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Enantioselective Synthesis and Chiroptical Properties of Optically Active Isoflavone Epoxides

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Dedicated to the late Prof. Dr. Günther Snatzke on the occasion of his 70th birth anniversary.

Abstract: Enantioselective epoxidation of isoflavones **1a-f** has been performed by using Mn(III)salen complexes (*R,R*)-**3** and (*S,S*)-**3** as catalysts and dimethyldioxirane (DMD) or NaOCl together with 4-phenylpyridine N-oxide (PPNO) axial ligand as oxygen donors to obtain nonracemic isoflavone epoxides **2a-f**. With the help of circular dichroism (CD) spectra of three enantiomeric pairs, and Snatzke's inverse octant rule, the absolute configurations of these optically active isoflavone epoxides have been determined.

INTRODUCTION

Isoflavones have been isolated from various plants and are well-known natural products.[1] However, their epoxidation has received less attention. The first representatives of their epoxides were prepared either by the alkaline hydrogen peroxide epoxidation of isoflavones[2] or by an intramolecular Darzens reaction of α-bromo-o-acyloxyacetophenones.[3] Recently we have demonstrated that dimethyldioxirane (DMD) is a convenient and effective reagent for the epoxidation of variously substituted isoflavones.[4] We have also succeeded to prepare the epoxides of isoflavone glycosides in high yields by this versatile oxidizing agent.[5] However, it has been observed that the presence of the chiral sugar auxiliary does not exercise any enantiofacial selectivity by using the achiral DMD oxidant such that a 1:1 mixture of the diastereomeric epoxides was isolated in each case. Since our aim was to synthesize nonracemic isoflavone epoxides, we have investigated the utility of enantiopure catalysts as the source of chirality instead of a chiral auxiliary connected to the isoflavone molecule.

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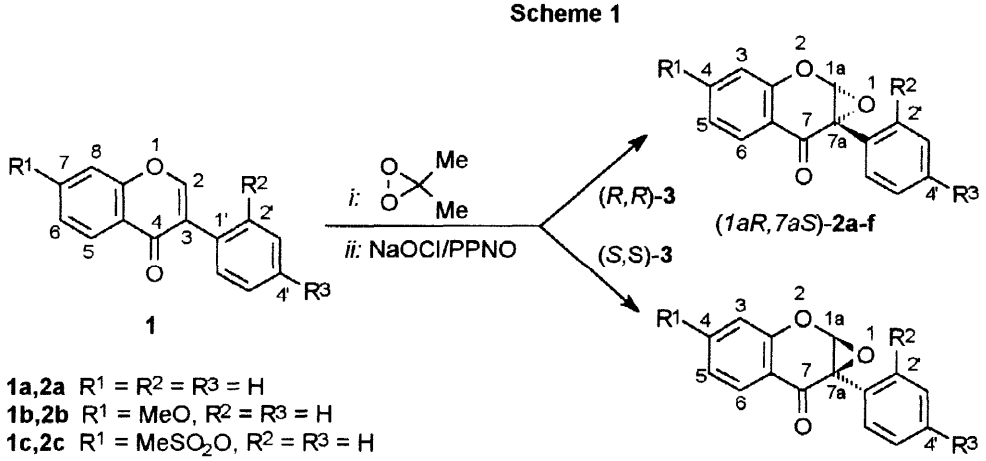
The Jacobsen's Mn(III)salen complexes have proven to be highly efficient catalysts for the enantioselective epoxidation of olefins by using various oxygen donors, e.g. NaOCl, H_2O_2, n-Bu_4IO_4 and iodosobenzene.[6] In our previous study on the enantioselective epoxidation of 2,2-dimethyl-2*H*-chromenes, the combination of optically active Mn(III)salen complexes and isolated DMD[7] proved to be advantageous for this purpose.[8] We present herein the application of the Jacobsen's Mn(III)salen catalysts[6] with DMD or NaOCl as oxygen-atom sources for the enantioselective epoxidation of isoflavones **1**, for which no catalytic asymmetric epoxidation has hitherto been reported.

RESULTS AND DISCUSSION

In the first series of our experiments the enantioselective epoxidation of isoflavones **1a-f** (Scheme 1) has been performed with the optically active complexes of (*R,R*)-**3** and (*S,S*)-**3** by using isolated dimethyldioxirane (ca. 0.05-0.1 M acetone solution)[7] as the oxygen source. Our experimental results (*Method i*) reveal that the use of 14-16 mol% catalyst in combination with 6-10 equiv. of DMD provides nonracemic isoflavone epoxides **2a-f** in moderate yields. The low yields are a consequence of incomplete conversion of the starting material due to the electron-poor double bond. The enantioselectivities varied from 20 to 92% e.e., which depended on the substitution pattern of the starting isoflavone (cf. Scheme 1).

