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Synthesis of novel C_2-symmetric and enantiomerically pure bisbenzoxazoles and bisbenzothiazoles derived from L- and D-tartaric acids

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Abstract—Five pairs of novel C_2-symmetric and enantiomerically pure bisbenzoxazoles and a pair of bisbenzothiazoles derived from L- and D-tartaric acids have been synthesized from L- and D-2,3-*O*-isopropylidenetartaric dichlorides and *o*-aminophenol derivatives or *o*-aminothiophenol, respectively, in two- or one-step reactions. The mechanism for the formation of bisbenzoxazoles and bisbenzothiazoles was suggested. The UV and ^{1}H NMR spectra showed that no coordination between the bisbenzoheterazoles and Cu(I) or Ni(II) cations occurred due to the lack of a sufficiently basic nitrogen donor atom in the benzoheterazole moiety.

1. Introduction

The C_2-symmetrical chiral bisoxazoline derivatives have recently been employed as ligands in a wide variety of metal-catalyzed asymmetric reactions,[1] including the cyclopropanation of olefins,[2] aziridination of olefins,[3] Diels–Alder and hetero-Diels–Alder reactions,[4] 1,3-dipolar cycloadditions,[5] allylic displacement,[6] addition of dialkylzinc to aldehydes,[7] organolithium addition to imines,[8] hydrosilylative reduction,[9] allylic oxidation of olefins,[10] hydrosilylation of ketones,[11] Friedel–Crafts reaction,[12] diene cyclization/hydrosilylation,[13] glyoxylate-ene reaction,[14] and so on. Over the last decade a wide range of C_2-symmetric chiral bisoxazoline ligands have been synthesized from readily available diacid derivatives and amino alcohols.[1] The Lewis basicity of the nitrogen donor atoms and the conformationally rigid framework of the chelate represent important structural features of this type of ligand. The influence of substitution at the oxazoline ring and the C_2-symmetric arrangement of the stereogenic centers in close proximity to the coordination site on the course of reactions mediated by bisoxazoline-ligated metal species has been studied.[2b] While the vast majority of bisoxazoline ligands are methylene, benzo and pyridyl linked with different substituents in the oxazoline ring, Corey and Andrus recently reported a set of biaryl-linked bisoxazoline ligands with different substituents in the oxazoline ring.[10c,15] Herein we report the preparation of a new kind of C_2-symmetric chiral bisbenzoxazoles **1a–e** and **2a–e**, and a pair of new C_2-symmetric chiral bisbenzothiazoles **1f** and **2f** (Scheme 1).

2. Results and discussion

Our design for these new ligands is such that it is possible for them to possess an obvious different structural feature to previously reported bisoxazoline ligands. In our ligands two stereogenic centers come from L- or D-tartaric acid **3** or **4**, and the rigid benzoxazole rings with different substituents on the benzene rings. The designed ligands may give a chiral environment with large specific rotation values. It may also produce an effective asymmetric environment in the course of reactions and induce good enantioselectivity in some asymmetric reactions.

Although there are several methods reported for the preparation of benzoxazoles from acids and *o*-aminophenol derivatives,[16] most of them require acidic and high temperature conditions, for example, reactions catalyzed by PPA or PPE,[17] $POCl_3$,[18] and $SOCl_2$.[19] In the case of preparing ligands such as **1a–f** and **2a–f**,

