection of acetal protecting groups,[1e] kinetic resolutions could possibly be observed on chiral racemic acetals with catalysts **1a** or **1b**. Commercially available racemic 4-phenyl-1,3-dioxane **9** was therefore submitted to our standard oxidation conditions using optically pure catalyst **1b** (Scheme 3). At half completion, remaining **9** was isolated, and its enantiomeric composition determined.[11] In this case, chiral recognition was very low (ee < 2%).

Better results were observed with dioxolanes **10a** and **10b** (Scheme 4). When oxidation of **10a** mediated by **1b** was run to half completion, remaining **10a** was isolated with an ee of 7%.[11] With dioxolane **10b**, an 8% ee of remaining **10b** was measured with catalyst **1a** and 18% was found with catalyst **1b** at half completion.[12] We have also carried out the oxidation of substrate **10b** using CuCl as a cocatalyst in the absence of acetaldehyde.[13] Slightly better results were observed, as catalyst **1a** led to 12% and **1b** led to 24% ee ($k_{rel} \approx 2$) at half completion. Experiments have been attempted at −20 °C with CuCl as cocatalyst, but virtually no oxidation has been observed after one week. In all of the cases studied here,

(8) Compound **1b** was first transformed into its OMe derivative (excess diazomethane, see: Santos, P. F.; Lobo, A. M.; Prabhakar, S. *Synth. Commun.* **1995**, *25*, 3509−3518), whose optical purity has been determined by HPLC on a Chiralpak AD column; elution, cyclohexane/*i*-PrOH (1/1), 0.5 mL min^{-1}.

(9) Determined by polarimetry, by comparison with literature data for optically pure **8a** (see: Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3081−3087).

(10) Determined by ^1H NMR at 200 MHz, adding increasing amounts of tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium ($Eu(hfc)_3$) to a dilute solution of ketone **8b**. Splitting of the OMe singlet was observed for racemic **8b**.

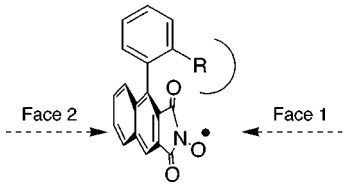
(11) Enantiomeric composition has been determined by GLC on a Chiraldex B-PM capillary column, with an oven temperature of 130 °C.

(12) Enantiomeric composition has been determined by HPLC on a Chiralpak AD column; elution, cyclohexane/*i*-PrOH (1/1), 0.5 mL min^{-1}.

(13) Einhorn, C.; Einhorn, J.; Marcadal, C.; Pierre, J. L., unpublished results.

catalyst **1b** exhibits chiral recognition noticeably higher than that of catalyst **1a**.

Although modest, these first results clearly indicate that asymmetric catalysis mediated by optically active *N*-hydroxyimides is possible. How do these catalysts lead to asymmetric induction? At this stage, a response to this question is necessarily speculative, as detailed reaction paths for these oxidations are lacking. A possible rationalization can be formulated as follows: The active species of these catalytic processes are most likely imide *N*-oxyl radicals obtained by one-electron oxidation of *N*-hydroxyimides. The first event of the substrate oxidation is probably benzylic atom abstraction by these highly reactive radicals. Imide *N*-oxyl radicals are nitroxydes and, as so, are π-radicals,[14] i.e., the unpaired electron occupies a molecular orbital whose medium plane is orthogonal to those of the phthalimide subunit. For hydrogen atom abstraction, a facial approach of the substrate can therefore be assumed. In the case of an axially chiral radical like **11** (derived from **1b** if R = Ph), the status of each face of the phthalimide subunit is very different. Substrate approaching from face 1 will be



11

positionned in a chiral environment induced by stereoelectronic effects of substituent R, allowing chiral discrimination. Face 2, however, is comparatively unhindered. Substrate approach from this face should therefore be favored, but with poor chiral discrimination. Following the preceding hypothesis, global chiral discrimination capacities of radical **11** should remain modest even with an optimal choice of substituent R.

In summary, we have prepared two original axially chiral *N*-hydroxyimides by a synthetic approach based on an isobenzofuran Diels−Alder reaction as the key step. Optically pure *N*-hydroxyimides, obtained via resolution of intermediate diacids, have been used as catalysts for some asymmetric oxidations. Although our catalysts display only modest chiral discrimination, these preliminary results are nevertheless promising as they constitute the first examples of asymmetric catalysis by optically active *N*-hydroxyimides. We are now investigating other catalysts, especially axially chiral *N*-hydroxyimides with C_2 symmetry, to improve the selectivity and to extend the scope of this type of oxidation to other substrates.

