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Axially chiral dimethylaminobenzimidazoles and their preliminary evaluation as acyl-transfer reagents†

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The synthesis of axially chiral benzimidazoles with a *peri*-substituted naphthalene and a dimethylamino group at positions 1 and 2, respectively, was developed. We evaluated these compounds in the desymmetrization reaction of *cis*-tetrahydrophthalic anhydride with benzyl alcohol, as the nucleophilic sp² imidazole nitrogen atom is able to catalyze the acyl-transfer reaction. The prepared benzimidazoles demonstrated catalytic activity and showed that their axial chirality impacts stereoselectivity.

Introduction

The acyl group transfer reaction represents one of the most common chemical transformations, occurring widely in both natural enzymatic processes and organic syntheses. ^{1,2} One family of chiral acyl transfer catalysts comprises derivatives based on the DMAP structure, ³ introduced by Vedejs in the late 1990s for the kinetic resolution of alcohols (Fig. 1). ^{4,5} Later, this family of catalysts was expanded to include other derivatives, differing in the variety of functional groups, the position of substitution at the pyridine ring and in the type of chirality. Examples of 3- or 4-substituted DMAP derivatives are shown in Fig. 1. ⁶⁻¹⁷

Another important group of acyl transfer catalysts is *N*-alkyl imidazole. These catalysts benefit from the sterically more accessible, nucleophilic sp² nitrogen atom of the imidazole ring, which kinetic studies have shown to be more efficient in acyl transfer reactions than pyridine-based catalysts.^{18,19} The imidazole moiety is naturally present in enzymes through histidine, which inspired Miller and colleagues to develop small peptide molecules incorporating histidine as acyl transfer catalysts.^{20–24} Zhang and colleagues developed a series of bicyclic imidazole catalysts (Fig. 1), featuring a rigid structure

in which a chiral center is directly adjacent to the nucleophilic sp² nitrogen atom. These imidazole catalysts were shown to catalyze asymmetric Steglich rearrangement with high enantioselectivities.²⁵

Further, the importance of the nucleophilic sp² nitrogen atom of the imidazole ring is not only associated with natural enzymatic acyl transfer reaction but also with hydrogen bonding as can be seen in acetyltransferases²⁶ and, for

Fig. 1 Examples of chiral acyl transfer catalysts.

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example, cyclin-dependent kinases interacting with the imidazole ring containing inhibitors.²⁷

While various chiral acyl transfer catalysts have been reported, the importance and broad application of the acylation reaction continues to drive research efforts. These efforts aim to extend the substrate scope, enable milder reaction conditions, improve stereochemical outcomes, and, more generally, a search for novel attractive chiral scaffolds with multiple chiral elements is also emerging. 28-32 Herein, we present a preliminary study of axially chiral N-naphthalenebenzimidazoles as a novel class of imidazole-based acvl transfer catalysts (Fig. 2). The chiral environment of the catalyst 5 is a result of restricted rotation around the C-N bond that connects the naphthalene and benzimidazole rings. We hypothesize that the chiral environment of the N-acylbenzimidazolium intermediates can be significantly modulated by the structure of the substituent R¹ at the *peri* position of the naphthalene ring. Additionally, the benzene ring of the benzimidazole and dimethylamino group are also expected to influence the stereochemical outcome. The presence of the dimethylamino group at position 2 of the benzimidazole ring not only enhances the stability of atropisomers but is primarily designed to increase the nucleophilicity of the catalyst. Moreover, the supposed distortion in the N-acyl bond of intermediate 5, induced by steric hindrance, may accelerate the kinetics of acyl transfer. In this report, we present the synthesis of benzimidazole-based catalysts, an evaluation of their catalytic activity, the stability of selected atropisomers, and preliminary results for the enantioselective desymmetrization reaction of a meso-anhydride.

Results and discussion

Synthesis of dimethylaminobenzimidazoles

The synthesis was initiated with naphthalene-1,8-diamine 1 and 1-fluoro-2-nitrobenzene, yielding diamine 2 as depicted in Scheme 1. Subsequently, the primary amine was sulfonylated using a slight molar excess of the corresponding sulfonyl chloride to provide derivatives 3a-e with good overall yields. Reduction of the nitro group to the corresponding amine was accomplished using powdered zinc in a mixture of methanol and acetic acid. The reaction proceeded smoothly without any side products. Typically, only a simple work up was needed to furnish intermediates 4a-e.

Nu
$$R^2$$
 $R^1 = ArSO_2NH$ pyrrolidin-1- yl piperidin-1-yl Bn_2N ArCONH

Fig. 2 Design of the catalyst and rationale for the enantioselective N-acyl transfer reaction.

Scheme 1 Synthesis of benzimidazoles 5a-e and 6a-b functionalized with sulfonamide moieties. Reagents and conditions: (a) 1-fluoro-2-nitrobenzene, KOH, DMSO, rt, 4 h; (b) RSO₂Cl, DCM/pyr 3:2, rt, 2 h; (c) Zn, MeOH/AcOH 25:2, rt, 2 h; (d) phosgene dimethyliminium chloride, CHCl₃, reflux, 2 h; (e) Zn, DMA-DMA, MeOH/AcOH 25:1, 60 °C, 4 h.

In the final cyclization step, phosgene dimethyliminium chloride was utilized to form benzimidazoles **5a-e** with dimethylamino group at position 2. The yields were moderate to good after purification by column chromatography.

According to NMR experiments, compound **5c** exists as a mixture of its free and zwitterionic forms. This behaviour can be attributed to the strongly electron-withdrawing nature of the 3,5-bis(trifluoromethyl)benzenesulfonyl group. As a result, obtaining a clear ¹H NMR spectrum of **5c** proved challenging under standard conditions. The spectrum became well-resolved only after the addition of a few drops of trifluoroacetic acid to the sample.

Two additional derivatives, **6a** and **6b**, bearing a methyl group at position 2 of the benzimidazole ring, were synthesized from nitroamines **3a** and **3b**. The transformation was achieved using a one-pot reduction/cyclization protocol with *N*,*N*-dimethylacetamide dimethylacetal as the cyclization reagent to expand the library of prepared compounds.³³

The synthesis of benzimidazoles **5f** and **5g**, functionalized with pyrrolidine and piperidine moieties at the *peri* position relative to the benzimidazole ring, commenced with the double alkylation of the primary amine using **1**,4-dibromobutane or **1**,5-dibromopentane (Scheme 2). The resulting compounds, **3f** and **3g**, were isolated in moderate yields. In the next step, an attempt to reduce the nitro group using powdered zinc, as described in Scheme **1**, led to the formation of significant amounts of impurities, complicating the isolation and results in reduced overall yields. Consequently, catalytic hydrogenation was employed to yield diamines **4f** and **4g** in quantitative yield. Finally, the target benzimidazoles **5f** and **5g**, were obtained under the same conditions used for sulfonamides **5a–e**.

Scheme 2 Synthesis of benzimidazoles 5f and 5g functionalized with pyrrolidine and piperidine moieties. Reagents and conditions: (a) 1,4dibromobutane or 1,5-dibromopentane, K₂CO₃, DMSO, rt, 24 h; (b) 10% Pd/C, hydrogen atmosphere, EtOAc, rt, 4 h; (c) phosgene dimethyliminium chloride, CHCl₃, reflux, 2 h.

The synthesis of dibenzylated derivative 5h closely followed the procedure for the synthesis benzimidazoles 5f and 5g; however, the reaction conditions required modification. An excess of benzyl bromide was employed, and the temperature was increased. Despite the presence of some unreacted starting material 2 in the reaction mixture, the reaction time could not be prolonged, as benzylation also occurred at the secondary amine, and the resulting impurity was challenging to separate from the desired product 3h. The subsequent reduction of the nitro group was carried out with powdered zinc, and the resulting diamine 4h was converted to the final benzimidazole 5h using the same methodology as for derivatives 5a-g (Scheme 3).

We also synthesized a derivative with the amide functionality, 5i (Scheme 4). The 3,5-bis(trifluoromethyl)benzoyl group was introduced in the first step. The reduction of nitro group with zinc initially resulted in the formation of a pyrimidine

Scheme 3 Synthesis of dibenzylated benzimidazole 5h. Reagents and conditions: (a) BnBr, K2CO3, MeCN, 70 °C, 16 h; (b) Zn, MeOH/AcOH 25: 2, rt, 2 h; (c) phosgene dimethyliminium chloride, CHCl₃, reflux, 2 h.

Scheme 4 Synthesis of benzimidazole 5i with amide functionality. Reagents and conditions: (a) 3,5-(bis)trifluoromethyl benzoyl chloride, DCM/pyr 3:2, rt, 2 h; (b) 10% Pd/C, hydrogen atmosphere, EtOAc, rt, 4 h; (c) phosgene dimethyliminium chloride, pyr, CHCl₃, rt, 2 h.

ring derivative rather than compound 4i. Additionally, ironcatalyzed reduction with hydrazine was unsuccessful.34 Consequently, we opted for catalytic hydrogenation to achieve the desired intermediate. The final step was performed using phosgene diminium chloride in the presence of pyridine to prevent the formation of impurities.

