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Preparation of chiral *trans*-5-substituted-acenaphthene-1,2-diols by baker's yeast-mediated reduction of 5-substituted-acenaphthylene-1,2-diones

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ABSTRACT

A series of *trans*-5-substituted-acenaphthene-1,2-diols were obtained in 21–72% yield with 97–100% ee by baker's yeast-mediated reduction of the corresponding acenaphthylene-1,2-diones, in the presence of DMSO as a co-solvent and under vigorous agitation. The absolute configuration of (−)-*trans*-5-methoxy-acenaphthene-1,2-diol *trans*-**3b** and (−)-*trans*-5-bromo-acenaphthene-1,2-diol *trans*-**3c** was assigned as (*S*,*S*) and (−)-*trans*-5-thiomorpholin-acenaphthene-1,2-diol *trans*-**3d** was established as (*R*,*R*) by exciton-coupled circular dichroism.

1. Introduction

Acenaphthene-1,2-diol derivatives are important structural units in biologically active compounds[1] and functional materials,[2,3] and also widely used as synthetic intermediates.[4,5] However, enantiomerically pure acenaphthene-1,2-diols have been scarcely used due to a lack of their efficient synthesis. As a powerful tool for enantioselective synthesis, enzymes provide a solution to this problem. Ziffer et al. have prepared enantiomerically pure acenaphthene-1,2-diol by hydrolysis of the corresponding racemic diacetate compound using *Rhizopus nigricans*.[6] In recent work, we have successfully reduced a series of substituted acenaphthylene-1,2-diones **1** to the corresponding chiral substituted 2-hydroxy-acenaphthylen-1-ones **2** using baker's yeast via control of the reaction time.[7] Herein, we report the preparation of chiral 5-substituted-acenaphthene-1,2-diols **3** by baker's yeast-mediated reduction of the corresponding substituted acenaphthylene-1,2-diones (Scheme 1), and for the first time assigned the absolute configuration of some products by exciton-coupled circular dichroism.

2. Results and discussion

2.1. Preparation of the substrates

The substrates **1b**–**e** were prepared from **1a** as shown in Scheme 2. Nitration and substitution of acenaphthylene-1,2-dione **1a** gave **1b** in 40% yield, and **1c** could be obtained in 90% yield by bromization of **1a**. Substitution of **1c** gave **1d** in 75% yield, and **1e** was obtained by diazotization and reduction of **1c** in 45% yield.

2.2. Choosing the optimal experimental conditions

In previous work, we have achieved the first example of using baker's yeast-mediated reduction of highly sterically hindered and hydrophobic fluorenones in which an orbital shaker was replaced by a mechanical stirrer in order to further improve mass transfer.[8] Acenaphthylene-1,2-diones **1** are also highly sterically hindered and hydrophobic, so a mechanical stirrer was used as a mass transfer driver in this reaction. Initially **1a** was chosen as a model to explore the feasibility of the reaction. In a typical experiment, substrate **1a** was added to the baker's yeast suspension and the reaction mixture was stirred by a mechanical stirrer with the stirring speed at 600 rpm. Based on monitoring of the reaction process by HPLC, di-alcohol **3a** was generated together with mono-alcohol **2a** from the beginning of the reaction and the substrate **1a** was consumed to about 70% in the initial 4 h of reaction time. At the same time, the content of **2a** reached its maximum value (about 50%) and this content remained for the next 6 h. The content of *trans*-**3a** increased dramatically after 12 h, while the content of *cis*-**3a** increased gradually. When the reaction proceeded for 48 h, **1a** and **2a** were almost consumed, and the content of *trans*-**3a** was over 85% and *cis*-**3a** was about 5% only. It indicated that the selectivity of the reduction towards *trans*-**3a** was higher than that towards *cis*-**3a**. This situation is similar with the yeast-mediated reduction of aliphatic α-diketones in which the *trans* configuration was also predominant.[9]

In our previous work, using an organic solvent (DMSO or DMF) as the co-solvent was found to not only improve the conversion,