Experimental Section

General Methods. Organometallic reactions were performed under an oxygen-free atmosphere of argon with exclusion of moisture from reagents and glassware. The solvents were dried using standard methods prior to use. Analytical thin-layer chromatography (TLC) was performed using Merck 60F 254 plates. Visualization of the developed chromatogram was performed by UV absorbance or ethanolic phosphomolybdic acid. Column chromatography was performed using Merk Geduran Si 60 silica gel (0.040−0.063 mm) with the indicated solvent system. GLC analyses were performed with a flame ionization detector using a 0.2 mm × 30 m OV 17 capillary column. ^{1}H NMR spectra were recorded at 200 or 250 MHz. Chemical shifts are reported in ppm on the δ scale relative to tretramethylsilan (TMS) as an internal standard. ^{13}C NMR spectra were recorded at 50 or 62.5 MHz with complete proton decoupling. Chemical shifts are reported in ppm relative to tetramethylsilan on the δ scale. Mass spectra were recorded under chemical ionization using NH_3 + isobutane. Melting points have been determined in unsealed capillary tubes and are uncorrected.

(2-Dimethoxymethyl-phenyl)-(2-methoxy-1-naphthalenyl)-methanol (3a). To a solution of dimethylacetal of 2-bromobenzaldehyde **2** (1.155 g, 5 mmol) in THF (20 mL) was added a 2 M solution of *n*-BuLi in hexanes (2.5 mL, 5 mmol) at −78 °C. The temperature was progressively raised to 0 °C, and the mixture was stirred at this temperature for 30 min. To this solution was added 2-methoxy-1-naphthaldehyde (931 mg, 5 mmol) in THF (10 mL). The mixture was stirred for an additional 3 h at room temperature. It was then poured into cold water (30 mL) and extracted with EtOAc. The organic extract was washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, leaving a slightly yellow solid. Recrystallization from toluene gave pure **3a** (1.52 g, 90%) as colorless crystals. Mp 136−138 °C. IR (KBr) 3469 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.42 (s, 3H), 3.51 (s, 3H), 3.93 (s, 3H), 4.76 (d, J = 8 Hz, 1H), 6.09 (s, 1H), 6.92−8.11 (m, 11H).[15] ^{13}C NMR (50 MHz, $CDCl_3$) δ 53.0, 54.2, 56.4, 68.3, 101.5, 113.3, 122.0, 123.7, 124.2, 126.6, 127.0, 127.3, 127.6, 128.4, 128.6, 128.9, 129.4, 132.4, 136.3, 140.5, 155.1.

Dimethyl 2′-Methoxy-1,4-epoxy-1,2,3,4-tetrahydro-[1,1′]-binaphthalenyl-2,3-dicarboxylate (4a). To a suspension of **3a** (338 mg, 1 mmol) in 1 mL of toluene was added *p*-toluenesulfonic acid monohydrate (5 mg). The solids solubilized progressively. After complete solubilization, dimethylfumarate (433 mg, 3 mmol) was added, and the mixture was refluxed under argon for 3 days. After the mixture cooled, solid Na_2CO_3 (about 100 mg) was added, and the mixture was stirred for 5 min. The solid was filtered, and the solvent was removed at reduced pressure. The crude product was purified by column chromatography (20% EtOAc/hexanes) to give **4a** as a 1:3 mixture of diastereomers[16] (238 mg, 57%). After several days at room temperature, the oily residue crystallized partially. Addition of 2 mL of pentane allowed the isolation of the less abundant isomer as a white crystalline solid. Mp 74−75 °C. IR (KBr) 1750 cm^{-1}. ^{1}H NMR (200 MHz), $CDCl_3$) δ 2.80 (d, J = 4.8 Hz, 1H), 3.60 (s, 3H), 3.82 (s, 3H), 3.92 (s, 3H), 4.66 (d, J = 4.8 Hz, 1H), 5.77 (s, 1H), 6.90−8.90 (m, 10H). The more abundant isomer has not been obtained in a pure form. Its ^{1}H NMR spectrum has been deduced from the spectrum of the mixture of isomers: δ 3.33 (s, 3H), 3.62 (s, 3H), 3.76 (dd, J = 5.4, 4.8 Hz, 1H), 3.97 (s, 3H), 4.02 (d, J = 4.8 Hz, 1H), 5.88 (d, J = 5.5 Hz, 1H), 6.90−8.90 (m, 10H).