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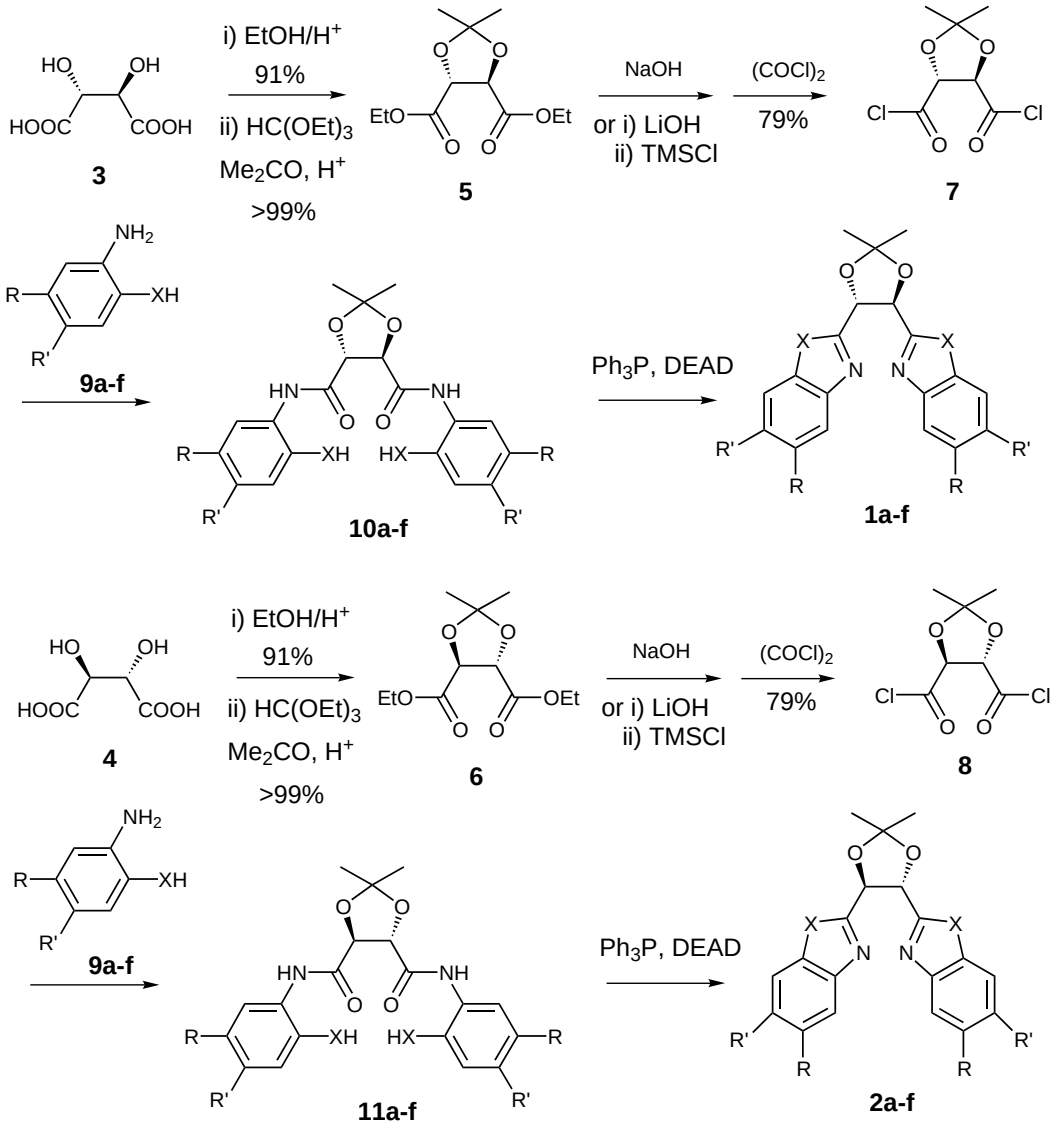


a X = O, R = R' = H,
b X = O, R = Me, R' = H,
c X = O, R = Cl, R' = H,
d X = O, R = NO_2, R' = H,
e X = O, R = Cl, R' = NO_2,
f X = S, R = R' = H

Scheme 1. Synthesis of enantiomerically pure 4,5-bis(benzoheterazol-2-yl)-2,2-dimethyl-1,3-dioxolanes.

however, these methods cannot be adopted because of the presence of acid-sensitive 1,3-dioxolane groups in the compounds. Instead, another approach using the Mitsunobu reaction for the preparation of oxazoline derivatives and benzoxazoles, under mild and neutral conditions, as investigated by Roush[20] and Wang,[21] respectively, was found to be successful in this synthesis.

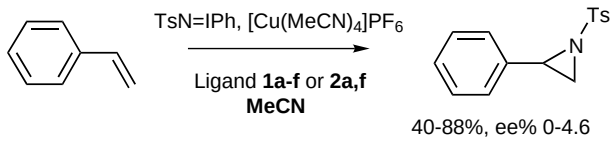
The diamides **10** and **11** are very important intermediates for the preparation of bisbenzoheterazoles **1** and **2** using the Mitsunobu reaction. Choi et al.[22] reported a method for the preparation of 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamides from amines and 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylic dichloride, which was prepared from dimethyl 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate through base-catalyzed hydrolysis in methanolic aqueous lithium hydroxide, conversion into di(trimethylsilyl) diester using 18-crown-6 as a phase transfer catalyst, followed by treatment with oxalyl chloride and a catalytic amount of DMF. We felt that it would be a useful method for us to synthesize diamides **10** and **11**. However, when we used this method to synthesize a pair of dihydroxy-

phenyl diamides **10a** and **11a** from 2-aminophenol and diethyl L- and D-tartrates **5** and **6**, we found that racemization occurred. Based on the structures of L- and D-2,3-*O*-isopropylidenetartaric dichlorides **7** and **8**, it should be unfavorable for them to racemize because they would convert into the less favored *meso*-2,3-*O*-isopropylidenetartaric dichloride bearing a dioxolane ring with *cis*-acyl chloride groups in the 4- and 5-positions, from an L- or D-2,3-*O*-isopropylidenetartaric dichloride bearing a dioxolane ring with *trans*-carboxylic chloride groups in the 4- and 5-positions. We rationalized that high temperature would be a major reason for the observed racemization. When we prepared dichlorides **7** and **8** at low temperature, followed by removal of solvent and excess oxalyl chloride, and reacted them directly with the aromatic amines **9a–e**, we successfully obtained the corresponding enantiomerically pure *N*,*N*′-bis(2-hydroxyphenyl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamides **10a–e** and **11a–e** in good yields. We also found another available method reported by Picard et al.[23] for the preparation of enantiomerically pure diacid chlorides **7** and **8** in high yields directly from L- and D-2,3-*O*-isopropylidenetartaric acid disodium salts, respectively, with an excess of oxalyl chloride in anhydrous benzene. Attempts to convert the L- and D-tartrates **5** and **6** into the corresponding dicarboxamides **10a** and **11a** directly under neutral conditions,[9c,24] under fluoride-[25] or cyanide-catalyzed neutral conditions,[26] or under basic conditions in the presence of sodium hydride[27] were unsuccessful due to the poor nucleophilicity of 2-aminophenol **9a**.