Scheme 1



1

1a,2a $R^1 = R^2 = R^3 = H$
1b,2b R^1 = MeO, $R^2 = R^3 = H$
1c,2c $R^1 = MeSO_2O$, $R^2 = R^3 = H$
1d,2d $R^1 = R^3$ = MeO, $R^2 = H$
1e,2e $R^1 = R^2$ = MeO, $R^3 = H$
1f,2f $R^1 = MeSO_2O$, R^2 =MeO, $R^3 = H$

(*R,R*)-**3**: (*R,R*)-N,N'-*bis*(3,5-di-*tert*butylsalicylidene)-1,2-cyclohexanediamino manganese chloride
(*S,S*)-**3**: (*S,S*)-N,N'-*bis*(3,5-di-*tert*butylsalicylidene)-1,2-cyclohexanediamino manganese chloride

As far as the substitution pattern is concerned, the electronic character of the substituent at the C-7 atom of substrate **1** does not significantly affect the rate and enantioselectivity of the reaction, although the electronic character of the substituent at this position may alter the reactivity of the isoflavone molecule. However, a methoxy group in the vicinity of the epoxidation site in derivatives **1e** and **1f** considerably enhanced the enantiofacial selectivity (cf. Experimental). In contrast, neither a higher molar ratio of the catalyst nor a larger

amount of the oxygen source improved either the yield or the enantiomeric excess. Prolongation of the reaction time (10 days) was also ineffective in enhancing the conversion of the isoflavones **1a-f**.

To improve both the yield and the enantioselectivity of the reaction, NaOCl as oxygen donor together with 4-phenylpyridine N-oxide (PPNO) as an axial ligand was used (*Method ii*) instead of dimethyldioxirane (*Method i*). The conversion of the isoflavone **1** generally ceases after 24 h and the use of 25 mol% Mn(III)salen complex **3** together with 7.5 equiv. of NaOCl and 0.5 equiv. of PPNO proved to be the optimum reaction conditions for the enantioselective epoxidation of isoflavones **1** by this method. The yields ranged between 25-31% which are comparable with those obtained by *Method i*. The enantiomeric excess is similarly high with both methods in the case of compounds **1e** and **1f** with a methoxy group at the C-2' atom. However, for the epoxidation of isoflavones **1a-d** the utilization of NaOCl together with PPNO resulted in somewhat higher enantiofacial selectivity. Thus, the use of NaOCl isntead of DMD as oxygen source does not offer any advantage.

The structural assignment of the epoxides **2a-f** rests on microanalyses, and IR and NMR spectroscopic data (cf. Experimental). In their ^{1}H NMR spectra, the disappearance of the singlet signal of the 2-H proton at ca. 8 ppm, characteristic of the isoflavone skeleton, and the appearance of a singlet signal between 5.36 and 5.56 ppm, assigned to the 1a-H proton of the isoflavone epoxide, established the presence of the oxirane ring. Chemical shifts of the C-1a (δ = 82-84 ppm) and C-7a (δ = 62-64 ppm) atoms in the ^{13}C NMR spectra also confirm the presence of an epoxide functionality. Moreover, the extreme high value of the heteronuclear coupling constant ^{1}J(1a-H,C-1a) = 224 Hz measured for the epoxide **2d** by a ^{13}C-coupled HMQC experiment confirms the epoxide ring.

In our preliminary account[9] we have reported that the absolute configuration of these optically active isoflavone epoxides has been determined by X-ray-diffraction analysis based on the Flack parameter (SHELXL >93). High-level optical purity of both enantiomers of the epoxides **2b,e,f** obtained either the considerable enantiofacial selectivity of the epoxidation or improved by recrystallization, made possible a correlation of their circular dichroism (CD) spectra with the absolute configuration of their centres of chirality. Circular dichroism spectroscopy was successfully exploited for the determination of the absolute configuration of optically active flavanones,[10] homoisoflavanones[11] and isoflavanones.[12] The utility of the modified octant rule[13] for this purpose was demonstrated as well.