Dimethyl 2′-Methoxy-[1,1′]binaphthalenyl-2,3-dicarboxylate (5a). To a solution of Diels−Alder adduct **4a** (mixture of diastereomers) (1.1 g, 2.63 mmol) in 2 mL of CH_2Cl_2 under argon was added methanesulfonic acid (341 μL, 5.26 mmol) at 0 °C. The mixture was stirred at the same temperature for 15 min. The reaction was quenched by addition of water (2 mL). The mixture was extracted with CH_2Cl_2; the organic extract was washed with saturated $NaHCO_3$ solution and with brine, dried (Na_2SO_4), and filtered; and the solvent was removed at reduced pressure. The remaining solid was recrystallized from ethyl acetate to give 1.5 g of **5a** (100%). Mp 178 °C. IR (KBr) 1715 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.30 (s, 3H), 3.77 (s, 3H), 3.96 (s, 3H), 6.99−8.69 (m, 11H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 51.7, 52.5 56.7, 113.4, 118.9, 123.6, 124.9, 125.3, 126.4, 126.6, 127.5, 127.6, 128.6, 129.1, 129.4, 130.4, 132.2, 132.4, 133.8, 134.1, 134.6, 155.1, 166.4, 168.9. Anal. Calcd for $C_{23}H_{20}O_5$: C, 74.98; H, 5.04; O, 19.99. Found: C, 74.49; H, 5.11; O, 18.89.

2′-Methoxy-[1,1′]binaphthalenyl-2,3-dicarboxylic Acid (6a). Diester **5a** (1.44 g, 3.6 mmol) was dissolved in 50 mL of a

(14) Aurich, H. G. In *Nitrones, Nitronates and Nitroxides* Patai, S., Rappoport, Z., Eds; John Wiley & Sons: New York, 1989; p 314.

(15) Doublet at 4.76 ppm (J = 8 Hz) was exchangeable with D_2O. After exchange, a doublet located at 7.12 ppm (J = 8 Hz) appeared as a singlet.

(16) Determined by ^{1}H NMR of the crude mixture.

2 M solution of potassium hydroxide in MeOH, and the solution was refluxed for 24 h. The solution was cooled, and the methanol was removed under reduced pressure. The remaining solid was dissolved in water (50 mL). The aqueous solution was made acidic (pH 1−2) with dilute HCl. The white precipitate that formed was collected by filtration, washed with water, and dried. Diacid **6a** so obtained (1.34 g, 100%) was analytically pure. Mp 274 °C. IR (KBr) 3500, 1702 cm^{-1}. ^1H NMR (200 MHz, Me_2SO-d_6) δ 3.70 (s, 3H), 6.84−8.68 (m, 11H). MS (CI, NH_3 + isobutane) *m*/*z* 372 (M^+, 100%).

2-Hydroxy-4-(2-methoxy-1-naphthalenyl)-benzo[*f*]isoindole-1,3-dione (1a). A solution of diacid **6a** (744 mg, 2 mmol) in acetic anhydride (2 mL) was refluxed for 15 min. The solvent was removed under reduced pressure. The yellow residue was dissolved in 3 mL of anhydrous pyridine. Hydroxylamine hydrochloride (153 mg, 2.2 mmol) was added, and the mixture was stirred overnight at room temperature under argon and then for 4 h at 95 °C. The solvent was removed at reduced pressure, and water (5 mL) was added. The mixture was acidified with diluted HCl (pH 1−2). The yellow precipitate was collected by filtration, washed with water, and dried. Crystallization from ethanol gave **1a** as a yellow powder (487 mg, 66%). Mp 250−251 °C. IR (KBr) 3300, 1783, 1721 cm^{-1}. ^1H NMR (200 MHz, Me_2SO-d_6) δ 3.71 (s, 3H), 6.85−8.58 (m, 11H), 10.79 (s, 1H). ^{13}C NMR (50 MHz, Me_2SO-d_6) δ 56.2, 113.7, 116.3, 122.9, 123.5, 123.8, 124.3, 125.1, 126.9, 127.2, 128.2, 128.4, 129.1, 129.5, 130.5, 132.9, 134.1, 135.1, 136.2, 154.4, 162.8, 163.3. MS (CI, NH_3 + isobutane) *m*/*z* 387 ($MH^+ + NH_3$, 100%). Anal. Calcd for $C_{23}H_{15}NO_4$: C, 74.78; H, 4.10; N, 3.79; O, 17.33. Found: C, 74.20; H, 3.97; N, 3.71; O, 17.12.