The enantiomerically pure dicarboxamides **10a–e** and **11a–e** were cyclized successfully into chiral bisbenzoxazole derivatives via Mitsunobu reaction using triphenylphosphine and diethyl azodicarboxylate (DEAD).[20,21] We found that the crude dihydroxyaryl diamides could be used directly to synthesize bisbenzoxazole derivatives in satisfactory yields without further purification. A pair of enantiomerically pure bisbenzothiazoles **1f** and **2f** were also synthesized from the dichlorides **7** and **8** and *o*-aminothiophenol **9f** using this one-pot method. This showed that in the synthesis of bisbenzoxazoles through the Mitsunobu reaction, the oxygen atoms in the benzoxazole ring originate in the hydroxyl group of the *o*-aminophenols **9a–e** and not the amide group.

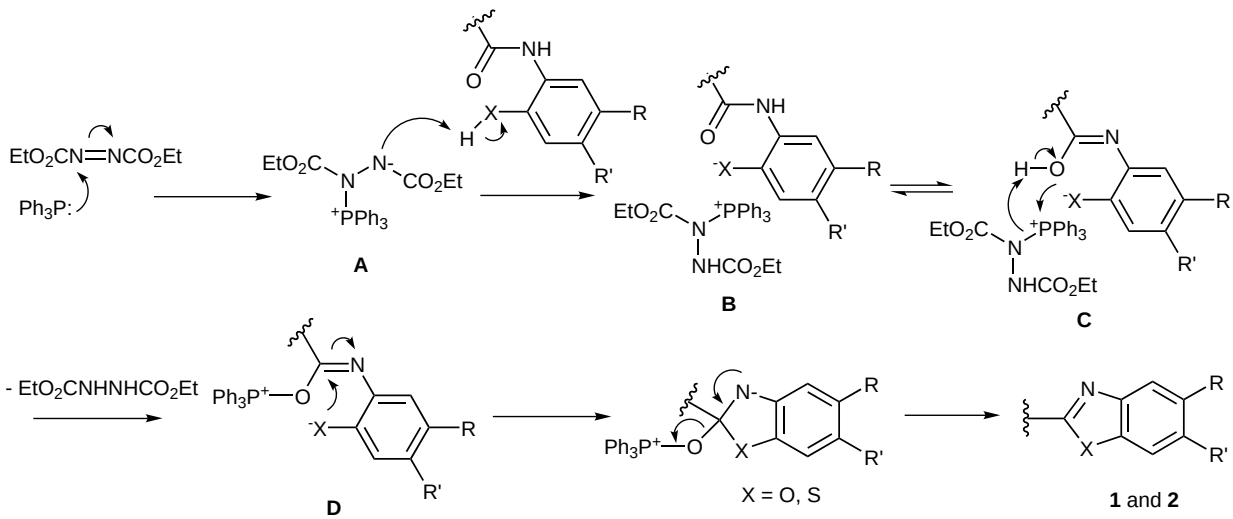
A suggested mechanism for the Mitsunobu reaction is as follows: triphenylphosphine attacks DEAD to form the zwitterionic adduct A, which abstracts an acidic hydrogen from the hydroxyl (or mercapto) group of the phenol (or thiophenol) to yield an azaphosphonium phenolate B. The amide in B then tautomerizes into a hydroxy imine form C, the hydroxyl group of which attacks the phosphonium ion to form an activated oxyphosphonium ion intermediate D, which then undergoes an addition–elimination process to produce the benzoxazole (or benzothiazole) ring and triphenylphosphine oxide (Scheme 2).

The efficiency of bisbenzoxazoles and bisbenzothiazoles **1** and **2** as ligands in asymmetric aziridination catalyzed by $[Cu(MeCN)_4]PF_6$ was evaluated.[28] Unfortunately, almost no enantiomeric excess has been obtained (Scheme 3). The asymmetric cyclopropanation of styrene with ethyl diazoacetate[2a] using **1** and **2** also gave a racemic mixture.



Scheme 3. Asymmetric aziridination of styrene using bisbenzoheterazoles.