In the UV spectra of the epoxides **2b,e,f** in acetonitrile (Fig. 1) displayed a distinct maximum between 253 and 277 nm, together with two other maxima or shoulders in the wavelength region of 211-222 nm and 301-307 nm. In their CD spectra 4-5 maxima, some cases with shoulders, have been detected (cf. Experimental). Both these UV and CD spectral characteristics reveal the complexity of the chromophore, which renders an unambiguous assignment of the UV bands and CD maxima to particular electronic transitions difficult. Fortunately, a complete assignment of all the CD maxima to the electronic transitions is not a prerequisite for a successful correlation of the chiroptical properties and the configuration of these epoxides.

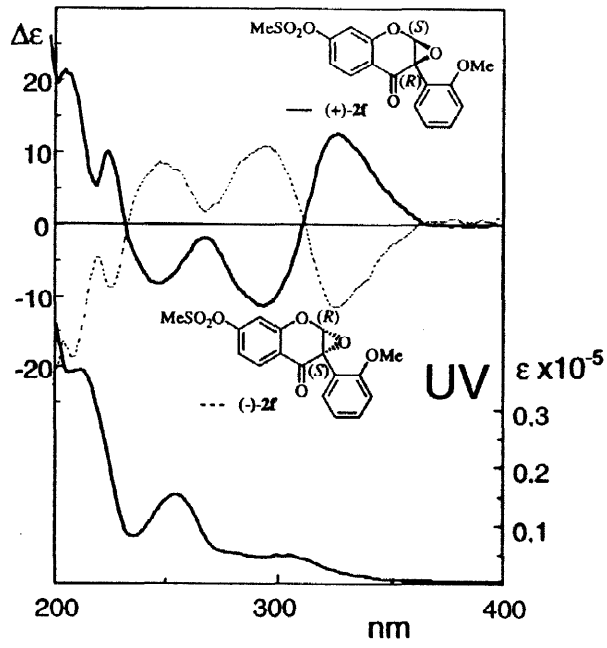


Figure 1. UV and CD spectra of the epoxide **2f** in MeCN.

Presumably the intense CD maximum (Δε 7-17) between 320-330 nm belongs to the n→π* transition of the carbonyl chromophore. The sign of this CD band, together with the modified octant rule is generally used for the determination of the absolute configuration of flavonoids with a chromanone skeleton.[10-13] However, for α,β-epoxyketones neither the octant rule nor the modified octant rule are valid, instead the so-called 'inverse octant rule' (Fig. 2), discovered by Snatzke,[13] applies to correlate the sign of the n→π* CD maximum and the configuration of such compounds. According to this rule, the negative n→π* CD maximum of the epoxides (-)-**2b,e,f** unequivocally prove the (*1aR,7aS*), while a positive sign of the same CD band of their (+)-enantiomers reveals the (*1aS,7aR*) absolute configuration, the latter established by X-ray-diffraction analysis.[9] Therefore, the absolute configuration of the optically active isoflavone epoxides was determined by two independent methods.

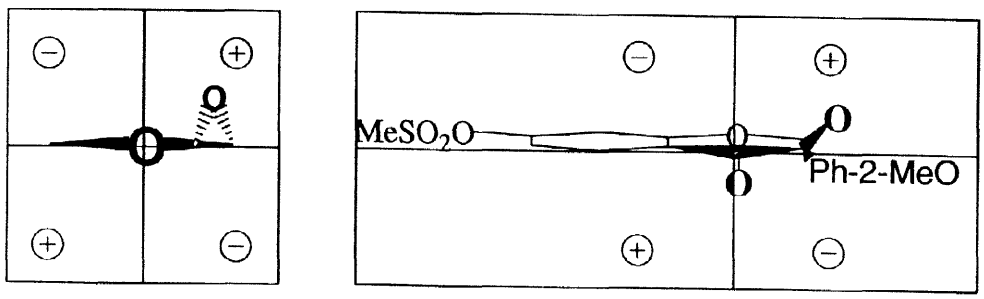


Figure 2. Inverse octant rule for α,β-epoxy ketones (left) and its application for epoxide (*1aS,7aR*)-**2f** (right).