Evaluation of catalytic activity

We then decided to evaluate the catalytic activity of benzimidazoles 5a-i in the reaction of cis-tetrahydrophthalic anhydride 6 with benzyl alcohol to obtain monoester 7. The experiments were performed using racemic catalysts (Table 1).

Table 1 Evaluation of the catalytic activity of racemic benzimidazoles in the reaction of cis-tetrahydrophthalic anhydride 6 with benzyl alcohol

Entry	Catalyst	Reaction time ^a (h)
1	_	6 days (21% of 6 left)
2	5a	20
3	5 b	21
4	5e	36
5	5 d	26
6	5e	36 (partly soluble in ether)
7	5 f	22
8	5g	22
9	5 h	50
10	5i	48
11	6a	>6 days (insoluble in ether)
12	6b	>6 days (insoluble in ether)

^a Monoesterification was monitored by ¹H NMR spectroscopy and was terminated once the anhydride 6 was completely consumed. The reaction yielded only monoester 7, which was not isolated.

The first experiment was conducted without a catalyst to demonstrate that the reaction was incomplete after 6 days (entry 1). Benzimidazoles with the sulfonamide moiety significantly accelerated the reaction rate (entries 1–6), with 5a and 5b proving to be the most efficient. The catalyst 5f, containing the pyrrolidine moiety, achieved full conversion after 22 hours (entry 7). A similar result was observed with 5g (entry 8). The steric hindrance of the dibenzylamino groups slowed the reaction rate, with full conversion of starting material occurring only after 50 hours (entry 9). The benzamide functionality did not improve the reaction rate (entry 10).

Additionally, we attempted to catalyze the monoesterification reaction with benzimidazoles **6a** and **6b**, expecting lower catalytic activity due to the substitution of the dimethylamino group with a methyl group. The reaction rate was found to be comparable to the conditions in entry 1 (without the catalyst), likely due to their insolubility in diethyl ether.

Furthermore, both atropisomers of compound **5f** were successfully separated by semi-preparative chiral HPLC. The thermal stability of atropisomer (-)-(R_a)-**5f** was evaluated by heating in ethylene glycol at three different temperatures: 80, 120, and 160 °C. Our investigation revealed that racemization occurred only at 160 °C, accompanied by partial thermal decomposition. The absolute configuration of both atropisomers of **5f** was determined through single-crystal X-ray crystallography (please see ESI†).

Desymmetrization experiments

Preliminary stereoselective desymmetrization experiments were conducted under the catalysis of benzimidazole (+)- (S_a) -5f at three concentrations, using the reaction conditions outlined in Table 1. Monobenzyl ester 7 was isolated as a mixture of enantiomers with a ratio of 11:89 when anhydride 6 was used at a concentration of 0.05 M. A lower concentration at 0.025 M resulted in worse enantioselectivity, with an enantiomeric ratio of 27:73, although the reaction time was extended to 48 hours. Further dilution of anhydride 6 to 0.01 M led to a significant decrease in reactivity, as residual anhydride 6 remained in the reaction mixture after 8 days, and racemic monoester 7 was formed. The dextrorotatory optical rotation of 7 (c = 1.0, MeOH), isolated as a mixture of enantiomers with a 27:73 enantiomeric ratio, indicated that (1R,6S)-6-((benzyloxy) carbonyl)cyclohex-3-ene-1-carboxylic acid was the predominant enantiomer.35,36

Conclusions

In summary, we successfully developed the synthesis of axially chiral benzimidazoles with a dimethylamino group at position 2, designed to mimic guanidine moiety. In total, 11 atropisomeric benzimidazoles were synthesized from readily available and inexpensive starting materials. The potential use of these benzimidazoles as acyl-transfer reagents was tested in a desymmetrization reaction of *cis*-tetrahydrophthalic anhydride with benzyl alcohol. The best catalytic activity was observed for ben-

zimidazoles **5a**, **5b**, **5f**, and **5g**. Benzimidazole **5f** was separated by semi-preparative HPLC into two atropisomers, which allowed us to confirm the high racemization barrier and evaluate the efficiency of chiral transfer from the axially chiral benzimidazole to the benzyl monoester **7**, obtained by desymmetrization of *cis*-tetrahydrophthalic anhydride **6**. In conclusion, it was demonstrated that benzimidazoles with a dimethylamino group at position 2 are capable of catalyzing acyl transfer reactions. Furthermore, their axial chirality presents potential for chiral transfer in asymmetric variants of these reactions. However, further optimization and development are necessary to improve their stereoselectivity.

Experimental

All starting materials, solvents, and reagents were bought from commercial suppliers (Merck, Fluorochem, Acros Organic, VWR, Lach-Ner, Apollo Scientific) and were used without further purification. NMR spectra were recorded on the spectrometer Jeol ECH400II (400 MHz for ¹H spectra, 100 MHz for ¹³C spectra), Jeol ECX-500SS (500 MHz for ¹H spectra, 126 MHz for ¹³C spectra) or Bruker Avance III HD 500 (500 MHz for ¹H spectra, 126 MHz for ¹³C spectra) at ambient temperature. Chemical shifts are quoted as particles per million (ppm) and are referenced as follows: CDCl₃: 7.26 ppm (1 H), 77.0 ppm (13 C) and DMSO- d_{6} : 2.50 ppm (1 H), 39.52 ppm (13 C). Coupling constants (J) are quoted in hertz. HRMS spectra were recorded by Thermo Exactive Plus high-resolution mass spectrometer with electrospray ionization (ESI) and Orbitrap analyser operating at a positive or negative full scan mode in the range of $60-800 \, m/z$. Thin-layer chromatography was performed on alumina sheets coated with Merck Silica gel 60 F254. The plates were developed and analyzed under UV light. Separations by column chromatography were carried out using SiliaFlash Irregular Silica Gel P60 (40-63 µm) as the stationary phase. Melting points were measured on a Boetius stage and are uncorrected. Chiral HPLC analyses were performed using HPLC Agilent 1260 II equipped with DA (diode array) detector. IR spectra were measured by DRIFT (Diffuse Reflectance Infrared Fourier Transform) on Thermo Nicolet AVATAR 370 FTIR spectrometer.

Synthetic procedures

N^{1} -(2-Nitrophenyl)naphthalene-1,8-diamine (2).

Naphthalene-1,8-diamine 1 (10 g, 0.063 mol) and potassium hydroxide (14.2 g, 0.253 mol) were suspended in dimethyl sulfoxide (350 mL). 1-Fluoro-2-nitrobenzene (6.67 mL, 0.063 mol) was added. The reaction mixture was stirred at room temperature for 4 hours. After the TLC analysis showed a full conversion of starting material, the reaction was poured into ice cold water (2 L) and carefully acidified to pH = 6 with concentrated aqueous hydrochloric acid. After stirring in an ice bath for 1 hour, the precipitate was collected by filtration to yield 13.45 g of 2 as a dark red solid (76%). Analytical sample was purified using column chromatography (dichloromethane/

n-hexane, 1:1). Mp 112–113 °C; ¹H NMR (500 MHz, CDCl₃) δ 9.60 (s, 1H), 8.24 (dd, J = 8.6, 1.6 Hz, 1H), 7.75 (dd, J = 8.2, 1.3 Hz, 1H), 7.39 (dd, J = 8.3, 7.3 Hz, 1H), 7.35-7.27 (m, 3H), 7.21(dd, J = 7.3, 1.3 Hz, 1H), 6.88-6.75 (m, 2H), 6.68 (dd, J = 6.0,2.7 Hz, 1H), 4.60 (br. s, 2H); 13 C NMR (126 MHz, CDCl₃) δ 144.87, 143.79, 137.18, 136.07, 135.29, 133.63, 128.79, 127.22, 126.41, 125.84, 125.02, 121.04, 118.85, 118.12, 117.80, 111.83; HRMS (ESI): m/z [M + H]⁺ calcd for C₁₆H₁₄N₃O₂: 280.1081, found: 280.1083.

General procedure for preparation of sulfonamides (3a-e)

Nitroamine 2 (279 mg, 1 mmol) was dissolved in a mixture of dichloromethane (3 mL) and pyridine (2 mL). The corresponding sulfonyl chloride (1.2 mmol) was added in one portion and the mixture was allowed to stir at room temperature for 2 hours. After the reaction was completed according to TLC, it was diluted with DCM (5 mL) and washed with 1 M aqueous hydrochloric acid (2 × 5 mL) and with water (1 × 5 mL). The organic layer was dried over magnesium sulfate and the crude compound was purified using column chromatography (dichloromethane) to yield the corresponding sulfonamide.