Resolution of Diacid 6a. Anhydrous brucine (394 mg, 1 mmol) was dissolved in 11 mL of acetone at reflux. A solution of racemic diacid **6a** (372 mg, 1 mmol) in 3 mL of acetone was added. After cooling, the mixture was left in the refrigerator (4 °C) overnight. The solid that formed was collected by filtration and air-dried, giving 490 mg of white crystals. They were redissolved in a mixture of 12 mL of MeOH and 10 mL of acetone at reflux. After the mixture stood overnight in the freezer (−18 °C), a crystalline solid was formed which was collected by filtration and air-dried, giving 224 mg of white crystals. They were added to a mixture of 5 mL of EtOAc and 5 mL of 2 N HCl. After complete dissolution of the solid, the organic phase was separated, washed twice with brine, dried over Na_2SO_4, and filtered. Removal of the solvent left 91 mg of levorotatory diacid **6a** (24%, theoretical yield 50%). ee > 99%.[6] $[\alpha]^{20.7}_D$ −43.7° (*c* = 2, MeOH).

Optically Active *N*-Hydroxyimide 1a. General procedure applied for the synthesis of racemic **1a** was used starting with optically pure levorotatory diacid **6a**. Dextrorotatory **1a** was obtained as a yellow powder. ee > 99%.[7] Mp 259 °C. $[\alpha]^{21.4}_D$ +88.3° (*c* = 0.2, THF).

(2-Dimethoxymethyl-phenyl)-(2-phenyl-phenyl)-methanol (3b). The reaction was performed as for the preparation of **3a**, replacing 2-methoxy-1-naphthaldehyde by biphenyl-2-carboxaldehyde (1.285 g, 40 mmol). Workup gives 9.85 g of **3b** (74%) as white crystals after recrystallization from toluene. Mp 110−112 °C. IR (KBr) 3600 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 3.08 (s, 3H), 3.20 (s, 3H), 3.22 (d, *J* = 2.9 Hz, 1H), 4.92 (s, 1H), 6.08 (d, *J* = 2.9 Hz, 1H), 7.01−7.81(m, 13H).[17] ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 52.4, 54.8, 68.6, 101.9, 126.4, 126.8, 127.1, 127.4, 127.7, 128.2, 128.7, 129.1, 129.8, 135.0, 139.5, 140.9, 142.0.

Dimethyl 1-(2-Phenyl-phenyl)-1,4-epoxy-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylate (4b). To a suspension of **3b** (6.68 g, 20 mmol) in 20 mL of xylenes was added *p*-toluenesulfonic acid monohydrate (50 mg). After complete solubilization, dimethyl fumarate (8.64 g, 60 mmol) was added, and the mixture was refluxed under argon for 4 days. After the mixture cooled, solid Na_2CO_3 (about 200 mg) was added, and the mixture was stirred for 5 min. The solid was filtered, and the solvent was removed at reduced pressure. The crude product contains Diels−Alder adduct **4b** as 9:1 mixture of diastereomers.[16] Column chromatography (10% EtOAc/hexanes) allows isolation of globally 5.25 g (63%) of **4b**. Slight differences between the elution rate of the diastereomers allowed isolation of pure samples. First eluted diastereomer (most abundant): mp 94 °C. ^1H NMR (250 MHz, $CDCl_3$) δ 2.97 (d, *J* = 3.8 Hz, 1H), 3.30 (s, 3H), 3.66 (s, 3H), 4.19 (d, *J* = 3.8 Hz, 1H), 5.59 (s, 1H), 6.77−8.06 (m, 13H). Second eluted diastereomer (less abundant): mp 177−178 °C. ^1H NMR (250 MHz, $CDCl_3$) δ 3.36 (d, *J* = 4.8 Hz, 1H), 3.42 (s, 3H), 3.53 (s, 3H), 3.61 (dd, *J* = 5.1, 4.8 Hz, 1H), 5.46 (d, *J* = 5.1 Hz, 1H), 7.09−7.65 (m, 13H).