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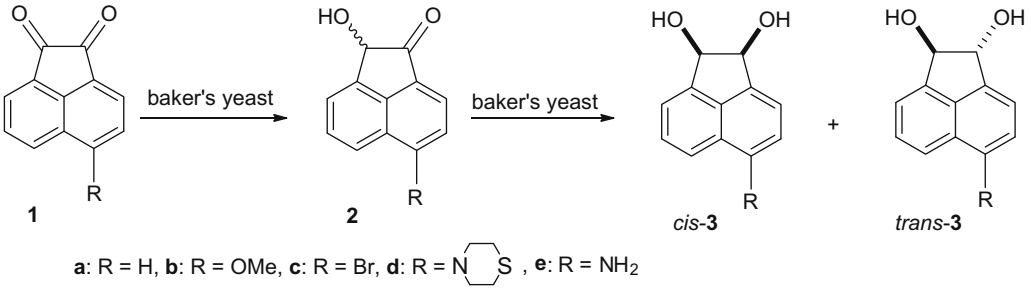
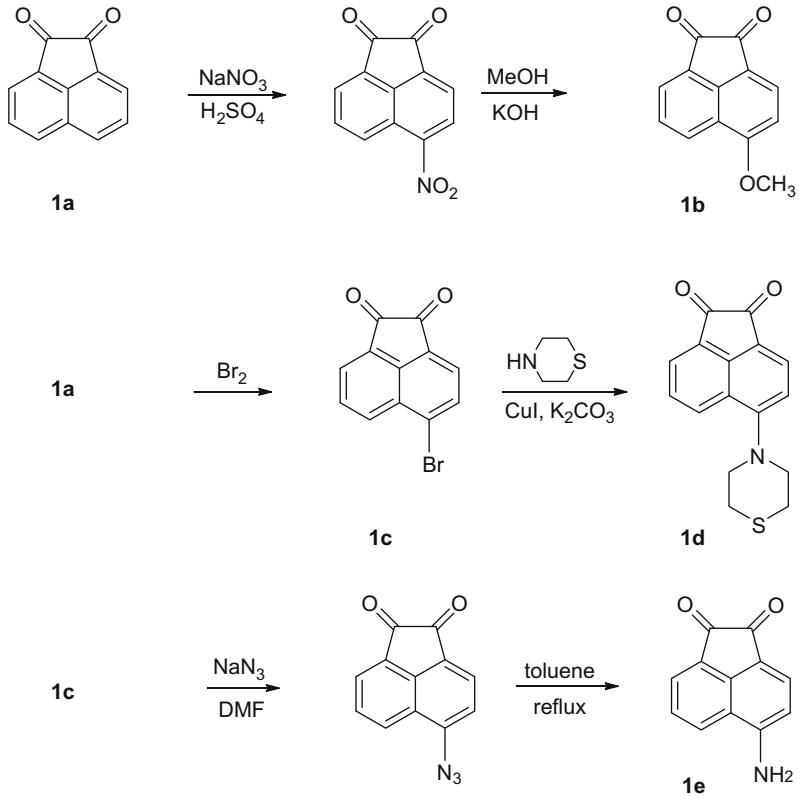


Scheme 1.



Scheme 2.

but also enhance the enantioselectivities and regioselectivities in baker's yeast-mediated reduction of fluorenones and acenaphthylene-1,2-diones **1**.[7,8] Therefore, the effects of DMSO and DMF as substrate co-solvents were investigated in this reduction system. As shown in Table 1, using DMF as the substrate co-solvent increased the enantioselectivity from 87% to 91% ee, but decreased the yield from 85% to 42%. On the other hand, using DMSO gave *trans*-**3a** with 97% ee and the yield was kept at 74%. The enhanced enantioselectivity was possibly caused by the sulfur atom in DMSO, which could modify enantiofacial discrimination in baker's yeast-mediated reduction.[10,11]

Table 1
Effect of co-solvent on the conversion and ee in the reduction of acenaphthylene-1,2-dione **1a** using baker's yeast[a]

Entry	Co-solvent	Conv.[b]%	*cis*-**3a** Yield[c] %	*trans*-**3a**		
				Yield[c] %	ee[d] %	$[\alpha]_D$[e]
1	No	98	5	85	87	−20.7
2	DMF	98	35	42	91	−21.1
3	DMSO	100	23	74	97	−24.1