Most of the ligands derived from chiral tartaric acid showed moderate to excellent enantiomeric excesses in asymmetric reactions.[2b,9c,29–35] To understand why the bisbenzoheterazoles **1** and **2** did not induce enantiose-



Scheme 2. Suggested mechanism for the formation of bisbenzoheterazoles.

lectivity in these reactions, it is necessary to check the validity of the coordination of the azoles with $[Cu(MeCN)_4]PF_6$. The UV spectra of bisbenzoxazole **1a**, the Cu catalyst, and bisbenzoxazole **1a** with the catalyst in molar ratios of 1:0.5 and 1:1 were determined in acetonitrile (Fig. 1). The results showed that no coordination occurred, as additive spectra were obtained for the samples of bisbenzoxazole **1a** with the Cu catalyst. To confirm the results, the ^1H NMR spectra of bisbenzoxazole **1a** and bisbenzoxazole **1a** with equimolar non-paramagnetic $NiCl_2$ were also determined in DMSO-d_6 solution (Fig. 2). There was no significant change in the chemical shifts in the spectra. Thus, we can conclude that no coordination between the bisbenzoxazole **1a** and Cu(I) or Ni(II) cations occurred, which explains why bisbenzoxazoles and bisbenzothiazoles **1** and **2** did not give asymmetric induction in the asymmetric aziridination and cyclopropanation reactions.

Bisbenzoxazole **1a** showed no coordination with the transition metals Cu(I) and Ni(II). The reason was

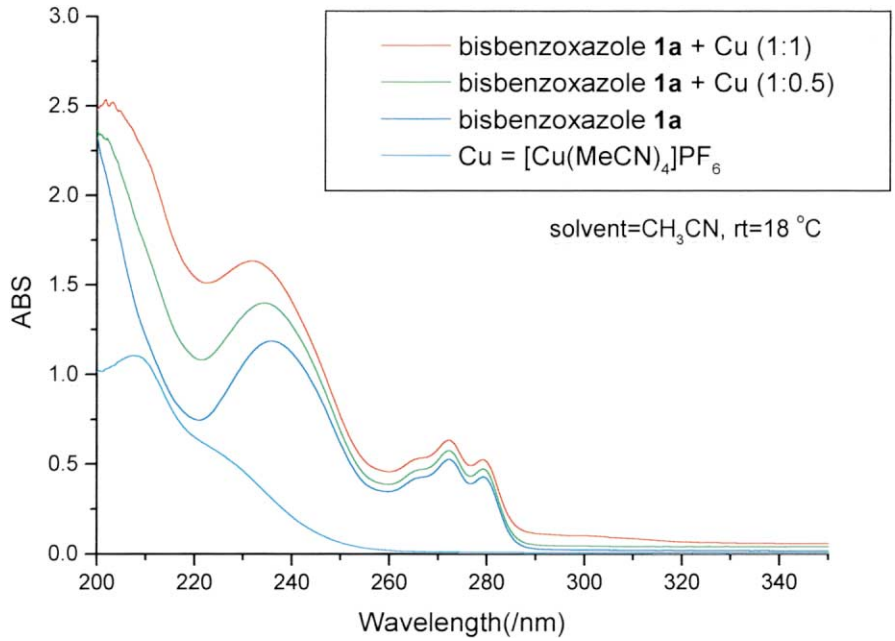


Figure 1. UV spectra of bisbenzoxazole **1a**, $[Cu(MeCN)_4]PF_6$, and bisbenzoxazole **1a** with $[Cu(MeCN)_4]PF_6$.

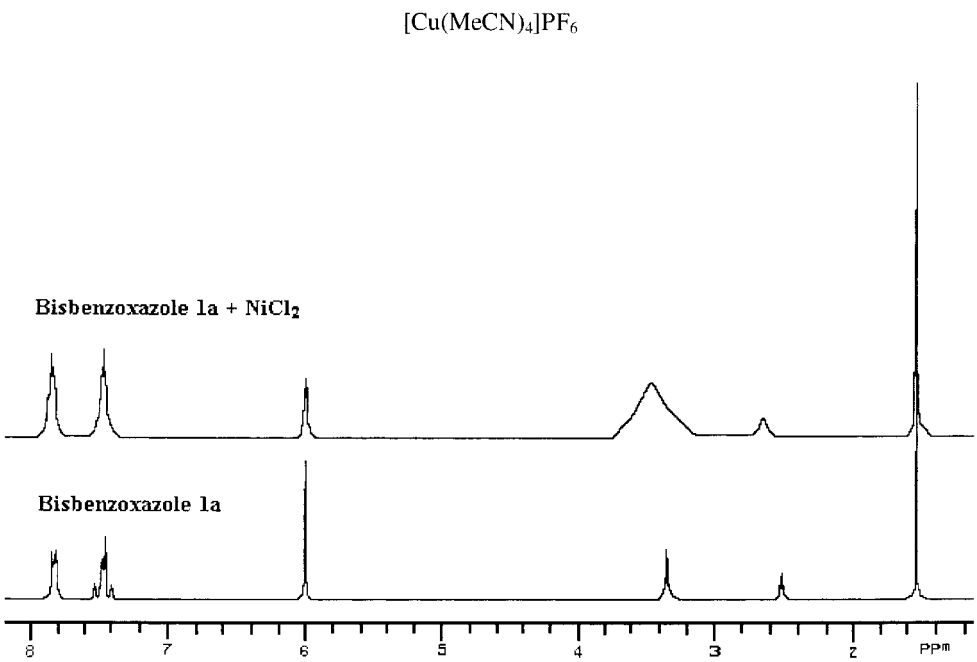


Figure 2. ^1H NMR spectra of bisbenzoxazole **1a** and bisbenzoxazole **1a** with $NiCl_2$ in DMSO-d_6.

rationalized that C_2-symmetrically chiral bisoxazolines are important and effective ligands in asymmetric catalytic reactions due to the suitable Lewis basic property of the nitrogen donor atoms in the oxazoline rings. However, the Lewis basicity of the nitrogen donor atoms in the bisbenzoheterazoles **1** and **2**, in which the oxazoline and thiazoline rings are fused with a benzene ring to become aromatic oxazoles and thiazoles, is weaker than that in bisoxazolines because of the lack of a sufficiently basic nitrogen donor atom in the azole moiety.