Dimethyl 1-(2-Phenyl-phenyl)-naphthalene-2,3-dicarboxylate (5b). The reaction was performed as for the preparation of **5a**. Starting from **4b** (mixture of diastereomers) (3.21 g, 7.75 mmol) **5b** was obtained as white crystals (2.58 g, 84%) after recrystallization from ethyl acetate. Mp 150−154 °C. IR (KBr) 1740 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.90 (s, 3H), 6.92−8.45 (m, 14H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 52.1, 52.5, 124.6, 126.5, 126.9, 127.1, 127.2, 127.5, 128.6, 128.7, 128.9, 129.1, 130.0, 131.9, 133.4, 134.8, 138.3, 140.8, 142.3, 166.5, 169.4. Anal. Calcd for $C_{26}H_{20}O_4$: C, 78.76; H, 5.09; O, 16.15. Found: C, 78.91; H, 5.28; O, 15.81.

1-(2-Phenyl-phenyl)-naphthalene-2,3-dicarboxylic Acid (6b). Saponification of **5b** (396 mg, 1 mmol) was performed with 15 mL of a 10 M solution of KOH in MeOH, at reflux for 24 h. Workup as described for the preparation of **6a** gave 327 mg (89%) of diacid **6b** as a white powder. Mp 174−179 °C. IR (KBr) 3500, 1690 cm^{-1}. ^1H NMR (200 MHz, Me_2SO-d_6) δ 6.94−8.51 (m, 14 H).

2-Hydroxy-4-(2-phenyl-phenyl)-benzo[*f*]isoindole-1,3-dione (1b). General procedure applied for the synthesis of **1a** was used, starting from diacid **6b** (552 mg, 1.5 mmol) and leading to 307 mg (56%) of **1b** after recrystallization from ethanol. Mp 227 °C. IR (KBr) 3200, 1780, 1715 cm^{-1}. ^1H NMR (200 MHz, Me_2SO-d_6) δ 7.34−8.39 (m, 14H); 10.86 (s, 1H). ^{13}C NMR (50 MHz, Me_2SO-d_6) δ 121.8, 123.9, 124.4, 126.8, 127.2, 127.7, 128.4, 128.9, 129.4, 129.7, 130.6, 132.9, 134.6, 138.5, 140.5, 141.4. MS (DCI, NH_3 + isobutane) *m*/*z* 366 (MH^+, 100%). Anal. Calcd for $C_{24}H_{15}NO_3$: C, 78.88; H, 4.14; N, 3.84; O, 13.14. Found: C, 78.98; H, 4.20; N, 3.54; O, 13.28.

Resolution of Diacid 6b. Anhydrous brucine (1,183 g, 3 mmol) was dissolved in 33 mL of acetone at reflux. A solution of 1.1 g (3 mmol) of racemic diacid **6b** was added. Solvent was removed at reduced pressure, leaving a partially crystallized yellow residue. A 20 mL portion of MeOH was added, and the mixture was refluxed for 10 min and then cooled at room temperature. The solid was collected by filtration, washed with MeOH, and air-dried, providing 1.00 g of white cristalline solid. It was added to a mixture of 20 mL of EtOAc and 20 mL of 2N HCl. After complete dissolution of the solid, the organic phase was separated, washed twice with brine, dried over Na_2SO_4, and filtered. Removal of the solvent under reduced pressure left 497 mg of levorotatory diacid **6b** (45%, theoretical yield 50%). ee > 99%.[6] Mp 138 °C. $[\alpha]^{21.7}_D$ −3.35° (*c* = 0.4, MeOH). The filtrate was concentrated at reduced pressure and treated as above, giving 515 mg of dextrorotatory diacid **6b** (47%). ee = 97%.[6] Mp 137 °C. $[\alpha]^{21.7}_D$ +3.25° (*c* = 0.4, MeOH).

Optically Active *N*-Hydroxyimide 1b. General procedure applied for the synthesis of **1a** was used, starting with optically active diacid **6b**. Dextrorotatory **6b** (ee = 97%) gave levorotatory **1b**, ee = 80%.[8] Mp 235 °C. $[\alpha]^{21.3}_D$ −11.6° (*c* = 0.2, THF); 338 mg of this sample of **1b** was recrystallized from 2.5 mL of ethanol, giving 245 mg of **1b**, ee >99%. Mp 251 °C. $[\alpha]^{20.9}_D$ −14.9° (*c* = 0.2, THF).