[a] Reaction conditions: substrate (100 mg), water (100 mL), co-solvent (10 mL), dry baker's yeast (10.0 g), sucrose (3.0 g), reaction time 48 h, at 30 °C.
[b] The conversion was determined by HPLC using a Zorbax RX-SIL column based on the consumed substrate.
[c] Isolated yield.
[d] The ee was determined by HPLC using a chiral AD-H column.
[e] The $[\alpha]_D$ was determined by WZZ-2S spectropolarimeter (*c* 0.28–0.32, $CHCl_3$), 20 °C.

2.3. Exploration of the reaction

In order to explore the reaction scope, a series of 5-substituted-acenaphthylene-1,2-diones **1b–e** were synthesized and then examined under the optimized conditions. As shown in Table 2, as with **1a**, the substrates **1b–d** could also be reduced to the corresponding *cis*- and *trans*-diols, and diols with the *trans* configuration were the dominant product; this may be a result of the thermodynamic stability of the *trans* configuration. Importantly, the *trans*-diols were highly enantiomerically pure (>97% ee), no matter what the electronic properties of the substituted group in the 5-position.

Table 2
Reduction of 5-substituted-acenaphthylene-1,2-dione **1** using baker's yeast[a]

Substrate	R	Conv.[b] %	**2**/**3**	*cis*-**3**				*trans*-**3**			
				Yield[c] %	ee[d] %	$[\alpha]_D$[f]	*R*/*S*	Yield[c] %	ee[d] %	$[\alpha]_D$[f]	*R*/*S*
1a	H	100	0/100	23	—	—	—	72	97	−24.1	1*S*,2*S*
1b	OCH_3	92	5/95	23	54	+3.0	—	56	100	−24.2	1*S*,2*S*
1c	Br	100	3/97	14	2	+3.4	—	60	99	+15.1[e]	1*S*,2*S*
1d		60	10/90	10	30	+5.5	—	21	100	−29.6	1*R*,2*R*
1e	NH_2	98	95/5	—	—	—	—	—	—	—	—

[a] Reaction conditions: substrate (100 mg), water (100 mL), DMSO (10 mL), dry baker's yeast (10.0 g), sucrose (3.0 g), reaction time 48 h, at 30 °C.
[b] The conversion was determined by HPLC using a Zorbax RX-SIL column based on the consumed substrate.
[c] Isolated yield.
[d] The ee was determined by HPLC using a chiral AD-H column.
[e] The $[\alpha]_D$ was determined by WZZ-2S spectropolarimeter (*c* 0.35–0.38, EtOAc, 20 °C).
[f] The $[\alpha]_D$ was determined by WZZ-2S spectropolarimeter (*c* 0.24–0.28, $CHCl_3$, 20 °C).

On the other hand, the *cis*-diols were obtained with low enantioselectivities. In previous research, substrate **1e** could be reduced to **2e** with 93% ee in the presence of DMF as the co-solvent.[7] However, substrate **1e** could hardly afford the corresponding diols in our experiment, probably due to the high electron density of the substituted group, which inhibited the activity of reductases towards the carbonyl group of **2e**. Similar results were observed for **1b** and **1d**, which also bore an electron-donating group in the 5-position, reductases towards the carbonyl group of **2b** and **2d** exhibiting lower activities than **2a** and **2c**.

2.4. The absolute stereochemistry determination

It had been reported that (+)-*trans*-acenaphthene-1,2-diol has an (1*R*,2*R*) configuration.[6] Therefore, the (−)-*trans*-**1a** obtained in our reduction system should be determined to be an (1*S*,2*S*) configuration. Unfortunately, there was no reported $[\alpha]_D$ for the newly synthesized chiral diols **3b**–**d**, so we turned to other methods for configuration assignment.

For the most part, the absolute configuration of alpha-diols could be achieved with exciton-coupled circular dichroism (ECCD).[12–14] Briefly, the ECCD method relies on the coupling of the electric transition dipole moments of two or more chromophores held in space in a chiral fashion.[15] The sign of the resultant ECCD couplet reflects the helicity of the interacting chromophores and consequently the chirality of the derivatized system. It was not possible to assign the absolute configuration of alpha-diols directly by ECCD because of a lack of chromophores. This can be accomplished via derivatization of the diol group with benzoates (or other similar chromophores).

