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Diastereoselective synthesis of boron-derivatives of resorcinarenes from amino alcohols and triethylborane

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Abstract—A diastereoselective synthesis of novel boron derivatives of resorcinarenes from chiral amino alcohols and triethylborane is described.

1. Introduction

Resorcinarenes are products of a one step synthesis starting from resorcinol and aliphatic, as well as aromatic aldehydes.[1] Due to their special structure, which is characterized by a cavity and a polar *upper rim*, and due to their easy functionalization, these macrocycles are often used as the stationary phase in HPLC,[2] as active substances in medicine[3] and as catalysts in asymmetric reactions.[4]

Chiral derivatives of resorcinarenes, including substituents displaying Lewis acid character, are particularly interesting. They may be used as catalysts, for example, in Diels–Alder reactions[5] as well as in asymmetric reduction.[6] So far we have reported the synthesis of several boron derivatives of resorcinarenes derived from chiral amino alcohols and $PhB(OH)_2$, with boron as a Lewis acid.[7] Herein we report a highly diastereoselective synthesis of new chiral boron derivatives of resorcinarenes starting from chiral amino alcohols and triethylborane.

2. Results and discussion

The general strategy of our synthesis of chiral boron-oxazine derivatives of resorcinarenes is shown in Scheme 1. We have used a series of primary amino alcohols with an increasing bulkiness of the R group ranging from methyl and branched alkyl groups to phenyl and have the modified method reported in our previous papers.[7]

In the first step, boron-chelates **3** were synthesized in a manner similar to a literature report[8] by dropping the corresponding amino alcohol **2** into a solution of BEt_3 in THF (1 M) at room temperature. In order to complete the transformation, heating at reflux was continued for 30 min. The course of the reaction can be followed by observing an intensive emission of 1 equiv of ethane. These bora-oxazole derivatives **3** were used for the Mannich reaction without further purification leading to the bora-oxazine-boraoxazolidine derivatives of resorcinarenes **4**. After evaporation of THF, we added paraformaldehyde, the resorcinarene as well as 1,4-dioxane to the oily residue and heated the mixture at reflux for 5 h. In all cases of the amino alcohols used, the main product precipitated from the reaction mixture as a fine-crystalline solid in good yield and with high diastereomeric excess suitable for spectral analysis without additional purification (Table 1).

The advantage of this procedure is the precipitation of only one of several diastereoisomers directly from the reaction mixture during the course of the reaction with high diastereoisomeric excess (de >98%). This can be caused by (i) larger rigidity of the boron-chelates compared to the aminomethylene derivative of the amino alcohol used in earlier studies and (ii) by using dioxane as a solvent facilitating the precipitation of only one diastereoisomer. In all cases, we observed the signals of dioxane protons (shifted upfield $\delta = 3.37$ ppm) in the ^{1}H NMR spectra, indicating a possible complexation of this solvent (Fig. 1).

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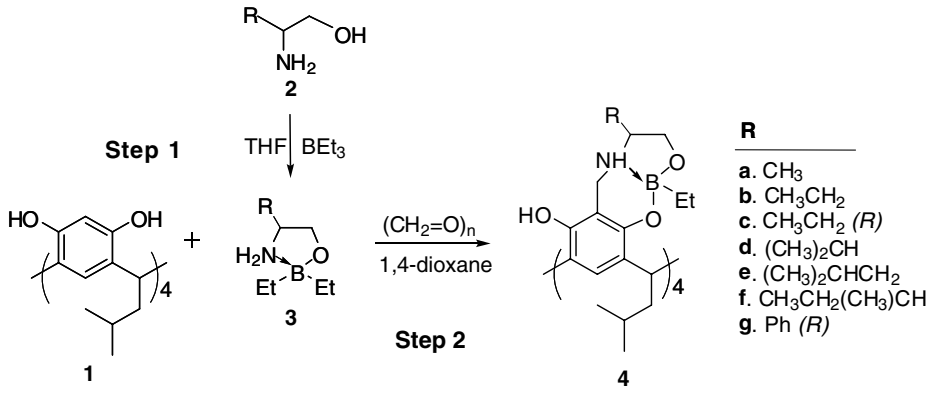


Scheme 1.