3. Conclusion

In conclusion, novel C_2-symmetric and enantiomerically pure bisbenzoxazoles and bisbenzothiazoles derived from L- and D-tartaric acids have been synthesized from L- and D-2,3-*O*-isopropylidenetartaric dichlorides and *o*-aminophenol derivatives or *o*-aminothiophenol, respectively, in two- or one-step reactions. The mechanism for the formation of bisbenzoxazoles and bisbenzothiazoles was suggested. The absence of coordination with Cu and Ni ions was rationalized as being the result of the poor Lewis basicity of the nitrogen donor atom in the benzoheterazole moiety.

4. Experimental

4.1. General method

Melting points were measured on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Mercury 200 (200 MHz) spectrometer in $CDCl_3$ with TMS as an internal standard or in DMSO-d_6. Mass spectra were obtained on a VG-ZAB-HS mass spectrometer. CHN analyses were recorded on an Elementar Vario EL analyzer. Optical rotations were measured on a Perkin Elmer 341LC polarimeter with a thermally jacketed 10 cm cell (concentration *c* given as g/100 mL). IR spectra were taken on a Brucker Vector 22 FT-IR spectrophotometer in KBr pellet.

L- and D-2,3-*O*-isopropylidenetartaric dichlorides **7** and **8** were synthesized according to a known method[23] and our modified method. All remaining chemicals were purchased from Beijing Chemical Co., Tokyo Kasei Kogyo Co., Ltd. or Acros Chemical Co., Inc. Benzene and THF were heated under reflux over sodium and distilled prior to use. Dichloromethane was heated under reflux over calcium hydride and distilled prior to use. Triethylamine and pyridine were heated under reflux over sodium hydroxide and distilled prior to use.

4.2. General procedure for the synthesis of 4,5-bis(benzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolanes 1a–b and 2a–b

To a solution of *N*,*N*′-bis(2-hydroxyaryl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamide **10a–b** or **11a–b** (10 mmol) and triphenylphosphine (5.76 g, 22 mmol) in dry THF (30 mL) was added dropwise a solution of DEAD (3.83 mL, 22 mmol) in dry THF (10 mL) under stirring and nitrogen atmosphere in an ice bath. The resulting mixture was stirred at room temperature for 8 h. After removal of the solvent, diethyl ether (60 mL) was added and the resulting mixture was stirred for 1 h. The insoluble solid was filtered off. The filtrate was concentrated and the residue was purified on a silica gel column with a mixture of petroleum ether (60–90°C) and ethyl acetate (10:1, v/v) as the eluent to give a solid product. If necessary, further crystallization could be carried out from a mixture of petroleum ether (60–90°C) and ethyl acetate to give pure crystals of product.

4.2.1. (4*R*,5*R*)-4,5-Bis(benzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 1a. Colorless needles; mp: 109–110°C; yield: 75%; $[\alpha]_D^{20}=-224$ (*c* 1.15, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.74–7.78 (m, 2H, ArH), 7.55–7.60 (m, 2H, ArH), 7.35–7.43 (m, 4H, ArH), 5.92 (s, 2H, 2CH), 1.66 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1616 (C=N). MS (EI) *m*/*z* (rel. intensity): 336 (1.82, M^+), 321 (5.96, $M-CH_3$), 278 (68.51, $M-CH_3COCH_3$), 251 (21.53), 189 (100.00), 172 (31.68), 160 (91.45), 148 (52.04), 132 (40.02), 120 (19.55), 119 (19.02), 103 (9.37), 77 (8.05). Anal. calcd for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.86; H, 4.71; N, 8.08%

4.2.2. (4*R*,5*R*)-4,5-Bis(5-methylbenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 1b. Colorless crystals; mp: 48–49°C; yield: 92%; $[\alpha]_D^{20}=-235$ (*c* 2.07, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.17–7.52 (m, 6H, ArH), 5.88 (s, 2H, 2CH), 2.46 (s, 6H, $2CH_3$), 1.65 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1614 (C=N). MS (EI) *m*/*z* (rel. intensity): 364 (1.31, M^+), 349 (2.63, $M-H_2O$), 306 (45.43, $M-CH_3COCH_3$), 279 (14.23), 203 (63.18), 186 (23.00), 174 (100.00), 162 (41.32), 146 (38.86), 133 (15.66), 116 (6.56), 78 (17.34). Anal. calcd for $C_{21}H_{20}N_2O_4$: C, 69.22; H, 5.53; N, 7.69. Found: C, 69.29; H, 5.40; N, 7.62%.