Chiral *trans*-bis-*p*-*N*,*N*-dimethylaminobenzoyloxy-1,2-dihydro-5-substituted-acenaphthenes (*trans*-**4b**–**d**) were prepared from the corresponding chiral *trans*-diols as shown in Scheme 3. To begin with, the stereochemistry of *trans*-**3a** was reexamined by ECCD. As shown in Figure 1, the strong CD peaks at 308 and 329 nm for *trans*-**4a**, which had arisen from coupling between the two *p*-*N*,*N*-(dimethylamino)benzoate groups, indicated a positive first Cotton effect.[12–14] According to the ECCD rules, the positive first

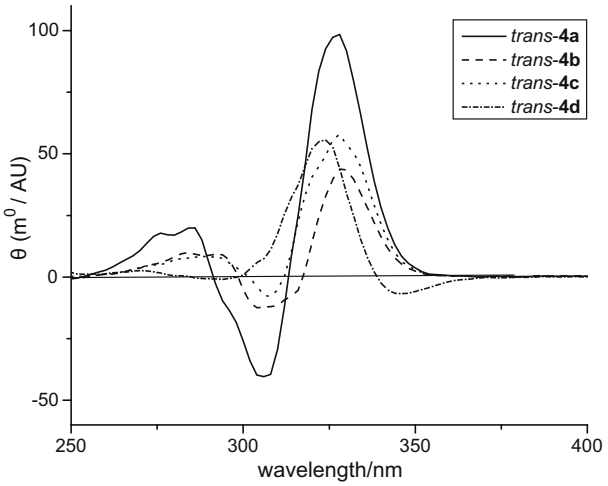
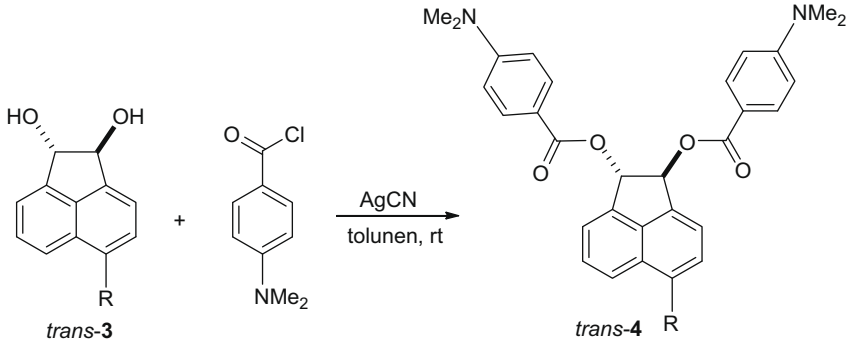


Figure 1. ECCD spectrum (5×10^{-5} mol/L in methanol) of *trans*-**4a**, -**4b**, -**4c** and -**4d**.



a: R = H, **b**: R = OMe, **c** :R = Br, **d**: R = 

Scheme 3.

Cotton effect requires a clockwise sense of the spatial arrangement between the two coupling chromophores.[12–14] The absolute stereochemical of *trans*-**4a** was established as (1*S*,2*S*), which was consistent with the previous assignment of *tran*-**3a** by $[\alpha]_D$ comparison, and the spatial arrangement of two bis-(*N*,*N*-dimethylamino)-benzoyl chromophores was shown in Figure 2.

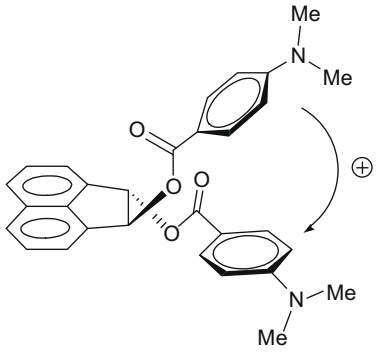


Figure 2. Assignment of the absolute configuration of *trans*-**4a** based on the observed positive chirality (positive first Cotton effect at 308 nm and 329 nm) which needed a clockwise sense (1*S*,2*S*) of spatial arrangement between the two (*p*-*N*,*N*-dimethylamino)-benzoyl chromophores.