Table 1. Yields of products **4** generated from resorcinarene **1** and the boron chelates of amino alcohols **2**

Amino alcohol	Product	Yield [%]	$[\alpha]_D^{25}$
(*S*)-Alaninol **2a**	*out*-(*P*,*S*,*S*,S_N,S_B)-**4a**	72	+1.6
(*S*)-2-Amino-1-butanol **2b**	*out*-(*P*,*S*,*S*,S_N,S_B)-**4b**	57	+11.4
(*R*)-2-Amino-1-butanol **2c**	*out*-(*M*,*R*,*R*,R_N,R_B)-**4c**	52	−11.2
(*S*)-Leucinol **2d**	*out*-(*P*,*S*,*S*,S_N,S_B)-**4d**	35	+0.5
(*S*)-Valinol **2e**	*out*-(*P*,*S*,*S*,S_N,S_B)-**4e**	42	+16.4
(*S*)-Iso-leucinol **2f**	*out*-(*P*,*S*,*S*,S_N,S_B)-**4f**	30	+20.7
(*R*)-Phenylglycinol **2g**	*out*-(*M*,*R*,*R*,R_N,R_B)-**4g**	27	−86.0

Analysing the data displayed in Table 1 in more detail, we observed reduced yields when increasing the bulkiness of the amino alcohol. This is caused by an increased solubility of the products with larger substituents. In accordance with this, we also observed only partial precipitation of the products directly from the reaction mixture when using (*S*)-valinol, (*S*)-isoleucinol, (*S*)-leucinol, and (*R*)-phenylglycinol as the amino alcohol component. The remaining quantities of diastereoisomers in dioxane solution were isolated by column chromatography. These observations led us to study whether the yield might be improved by using less solvent. Indeed, decreasing the quantity of 1,4-dioxane led to an increased precipitation and an increased yield of up to 60% in the case of (*S*)-leucinol and (*R*)-phenylglycinol.

The stereochemical nomenclature of this type of compounds was proposed on the basis of three components: (i) the nomenclature defining the priority of substituents around an axis of chirality proposed by Heaney;[4b,c] (ii)

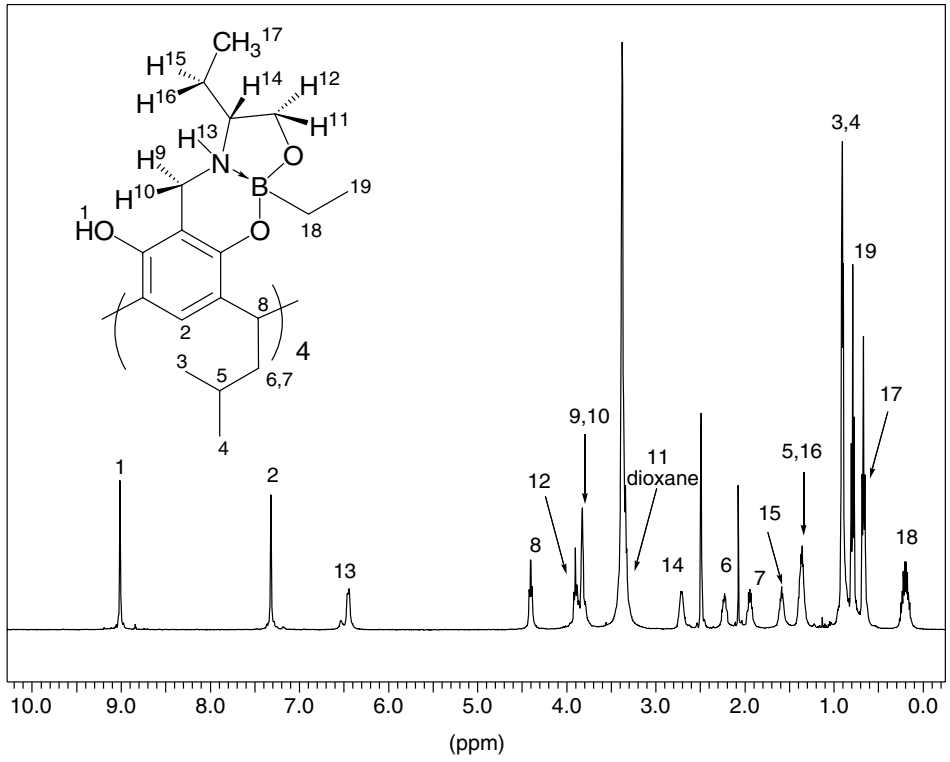


Figure 1. ^{1}H NMR spectra of *out*-(*M*,*R*,*R*,R_N,R_B)-**4c**.

two possibilities of orientation of the bora-oxazine-oxazolidine rings *in* or *out* of the resorcinarene cavity;[7d] (iii) generating two new stereocenters at the nitrogen and at the boron atoms during the course of the reaction as a result of forming the bora-oxazine and bora-oxazolidine rings.