4.2.3. (4*S*,5*S*)-4,5-Bis(benzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 2a. Colorless needles; mp: 110–111°C; yield: 78%; $[\alpha]_D^{20}=+220$ (*c* 0.98, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.74–7.78 (m, 2H, ArH), 7.56–7.60 (m, 2H, ArH), 7.35–7.40 (m, 4H, ArH), 5.92 (s, 2H, 2CH), 1.66 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1613 (C=N). MS (EI) *m*/*z* (rel. intensity): 336 (1.61, M^+), 321 (10.15, $M-CH_3$), 278 (100.00, $M-CH_3COCH_3$), 251 (39.93), 189 (100.00), 172 (47.23), 160 (99.17), 148 (80.20), 132 (70.18), 120 (31.49), 119 (30.11), 103 (18.11), 77 (15.23). Anal. calcd for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.79; N, 8.33. Found: C, 67.72; H, 4.70; N, 8.22%.

4.2.4. (4*S*,5S)-4,5-Bis(5-methylbenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 2b. Colorless crystals; mp: 49–50°C yield: 99%; $[\alpha]_D^{20}=+235$ (*c* 1.06, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.16–7.52 (m, 6H, ArH), 5.88 (s, 2H, 2CH), 2.46 (s, 6H, $2CH_3$), 1.65 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1614 (C=N). MS (EI) *m*/*z* (rel. intensity): 364 (3.59, M^+), 349 (6.11, $M-H_2O$), 306 (93.59, $M-CH_3COCH_3$), 279 (26.41), 203 (100.00), 186 (37.23), 174 (99.18), 162 (66.54), 146 (58.18), 133

(23.25), 116 (9.15), 78 (21.62). Anal. calcd for $C_{21}H_{20}N_2O_4$: C, 69.22; H, 5.53; N, 7.69. Found: C, 69.15; H, 5.71; N, 7.54%.

4.3. General procedure for the one-pot synthesis of 4,5-bis(benzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolanes 1c–e and 2c–e, and 4,5-bis(benzothiazol-2-yl)-2,2-dimethyl-1,3-dioxolanes 1f and 2f

To a solution of L- or D-dichloride **7** or **8** (2.03 g, 10 mmol) in anhydrous THF (10 mL) in an ice bath was added dropwise a solution of one of the aromatic amines **9c–f** (30 mmol) in anhydrous THF (50 mL). The resulting mixture was stirred at room temperature for 1 h, and then the solid amine salt was filtered off. The filtrate was concentrated to give a solid product.

The above product and triphenylphosphine (5.76 g, 22 mmol) was dissolved in dry THF (30 mL). A solution of DEAD (3.83 mL, 22 mmol) in dry THF (10 mL) was added dropwise under stirring and a nitrogen atmosphere in an ice bath. The resulting mixture was stirred at room temperature for 8 h. After removal of the solvent, diethyl ether (60 mL) was added and the resulting mixture was stirred for 1 h. The insoluble solid was filtered off. The filtrate was concentrated and the residue was purified on a silica gel column with a mixture of petroleum ether (60–90°C) and ethyl acetate (10:1, v/v) as an eluent to give a solid product except products **1c** and **2c**. If necessary, further crystallization could be carried out from a mixture of petroleum ether (60–90°C) and ethyl acetate to give pure crystal.

4.3.1. (4*R*,5*R*)-4,5-Bis(5-chlorobenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 1c. Colorless oil; yield: 79%; $[\alpha]_D^{20}=-214$ (*c* 0.74, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.34–7.74 (m, 6H, ArH), 5.87 (s, 2H, 2CH), 1.64 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1638 (C=N). MS (EI) *m*/*z* (rel. intensity): 404 (0.99, M^+), 389 (5.38, M–CH_3), 346 (45.20, M–CH_3COCH_3), 319 (14.01), 223 (100.00), 206 (18.58), 194 (86.98), 182 (36.43), 166 (41.73), 154 (14.62), 138 (8.98). Anal. calcd for $C_{19}H_{14}Cl_2N_2O_4$: C, 56.31; H, 3.48; N, 6.91. Found: C, 56.28; H, 3.57; N, 6.81%.

4.3.2. (4*R*,5*R*)-4,5-Bis(5-nitrobenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 1d. Yellowish crystal; mp: 101–102°C; yield: 67%; $[\alpha]_D^{20}=-243$ (*c* 1.03, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.71–8.68 (m, 6H, ArH), 5.96 (s, 2H, 2CH), 1.67 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1621 (C=N), 1533 (NO_2). MS (EI) *m*/*z* (rel. intensity): 426 (0.20, M^+), 411 (27.43, M–CH_3), 368 (56.56, M–CH_3COCH_3), 341 (15.80), 234 (100.00), 217 (36.73), 205 (93.24), 193 (48.32). Anal. calcd for $C_{19}H_{14}N_4O_8$: C, 53.53; H, 3.31; N, 13.14. Found: C, 53.67; H, 2.96; N, 13.02%.