The observed absolute configuration of the isoflavone epoxides, prepared herein by the catalytic enantioselective epoxidation with the Mn(III)salen catalyst, may be rationalized by means of the Katsuki model[6f,14] for the epoxidation mechanism. Figure 3 shows the trajectory for the attack of isoflavone **1b** to the oxo species of the (*S,S*)-**3** catalyst which results in the (*1aS,7aR*)-**2b**.[14]

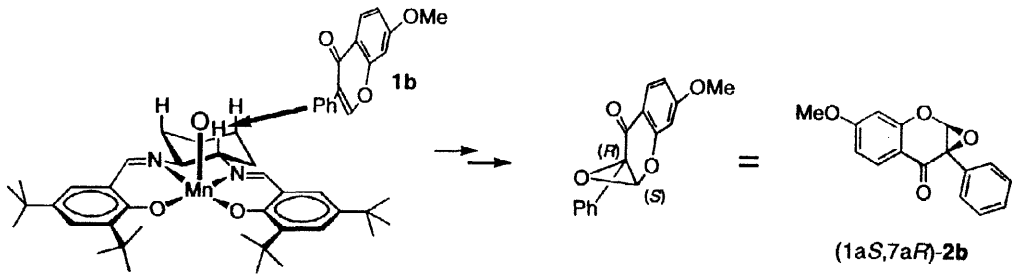


Figure 3. Trajectory for the attack of isoflavone **1b** to the oxo species of the (*S,S*)-**3** catalyst.

In summary, optically active isoflavone epoxides have been sythesized for the first time by a catalytic enantioselective epoxidation. It has been demonstrated that the combination of the Jacobsen's Mn(III)salen catalysts either with dimethyldioxirane or with NaOCl as oxygen donors may be used for the enantioselective epoxidation of even such electron-poor compounds as the isoflavones. The absolute configuration of the nonracemic epoxides **2** have been successfully determined by two independent methods, *viz.* X-ray diffraction analysis[9] and by circular dichroism (CD) spectroscopy, the latter utilized Snatzke's inverse octant rule.[13]

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EXPERIMENTAL

All reagents and catalysts were of commercial purity. Caroat (potassium monoperoxosulfate), the triple salt $2KHSO_5.KHSO_4.K_2SO_4$, was used as received, a generous gift from the Peroxid-Chemie GmbH (München, Germany). Analytical TLC plates and silica gel for chromatography were purchased from the Merck. Melting points were determined on a Reichert Thermovar hot-stage apparatus and are uncorrected. Microanalyses were performed in-house on a Carlo-Erba 1106 CHN Analyzer. ^1H and ^{13}C NMR spectra were acquired on Bruker AC 250 (250/63 MHz), on Bruker AC 200 (200/50 MHz) or on Bruker DRX-500 (500/125 MHz) spectrometers in $CDCl_3$ (TMS, δ 0.0 ppm) at room temperature (ca. 20 °C). IR spectra were measured with a FT-IR Perkin-Elmer 1600 spectrometer. Thin-layer chromatography (TLC) was performed on Kieselgel 60 F_{254} (Merck) layer by using toluene:ethyl acetate (4:1 v/v) as eluent. Optical purity was determined by HPLC on

Chiracel OD, OD-H or OB-H columns (Diacel Chemical Industries, 0.46 cm x 25 cm) with hexane:2-propanol (5:1 or 9:1 v/v) as mobil phase. The optical rotations were determined by using a Perkin-Elmer 241 polarimeter in $CHCl_3$ (c ca. 1). UV spectra were measured on a Hitachi U-3200 instrument or on a Shimadzu UV 2101 PC UV-VIS scanning spectrometer in MeCN. CD spectra were recorded on a Jasco J 600 spectrometer in MeCN at room temperature (ca. 20 °C).

Dimethyldioxirane (DMD, as acetone solution) was prepared as described[7] and its peroxide content was determined iodometrically. The starting materials **1a,b** and **1d,e** were synthesized according to published procedures.[15]

Since the UV, IR, ^1H and ^{13}C NMR spectra of the enantiomeric pairs are identical, only for the (*1aS,7aR*) enantiomers have been given.

7-Mesyloxyisoflavone (1c)

Mesyl chloride (6.0 ml) was added in small portions to a cooled and stirred mixture of 7-hydroxyisoflavone[15f] (4.70 g) and anhydrous pyridine (100 ml). The mixture was left to stand in refrigerator for 48 h and then poured onto crushed ice. The precipitated material was collected by filtration, washed with water and crystallized from methanol to yield 5.90 g (93%), m.p. 177-178 °C (MeOH), colorless plates. Anal. Calcd for $C_{16}H_{12}O_5S$: C 60.75, H 3.82; found C 60.88, H 3.80%. IR [KBr, ν (cm^{-1})]: 3085, 3030, 2935, 1630, 1615, 1440, 1370, 1225, 1170, 950. ^1H NMR (δ): 3.24 (s, 3H, $MeSO_2O$), 7.33-7.57 (m, 7 arom. H), 8.03 (s, 1H, 2-H), 8.37 (d, J = 8.9 Hz, 1H, 5-H); ^{13}C NMR (δ): 38.6 (Me), 112.0 (C-2), 119,7 (C-8), 126.3 (C-3), 128.9 C-4'), 129.0 C-2',6'), 129.1 (C-6), 129.3 (C-3',5'), 131.6 (C-1'), 152.7 (C-4a), 153.1 (C-8a), 153.7 (C-5), 158.0 C-7), 175.6 (C-4).