In accordance with these stereochemical components, the structural analysis of all the received derivatives of resorcinarenes **4** was done on the basis of 1D and 2D NMR spectra (^{1}H,^{1}H COSY and ^{1}H,^{1}H NOESY). Spectral analysis of the derivatives of resorcinarene **4**, obtained from (*S*)-amino alcohols, indicates that these derivatives can be classified as *out*-(*P*,*S*,*S*,S_N,S_B) whereas in the case of using (*R*)-amino alcohols derivatives *out*-(*M*,*R*,*R*,R_N,R_B) were prepared.

Figure 2 shows the ^{1}H,^{1}H NOESY spectrum (500 MHz) of bora-oxazine-oxazolidine derivative *out*-(*M*,*R*,*R*,R_N,R_B)-**4c** with marked signals of coupling protons indicating the spatial structure of this compound.

There is a coupling of proton H^{14} with both of the isochronous protons: H^9 and H^{10} of the methylene bridge of the bora-oxazine ring (observed at the same value of $\delta = 3.83$ ppm in ^{1}H NMR spectra) depicted in Figure 2. Moreover, the methylene protons of the bora-oxazolidine ring, H^9 and H^{10}, couple with the protons of the alkyl group, H^{15} and H^{16}, as well as with methylene protons of ethyl group, H^{18}. In such spatial structure of compound *out*-(*M*,*R*,*R*,R_N,R_B)-**4c**, the proton of the tertiary amino group (NH^{13}), located in the ^{1}H NMR spectra at $\delta = 6.45$ ppm, couples with protons H^{18}. The position of the signal of the amine proton (NH^{13}), which is strongly shifted downfield, also indicates a clockwise closing of the bora-oxazine ring. It also suggests that the amine proton is located outside the resorcinarene cavity.

In order to establish the influence of the stereocenter on the direction of closing of the bora-oxazine ring, we also carried out the synthesis with both enantiomers of 2-amino-1-butanol **2b** and **2c**. The ^{1}H NMR (Fig. 1), ^{13}C NMR and ^{1}H,^{1}H COSY spectra of both products obtained either from **2b** or **2c** are identical. In the case of compound **4b**, the bora-oxazine rings are closed in the opposite direction relative to **4c**. The location of the ethyl group linked to the boron atom, as well as the orientation of