4.3.3. (4*R*,5*R*)-4,5-Bis(5-chloro-6-nitrobenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 1e. Yellowish crystal; mp: 154–156°C; yield: 51%; $[\alpha]_D^{20}=-213$ (*c* 1.23, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 8.16 (s, 2H, ArH), 7.94 (s, 2H, ArH), 5.91 (s, 2H, 2CH), 1.64 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1622 (C=N), 1530 (NO_2). MS (EI) *m*/*z* (rel. intensity): 479 (5.01, M–CH_3), 436 (9.84, M–CH_3COCH_3), 268 (100.00), 239 (41.83), 227 (20.59), 211 (12.21), 198 (13.84). Anal. calcd for $C_{19}H_{12}Cl_2N_4O_8$: C, 46.08; H, 2.44; N, 11.31. Found: C, 46.00; H, 2.54; N, 11.61%.

4.3.4. (4*S*,5*S*)-4,5-Bis(5-chlorobenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 2c. Colorless oil; yield: 75%; $[\alpha]_D^{20}=+216$ (*c* 0.81, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.34–7.74 (m, 6H, ArH), 5.87 (s, 2H, 2CH), 1.64 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1630 (C=N). MS (EI) *m*/*z* (rel. intensity): 404 (0.76, M^+), 389 (3.67, M–CH_3), 346 (31.92, M–CH_3COCH_3), 319 (9.64), 223 (100.00), 206 (16.01), 194 (70.74), 182 (48.48), 166 (51.80), 153 (16.51), 138 (10.57). Anal. calcd for $C_{19}H_{14}Cl_2N_2O_4$: C, 56.31; H, 3.48; N, 6.91. Found: C, 56.51; H, 3.37; N, 6.99%.

4.3.5. (4*S*,5*S*)-4,5-Bis(5-nitrobenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 2d. Yellowish crystal; mp: 102–103°C; yield: 62%; $[\alpha]_D^{20}=+238$ (*c* 1.04, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.71–8.67 (m, 6H, ArH), 5.96 (s, 2H, 2CH), 1.67 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1618 (C=N), 1531 (NO_2). MS (EI) *m*/*z* (rel. intensity): 426 (0.31, M^+), 411 (28.97, M–CH_3), 368 (60.07, M–CH_3COCH_3), 341 (15.96), 234 (100.00), 217 (39.11), 205 (88.38). Anal. calcd for $C_{19}H_{14}N_4O_8$: C, 53.53; H, 3.31; N, 13.14. Found: C, 53.71; H, 2.97; N, 12.90%.

4.3.6. (4*S*,5*S*)-4,5-Bis(5-chloro-6-nitrobenzoxazol-2-yl)-2,2-dimethyl-1,3-dioxolane 2e. Yellowish crystal; mp: 153–155°C; yield: 52%; $[\alpha]_D^{20}=+215$ (*c* 1.33, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 8.16 (s, 2H, ArH), 7.94 (s, 2H, ArH), 5.90 (s, 2H, 2CH), 1.64 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1621 (C=N), 1529 (NO_2). MS (EI) *m*/*z* (rel. intensity): 479 (8.50, M–CH_3), 436 (14.47, M–CH_3COCH_3), 409 (3.93), 268 (100.00), 239 (58.12), 227 (27.25), 211 (15.71), 199 (13.00). Anal. calcd for $C_{19}H_{12}Cl_2N_4O_8$: C, 46.08; H, 2.44; N, 11.31. Found: C, 46.37; H, 2.39; N, 11.48%.

4.3.7. (4*R*,5*R*)-4,5-Bis(benzothiazol-2-yl)-2,2-dimethyl-1,3-dioxolane 1f. Colorless crystals; mp: 114–115°C; yield: 35%; $[\alpha]_D^{20}=-249$ (*c* 0.68, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.90–8.06 (m, 4H, ArH), 7.40–7.49 (m, 4H, ArH), 5.80 (s, 2H, 2CH), 1.68 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1639 (C=N). MS (EI) *m*/*z* (rel. intensity): 368 (4.39, M^+), 353 (1.99, M–CH_3), 310 (100.00, M–CH_3COCH_3), 282 (41.42), 205 (56.12), 190 (46.76), 176 (64.89), 164 (52.38), 148 (29.18), 135 (69.22), 108 (14.14). Anal. calcd for $C_{19}H_{16}N_2O_2S_2$: C, 61.93; H, 4.38; N, 7.60. Found: C, 61.79; H, 4.21; N, 7.43%.

4.3.8. (4*S*,5*S*)-4,5-Bis(benzothiazol-2-yl)-2,2-dimethyl-1,3-dioxolane 2f. Colorless crystals; mp: 115–116°C; yield: 34%; $[\alpha]_D^{20}=+249$ (*c* 0.96, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$/TMS) δ (ppm): 7.90–8.06 (m, 4H, ArH), 7.37–7.53 (m, 4H, ArH), 5.81 (s, 2H, 2CH), 1.68 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 1629 (C=N). MS (EI) *m*/*z* (rel. intensity): 368 (9.80, M^+), 353 (3.14, M–CH_3), 310 (100.00, M–CH_3COCH_3), 282 (45.47), 205 (74.95), 190

(51.00), 176 (71.67), 164 (59.88), 148 (30.36), 135 (99.38), 108 (27.86). Anal. calcd for $C_{19}H_{16}N_2O_2S_2$: C, 61.93; H, 4.38; N, 7.60. Found: C, 61.76; H, 4.50; N, 7.57%.