Based on the same principle, the absolute configuration of *trans*-**3b** and -**3c** could be determined to be (1*S*,2*S*) because *trans*-**4b** and -**4c** exhibited a positive first Cotton effect. Contrary to others, the CD curve of *trans*-**4d** presented a negative first cotton effect at 348 nm and 320 nm, which required an anticlockwise sense of spatial arrangement between the two bis-(*p*-*N*,*N*-dimethylamino)-benzoyl chromophores. Thus it can be concluded that *trans*-**3d** had an absolute configuration of (1*R*,2*R*). Due to the low enantiomeric excess of *cis*-**3b**, -**3c** and -**3d** obtained by the yeast reduction, the absolute configuration of *cis*-**3b**, -**3c** and -**3d** cannot be given at this time.

2.5. Proposed mechanism for reductases

It has been demonstrated that there are several reductases in baker's yeast cells and each of the reductase exhibits high enantioselectivity towards different substrates.[16–19] Based on these facts, it could be assumed that there are two kinds of reductases, reductase-(*R*) and -(*S*), towards the first carbonyl group of substituted acenaphthylene-1,2-diones **1** and four kinds of reductases, reductase-(*R*,*R*), -(*S*,*S*), -(*R*,*S*) and -(*S*,*R*), towards the second residual carbonyl group of substituted 2-hydroxyacenaphthylen-1-ones **2**, although it is worthy of a further test by isolating the reductases from the cells of baker's yeast. In the reduction of substituted acenaphthylene-1,2-diones by baker's yeast, the low enantiomeric excess of 2-hydroxyacenaphthylen-1-one[7] and *cis*-acenaphthene-1,2-diol reveals that both reductase-(*R*) and -(*S*) and both reductase-(*R*,*S*) and -(*S*,*R*) work actively at the same time, respectively. The very high enantioselectivity of *trans*-diols exhibits either reductase-(*S*,*S*) or reductase-(*R*,*R*) work only towards different substrates.

3. Conclusions

We have reported a method to obtain a series of substituted *trans*-acenaphthene-1,2-diols with very high enantiomeric excess by baker's yeast-mediated reduction of the corresponding acenaphthylene-1,2-diones. As the second example for baker's yeast-catalyzed reduction of rigid and polycyclic aromatic ketones, the research extends the substrates of the enzymatic reductions further.

4. Experimental and characterization

4.1. Experimental details

Baker's yeast was produced by Angel Yeast Co., Ltd. All solvents were analytical grade unless specified. Normal phase HPLC analysis was performed on an Agilent 1100 series. The chiracel AD-H column was produced by Daicel chemical Industries, Ltd. The length/internal diameter of column was 250/4.6 mm, and all the reagents of mobile phase were chromatographic pure. ^{1}H NMR and ^{13}C NMR were recorded on Varian INOVA 400 MHz or Bruker Avance II 400 MHz. Chemical shifts are reported in parts per million (δ) downfield from TMS. Optical rotations were determined by WZZ-2S. ECCD was measured with J-810.

4.2. Experimental procedure for the synthesis of substrates 1b–e

4.2.1. 5-Methoxy-acenaphthylene-1,2-dione 1b

Powdered $NaNO_3$ 2.94 g (34.6 mmol) was slowly added into a mixture of acenaphthylene-1,2-dione 6.00 g (32.9 mmol) in 15 mL of concentrated sulfuric acid and the reaction mixture was stirred for 2 h in an ice-water-bath. The mixture was slowly transferred into crushed ice. After filtration and dryness, crude 5-nitro-acenaphthylene-1,2-dione was obtained.[20]