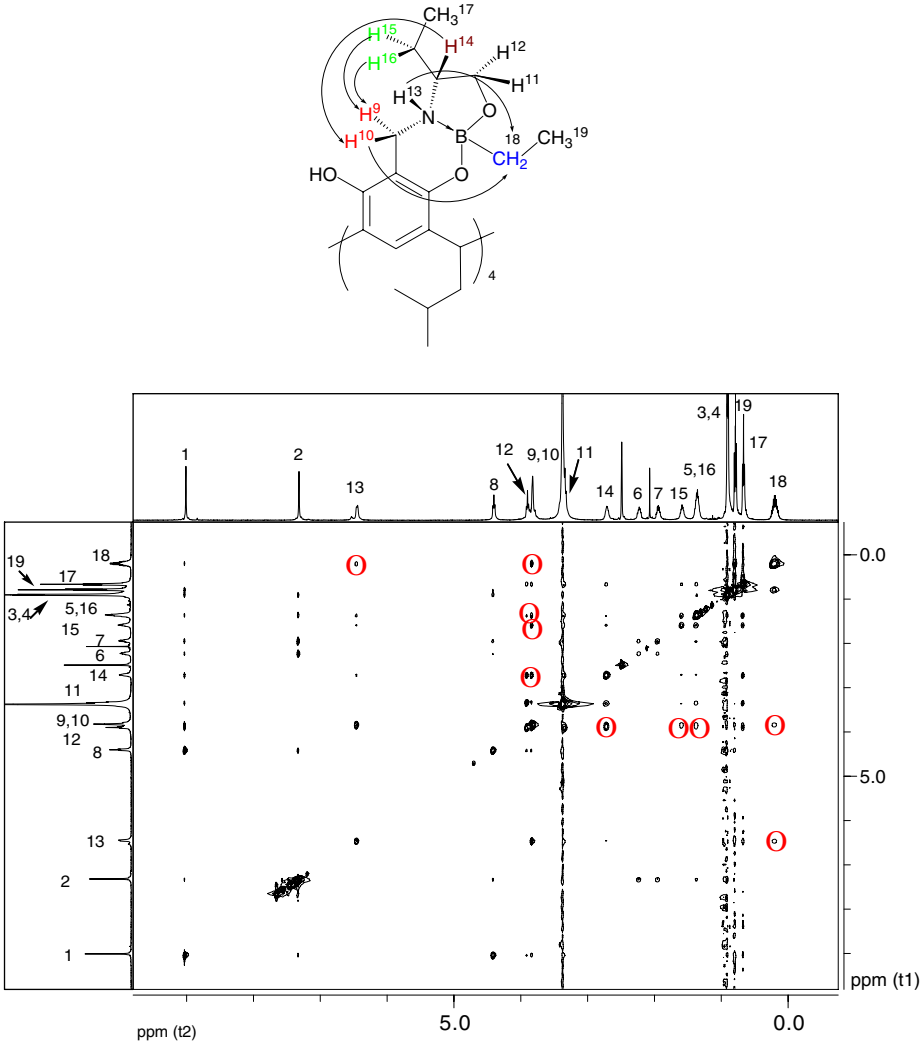
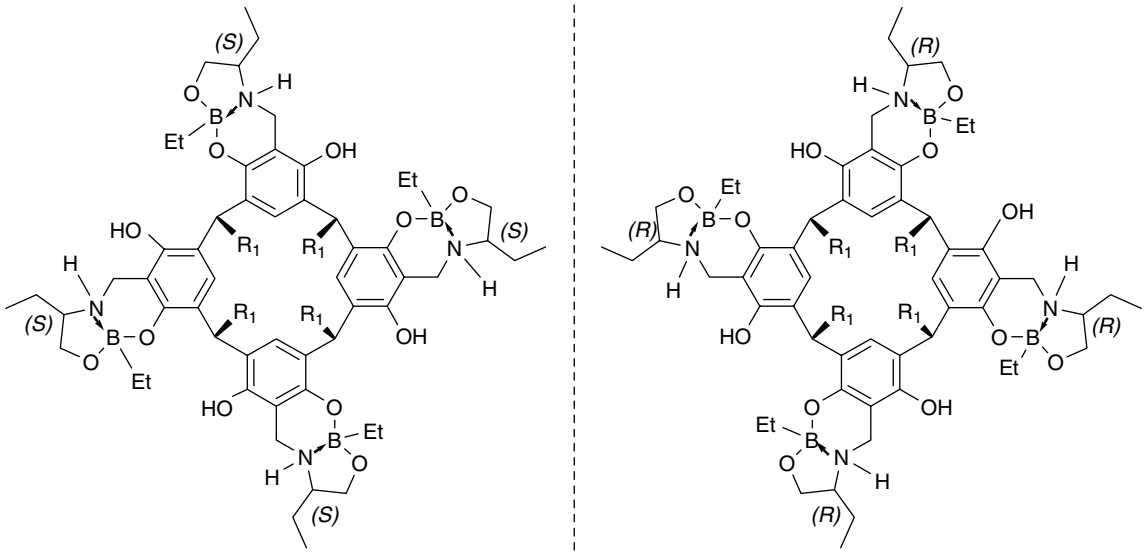


Figure 2. The ^{1}H,^{1}H NOESY spectra (500 MHz) of *out*-(*M*,*R*,*R*,R_N,R_B)-**4c** with marked coupling protons.



out-(*P*,*S*,*S*,S_N,S_B)-**4b** *out*-(*M*,*R*,*R*,R_N,R_B)-**4c**

Figure 3.

the bora-oxazine-oxazolidine rings in relation to the resorcinarene cavity, is the same in both cases. Consequently, *out*-(*P*,*S*,*S*,S_N,S_B)-**4b** and *out*-(*M*,*R*,*R*,R_N,R_B)-**4c** are enantiomers with different directions of closing the bora-oxazine rings (Fig. 3).

3. Conclusion

Herein we have described the synthesis of new chiral boron derivatives of resorcinarenes via Mannich reaction from boron-chelates obtained from chiral amino alcohols and triethylborane. All bora-oxazine-oxazolidine derivatives were isolated with high diastereomeric excess and their structures were confirmed by NMR-spectroscopy. On the basis of the experiments performed with both enantiomers of 2-amino-1-butanol, we were able to confirm the influence of the stereocenter of the starting amino alcohol on the direction of closing the bora-oxazine ring. Reactions with the (*S*)-amino alcohol led to boron derivatives *out*-(*P*,*S*,*S*,S_N,S_B)-**4**. In the reactions with the part (*R*)-amino alcohol, *out*-(*M*,*R*,*R*,R_N,R_B)-**4** diastereoisomers were prepared, but with the same location of the ethyl group linked to the boron atom, as well as the orientation of the bora-oxazine-oxazolidine rings in relation to the resorcinarene cavity. These compounds might have a high potential for the synthesis of boron-macrocycles related to Corey's oxaborolidine ligands,[5] which will be object of our successive investigations.