General Procedures of *N*-Hydroxyimides-Mediated Oxidations. (1) In the Presence of Acetaldehyde.[3] To 1 mmol of substrate dissolved in 3 mL of anhydrous acetonitrile was added 0.1 mmol of *N*-hydroxyimide. The mixture was vigorously stirred under an oxygen atmosphere while a solution of 56 μL (1 mmol) of acetaldehyde in 3 mL of anhydrous acetonitrile was added via a syringe pump over 5 h. Progress of the reaction was followed by TLC and/or GLC.

(2) In the Presence of CuCl. To a solution of 1 mmol of substrate dissolved in 5 mL of anhydrous acetonitrile were added 0.1 mmol of *N*-hydroxyimide and 0.1 mmol of CuCl. The mixture was vigorously stirred under an oxygen atmosphere, and progress of the reaction was followed by TLC and/or GLC.

(17) Doublet at 3.22 ppm (*J* = 2.9 Hz) was exchangeable with D_2O. After exchange, doublet at 6.08 ppm (*J* = 2.9 Hz) appeared as a singlet.

Substrates for Asymmetric Oxidations. 2-Methylindane (7a). Prepared according to literature procedure.[18]

2-Methoxy-2-phenylindane (7b). A commercial 35 wt % dispersion in oil of potassium hydride (1.6 g, 14 mmol) was washed twice with anhydrous pentane, and 14 mL of anhydrous THF was added. While the mixture stirred under argon, a solution of 2-phenylindan-2-ol[19] (2.51 g, 12 mmol) in 24 mL of THF was added dropwise, and the temperature of the reaction medium was maintained below 20 °C. After the end of hydrogen evolution, a solution of iodomethane (0.82 mL, 13.2 mmol) in 14 mL of THF was added dropwise. The mixture was stirred for 6 h at room temperature. It was quenched with 5 mL of MeOH followed by 50 mL of water and extracted with ether. The organic extract was washed with brine and dried over Na_2SO_4. The solvents were removed under reduced pressure. The crude product was purified by column chromatography (5% EtOAc/hexanes), giving 1.72 g of **7b** (64%) as a colorless liquid. IR (neat) 1480 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 3.08 (s, 3H), 3.23−3.54 (m, 4H), 7.10−7.68 (m, 9H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 44.1, 51.6, 89.7, 124.4, 126.6, 127.3, 128.3, 141.0, 143.0.

2-Dimethyl-4-phenyl-1,3-dioxolane (10a). Prepared according to literature procedure.[20]

2,2-Diphenyl-4-phenyl-1,3-dioxolane (10b). Benzophenone dimethyl acetal (2.28 g, 10 mmol) and 1-phenyl-1,2-ethanediol (1.38 g, 10 mmol) were dissolved in 100 mL of toluene. After addition of a catalytic amount of *p*-toluenesulfonic acid monohydrate, the mixture was refluxed for 1 h. After cooling at room temperature, the solution was washed with a saturated solution of $NaHCO_3$ and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the solid residue was recrystallized from hexanes, giving 2.42 g (80%) of **10b** as colorless crystals. Mp 98 °C. IR (KBr) 1453 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 3.85−3.93 (m, 1H), 4.32−4.40 (m, 1H), 5.08−5.16 (m, 1H), 7.28−7.63 (m, 15H). ^{13}C NMR (50 MHz, CDCl3) δ 72.2, 78.5, 110.4, 126.2, 126.6, 128.1, 128.2, 128.6, 138.8, 142.4, 142.6.

Oxidation Products. 2-Methylindan-1-one (8a). Identified by comparison with literature data.[9]

2-Methoxy-2-phenylindan-1-one (8b). After completion of the oxidation of **7b** (method 1 or 2), the solvent was removed at reduced pressure. The residue was purified by column chromatography (10% EtOAc/hexanes), and **8b** was isolated as a colorless oil. IR (neat) 1739, 1450 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ 3.34 (s, 3H), 3.59 (s, 2H), 7.23−7.69 (m, 9H). ^{13}C NMR (62.5 MHz, $CDCl_3$) 40.5, 52.8, 86.3, 125.2, 126.0, 126.4, 127.5, 127.8, 128.1, 128.6, 130.0, 134.1, 134.7, 138.4, 150.8, 202.4.

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