4-Methyl-N-(8-[(2-nitrophenyl)amino]naphthalen-1-yl)benzenesulfonamide (3a). Nitroamine 2 (1 g, 3.58 mmol) was sulfonylated to give sulfonamide 3a (1.16 g, 81%) as an orange solid after purification. Mp 161-162 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.95 (s, 1H), 9.24 (s, 1H), 8.31 (dd, J = 8.6, 1.5 Hz, 1H), 7.81 (dt, J = 8.1, 0.6 Hz, 1H), 7.64 (td, J = 8.0, 1.0 Hz, 2H), 7.59-7.49(m, 2H), 7.49-7.37 (m, 2H), 7.35-7.24 (m, 1H), 7.22 (dt, <math>J = 7.3, 1.2 Hz, 1H), 7.17-7.07 (m, 2H), 6.96 (ddd, J = 8.5, 7.1, 1.2 Hz, 1H), 6.46 (dd, J = 8.5, 1.2 Hz, 1H), 2.33 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 144.4, 143.9, 136.6, 136.5, 136.2, 135.1, 134.9, 133.8, 129.7, 129.6, 128.0, 127.4, 126.7, 126.7, 126.4, 125.2, 122.9, 119.8, 118.6, 117.5, 21.6; HRMS (ESI): m/z [M + H_{20}^{+} calcd for $C_{23}H_{20}N_3O_4S$: 434.1168, found: 434.1169.

N-(8-[(2-Nitrophenyl)amino]naphthalen-1-naphthaleneyl)-2sulfonamide (3b). Nitroamine 2 (1 g, 3.58 mmol) was sulfonylated to give sulfonamide 3b (1.36 g, 75%) as an orange solid after purification. Mp 185–186 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.10 (s, 1H), 9.27 (s, 1H), 8.34–8.25 (m, 2H), 7.90–7.76 (m, 1H), 7.82-7.77 (m, 2H), 7.79-7.70 (m, 2H), 7.67-7.56 (m, 2H), 7.61-7.50 (m, 2H), 7.43 (t, J = 7.9 Hz, 1H), 7.45-7.34 (m, 1H), 7.20-7.12 (m, 2H), 6.90 (ddd, J = 8.5, 7.1, 1.2 Hz, 1H), 6.39 (dd, J = 8.5, 1.2 Hz, 1H; ¹³C NMR (101 MHz, CDCl₃) δ 144.4, 136.5, 136.5, 136.1, 135.1, 135.0, 134.9, 133.7, 132.1, 129.6, 129.5, 129.4, 129.0, 128.9, 128.1, 127.9, 127.6, 126.7, 126.7, 126.4, 125.3, 122.9, 122.4, 119.9, 118.5, 117.6; HRMS (ESI): m/z [M + H⁺ calcd for $C_{26}H_{20}N_3O_4S$: 470.1169, found: 470.1178.

N-(8-[(2-Nitrophenyl)amino)naphthalen-1-yl]-3,5-bis(trifluoromethyl)benzenesulfonamide (3c). Nitroamine 2 (0.15 g, 0.53 mmol) was sulfonylated to give sulfonamide 3c (0.23 g, 79%) as a dark red solid. Mp 158-159 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.19 (s, 1H), 9.24 (s, 1H), 8.33 (dd, J = 8.5, 1.6 Hz, 1H), 8.10-8.06 (m, 2H), 7.96-7.92 (m, 1H), 7.86 (dt, J = 8.3, 0.4 Hz, 1H), 7.73 (dd, J = 8.3, 1.2 Hz, 1H), 7.59 (dd, J = 7.7, 1.2 Hz, 1H), 7.51-7.45 (m, 2H), 7.35-7.23 (m, 2H), 6.98 (ddd, J = 8.5,

7.1, 1.3 Hz, 1H), 6.43 (dd, I = 8.5, 1.2 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 144.0, 142.3, 136.5, 136.3, 135.3, 134.5, 132.9 (q, J = 34.5 Hz), 132.5, 129.7, 128.3, 127.56, 127.55 126.8, 126.6, 126.5, 123.8, 123.2, 121.0, 120.3, 118.4, 118.0; HRMS (ESI): $m/z [M - H]^-$ calcd for $C_{24}H_{14}F_6N_3O_4S$: 554.0604, found: 554.0614.

N-(8-((2-Nitrophenyl)amino)naphthalen-1-yl)quinoline-8-sulfonamide (3d). Nitroamine 2 (0.4 g, 1.43 mmol) was sulfonylated to give sulfonamide 3d (0.52 g, 77%) as a red solid. Mp 111–112 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.16 (s, 1H), 10.05 (s, 1H), 9.05 (dd, J = 4.3, 1.8 Hz, 1H), 8.31 (dd, J = 7.3, 1.5 Hz, 1H), 8.21 (dd, J = 8.4, 1.8 Hz, 1H), 8.17 (dd, J = 8.6, 1.6 Hz, 1H), 7.98 (dd, J = 8.4, 1.6 Hz, 1H), 7.71 (dd, J = 7.8, 1.7 Hz, 1H), 7.61 (dd, J = 8.1, 1.3 Hz, 1H), 7.58-7.46 (m, 2H), 7.46-7.38 (m, 2H),7.37–7.30 (m, 2H), 7.24 (t, J = 7.9 Hz, 1H), 6.89 (dd, J = 8.6, 1.2 Hz, 1H), 6.82 (ddd, J = 8.6, 7.0, 1.3 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 151.5, 144.4, 143.4, 137.0, 136.7, 135.9, 135.7, 135.4, 134.4, 133.7, 132.9, 131.6, 128.9, 128.1, 126.5, 126.5, 126.3, 126.1, 126.0, 125.6, 124.4, 122.5, 119.7, 118.4, 118.2; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{25}H_{19}N_4O_4S$: 471.1122, found: 471.1121.

N-(8-[(2-Nitrophenyl)amino)naphthalen-1-yl]methanesulfonamide (3e). Nitroamine 2 (0.4 g, 1.43 mmol) was sulfonylated to give sulfonamide 3e (0.41 g, 79%) as a red solid. Mp 189–190 °C; ¹H NMR (400 MHz, CDCl₃) δ 9.79 (s, 1H), 9.35 (s, 1H), 8.30 (dd, J = 8.5, 1.5 Hz, 1H), 7.90 (dd, J = 8.2, 1.1 Hz, 1H), 7.71 (ddd, J = 7.8, 3.7, 1.1 Hz, 2H), 7.56–7.47 (m, 2H), 7.38-7.31 (m, 2H), 6.95 (ddd, J = 8.5, 7.1, 1.3 Hz, 1H), 6.58 (dd, $J = 8.5, 1.2 \text{ Hz}, 1\text{H}), 2.89 (s, 3\text{H}); {}^{13}\text{C NMR} (101 \text{ MHz}, \text{DMSO-}d_6)$ δ 143.5, 136.5, 135.7, 134.8, 133.4, 132.6, 127.8, 127.3, 126.4, 126.0, 126.0, 125.4, 125.1, 123.9, 117.5, 117.0, 38.4; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{17}H_{16}N_3O_4S$: 358.0856, found: 358.0857.

General procedure for preparation of nitro compounds (3f-g)

Nitroamin 2 (1 g, 3.58 mmol) and potassium carbonate (2.18 g, 15.77 mmol) were suspended in dimethyl sulfoxide (10 mL). The corresponding dibromoalkane was subsequently added. The reaction mixture was allowed to stir at room temperature for 24 hours. After the reaction was completed, the resulting mixture was poured into water (50 mL) and extracted with dichloromethane (3 × 30 mL). The combined extracts were dried over magnesium sulfate and the solvent was evaporated on a rotavap. A crude oily residue was purified by column chromatography (dichloromethane/n-hexane, 1:1) to yield corresponding nitro compound 3f or 3g.

N-(2-Nitrophenyl)-8-(pyrrolidin-1-yl)naphthalen-1-amine (3f). 1,4-Dibromobutane (0.94 mL; 7.87 mmol); 775 mg of 3f was isolated as a red solid (65%). Mp = 79–80 °C; ¹H NMR (400 MHz, DMSO- d_6) δ 12.02 (s, 1H), 8.12 (dd, J = 8.5, 1.6 Hz, 1H), 7.74 (dd, J = 8.6, 1.2 Hz, 1H), 7.67 (dd, J = 8.0, 1.3 Hz, 1H), 7.58 (dd, J = 8.0, 1.3 Hz, 1H), 7.56 (ddd, J = 8.7, 7.2, 1.6 Hz, 1H), 7.51-7.35 (m, 4H), 6.96 (ddd, J = 8.4, 7.0, 1.2 Hz, 4H), 3.23(br. s., 2H), 2.85 (br. s., 2H), 1.81 (br. s., 4H); ¹³C NMR (101 MHz, DMSO- d_6) δ 147.5, 140.0, 137.0, 136.5, 136.2, 135.6, 126.3, 126.3, 125.6, 125.1, 123.1, 121.3, 119.1, 118.2, 117.3,

114.9, 54.5, 23.6; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{20}H_{20}N_3O_2$: 334.1550, found: 334.1549.