4. Experimental

4.1. General experimental detail

All ^{1}H and ^{13}C NMR, 2D NMR (^{1}H,^{1}H COSY and ^{1}H,^{1}H NOESY) spectra were measured at 499.893 MHz, with a Bruker DRX 500 spectrometer. Mass spectra were recorded with an Esquire 3000 ion trap mass spectrometer (Bruker Daltonik) and on a Bruker APEX III FT MS at the University of Bielefeld, with the electrospray (ES) technique. Melting points were recorded with a Boëtius melting point instrument and are uncorrected. Optical rotations were measured with an Optical Perkin–Elmer 341 Model polarimeter that was operated at $\lambda = 589$ nm, which corresponds to the sodium D line, at 25 °C. All chromatographic manipulations used silica gel 60 (SiO_2, Merck, particle size 0.040–0.063 mm, 230–240 mesh) as the adsorbent. Reactions were monitored by thin layer chromatography (TLC) on plastic sheets coated with Merck Kieselgel 60 F254 silica gel. TLC plates were visualized by UV radiation at a wavelength of 254 nm. Reagents and solvents were obtained from Fluka and Merck and were used without purification.

4.2. General procedure for the synthesis of boron derivative resorcinarene from amino alcohol 4

To a solution of 1 M BEt_3 in THF (2.81 ml), amino alcohol **2** (2.81 mmol) was added and the reaction mixture was gently heated to boiling for 30 min. After evaporation of the solvent, a colorless oil was obtained. 1,4-Dioxane (20 ml), resorcinarene **1** (0.50 g; 0.70 mmol) and paraformaldehyde (0.10 g; 3.51 mmol) were added and the mixture was refluxed for 5 h. The yellow solid precipitate was collected and washed with 1,4-dioxane to give pure product **4**.

4.3. *out*-(*P*,*S*,*S*,S_N,S_B)-4a

The reaction led to 0.61 g (0.50 mmol, 72%) of product as yellow crystals, which can be further purified by crystallization using ethyl acetate as the solvent. Mp > 300 °C; $[\alpha]_D^{25} = +1.6$ (*c* 0.46, CH_3OH, $\lambda = 589$ nm) ^{1}H NMR (500 MHz, acetone-d_6) δ: 0.38–0.43 (q, $J = 7.6$ Hz, 16H,

CH_3CH_2B–), 0.88 (t, $J = 7.6$ Hz, 12H, CH_3CH_2B–), 0.93 (dd, $J = 6.9$ Hz, $J = 6.2$ Hz, 24H, $(CH_3)_2CHCH_2$–), 1.13 (d, $J = 6.9$ Hz, 12H, $CH_3CH(CH_2O$–)NH–), 1.44–1.50 (m, 4H, $(CH_3)_2CHCH_2$–), 2.03–2.06 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.21–2.27 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.94 (m, 4H, $CH_3CH(CH_2O$–)NH–) 3.42 (t, $J = 8.8$ Hz, 4H, –CH_aH_bO–), 4.02–4.06 (m, 8H, $ArCH_aH_bNH$–, –CH_aH_bO–), 4.11 (br s, 4H, $ArCH_aH_bNH$–), 4.60 (t, $J = 8.2$ Hz, $J = 7.6$ Hz, 4H, $ArCHCH_2CH(CH_3)_2$), 5.72 (d, $J = 8.8$ Hz, 4H, NH), 7.43 (s, 4H, ArH), 9.06 (s, 4H, OH). ^{13}C NMR (500 MHz, acetone-d_6) δ: 8.5, 12.4, 21.1, 21.5, 24.9, 29.9, 39.2, 41.3, 52.8, 102.5, 122.1, 122.9, 124.5, 147.6, 149.2. MS-ESI: M+Cl^-: 1248.2 (calculated: 1248.276).