7-Mesyloxy-2'-methoxyisoflavone (1f)

7-Hydroxy-2'-methoxyisoflavone[15c] (5.40 g) dissolved in anhydrous pyridine (150 ml) was allowed to react with mesyl chloride (6.0 ml) as described for compound **1c** to afford 4.80 g (69%), m.p. 169-170 °C (MeOH), colorless plates. Anal. Calcd for $C_{17}H_{14}O_6S$: C 58.96, H 4.07; found C 58.81, H 4.09%. IR [KBr, ν (cm^{-1})]: 3084, 3028, 2932, 1630, 1612, 1450, 1372, 1227, 1180, 948. ^1H NMR (δ): 3.21 (s, 3H, $MeSO_2O$), 3.80 (s, 3H, MeO), 6.99-7.48 (m, 6 arom. H), 7.99 (s, 1H, 2-H), 8.36 (d, J = 8.7 Hz, 1H, 5-H); ^{13}C NMR (δ): 38.0 (Me), 55.7 (Me), 111.2 (C-2), 111.5 (C-3'), 119.1 (C-8), 120.2 (C-1'), 120.6 (C-5'), 123.2 (C-3), 123.4 (C-4'), 128.6 (C-6'), 130.0 (C-6), 131.6 (C-2'), 152.2 (C-4a), 154.5 (C-8a), 156.6 (C-5), 157.4 (C-7), 175.0 (C-4).

General procedures for the enantioselective epoxidation of isoflavones 1a-f

Method i: Dimethyldioxirane (ca. 0.05-0.1 M acetone solution) was added to a stirred solution of the particular isoflavone **1** (1.00 mmol) and Mn(III)salen complex **3** (14-16 mol%) in anhydrous CH_2Cl_2 (10.0 ml) and the stirring was continued at room temperature (ca. 20 °C). The progress of the reaction was monitored by TLC and new batches of DMD were added in 24-h intervals until the conversion of the starting material halted

(10 d). The solvent was evaporated (ca. 25 °C/15 Torr) and the epoxides **2a-f** were purified by silica-gel chromatography by using toluene:ethyl acetate (4:1 v/v) as eluent.

Method ii: A 2N NaOCl solution (4.0 ml, 7.50 mmol) in 0.05 N Na_2HPO_4 buffer (12.0 ml, pH 11.3) was added to a stirred solution of isoflavone **1** (1.00 mmol), Mn(III)salen complex **3** (25 mol%) and 4-phenylpyridine N-oxide (0.50 mmol). Stirring was continued for 24 h, the mixture was extracted with CH_2Cl_2 (3 x 10 ml), the solution was dried over Na_2SO_4, the solvent was evaporated (ca. 25 °C/15 Torr), and the residue was purified as described for *Method i* to afford the epoxides **2a-f**.

(1aR,7aS)-1a,7a-Dihydro-7a-phenyl-7H-oxireno[b][1]benzopyran-7-one [(*1aR,7aS*)-**2a**]

Method i: DMD (9 equiv.) and (*R,R*)-**3** (14 mol%), yield 31%, $[\alpha]_D^{23}$ = -153 (c = 1, $CHCl_3$, 52% e.e.), m.p. 83-84 °C. Anal. Calcd for $C_{15}H_{10}O_3$: C 75.62, H 4.32; found C 75.57, H 4.35%.

(1aS,7aR)-1a,7a-Dihydro-7a-phenyl-7H-oxireno[b][1]benzopyran-7-one [(*1aS,7aR*)-**2a**]

Method i: DMD (9 equiv.) and (*S,S*)-**3** (14 mol %), yield 34%, $[\alpha]_D^{23}$ = +200 (c 7 1, $CHCl_3$, 56% e.e.); *Method ii:* (*S,S*)-**3** (25 mol%), yield 25%, $[\alpha]_D^{23}$ = +204 (c = 1, $CHCl_3$, 65% e.e.), m.p. 83-84 °C. Anal. Calcd for $C_{15}H_{10}O_3$: C 75.62, H 4.32; found C 75.66, H 4.30%. IR [KBr, ν (cm^{-1})]: 3065, 1685, 1610, 1465, 1350, 1270, 1215, 1125, 1090. ^1H NMR (δ): 5.53 (s, 1H, 1a-H), 7.11-7.65 (m, 8 arom. H), 8.03 (dd, J = 7.6, 1.5 Hz, 1-H, 6-H); ^{13}C NMR (δ): 63.1 (C-7a), 83.0 (C-1a), 118.0 (C-3), 120.2 (C-6a), 123.5 (C-5), 127.3 (C-2',6'), 127.8 (C-6), 128.4 (C-3',5'), 129.1 (C-4'), 130.1 (C-1'), 136.2 (C-4), 155.1 (C-3a), 187.5 (C-7).