4.4. General procedure for the synthesis of *N*,*N*′-bis(2-hydroxyaryl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamides 10a–b and 11a–b

To a solution of L- or D-2,3-*O*-isopropylidenetartaric dichloride **7** or **8** (2.03 g, 10 mmol) in anhydrous THF (10 mL) in an ice bath was added dropwise a solution of 2-aminophenol **9a** or **9b** (30 mmol) in anhydrous THF (50 mL). The resulting mixture was stirred at room temperature for 1 h, and the solid amine salt was filtered off. The filtrate was concentrated to give a solid product. After washing with diethyl ether, the crude product was crystallized from acetonitrile to give crystals of pure product.

4.4.1. (4*R*,5*R*)-*N*,*N*′-Bis(2-hydroxyphenyl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamide 10a. Colorless crystals; mp: 205–207°C; yield 88%; $[\alpha]_D^{20}=-105$ (*c* 0.96, acetone). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 10.15 (s, 2H, 2OH), 9.18 (s, 2H, 2CONH), 8.04 (d, $J=8.0$ Hz, 2H, ArH), 6.75–6.99 (m, 6H, ArH), 4.96 (s, 2H, 2CH), 1.51 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 3378 (O–H), 1666 (C=O). MS (EI) *m*/*z* (rel. intensity): 372 (9.82, M^+), 354 (11.43, M^+-H_2O), 236 (5.71), 188 (9.63), 162 (44.38), 134 (20.07), 109 (73.70, H_2NPhOH^+). Anal. calcd for $C_{19}H_{20}N_2O_6$: C, 61.28; H, 5.41; N, 7.52. Found: C, 61.21; H, 5.59; N, 7.47.

4.4.2. (4*R*,5*R*)-*N*,*N*′-Bis(2-hydroxy-5-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamide 10b. Colorless crystals; mp: 181–182°C; yield 86%; $[\alpha]_D^{20}=-90$ (*c* 1.19, acetone). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 9.86 (s, 2H, 2OH), 9.12 (s, 2H, 2CONH), 7.88 (s, 2H, ArH), 6.76 (s, 4H, ArH), 4.92 (s, 2H, 2CH), 2.19 (s, 6H, $2CH_3Ar$), 1.50 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 3354 (O–H), 1665 (C=O). MS (EI) *m*/*z* (rel. intensity): 400 (31.90, M^+), 382 (27.11, $M-H_2O$), 250 (12.21), 202 (17.23), 176 (100.00), 149 (32.78), 122 (68.99, HNPh(Me)OH). Anal. calcd for $C_{21}H_{24}N_2O_6$: C, 62.99; H, 6.04; N, 7.00. Found: C, 63.06; H, 5.83; N, 6.82%.

4.4.3. (4*S*,5*S*)-*N*,*N*′-Bis(2-hydroxyphenyl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamide 11a. Colorless crystals; mp: 203–205°C; yield 91%; $[\alpha]_D^{20}=+107$ (*c* 0.90, acetone). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 10.15 (s, 2H, 2OH), 9.18 (s, 2H, 2CONH), 8.04 (d, $J=8.0$ Hz, 2H, ArH), 6.75–6.99 (m, 6H, ArH), 4.96 (s, 2H, 2CH), 1.51 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 3375 (O–H), 1667 (C=O). MS (EI) *m*/*z* (rel. intensity): 372 (5.24, M^+), 354 (3.26, M^+-H_2O), 236 (3.54), 188 (3.61), 162 (13.86), 134 (27.31), 109 (100, H_2NPhOH^+). Anal. calcd for $C_{19}H_{20}N_2O_6$: C, 61.28; H, 5.41; N, 7.52. Found: C, 61.01; H, 5.43; N, 7.37%.

4.4.4. (4*S*,5*S*)-*N*,*N*′-Bis(2-hydroxy-5-methylphenyl)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxamide 11b. Colorless crystal; mp: 182–183°C; yield 64%; $[\alpha]_D^{20}=+90$ (*c* 1.47, acetone). ^{1}H NMR (200 MHz, DMSO-d_6) δ (ppm): 9.86 (s, 2H, 2OH), 9.12 (s, 2H, 2CONH), 7.89 (s, 2H, ArH), 6.76 (s, 4H, ArH), 4.93 (s, 2H, 2CH), 2.20 (s, 6H, $2CH_3Ar$), 1.50 (s, 6H, $2CH_3$). IR (KBr pellet, cm^{-1}): 3354 (O–H), 1665 (C=O). MS (EI) *m*/*z* (rel. intensity): 400 (17.45, M^+), 382 (19.30, $M-H_2O$), 250 (6.74), 202 (11.32), 176 (74.36), 149 (19.41), 123 (100.00), 122 (40.05, HNPh(Me)OH). Anal. calcd for $C_{21}H_{24}N_2O_6$: C, 62.99; H, 6.04; N, 7.00. Found: C, 62.93; H, 5.83; N, 6.72%.

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