4.4. *out*-(*P*,*S*,*S*,S_N,S_B)-4b

The reaction led to 0.51 g (0.40 mmol, 57%) of product as yellow crystals, which can be further purified by crystallization using acetone/ethyl acetate as the solvent. Mp > 300 °C; $[\alpha]_D^{25} = +11.4$ (*c* 0.31, CH_3OH, $\lambda = 589$ nm). ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.13–0.26 (m, 8H, CH_3CH_2B–), 0.67 (t, $J = 7.55$ Hz, $J = 7.5$ Hz, 12H, $CH_3CH_2CH(CH_2O$–)NH–), 0.79 (t, $J = 8.15$ Hz, $J = 7.55$ Hz, 16H, CH_3CH_2B–), 0.90 (dd, $J = 5.05$ Hz, 24H, $(CH_3)_2CHCH_2$–), 1.36 (m, 8H, $(CH_3)_2CHCH_2$–, $CH_3CH_aH_bCH(CH_2O$–)NH–), 1.59 (m, 4H, $CH_3CH_aH_bCH(CH_2O$–)NH–), 1.94 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.23 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.71 (m, 4H, $CH_3CH_2CH(CH_2O$–)NH–), 3.32–3.38 (m, 4H, –CH_aH_bO–), 3.82 (br s, 8H, $ArCH_2NH$–), 3.90 (t, $J = 8.2$ Hz, 4H, –CH_aH_bO–), 4.40 (t, $J = 8.2$ Hz, $J = 7.6$ Hz, 4H, $ArCHCH_2CH(CH_3)_2$), 6.45 (d, $J = 8.8$ Hz, 4H, NH), 7.31 (s, 4H, ArH), 9.01 (s, 4H, OH). ^{13}C NMR (500 MHz, DMSO-d_6) δ: 8.5, 9.7, 22.6, 23.0, 23.2, 26.0, 30.7, 40.8, 41.8, 58.7, 103.9, 122.9, 123.6, 125.2, 148.4, 149.5. MS-ESI: M+Na^+: 1292.2 (calculated: 1291.922).

4.5. *out*-(*M*,*R*,*R*,R_N,R_B)-4c

The reaction led to 0.45 g (0.35 mmol, 52%) of the product as yellow crystals, which can be further purified by crystallization using acetone/ethyl acetate as the solvent. Mp > 300 °C; $[\alpha]_D^{25} = -11.2$ (*c* 0.462, CH_3OH, $\lambda = 589$ nm). ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.13–0.26 (m, 8H, CH_3CH_2B–), 0.67 (t, $J = 7.6$ Hz, $J = 6.9$ Hz, 12H, $CH_3CH_2CH(CH_2O$–)NH–), 0.79 (t, $J = 8.2$ Hz, $J = 7.6$ Hz, 12H, CH_3CH_2B–), 0.90 (dd, $J = 4.4$ Hz, 24H, $(CH_3)_2CHCH_2$–), 1.36 (m, 8H, $(CH_3)_2CHCH_2$–, $CH_3CH_aH_bCH(CH_2O$–)NH–), 1.59 (m, 4H, $CH_3CH_aH_bCH(CH_2O$–)NH–), 1.94 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.23 (m, 4H, $(CH_3)_2$+ $CHCH_aH_b$–), 2.71 (m, 4H, $CH_3CH_2CH(CH_2O$–)NH–), 3.34 (t, $J = 8.8$ Hz, $J = 8.2$ Hz, 4H, –CH_aH_bO–), 3.83 (br s, 8H, $ArCH_2NH$–), 3.91 (t, $J = 8.2$ Hz, $J = 7.6$ Hz, 4H, –CH_aH_bO–), 4.41 (t, $J = 7.6$ Hz, 4H, $ArCHCH_2CH(CH_3)_2$), 6.45 (d, $J = 7.0$ Hz, 4H, NH), 7.31 (s, 4H, ArH), 9.02 (s, 4H, OH). ^{13}C NMR (500 MHz, DMSO-d_6) δ: 8.5, 9.6, 22.6, 23.0, 23.2, 26.0, 30.7, 40.8, 41.8, 58.7, 103.9, 122.9, 123.6, 125.2, 148.3, 149.5. MS-ESI: M+Cl^-: 1304.4 (calculated: 1304.384).