(1aR,7aS)-1a,7a-Dihydro-4-methoxy-7a-phenyl-7H-oxireno[b][1]benzopyran-7-one [(*1aR,7aS*)-**2b**]

Method i: DMD (6 equiv.) and (*R,R*)-**3** (14 mol%), yield 27%, $[\alpha]_D^{23}$ = -122 (c = 1, $CHCl_3$, 37% e.e.); *Method ii:* (*R,R*)-**3** (25 mol%), yield 30%, $[\alpha]_D^{23}$ = -367 (c = 1, $CHCl_3$ 99% e.e., recrystallized from MeOH, crude product 71% e.e.), m.p. 124-125 °C. Anal. Calcd for $C_{16}H_{12}O_3$: C 71.63, H 4.51; found C 71.54, H 4.53%. CD [MeCN, λ (nm), Δε]: 208 sh (-6.54), 233 (-3.66), 225 (-3.74), 243 (+0.11), 250 (-0.03), 277 sh (+4.04), 295 (+5.84), 328 (-6.80).

(1aS,7aR)-1a,7a-Dihydro-4-methoxy-7a-phenyl-7H-oxireno[b][1]benzopyran-7-one [(*1aS,7aR*)-**2b**

Method i: DMD (6 equiv.) and (*S,S*)-**3** (14 mol%), yield 36%, $[\alpha]_D^{23}$ = +133 (c = 1, $CHCl_3$, 39% e.e.); *Method ii*: (*S,S*)-**3** (25 mol%), yield 26%, $[\alpha]_D^{23}$ = +358 (c = 1, $CHCl_3$, 99% e.e., recrytallized from MeOH, crude product 77% e.e.), m.p. 124-125 °C. Anal. Calcd for $C_{16}H_{13}O_3$: C 71.63, H 4.51; found C 71.75, H 4.48%. UV [MeCN, λ, (nm), ε]: 222 sh (11180), 277 (6463), 307 sh (3861). CD [MeCN, λ (nm), Δε]: 203 (+3.86), 206 (+4.73), 223 (+3.06), 226 (+3.42), 240 (-1.62), 248 (-0.56), 276 (-5.21), 287 (-4.54), 326 (+8.06). IR [KBr, ν (cm^{-1})]: 3415, 2940, 2360, 1670, 1620, 1580, 1440, 1270, 1245, 1120. ^1H NMR (δ): 3.88 (s, 3H, MeO), 5.49 (s, 1H, 1a-H), 6.55-7.47 (m, 7 arom. H), 7.96 (d, J = 8.8 Hz, 1H, 6-H); ^{13}C NMR (δ): 55.8 (Me),

62.4 (C-7a), 83.3 (C-1a), 101.1 (C-3), 113.5 (C-6a), 113.6 (C-5), 127.2 (C-2',6'), 128.3 (C-3',5'), 128.9 (C-4'), 129.5 (C-6), 130.7 (C-1'), 157.2 (C-3a), 166.2 (C-4), 186.1 (C-7).

(1aR,7aS)-1a,7a-Dihydro-4-mesyloxy-7a-phenyl-7H-oxireno[b][1]benzopyran-7-one [(*1aR,7aS*)-**2c**]

Method i: DMD (10 equiv.) and (*R,R*)-**3** (14 mol%), yield 22%, $[\alpha]_D^{23}$ = -47 (c = 1, $CHCl_3$, 21% e.e.), m.p. 118-120 °C. Anal. Calcd for $C_{16}H_{12}O_6S$: C 57.83, H 3.64; found C 57.92, H 3.67%.