N-(2-Nitrophenyl)-8-(piperidin-1-yl)naphthalen-1-amine (3g). 1,5-Dibromopentane (1.03 mL, 7.87 mmol); 760 mg of 3g was isolated as a red solid (61%). Mp = 144–145 °C; ¹H NMR (400 MHz, DMSO- d_6) δ 11.59 (s, 1H), 8.15 (dd, J = 8.5, 1.6 Hz, 1H), 7.75 (dd, J = 8.6, 1.0 Hz, 1H), 7.67 (dd, J = 8.2, 0.9 Hz, 1H), 7.65–7.51 (m, 2H), 7.45 (t, J = 7.8 Hz, 1H), 7.41–7.30 (m, 3H), 7.01 (ddd, J = 8.4, 7.0, 1.2 Hz, 1H), 3.19–3.11 (m, 2H), 2.72–2.55 (m, 2H), 1.67–1.57 (m, 1H), 1.59–1.44 (m, 4H), 1.31–1.13 (m, 1H); ¹³C NMR (101 MHz, DMSO- d_6) δ 151.4, 140.3, 138.0, 137.6, 137.3, 136.2, 126.7, 126.2, 125.7, 123.7, 120.7, 120.2, 120.2, 117.3, 115.0, 55.8, 25.4, 23.9; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₁H₂₂N₃O₂: 348.1707, found: 348.1690.

 N^{1} , N^{1} -Dibenzyl- N^{8} -(2-nitrophenyl) naphthalene-1,8-diamine (3h). Nitroamine 2 (400 mg, 1.43 mmol) and potassium carbonate (593 mg, 4.29 mmol) were suspended in acetonitrile (5 mL). Benzyl bromide (0.551 mL; 4.29 mmol) was added and the reaction mixture was allowed to stir for 16 hours at 70 °C. After the reaction was completed, the resulting mixture was poured into water (20 mL) and extracted with dichloromethane (3 × 15 mL). The combined extracts were dried over magnesium sulfate and the solvent was evaporated on a rotavap. The crude oily residue was purified by column chromatography (dichloromethane/n-hexane; 1:1) to yield 402 mg of 9 as a red solid (61%). Mp = 127-128 °C; ¹H NMR (400 MHz, CDCl₃) δ 12.60 (s, 1H), 8.20 (dd, J = 8.4, 1.5 Hz, 1H), 7.63 (dd, J= 8.6, 0.6 Hz, 1H), 7.58-7.49 (m, 1H), 7.51-7.39 (m, 1H), 7.44 (dd, J = 7.7, 1.1 Hz, 1H), 7.38-7.25 (m, 2H), 7.18 (t, J = 7.8 Hz,1H), 7.11-6.96 (m, 6H), 7.02-6.92 (m, 4H), 6.89-6.76 (m, 2H), 4.45 (d, J = 13.4 Hz, 2H), 4.29 (d, J = 13.4 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 144.7, 141.9, 137.6, 137.1, 137.0, 135.7, 134.9, 130.3, 127.9, 127.2, 126.8, 126.0, 125.2, 124.9, 123.9, 123.6, 123.0, 118.4, 118.0, 116.6, 59.8; HRMS (ESI): m/z [M + H_{30}^{+} calcd for $C_{30}H_{26}N_{3}O_{2}$: 460.2020, found: 460.2025.

N-(8-((2-Nitrophenyl)amino)naphthalen-1-yl)-3,5-bis(trifluoromethyl)benzamide (3i). Nitroamine 2 (400 mg, 1.43 mmol) was dissolved in a mixture of dichloromethane (4 mL) and pyridine (2.6 mL). 3,5-Bis(trifluoromethyl)benzoyl chloride (0.312 ml, 1.72 mmol) was added in one portion and the mixture was allowed to stir at room temperature for 2 hours. After the reaction was completed according to TLC, it was diluted with dichloromethane (4 mL) and washed with 1 M aqueous solution of hydrochloric acid (2 × 8 mL) and with water (1 × 8 mL). The organic layer was dried over magnesium sulfate and the crude oily residue was purified using column chromatography (dichloromethane/n-hexane, 1:1) to yield 564 mg of nitroamine 3i as an orange solid (76%). Mp = 206–207 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.81 (s, 1H), 9.34 (s, 1H), 8.36 (dd, J = 7.7, 1.2 Hz, 1H), 7.98–7.91 (m, 4H), 7.88 (dd, J = 8.6, 1.5 Hz, 1H, 7.83 (dd, J = 8.3, 1.0 Hz, 1H), 7.63 (t, J = 8.0Hz, 1H), 7.52 (dd, J = 8.2, 7.3 Hz, 1H), 7.33-7.27 (m, 2H), 6.78(ddd, J = 8.5, 7.1, 1.3 Hz, 1H), 6.58 (dd, J = 8.5, 1.2 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 163.0, 144.2, 137.4, 136.4, 136.4, 134.3, 134.2, 132.9, 132.3 (q, J = 34.0 Hz), 129.8, 127.8, 126.8, 126.6, 126.4, 126.1, 125.3, 123.8, 122.9 (q, J = 273.0 Hz), 121.9,

119.7, 118.0; HRMS (ESI): m/z [M - H]⁻ calcd for $C_{25}H_{14}F_6N_3O_2$: 518.0934, found: 518.0945.

General procedure for preparation of diamines (4a-e)

Sulfonamide 3a-e (1 mmol) and powdered zinc (262 mg; 4 mmol) were suspended in methanol (4.5 mL). Acetic acid (0.36 mL; 6.3 mmol) was added in one portion and the resulting mixture was allowed to stir at room temperature for 2 hours. After the reaction was completed, residual zinc was filtered off, and the filtrate was diluted with 5% aqueous solution of sodium carbonate (10 mL). Product was extracted with dichloromethane (3 \times 10 mL vol.) and combined extracts were dried over magnesium sulfate. A solvent was evaporated to yield corresponding diamine **4a-e**. The isolated compound was purified using column chromatography, where noted.

N-(8-((2-Aminophenyl)amino)naphthalen-1-yl)-4-methyl-benzenesulfonamide (4a). Nitrosulfonamide 3a (250 mg, 0.58 mmol) was reduced to give amine 4a (220 mg, 86%) as a brown solid after the extraction. Mp 197–199 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.33 (s, 1H), 7.65 (dd, J = 8.3, 1.2 Hz, 1H), 7.51 (dd, J = 7.9, 1.4 Hz, 1H), 7.44–7.33 (m, 1H), 7.37–7.26 (m, 1H), 7.31–7.21 (m, 3H), 7.04 (dd, J = 7.5, 1.2 Hz, 1H), 7.03–7.00 (m, 2H), 6.96 (td, J = 7.5, 1.4 Hz, 1H), 6.91 (dd, J = 7.8, 1.7 Hz, 1H), 6.60 (ddd, J = 7.8, 7.2, 1.7 Hz, 1H), 6.06 (dd, J = 7.9, 1.4 Hz, 1H), 5.92 (s, 1H), 3.83 (s, 2H), 2.30 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 143.5, 142.1, 141.6, 136.2, 135.4, 132.8, 129.5, 128.7, 127.5, 126.7, 126.5, 125.0, 124.7, 123.1, 121.0, 120.4, 119.9, 116.8, 115.1, 114.9, 20.7; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{23}H_{21}N_3O_2S$: 404.1423, found: 404.1427.

N-(8-((2-Aminophenyl)amino)naphthalen-1-yl)naphthalene-2-sulfonamide (4b). Nitrosulfonamide 3b (272 mg, 0.58 mmol) was reduced to give amine 4b (224 mg, 88%) as a brown solid after the extraction. 1 H NMR (400 MHz, CDCl₃) δ 11.58 (s, 1H), 8.19 (d, J = 1.9 Hz, 1H), 7.82 (dd, J = 8.4, 1.4 Hz, 1H), 7.78 (dd, J = 8.4, 1.4 Hz, 1H), 7.J = 8.1, 1.5 Hz, 1H), 7.64 (dd, J = 8.4, 1.1 Hz, 1H), 7.63 (d, J =8.8 Hz, 1H), 7.60-7.51 (m, 2H), 7.49 (dd, J = 8.1, 1.2 Hz, 1H), 7.40 (dd, J = 7.7, 1.2 Hz, 1H), 7.38 (dt, J = 7.9, 0.8 Hz, 1H), 7.26(t, J = 7.9 Hz, 1H), 7.18 (dd, J = 8.8, 1.9 Hz, 1H), 7.05 (dd, J =7.4, 1.2 Hz, 1H), 6.99 (ddd, J = 8.2, 7.0, 1.3 Hz, 1H), 6.95 (dd, J= 7.9, 1.9 Hz, 1H), 6.57 (ddd, J = 7.9, 7.0, 1.9 Hz, 1H), <math>6.04 (dd, J = 7.9, 7.0, 1.9 Hz, 1H)J = 7.9, 1.3 Hz, 1H), 5.92 (s, 1H), 3.86 (s, 2H); ¹³C NMR (101 MHz, DMSO- d_6) δ 142.5, 141.7, 136.2, 135.3, 134.3, 132.7, 131.4, 129.3, 129.1, 128.9, 128.5, 127.8, 127.6, 126.8, 126.7, 125.0, 124.8, 123.3, 122.6, 120.8, 120.4, 120.3, 116.7, 115.1, 114.5; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{26}H_{22}N_3O_2S$: 440.1427, found: 440.1427.