A mixture of crude 5-nitro-acenaphthylene-1,2-dione 1.00 g and KOH 0.25 g (4.46 mmol) in 30 mL of methanol was refluxed for 2.0 h. After the solvent was removed from the reaction mixture, the crude product was purified by silica gel column chromatography using CH_2Cl_2 as an eluent to afford the pure 5-methoxy-acenaphthylene-1,2-dione **1b** as a yellow solid in 40% yield. ^{1}H NMR (400 MHz, DMSO-d_6): 8.38 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 6.8 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 3.35 (s, 3H); ^{13}C NMR (400 MHz, DMSO-d_6): 189.1, 186.0, 160.1, 146.7, 128.4, 128.1, 127.5, 124.8, 122.3, 122.2, 107.6, 57.1; IR (KBr, cm^{-1}): 1719, 1248; HRMS-EI (70 eV) *m*/*z*, calcd for $C_{13}H_8O_3$ 212.0473, found 212.0473; mp: 230.3–231.5 °C.

4.2.2. 5-Bromo-acenaphthylene-1,2-dione 1c[21]

A mixture of acenaphthylene-1,2-dione 20 g (109.8 mmol) and bromine liquid (20 mL) was refluxed for 2 h. Off-gas was absorbed by saturated NaOH solution. After the mixture had cooled, saturated $Na_2S_2O_3$ solution was slowly added until the colour of the reaction mixture changed from red to colourless. Then the reaction mixture was poured into 700 mL of water and some primrose precipitates were separated out. After filtration, the filter cake was recrystallized in glacial acetic acid for four times and a yellow needle crystalloid was afforded in 90% yield. ^{1}H NMR (400 MHz, DMSO-d_6): 8.39 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 7.6 Hz, 1H), 8.15 (d, J = 7.2 Hz, 1H), 8.04 (t, J = 7.8 Hz, 1H), 7.96(d, J = 7.6 Hz, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): 187.2, 187.1, 144.7, 132.4, 131.0, 130.5, 130.1, 129.9, 129.3, 126.9, 122.6, 122.5; IR (KBr, cm^{-1}) 1726, 766; HRMS-EI (70 eV) *m*/*z*, calcd for $C_{12}H_6O_2$ 259.9473, found 259.9475; mp: 236.0–236.8 °C (Lit.[22] 238 °C).

4.2.3. 5-Thiomorpholin-acenaphthylene-1,2-dione 1d

A mixture of 5-bromo-acenaphthylene-1,2-dione **1c** (1.30 g, 5 mmol), K_2CO_3 (1.38 g, 10.0 mmol), CuI (190 mg, 1.0 mmol) and thiomorpholine (1.50 ml, 7.5 mmol) in 50 mL of DMF was stirred for 30 min at room temperature and then heated to 130 °C for 1.5 h under N_2 protection. After the mixture was cooled to ambient temperature, it was poured into 500 mL of water and some red precipitates were separated out. After filtration, the filter cake was dried under an infrared dryer. The crude mixture was purified by silica gel column chromatography using CH_2Cl_2 as the eluent to afford the pure 5-thiomorpholin-acenaphthylene-1,2-dione **1d** as a red solid in 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): 8.22 (d,

J = 8.8 Hz, 1H), 8.07 (d, J = 7.6 Hz, 1H), 8.02 (d, J = 6.8 Hz, 1H), 7.76 (t, J = 8.0 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 3.65 (t, J = 5.2 Hz, 4H), 2.99 (t, J = 4.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 189.5, 186.2, 155.7, 148.0, 129.5, 128.8, 127.2, 126.2, 124.0, 123.4, 121.9, 116.1, 54.7, 28.1; IR (KBr, cm^{-1}): 1717, 1318; HRMS-EI (70 eV) *m/z*, calcd for $C_{16}H_{13}NO_2S$ 283.0667, found 283.0677; mp: 190.6–192.7 °C.

4.2.4. 5-Amino-acenaphthylene-1,2-dione 1e

A mixture of 5-bromo-acenaphthylene-1,2-dione **1c** (2.0 g, 7.7 mmol) and NaN_3 (0.9 g, 13.8 mmol) in 30 mL of DMF was stirred at 100 °C for 5 min. When the reaction mixture was cooled to ambient temperature, it was poured into 50 mL of water and a yellow precipitate was separated out. After filtration, the filter cake was dried under vacuum dryer to give crude 5-azido-acenaphthylene-1,2-dione.