(1aS,7aR)-1a,7a-Dihydro-4-mesyloxy-7a-phenyl-7H-oxireno[b][1]benzopyran-7-one [(*1aS,7aR*)-**2c**]

Method i: DMD (10 equiv.) and (*S,S*)-**3** (14 mol%), yield 27%, $[\alpha]_D^{23}$ = +60 (c = 1, $CHCl_3$, 48% e.e.); *Method ii:* (*S,S*)-**3** (25 mol%), yield 23%, $[\alpha]_D^{23}$ = +70 (c = 1, $CHCl_3$, 56% e.e.), m.p. 117- 119 °C. Anal. Calcd for $C_{16}H_{12}O_6S$: C 57.83, H 3.64; found C 57.74, H 3.62%. IR [KBr, ν (cm^{-1})]: 3060, 2945, 1690, 1620, 1440, 1370, 1230, 1175, 1135, 955. ^1H NMR (δ): 3.23 (s, 3H, $MeSO_2O$), 5.56 (s, 1H, 1a-H), 7.10-7.47 (m, 7 arom. H), 8.10 (d, J = 8.3 Hz, 1H 6-H); ^{13}C NMR (δ): 38.1 (Me), 62.9 (C-7a), 83.2 (C-1a), 111.4 (C-3), 117.2 (C-5), 118.9 (C-6a), 127.2 (C-2',6'), 128.3 (C-3',5'), 129.2 (C-4'), 129.8 (C-1'), 129.9 (C-6), 154.3 (C-4), 156.0 (C-3a), 186.2 (C-7).

(1aR,7aS)-1a,7a-Dihydro-4-methoxy-7a-(4-methoxyphenyl)-7H-oxireno[b][1]benzopyran-7-one [(*1aR,7a*)-**2d**]

Method i: DMD (10 equiv.) and (*R,R*)-**3** (16 mol%), yield 39%, $[\alpha]_D^{23}$ = -112 (c = 1, $CHCl_3$, 52% e.e.), m.p. 159-160 °C. Anal. Calcd for $C_{17}H_{14}O_5$: C 68.45, H 4.73; found C 68.57, H 4.70%.

(1aS,7aR)-1a,7a-Dihydro-4-methoxy-7a-(4-methoxyphenyl)-7H-oxireno[b][1]benzopyran-7-one [(*1aS,7aR*)-**2d**]

Method i: DMD (10 equiv.) and (*S,S*)-**3** (16 mol%), yield 29%, $[\alpha]_D^{23}$ = +65 (c = 1, $CHCl_3$, 22% e.e.); *Method ii:* (*S,S*)-**3** (25 mol%), yield 30%, $[\alpha]_D^{23}$ = +321 (c = 1, $CHCl_3$, 98% e.e., recrystallized from MeOH, crude product 76% e.e.), m.p. 160-161 °C. Anal. Calcd for $C_{17}H_{14}O_5$: C 68.45, H 4.73; found C 68.37, H 4.76%. IR [KBr, ν (cm^{-1})]: 3390, 2960, 2840, 1670, 1610, 1580, 1440, 1245, 1165, 1120. ^1H NMR (δ): 3.80 (s, 3H, MeO), 3.88 (s, 3H, MeO), 5.49 (s, 1H, 1a-H), 6.54-7.40 (m, 6 arom. H), 7.95 (d, J = 8.9 Hz, 1H, 6-H); ^{13}C NMR (δ): 55.4 (Me), 55.8 (Me), 62.3 (C-7a), 83.4 (C-1a), 101.1 (C-3), 111.6 (C-5), 113.6 (C-6a), 113.9 (C-3',5'), 122.7 (C-1'), 128.7 (C-2',6'), 129.5 (C-6), 157.2 (C-3a), 160.1 (C-4'), 166.2 (C-4), 186.4 (C-7).

(1aR,7aS)-1a,7a-Dihydro-4-methoxy-7a-(2-methoxyphenyl)-7H-oxireno[b][1]benzopyran-7-one [(*1aR,7aS*)-**2e**]

Method i: DMD (6 equiv.) and (*R,R*)-**3** (16 mol%), yield 31%, $[\alpha]_D^{23}$ = -122 (c = 1, $CHCl_3$, 82% e.e.), m.p. 126-127 °C. Anal. Calcd for $C_{17}H_{14}O_5$: C 68.45, H 4.73; found C 68.35, H 4.70%. CD [MeCN, λ (nm), Δε]: 206 (-17.68), 208 (-18.68), 224 (+4.88), 232 (-7.13), 242 sh (+2.15), 295 (+15.57), 325 (-16.99).