N-(8-((2-Aminophenyl)amino)naphthalen-1-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide (4c). Nitrosulfonamide 3c (100 mg, 0.18 mmol) was reduced to give amine 4c (89 mg, 94%) as a brown solid after the extraction. Compound 4c (494 mg) was obtained after the extraction as a brown solid (94%). Mp 172–174 °C; ¹H NMR (400 MHz, CDCl₃) δ 12.12 ppm (br. s., 1H), 8.02–7.97 (m, 2H), 7.92–7.87 (m, 1H), 7.72 (dd, J = 8.3, 1.0 Hz, 1H), 7.61 (dd, J = 8.2, 1.0 Hz, 1H), 7.47 (dd, J = 7.7, 1.2 Hz, 1H), 7.42 (dd, J = 8.2, 7.4 Hz, 1H), 7.38 (t, J = 7.9 Hz, 1H), 7.10 (dd, J = 7.3, 1.2 Hz, 1H), 6.90–6.87 (m, 2H),

6.55-6.47 (m, 1H), 6.01 (d, I = 7.8 Hz, 1H), 5.79 (br. s., 1H), 3.68 (s, 2H); 13 C NMR (101 MHz, DMSO- d_6) δ 142.7, 142.2, 140.9, 136.4, 131.9, 131.2 (q, J = 34.0 Hz), 127.9, 127.5, 127.2, 126.9, 125.3, 124.8, 124.5, 122.6, 122.5 (q, J = 273.5 Hz), 120.4, 119.3, 117.0, 115.4, 111.7; HRMS (ESI): $m/z [M + H]^+$ calcd for C₂₄H₁₈F₆N₃O₂S: 526.1018, found: 526.1025.

N-(8-((2-Nitrophenyl)amino)naphthalen-1-yl)quinoline-8-sulfonamide (4d). Nitrosulfonamide 3d (272 mg, 0.58 mmol) was reduced to give amine 4d (245 mg, 96%) as a brown solid after the extraction. Mp 205–207 °C; 1 H NMR (500 MHz, CDCl₃) δ 10.33 (s, 1H), 9.11 (d, J = 3.0 Hz, 1H), 8.33 (d, J = 7.3 Hz, 1H), 8.30 (d, J = 8.2 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H), 7.82 (s, 1H), 7.64-7.54 (m, 2H), 7.53 (d, J = 8.3 Hz, 1H), 7.33-7.24 (m, 2H), 7.05 (t, I = 7.8 Hz, 1H), 7.02–6.92 (m, 2H), 6.88 (d, I = 7.8 Hz, 1H), 6.81-6.71 (m, 2H), 6.67 (d, J = 7.3 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 151.6, 143.4, 142.3, 141.9, 137.5, 136.9, 135.2, 134.0, 132.9, 132.6, 129.3, 129.1, 127.8, 127.1, 125.9, 125.8, 125.3, 124.9, 122.6, 121.0, 120.7, 120.2, 119.2, 116.7, 113.8. HRMS (ESI): m/z [M + H]⁺ calcd for $C_{25}H_{21}N_4O_2S$: 441.1380, found: 441.1376.

N-(8-((2-Aminophenyl)amino)naphthalen-1-yl)methanesulfonamide (4e). Nitrosulfonamide 3e (200 mg, 0.56 mmol) was reduced to give amine 4e (166 mg, 91%) as a white solid after the purification using a column chromatography (dichloromethane/ethyl acetate, 10:1). Mp 149-150 °C; ¹H NMR (400 MHz, CDCl₃) δ 11.06 (br. s, 1H), 7.75 (t, J = 8.3, 1.1 Hz, 1H), 7.65 (dd, J = 7.6, 1.1 Hz, 1H), 7.62 (dd, J = 8.3, 0.9 Hz, 1H), 7.49–7.38 (m, 2H), 7.13 (dd, J = 7.3, 1.2 Hz, 1H), 6.91–6.82 (m, 2H), 6.57 (ddd, J = 8.0, 5.9, 2.9 Hz, 1H), 6.04 (dd, J = 7.6, 0.9 Hz, 1H), 5.79 (br. s, 1H), 2.38 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 142.9, 142.2, 136.9, 134.1, 129.1, 127.3, 127.3, 126.0, 125.2, 123.6, 121.5, 120.9, 120.8, 117.1, 115.6, 115.1, 38.6; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{17}H_{18}N_3O_2S$: 328.1114, found: 328.1112.

General procedure for preparation of diamines (4f-g)

10% palladium on activated charcoal (53 mg, 0.01 mmol) was placed at the bottom of the flask. The solution of nitro compound 3f or 3g (1 mmol) in ethyl acetate (25 mL) was carefully added. The resulted suspension was stirred at RT for 4 hours under hydrogen atmosphere. After the reaction was completed, palladium on activated charcoal was removed using filtration and the filtrate was evaporated on a rotavap to yield the corresponding diamine 4f or 4g.

 N^{1} -(8-(Pyrrolidin-1-yl)naphthalen-1-yl)benzene-1,2-diamine (4f). Nitro compound 3f (333 mg, 1 mmol); 303 mg of 4f was isolated as a grey oil (quantitative). ¹H NMR (400 MHz, DMSO d_6) δ 10.70 (s, 1H), 7.56 (dd, J = 7.3, 2.1 Hz, 1H), 7.42–7.29 (m, 2H), 7.19 (t, J = 7.8 Hz, 2H), 7.13 (dd, J = 8.1, 1.4 Hz, 1H), 6.87 (ddd, J = 8.6, 7.2, 1.5 Hz, 1H), 6.80 (dd, J = 7.9, 1.6 Hz, 1H),6.64 (dd, J = 7.6, 1.3 Hz, 1H), 6.60 (ddd, J = 7.7, 7.2, 1.6 Hz, 1H), 4.74 (s, 2H), 3.48-3.34 (m, 2H), 2.99-2.75 (m, 2H), 1.97-1.76 (m, 4H); 13 C NMR (101 MHz, DMSO- d_6) δ 147.7, 143.8, 143.0, 136.5, 127.7, 126.3, 125.6, 125.3, 124.2, 122.7, 119.2, 116.8, 116.5, 116.4, 115.3, 106.4, 54.3, 23.7; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₀H₂₁N₃: 304.1803, found: 304.1808.

N¹-(8-(Piperidin-1-yl)naphthalen-1-yl)benzene-1,2-diamine (4g). Nitro compound 3g (347 mg; 1 mmol); 317 mg of 4g was isolated as a grey oil (quantitative). ¹H NMR (400 MHz, CDCl₃) δ 11.03 (s, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.36 (t, J = 7.9 Hz, 1H), 7.30-7.19 (m, 3H), 7.16 (dd, J = 7.9, 1.3 Hz, 1H), 7.07 (td, J =7.6, 1.3 Hz, 1H), 6.86 (dd, J = 7.9, 1.3 Hz, 1H), 6.81 (td, J = 7.5, 1.2 Hz, 1H), 6.57 (d, J = 7.4 Hz, 1H), 3.89 (s, 2H), 3.39–3.25 (m, 2H), 2.88-2.68 (m, 2H), 1.87-1.65 (m, 5H), 1.46-1.30 (m, 1H); 13 C NMR (101 MHz, CDCl₃) δ 151.5, 144.8, 143.1, 137.2, 128.7, 126.8, 126.3, 126.2, 125.8, 125.5, 119.1, 118.8, 117.5, 116.8, 116.0, 107.3, 55.7, 26.5, 24.1; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₁H₂₄N₄: 318.1965, found: 318.1952.

N¹-(2-Aminophenyl)-N⁸,N⁸-dibenzylnaphthalene-1,8-diamine (4h). Dibenzylamin 3h (260 mg, 0.58 mmol) and powdered zinc (150 mg, 2.29 mmol) were suspended in methanol (3.7 mL). Acetic acid (0.3 mL; 5.27 mmol) was added. The reaction mixture was allowed to stir at room temperature for 2 hours. After the reaction was completed, residual zinc was filtrated-off and the filtrate was diluted with 5% aqueous solution of potassium carbonate (5 mL). The product was extracted with dichloromethane (3 × 5 mL) and the combined extracts were dried over magnesium sulfate. After the solvent was evaporated, 216 mg of 4h was obtained as a red solid (87%). Mp 139–141 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.79 (br. s, 1H), 7.57 (dd, J = 8.2, 1.0 Hz, 1H), 7.29-7.05 (m, 10H), 7.16-7.06 (m, 5H),6.92 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.87 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.81 (dt, J = 7.4, 1.6 Hz, 1H), 6.47 (dd, J = 7.3, 1.5 Hz, 1H), 4.33-4.20(m, 4H), 3.71 (br. s, 2H); 13 C NMR (101 MHz, CDCl₃) δ 147.1, 144.7, 143.2, 137.3, 136.1, 130.1, 128.9, 128.6, 128.4, 127.6, 127.4, 126.8, 126.7, 126.5, 126.3, 124.8, 120.5, 119.5, 117.6, 116.4, 58.9; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{30}H_{28}N_3$: 430.2278, found: 430.2278.