4.6. *out*-(*P*,*S*,*S*,S_N,S_B)-4d

The reaction afforded 0.15 g spectrally pure product as yellow crystals. After evaporation of the solvent from 1,4-dioxane solution, 0.2 g of the same product *out*-(*P*,*S*,*S*,S_N,S_B)-**4d** was isolated by column chromatography with ethyl acetate as the eluent. The overall yield of the reaction was 0.35 g (0.25 mmol, 35%). Mp > 300 °C; $[\alpha]_D^{25} = +0.5$ (*c* 0.35; CH_3OH, $\lambda = 589$ nm). ^{1}H NMR (500 MHz, DMSO-d_6) δ: 0.10–0.23 (m, 8H, CH_3CH_2B–), 0.66 (d, $J = 5.6$ Hz, 12H, $CH_3(CH_3)CHCH_2CH(CH_2O)$), 0.74 (d, $J = 6.25$ Hz, 12H, $CH_3(CH_3)CHCH_2CH(CH_2O)$), 0.77 (d, $J = 7.5$ Hz,12H, CH_3CH_2B–) 0.90 (d, $J = 6.9$ Hz, 24H, $(CH_3)_2CHCH_2$–), 1.34–1.38 (m, 8H, $(CH_3)_2CHCH_2$–, $(CH_3)_2CHCH_aCH_bCH(CH_2O)$), 1.40–1.48 (m, 8H, $(CH_3)_2CHCH_aCH_bCH(CH_2O)$, $(CH_3)_2CHCH_2CH(CH_2O)$) 1.96 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.21 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.86 (m, 4H, $(CH_3)_2CHCH_2CH(CH_2O$–)NH–), 3.37 (m, 4H, –CH_aH_bO–), 3.71(d, $J = 16.4$ Hz, 4H, $ArCH_aH_bNH$–), 3.86 (dd, $J = 17.0$ Hz, $J = 5.0$ Hz, 4H, $ArCH_aH_bNH$–), 3.93 (t, $J = 8.2$ Hz, $J = 7.5$ Hz, 4H, –CH_aH_bO–), 4.39 (t, $J = 7.6$ Hz, 4H, $ArCHCH_2CH(CH_3)_2$), 6.38 (d, $J = 7.6$ Hz, 4H, NH), 7.30 (s, 4H, ArH), 8.91 (s, 4H, OH). ^{13}C NMR (500 MHz, DMSO-d_6) δ: 7.3, 21.1, 21.6, 21.8, 22.0, 23.7, 24.8, 29.5, 40.0, 40.7, 56.4, 65.6, 103.2, 121.5, 122.4, 124.1, 147.3, 148.2. MS-ESI: M+Na^+: 1404.4 (calculated: 1404.1358).

4.7. *out*-(*P*,*S*,*S*,S_N,S_B)-4e

The reaction afforded 0.19 g spectrally pure product as yellow crystals. After evaporation of the solvent from 1,4-dioxane solution, 0.2 g of the same product *out*-(*P*,*S*,*S*,S_N,S_B)-**4e** was isolated by column chromatography with ethyl acetate/methanol (8:1) as the eluent. The overall yield of the reaction was 0.39 g (0.29 mmol, 42%). Mp > 300 °C; $[\alpha]_D^{25} = +16.4$ (*c* 0.5; CH_3OH, $\lambda = 589$ nm). ^{1}H NMR (500 MHz, acetone-d_6) δ: 0.35 (q, $J = 7.6$ Hz, 8H, CH_3CH_2B–), 0.96–0.88 (m, 60H, $(CH_3)_2CH(CH_2O$–)NH–, $(CH_3)_2CHCH_2$–, CH_3CH_2B–), 1.47 (m, 4H, $(CH_3)_2CHCH_2$–), 1.98 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.06 (m, 4H, $(CH_3)_2CHCH(CH_2O$–)NH–), 2.23 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.69 (m, 4H, $(CH_3)_2CHCH(CH_2O$–)NH–), 3.58 (m, 4H, –CH_aH_bO–), 3.94 (t, $J = 8.8$ Hz, $J = 8.2$ Hz, 4H, –CH_aH_bO–), 4.10 (dd, $J = 16.4$ Hz, $J = 4.4$ Hz, 4H, $ArCH_aH_bNH$–), 4.23 (d, $J = 16.4$ Hz, 4H, $ArCH_aH_bNH$–), 4.61 (t, $J = 8.2$ Hz, $J = 7.6$ Hz, 4H, $ArCHCH_2CH(CH_3)_2$), 5.38 (br s, 4H, NH), 7.51 (s, 4H, ArH), 8.83 (s, 4H, OH). ^{13}C NMR (500 MHz, acetone-d_6) δ: 8.9, 17.4, 20.0, 23.1, 23.4, 26.8, 30.5, 43.6, 64.2, 64.9, 105.0, 124.1, 124.9, 126.5, 150.4, 151.1. MS-ESI: M+Cl^-: 1360.2 (calculated: 1360.491).