(1aS,7aR)-1a,7a-Dihydro-4-methoxy-7a-(2-methoxyphenyl)-7H-oxireno[b][1]benzopyran-7-one [(*1aS,7aR*)-**2e**]

Method i: DMD (6 equiv.) and (*S,S*)-**3** (16 mol%), yield 32%, $[\alpha]_D^{23}$ = +126 (c = 1, $CHCl_3$, 86% e.e.); *Method ii:* (*S,S*)-**3** (25 mol%), yield 30%, $[\alpha]_D^{23}$ = +165 (c = 1, $CHCl_3$, 90% e.e.), m.p. 127-129 °C. Anal. Calcd for $C_{17}H_{14}O_5$: C 68.45, H 4.73; found C 68.40, H 4.78. UV [MeCN, λ (nm), ε]: 213 sh (30769), 277 (17975), 301 sh (9487). CD [MeCN, λ (nm), Δε]: 204 (+13.86), 210 (+16.47), 224 (-4.92), 232 (+6.73), 244 sh (-2.90), 295 (-15.09), 324 (+15.51). IR [KBr, ν (cm^{-1})]: 3415, 2940, 2840, 2360, 1680, 1605, 1495, 1440, 1275, 1240. ^{1}H NMR (δ): 3.61 (s, 3H, MeO), 3.68 (s, 3H, MeO), 5.36 (s, 1H, 1a-H), 6.41-7.26 (m, 6 arom. H), 7.80 (d, J = 8.9 Hz, 1H, 6-H). ^{13}C NMR (δ): 55.6 (Me), 55.8 (Me), 61.2 (C-7a), 82.9 (C-1a), 101.1 (C-3), 110.5 (C-3'), 111.4 (C-5), 113.0 (C-6a), 120.7 (C-1',5'), 128.3 (C-6'), 129.5 (C-6), 130.4 (C-4'), 157.4 (C-3a,2'), 166.0 (C-4), 185.5 (C-7).

(1aR,7aS)-1a,7a-Dihydro-4-mesyloxy-7a-(2-methoxyphenyl)-7H-oxireno[b][1]benzopyran-7-one [(*1aR,7aS*)-**2f**]

Method i: DMD (6 equiv.) and (*R,R*)-**3** (16 mol%), yield 25%, $[\alpha]_D^{23}$ = -58 (c = 1, $CHCl_3$, 72% e.e.), m.p. 144-145 °C. Anal. Calcd for $C_{17}H_{14}O_7S$: C 56.35, H 3.89; found C 56.27, H 3.91%. CD [MeCN, λ (nm), Δε]: 203 (-21.62), 205 (-25.57), 209 sh (-24.39), 220 (-1.37), 227 (-9.75), 248 (+12.16), 268 (+3.98), 297 (+15.73), 330 (-13.57).

(1aS,7aR)-1a,7a-Dihydro-4-mesyloxy-7a-(2-methoxyphenyl)-7H-oxireno[b][1]benzopyran-7-one [(*1aS,7aR*)-**2f**]

Method i: DMD (6 equiv.) and (*S,S*)-**3** (16 mol%), yield 23%, $[\alpha]_D^{23}$ = +86 (c = 1, $CHCl_3$, 90% e.e.); *Method ii:* (*S,S*)-**3** (25 mol%), yield, 31%, $[\alpha]_D^{23}$ = +87 (c = 1, $CHCl_3$, 94% e.e.), m.p. 145-146 °C. Anal. Calcd for $C_{17}H_{14}O_7S$: C 56.35, H 3.89; found C 56.41, H 3.86%. UV [MeCN, λ (nm), ε]: 211 (41864), 253 (17158), 306 (5129). CD [MeCN, λ (nm), Δε]: 204 (+20.95), 207 (+23.28), 220 (+5.56), 226 (+10.76), 248 (-9.24), 270 (-2.36), 296 (-12.77), 329 (+13.48). IR [KBr, ν (cm^{-1})]: 3075, 3025, 2940, 1685, 1610, 1585, 1500, 1440, 1355. ^{1}H NMR (δ): 3.22 (s, 3H, $MeSO_2O$), 3.78 (s, 3H, MeO), 5.54 (s, 1H, 1a-H), 6.93-7.44 (m, 6 arom. H), 8.08 (m, 1H, 6-H). ^{13}C NMR (δ): 38.2 (Me), 55.7 (Me), 61.6 (C-7a), 83.0 (C-1a), 110.5 (C-3'), 111.5 (C-3), 117.0 (C-5), 118.4 (C-6a), 119.8 (C-1'), 120.8 (C-5'), 128.2 (C-6'), 130.0 (C-6), 130.8 (C-4'), 154.3 (C-4), 156.4 (C-3a), 157.4 (C-2'), 185.5 (C-7).

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