N-(8-((2-Aminophenyl)amino)naphthalen-1-yl)-3,5-bis(trifluoromethyl)benzamide (4i). 10% palladium on activated charcoal (15 mg, 0.015 mmol) was placed at the bottom of the flask. The solution of nitro compound 3i (150 mg, 0.289 mmol) in ethyl acetate (10 mL) was carefully added. A suspension was stirred at room temperature for 4 hours under hydrogen atmosphere. After the reaction was completed, palladium on activated charcoal was removed using filtration and the filtrate was evaporated on a rotavap to yield 134 mg of diamine 4i as a yellow solid (95%). Mp 152–154 °C; ¹H NMR (400 MHz, CDCl₃) δ 12.34 (s, 1H), 8.57 (d, J = 7.6 Hz, 1H), 8.12 (s, 2H), 7.92 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.70 (dd, J = 8.2, 1.1 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.13 (dd, J = 7.2, 0.8 Hz, 1H), 6.80 (td, J = 7.6, 1.3 Hz, 1H), 6.69 (td, J = 7.7, 1.3 Hz, 1H), 6.57 (dd, J = 7.7, 1.2 Hz, 1H), 6.46 (dd, J = 7.8, 1.3 Hz, 1H), 5.75 (s, 1.4 Hz, 1.4 Hz,1H), 3.30 (s, 2H); 13 C NMR (101 MHz, DMSO- d_6) δ 162.4, 140.8, 140.7, 137.4, 135.9, 133.8, 130.4 (q, J = 33.4 Hz), 129.5, 127.9, 126.3, 126.0, 125.4, 124.8, 123.5, 123.0 (q, J = 273.0 Hz), 122.4, 121.2, 121.1, 120.7, 116.8, 116.5, 114.8; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{25}H_{18}F_6N_3O$: 490.1349, found: 490.1332.

General procedure for preparation of benzimidazoles (5a-e)

Diamine 4a-e (1 mmol) was dissolved in chloroform (5 mL). Phosgene dimethyliminium chloride (244 mg; 1.5 mmol) was added in one portion and the reaction mixture was refluxed for 2 hours. After the reaction was completed, the resulting mixture was diluted with dichloromethane (10 mL) and washed with 5% aqueous solution of sodium carbonate (2 \times 5 mL) and water (1 \times 5 mL). The organic layer was dried over magnesium sulfate and the solvent was evaporated on a rotavap. A crude solid was purified by column chromatography to yield corresponding benzimidazole **5a–e**.

N-(8-(2-(Dimethylamino)-1H-benzimidazol-1-yl)naphthalen-1-yl)-4-methylbenzenesulfonamide (5a). Diamine 4a (1.2 g, 2.98 mmol) was transformed by cyclization to give benzimidazole 5a (0.94 g, 69%) as a brown solid after the purification using a column chromatography (dichloromethane/ethyl acetate, 1:1). Mp 185–187 °C; 1 H NMR (400 MHz, CDCl₃) δ 8.27 (s, 1H), 7.93 (dd, J = 8.3, 1.1 Hz, 1H), 7.70 (d, J = 8.1 Hz, 2H), 7.64 (d, J = 7.9 Hz, 1H), 7.49 (t, J = 7.9 Hz, 1H), 7.46 (t, J = 8.0 Hz, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.29–7.16 (m, 2H), 7.12-7.03 (m, 2H), 6.90 (t, J = 7.6 Hz, 1H), 6.40 (d, J = 7.8 Hz, 1H), 2.89 (s, 6H), 2.33 (s, 3H); 13 C NMR (101 MHz, CDCl₃) δ 158.4, 143.8, 142.3, 138.2, 136.6, 132.7, 130.9, 129.6, 128.5, 127.6, 126.9, 126.2, 125.3, 123.5, 122.2, 121.0, 117.9, 117.2, 109.7, 40.8, 21.6; IR (FTIR): 2941, 2831, 2362, 2343, 1570, 1462, 1297, 1158, 1035, 918, 841, 740, 658 cm⁻¹; HRMS (ESI): m/z [M +H]⁺ calcd for C₂₆H₂₅N₄O₂S: 357.1693, found: 357.1688.

N-(8-(2-(Dimethylamino)-1H-benzimidazol-1-yl)naphthalen-1-yl)naphthalene-2-sulfonamide (5b). Diamine 4b (127 mg, 0.29 mmol) was transformed by cyclization to give benzimidazole 5b (106 mg, 74%) as a brown solid after the purification using a column chromatography (dichloromethane/methanol, 20:1). Mp = 187–188 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.27 (s, 1H), 8.17 (d, J = 1.7 Hz, 1H), 7.91 (dd, J = 8.2, 1.1 Hz, 1H), 7.88-7.79 (m, 3H), 7.75-7.64 (m, 2H), 7.65-7.51 (m, 3H), 7.53-7.42 (m, 2H), 7.32 (dd, J = 8.7, 1.9 Hz, 1H), 7.18 (ddd, J =15.9, 7.9, 1.2 Hz, 2H), 6.77 (td, J = 7.9, 1.1 Hz, 1H), 6.31 (d, J = 7.7 Hz, 1H), 2.85 (s, 6H); $^{13}\mathrm{C}$ NMR (101 MHz, CDCl $_3$) δ 158.5, 142.6, 138.2, 136.5, 135.0, 132.8, 132.6, 132.0, 130.8, 129.5, 129.3, 128.9, 128.9, 128.4, 127.8, 127.4, 126.9, 126.2, 125.4, 123.5, 122.6, 122.0, 120.9, 117.7, 117.3, 109.5, 40.7; IR (FTIR): 2941, 2832, 2362, 2343, 1685, 1569 1462, 1297, 1158, 1034, 919, 842, 764, 740, 669 cm⁻¹; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₉H₂₅N₄O₂S: 493.1693, found: 493.1686.

N-(8-(2-(Dimethylamino)-1*H*-benzimidazol-1-yl)naphthalen-1-yl)-3,5-bis(trifluoromethyl)benzenesulfonamide (5c). Diamine 4c (323 mg, 0.56 mmol) was transformed by cyclization to give benzimidazole 5c (232 mg, 72%) as a yellow solid after the purification using a column chromatography (dichloromethane/ethyl acetate, 1:1). Mp 210–212 °C; ¹H NMR (400 MHz, CDCl₃ with one drop of TFA) δ 8.23 (dd, J = 8.0, 1.5 Hz, 1H), 8.11–8.05 (m, 2H), 7.95 (s, 2H), 7.87–7.77 (m, 2H), 7.68 (s, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.45–7.36 (m, 2H), 7.27–7.16 (m, 1H), 6.79 (d, J = 8.1 Hz, 1H), 6.60 (dd, J = 7.3, 0.8 Hz, 1H), 2.99 (s, 6H); ¹³C NMR (126 MHz, CDCl₃ with one drop of TFA) δ 150.4, 141.7, 136.7, 133.6, 132.8 (q, J = 34.5 Hz), 132.7, 131.1, 130.3, 129.8, 129.6, 129.0, 128.7, 128.4, 128.3 (q, J = 2.7 Hz), 126.9, 126.6, 126.5, 125.5, 124.1, 122.4 (q, J = 272.6 Hz), 112.7, 111.5, 40.9; IR (FTIR): 2923, 2938, 2362, 2342, 1570,

1458, 1358, 1277, 1123, 1054, 1033, 1017, 904, 843, 817, 764, 737 cm $^{-1}$; HRMS (ESI): m/z [M + H] $^{+}$ calcd for $C_{27}H_{21}F_6N_4O_2S$: 579.1284, found: 579.1295.

N-(8-(2-(Dimethylamino)-1H-benzimidazol-1-yl)naphthalen-1-yl)quinoline-8-sulfonamide (5d). Diamine 4d (127 mg, 0.29 mmol) was transformed by cyclization to give benzimidazole 5d (90 mg, 64%) as a yellow solid after the purification using a column chromatography (dichloromethane/ethyl acetate, 1:1). Mp 196–197 °C; 1 H NMR (500 MHz, CDCl₃) δ 8.55 (s, 1H), 8.25 (dd, J = 7.3, 1.4 Hz, 1H), 8.24–8.14 (m, 2H), 8.01 (dd, J = 8.2, 1.2 Hz, 1H), 7.96 (dd, J = 8.2, 1.1 Hz, 1H), 7.86 (dd, J = 8.2, 1.0 Hz, 1H), 7.76 (dd, J = 7.5, 0.8 Hz, 1H), 7.58 (dd, J = 7.5, 0.8 Hz, 1H)J = 7.9, 7.4 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.49 (dd, J = 8.0, 7.4)Hz, 1H), 7.38 (dd, I = 8.2, 4.3 Hz, 1H), 7.19 (dd, I = 7.3, 1.2 Hz, 1H), 7.07 (d, J = 7.9 Hz, 1H), 6.96 (ddd, J = 8.3, 7.7, 1.0 Hz, 1H), 6.78 (ddd, J = 8.1, 7.7, 0.9 Hz, 1H), 6.40 (d, J = 7.8 Hz, 1H), 2.75(s, 6H); 13 C NMR (101 MHz, DMSO- d_6) δ 157.8, 151.2, 142.3, 141.8, 138.0, 137.2, 136.6, 136.0, 133.9, 132.3, 131.4, 130.3, 129.0, 128.5, 128.4, 126.7, 126.5, 126.3, 125.8, 124.1, 122.6, 121.8, 121.4, 119.7, 116.1, 108.6; IR (FTIR): 2942, 2832, 2361, 2343, 1686, 1566, 1458, 1429, 1166, 1147, 1034, 921, 766, 736, 669 cm⁻¹; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{28}H_{23}N_5O_2S$: 494.1844, found: 494.1645.