4.8. *out*-(*P*,*S*,*S*,S_N,S_B)-4f

The reaction afforded 0.19 g spectrally pure product as yellow crystals. After evaporation of the solvent from 1,4-dioxane solution, 0.19 g of the same product *out*-(*P*,*S*,*S*,S_N,S_B)-**4f** was isolated by column chromatography with ethyl acetate as the eluent. The overall yield of the reaction was 0.38 g (0.28 mmol, 30%). Mp > 300 °C; $[\alpha]_D^{25} = +20.7$ (*c* 0.46; CH_3OH, $\lambda = 589$ nm). ^{1}H NMR

(500 MHz, acetone-d_6) δ: 0.35 (q, $J = 7.6$ Hz, 8H, CH_3-CH_2B–), 0.82 (t, $J = 7.6$ Hz, $J = 6.9$ Hz, 12H, CH_3CH_2B–), 0.88 (d, $J = 8.2$ Hz, 12H, $CH_3CH_2CH(CH_3)$–), 0.92–0.95 (m, 36H, $CH_3CH_2CH(CH_3)$–, $(CH_3)_2CHCH_2$–), 1.41–1.52 (m, 12H, $CH_3CH_2CH(CH_3)$, $(CH_3)_2CHCH_2$–), 1.73–1.78 (m, 4H, $CH_3CH_2CH(CH_3)$–), 1.98–2.08 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.21–2.26 (m, 4H, $(CH_3)_2$-$CHCH_aH_b$–), 2.80–2.86 (m, 4H, $CH_3CH_2CH(CH_3)$-$CH(CH_2O$–)NH–), 3.57 (m, 4H, –CH_aH_bO–), 3.90 (t, $J = 8.8$ Hz, $J = 8.2$ Hz, 4H, –CH_aH_bO–), 4.12 (m, 8H, $ArCH_2NH$–), 4.61 (t, $J = 8.2$ Hz, $J = 8.2$ Hz, 4H, $ArCH$-$CH_2CH(CH_3)_2$), 5.28 (dd, $J = 9.45$ Hz, $J = 3.75$ Hz, 4H, NH), 7.50 (s, 4H, ArH), 8.86 (s, 4H, OH). ^{13}C NMR (500 MHz, acetone-d_6) δ: 8.9, 12.1, 12.6, 23.2, 23.4, 26.8, 27.0, 31.8, 36.0, 43.3, 43.5, 63.6, 63.7, 104.8, 124.0, 124.8, 126.5, 150.2, 151.1. MS-ESI: M+Na^+: 1404.4 (calculated: 1404.1358).

4.9. *out*-(*M*,*R*,*R*,*R*$_N$,*R*$_B$)-4g

The reaction afforded 0.12 g spectrally pure product as yellow crystals. After evaporation of the solvent from 1,4-dioxane solution, 0.15 g of the same product *out*-(*M*,*R*,*R*,*R*$_N$,*R*$_B$)-**4g** was isolated by column chromatography with hexane/ethyl acetate (4:1) as the eluent. The overall yield of the reaction was 0.27 g (0.18 mmol, 26%). Mp > 300 °C; $[\alpha]_D^{25} = -86.1$ (*c* 0.212; CH_3OH, $\lambda = 589$ nm). ^{1}H NMR (500 MHz, THF-d_8) δ: 0.45 (q, $J = 7.6$ Hz, 8H, CH_3CH_2B–), 0.99 (m, 36H, $(CH_3)_2CHCH_2$–, CH_3CH_2B–), 1.50–1.55 (m, 4H, $(CH_3)_2CHCH_2$–), 2.06–2.10 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 2.16–2.21 (m, 4H, $(CH_3)_2CHCH_aH_b$–), 3.80 (t, $J = 8.8$ Hz, 4H, $ArCH$-(NH)CH_2O), 3.88–3.95 (m, 8H, $ArCH(NH)CH_aH_bO$, $ArCH_aH_bNH$–), 4.04–4.10 (m, 8H, $ArCH(NH)CH_aH_bO$, $ArCH_aH_bNH$–), 4.76 (t, $J = 8.2$ Hz, $J = 7.6$ Hz, 4H, $ArCHCH_2CH(CH_3)_2$), 5.88 (d, $J = 5.0$ Hz, 4H, NH), 7.07–7.37 ($24H_{Ar}$), 8.67 (s, 4H, OH). ^{13}C NMR (500 MHz, THF-d_8) δ: 9.0, 23.4, 23.5, 27.0, 30.4, 31.8, 41.9, 44.4, 64.0, 69.0, 105.7, 123.9, 125.1, 126.8, 129.3, 129.5, 129.6, 137.1, 150.7, 151.7. MS-ESI: M+H^+: 1462.0 (calculated: 1462.111).

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