N-(8-(2-(Dimethylamino)-1H-benzimidazol-1-yl)naphthalen-1-yl)methanesulfonamide (5e). Diamine 4e (80 0.25 mmol) was transformed by cyclization to give benzimidazole 5e (55 mg, 58%) as a vellow solid after the purification using a column chromatography (ethyl acetate). Mp = 216–218 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.02 (dd, J = 8.3, 1.2 Hz, 1H), 7.85 (dd, J = 7.7, 1.1 Hz, 1H), 7.82 (dd, J = 8.3, 1.0 Hz, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.60–7.54 (m, 2H), 7.34 (dd, J =7.3, 1.3 Hz, 1H), 7.20 (td, J = 7.7, 1.1 Hz, 1H), 6.94 (td, J = 7.7, 1.1 Hz, 1H), 6.58 (d, J = 7.9 Hz, 1H), 2.91 (s, 6H), 2.53 (s, 3H); ¹³C NMR (101 MHz, DMSO- d_6) δ 157.6, 142.0, 137.9, 136.2, 132.2, 131.9, 130.2, 128.4, 127.3, 126.5, 126.3, 125.1, 124.0, 121.6, 119.7, 115.7, 109.4, 40.3, 40.2; IR (FTIR): 3288, 2922, 2844, 2362, 2343, 1618, 1570, 1463, 1419, 1296, 1277, 1157, 1058, 997, 976, 857, 765, 743 cm⁻¹; HRMS (ESI): m/z [M + H] calcd for C₂₀H₂₀N₄O₂S: 381.1378, found: 381.1380.

General procedure for preparation of benzimidazoles (5f and 5g)

Diamine **4f** or **4g** (0.91 mmol) was dissolved in chloroform (6 mL). Phosgene dimethyliminium chloride (221 mg, 1.36 mmol) was added in one portion and the reaction mixture was refluxed for 2 hours. After the reaction was completed, the resulting mixture was diluted with dichloromethane (12 mL) and washed with 5% aqueous solution of sodium carbonate (2×10 mL) and water (1×10 mL). The organic layer was dried over magnesium sulfate and the solvent was evaporated on a rotavap. A crude yellow solid was purified by column chromatography (dichloromethane/ethyl acetate, 3:2) to yield benzimidazole **5f** or **5g**.

N,N-Dimethyl-1-(8-(pyrrolidin-1-yl)naphthalen-1-yl)-1*H*-benzimidazol-2-amine (5f). Diamine 4f (276 mg, 0.91 mmol); 243 mg of 5f was isolated as an yellow solid (75%). Mp =

138–139 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.98–7.89 (m, 1H), 7.64 (d, J = 8.1 Hz, 1H), 7.64–7.54 (m, 3H), 7.46 (td, J = 8.1, 1.2 Hz, 1H), 7.21 (d, J = 7.5 Hz, 1H), 7.25–7.06 (m, 1H), 7.12–7.08 (m, 1H), 7.08-6.97 (m, 1H), 2.69-2.54 (m, 2H), 2.49 (s, 6H), 1.47-1.15 (m, 4H), 1.10-0.65 (m, 2H); ¹³C NMR (101 MHz, $CDCl_3$) δ 157.8, 148.3, 137.0, 136.5, 132.5, 129.8, 127.0, 126.9, 125.6, 125.5, 124.0, 121.6, 120.3, 117.2, 116.5, 108.7, 54.0, 40.4, 23.3; IR (FTIR): 2981, 2940, 2867, 2813, 2362, 2343, 1614, 1542, 1461, 1399, 1276, 1057, 1003, 938, 756, 738 cm⁻¹; HRMS (ESI): $m/z [M + H]^+$ calcd for $C_{23}H_{25}N_4$: 357.2074, found: 357.2071.

Chiral resolution of N,N-dimethyl-1-(8-(pyrrolidin-1-yl) naphthalen-1-vl)-1H-benzimidazol-2-amine (5f). Both enantiomers of (-)- (R_a) -5f and (+)- (S_a) -5f were isolated using semi-preparative chiral HPLC (column Lux Cellulose-3 (250 × 10 mm; 5 μ m), mobile phase: n-hexane: MeOH: EtOH 40:1:1 (v/v/v), flow rate: 5 mL min⁻¹), T = 35 °C, loading: 1000 μ l, UV detection: $\lambda = 274$ nm. Amount of racemic 5f was 110 mg.

(-)-N,N-Dimethyl-1-(8-(pyrrolidin-1-yl)naphthalen-1-yl)-1H-benzimidazol-2-amine (-)- (R_a) -5f. First eluted atropisomer was (-)-(R_a)-5f (55 mg isolated). [α]_D²² -20.86° (c = 0.2, MeOH).

(+)-N,N-Dimethyl-1-(8-(pyrrolidin-1-yl)naphthalen-1-yl)-1Hbenzimidazol-2-amine (+)- (S_a) -5f. Second eluted atropisomer was (+)-(S_a)-5f (45 mg isolated). $[\alpha]_D^{22}$ +23.14° (c = 0.6, MeOH).

N,N-Dimethyl-1-(8-(piperidin-1-yl)naphthalen-1-yl)-1H-benzimidazol-2-amine (5g). Diamine 4g (288 mg, 0.91 mmol); 255 mg of 5g was isolated as an yellow solid (78%). Mp = 145–147 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.94 (dd, J = 8.0, 1.5 Hz, 1H), 7.69 (dd, J = 8.2, 1.2 Hz, 1H), 7.59 (dt, J = 7.9, 0.9 Hz, 1H), 7.60-7.48 (m, 1H), 7.52-7.47 (m, 2H), 7.31 (dd, J = 7.6, 1.2 Hz, 1H), 7.14 (ddd, J = 7.9, 7.2, 1.3 Hz, 1H), 6.98 (ddd, J = 8.2, 7.2, 1.2 Hz, 1H), 6.91 (ddd, J = 7.9, 1.3, 0.7 Hz, 1H), 3.00–2.91 (m, 1H), 2.59 (s, 6H), 2.63-2.53 (m, 1H), 2.47-2.40 (m, 1H), 1.96 (td, J = 11.9, 2.8 Hz, 1H), 1.53-1.41 (m, 1H), 1.38-1.23 (m, 2H), 0.86 (tdt, J = 13.7, 9.3, 4.3 Hz, 1H), 0.75-0.65 (m, 1H), -0.42 (qt, J = 13.1, 4.1 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 157.6, 152.5, 141.9, 137.6, 137.2, 132.6, 130.0, 127.5, 127.0, 125.8, 125.4, 124.9, 121.4, 120.1, 119.4, 116.6, 108.8, 57.6, 54.1, 40.6, 25.8, 24.2, 23.9; IR (FTIR): 2931, 2362, 1616, 1542, 1399, 1282, 1225, 1129, 1052, 988, 923, 843, 820, 766, 659 cm⁻¹; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{24}H_{27}N_4$: 371.2230, found: 371.2228.

1-[8-(Dibenzylamino)naphthalen-1-yl]-N,N-dimethyl-1H-benzimidazol-2-amine (5h). Diamine 4h (200 mg, 0.47 mmol) was dissolved in chloroform (5 mL). Phosgene dimethyliminium chloride (115 mg, 0.705 mmol) was added in one portion and the reaction mixture was refluxed for 2 hours. After the reaction was completed, the resulting mixture was diluted with dichloromethane (10 mL) and washed with 5% aqueous solution of sodium carbonate (2 \times 10 mL) and water (1 \times 10 mL). Organic layer was dried over magnesium sulfate and the solvent was evaporated on a rotavap. The crude solid was purified using column chromatography (dichloromethane) to yield 147 mg of **5h** as a brown solid (65%). Mp = 161-162 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (dd, J = 8.0, 1.6 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H, 7.74 (d, J = 7.9 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H),7.56 (dd, J = 7.2, 1.6 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 7.32–7.27

(m, 1H), 7.24-7.17 (m, 2H), 7.10-7.00 (m, 3H), 7.00-6.92 (m, 5H), 5.94 (d, J = 7.5 Hz, 2H), 3.98 (d, J = 13.7 Hz, 1H), 3.89-2.78 (m, 2H), 3.19 (d, J = 14.2 Hz, 1H), 2.62 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 155.6, 148.6, 137.6, 136.5, 136.2, 134.6, 132.1, 130.9, 129.7, 129.5, 128.4, 127.7, 127.6, 127.4, 127.3, 127.2, 126.5, 125.6, 124.8, 124.3, 122.6, 121.4, 120.5, 116.3, 109.7, 57.5, 55.4, 40.9; IR (FTIR): 2945, 2361, 1636, 1541, 1426, 1394, 1279, 1032, 908, 841, 759, 689 cm⁻¹; HRMS (ESI): m/z [M + H⁺ calcd for C₃₃H₃₁N₄: 483.2543, found: 483.2554.

N-(8-(2-(Dimethylamino)-1H-benzimidazol-1-yl)naphthalen-1-yl)-3,5-bis(trifluoromethyl)benzamide (5i). Diamine (60 mg, 0.123 mmol) and pyridine (0.04 mL; 0.492 mmol) were dissolved in dichloromethane (2.5 mL). Phosgene dimethyliminium chloride (30 mg, 0.184 mmol) was added in one portion and the reaction mixture was stirred at room temperature for 2 hours. After the reaction was completed, the resulting mixture was diluted with dichloromethane (5 mL) and washed with 5% aqueous solution of sodium carbonate (2 \times 5 mL) and water (1 \times 5 mL). The organic layer was dried over magnesium sulfate and the solvent was evaporated on a rotavap. The residue was purified using column chromatography (dichloromethane/ethyl acetate, 12:1) to yield 36 mg of 5i as a white solid (54%). Mp = 74-75 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (dd, J = 8.3, 1.1 Hz, 1H), 7.98 (dd, J = 8.2, 0.9 Hz, 1H), 7.94 (s, 1H), 7.85 (d, J = 7.4 Hz, 1H), 7.73 (s, 1H), 7.67 (t, J = 7.7 Hz, 1H, 7.65 - 7.58 (m, 3H), 7.47 (dd, J = 7.3, 1.2 Hz, 1H),7.13 (d, J = 7.8 Hz, 1H), 7.08 (td, J = 7.3, 0.9 Hz, 1H), 6.97 (td, J= 7.9, 1.3 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 2.71 (s, 6H); ¹³C NMR (101 MHz, CDCl₃) δ 163.3, 137.2, 136.5, 136.0, 132.0 (q, J = 33.7 Hz), 131.6, 131.1, 130.7, 129.1, 128.3, 127.2, 127.0, 126.9, 126.1, 125.3, 125.3, 123.4, 121.5 (q, J = 273.0 Hz), 121.1, 118.1, 117.1, 108.6, 40.7; IR (FTIR): 2942, 2831, 2362, 2344, 1686, 1496 1462, 1277, 1129, 1031, 904, 844, 764, 739, 681 cm⁻¹; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₈H₂₁F₆N₃O: 544.1614, found: 544.1624.

General procedure for preparation of benzimidazoles (6a-b)

The corresponding nitro compound 3a or 3b (0.29 mmol) and powdered zinc (75 mg, 1.16 mmol) were suspended in methanol (1.8 mL). N,N-Dimethylacetamide dimethyl acetal (0.424 mL, 2.9 mmol) and AcOH (0.148 mL, 2.59 mmol) were subsequently added. The reaction mixture was allowed to stir at 60 °C for 4 hours. After the reaction was completed, residual zinc was filtered off, and the filtrate was diluted with 5% aqueous solution of sodium bicarbonate (5 mL). The product was extracted with dichloromethane (3 × 6 mL). The combined extracts were dried over magnesium sulfate and the solvent was evaporated to yield an oily residue which was purified by column chromatography.

4-Methyl-N-(8-(2-methyl-1H-benzimidazol-1-yl)naphthalen-1yl)benzenesulfonamide (6a). Nitrosulfonamide 3a (125 mg, 0.29 mmol) was transformed by reduction and cyclization to give benzmidazole 6a (87 mg, 70%) as a yellow solid after the purification using column chromatography (dichloromethane/ methanol, 12:1). Mp 229–230 °C; 1 H NMR (400 MHz, CDCl₃) δ 8.02 (dd, J = 8.4, 1.2 Hz, 1H), 7.87 (dt, J = 8.0, 0.8 Hz, 1H), 7.78

(dd, J = 8.3, 1.1 Hz, 1H), 7.63–7.53 (m, 2H), 7.46 (t, J = 7.9 Hz, 1H), 7.42–7.31 (m, 3H), 7.29 (dd, J = 7.3, 1.3 Hz, 1H), 7.20 (ddd, J = 8.1, 7.3, 1.0 Hz, 1H), 7.17–7.13 (m, 2H), 6.81 (dt, J = 8.0, 0.9 Hz, 1H), 6.15 (s, 1H), 2.35 (s, 3H), 2.27 (s, 3H); 13 C NMR (101 MHz, DMSO- d_6) δ 152.2, 142.7, 142.5, 137.6, 136.2, 136.0, 131.4, 131.1, 129.9, 129.2, 128.9, 128.8, 127.6, 127.4, 127.2, 126.1, 125.8, 121.6, 121.1, 118.1, 110.4, 20.9, 14.5; IR (FTIR): 3261, 2945, 2833, 2361, 2343, 1653, 1404, 1332, 1157, 1093, 765, 737, 663 cm⁻¹; HRMS (ESI): m/z [M + H]⁺ calcd for $C_{25}H_{21}N_3O_2S$: 428.1425, found: 428.1427.

N-(8-(2-Methyl-1H-benzimidazol-1-yl)naphthalen-1-yl)naphthalene-2-sulfonamide (6b). Nitrosulfonamide 3b (136 mg, 0.29 mmol) was transformed by reduction and cyclization to give benzmidazole 6b (115 mg, 80%) as a yellow solid after the purification using column chromatography (dichloromethane/ methanol, 12:1). Mp 300-302 °C; ¹H NMR (400 MHz, DMSO d_6) δ 8.12 (d, J = 1.8 Hz, 1H), 8.01 (dd, J = 8.3, 1.3 Hz, 1H), 7.90-7.86 (m, 2H), 7.85-7.81 (m, 1H), 7.80-7.76 (m, 2H), 7.64-7.54 (m, 4H), 7.44 (t, J = 7.9 Hz, 1H), 7.39-7.33 (m, 2H), 7.29 (dd, J = 7.3, 1.3 Hz, 1H), 7.16 (ddd, J = 8.2, 7.3, 1.1 Hz, 1H), 6.77 (dt, J = 8.1, 0.9 Hz, 1H), 6.25 (s, 1H), 2.26 (s, 3H); ¹³C NMR (126 MHz, DMSO- d_6) δ 152.3, 142.4, 137.6, 136.1, 134.1, 131.4, 131.4, 130.9, 130.0, 129.1, 128.9, 128.8, 128.7, 128.2, 127.9, 127.8, 127.5, 127.4, 126.2, 125.8, 122.8, 121.6, 121.2, 118.1, 110.5, 14.6; IR (FTIR): 2972, 2940, 2865, 2844, 2362, 1597, 1399, 1330, 1054, 1016, 1031, 761, 740 cm⁻¹; HRMS (ESI): m/z [M + H]⁺ calcd for C₂₈H₂₁N₃O₂S: 484.1427, found: 484.1427.

General procedure for monoester (7) by desymmetrization of *cis*-tetrahydrophthalic anhydride (6)

cis-Tetrahydrophthalic anhydride (30 mg, 0.197 mmol) and the corresponding benzimidazole catalyst (0.0197 mmol) were dissolved in dry diethyl ether (3.9 mL). Benzyl alcohol (0.204 mL, 1.97 mmol) was added drop-wise and the resulting solution was stirred at room temperature until meso-anhydride 6 was not detected (monitored by TLC). Then, diethyl ether was evaporated and the residue was dissolved in dichloromethane (5 mL) and extracted with saturated aqueous solution of sodium bicarbonate (2 × 5 mL). The aqueous layer was washed with dichloromethane (1 × 5 mL; to remove traces of benzyl alcohol and catalyst), acidified with conc. hydrochloric acid to pH = 1, and extracted with ethyl acetate (2 × 5 mL). Organic layer was dried over magnesium sulfate and concentrated on a rotovap to give benzyl ester 7.

¹H NMR (500 MHz, CDCl₃) δ 7.42–7.27 (m, 5H), 5.69 (t, J = 1.8 Hz, 2H), 5.21–5.08 (m, 2H), 3.14–3.06 (m, 2H), 2.67–2.53 (m, 2H), 2.45–2.32 (m, 2H);³⁵ [α]_D²² +4.51° (c = 1.0, MeOH), ratio: 27:73.^{35,36}

Author contributions

D. T. performed all synthesis and wrote the original draft. I. N. did the X-ray crystallography. O. K. developed chiral analytical and semi-preparative methods and separated both individual

atropisomers (–)-5f and (+)-5f. A. P. developed separation method at analytical level and analysed products after desymmetrization reaction by chiral HPLC. P. C. supervised the project and participated in writing – review and editing.

Data availability

The authors confirm that the data supporting the findings of this study are available within the article and its ESI† or upon request from the corresponding authors.

Conflicts of interest

There are no conflicts to declare.

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