The crude 5-azido-acenaphthylene-1,2-dione (0.8 mg, 3.6 mmol) in 60 mL of toluene was kept at reflux for 36 h. When the reaction mixture was cooled to ambient temperature, some brown precipitates were separated out. After filtration, the filter cake was dried under vacuum dryer. The crude 5-amino-acenaphthylene-1,2-dione was purified by silica gel column chromatography using CH_2Cl_2 as the eluent to give pure 5-amino-acenaphthylene-1,2-dione **1e** in 45% yield. ^{1}H NMR (400 MHz, DMSO-d_6): 8.45 (d, J = 8.4 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 6.8 Hz, 1H), 7.64 (t, J = 7.6 Hz, 1H), 7.31 (s, 2H), 6.90 (d, J = 8.0 Hz, 1H); ^{13}C NMR (400 MHz, DMSO-d_6): 191.9, 183.1, 152.5, 148.9, 128.5, 127.6, 126.0, 125.9, 121.5, 118.3, 117.0, 109.6; IR (KBr, cm^{-1}): 3456, 3363, 1592, 1344; mp >200 °C.

4.3. Experimental procedure for 3a–3d

A mixture of dry baker's yeast (10.0 g) and sucrose (3.0 g) in water (100 mL) was stirred at 30 °C for 0.5 h. Then the substrate (100 mg) dissolved in the organic solvent of DMSO (10 mL) was added to the mixture and vigorous stirring (600 rpm) was continued at the same temperature (30 °C) for 48 h. After removal of the baker's yeast by filtration, the filtrates were extracted with ethyl acetate (3 × 100 mL). The separated organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude products were purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 20:1) to afford the pure 1,2-dihydroxy product as the white solid.

4.3.1. *cis*-Acenaphthene-1,2-diol *cis*-3a

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.77 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 5.29 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 149.0, 146.7, 138.7, 128.3, 124.1, 120.8, 72.0; IR (KBr, cm^{-1}): 3333; HRMS-EI (70 eV) *m/z*, calcd for $C_{12}H_{10}O_2$ 186.0681, found 186.0681; mp: 170.8–172.4 °C (Lit.[23] 208–209 °C).

4.3.2. *trans*-(1*S*,2*S*)-Acenaphthene-1,2-diol *trans*-3a

^{1}H NMR (400 MHz, DMSO-d_6): 7.76 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 7.8 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 5.18 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): 143.8, 135.4, 130.3, 128.3, 123.9, 120.0, 82.4; IR (KBr, cm^{-1}): 3266; HRMS-EI (70 eV) *m/z*, calcd for $C_{12}H_{10}O_2$ 186.0681, found 186.0683; mp: 153.7–154.6 °C (Lit.[24] 160–163 °C). $[\alpha]_D^{20} = -24.1$ (c 0.28, $CHCl_3$); The enantiomeric excess was determined by HPLC with a chiral AD-H column (*n*-hexane/isopropyl alcohol = 85:15, UV detection at 254 nm, flow rate = 1.0 mL /min), retention time: (*S*,*S*)-*trans*-**3a** = 8.06 min, (*R*,*R*)-*trans*-**3a** = 10.49 min.

4.3.3. *cis*-5-Methoxy-acenaphthene-1,2-diol *cis*-3b

^{1}H NMR (400 MHz, DMSO-d_6): 7.84 (d, J = 8.0 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 5.29–5.20 (m, 2H), 5.12 (d, J = 6.8 Hz, 2H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 154.1, 144.6, 137.2, 136.7, 127.7, 122.6, 121.7, 121.6, 119.5, 106.8, 73.8, 72.4, 56.1; IR (KBr, cm^{-1}): 3359; HRMS-EI (70 eV) *m/z*, calcd for $C_{13}H_{12}O_3$ 216.0786, found 216.0790; mp: 170.1–171.5 °C (Lit.[25] 172–173 °C). $[\alpha]_D^{20} = +3.0$ (c 0.38, EtOAc); The enantiomeric excess was determined by HPLC with a chiral AD-H column, (*n*-hexane/isopropyl alcohol = 85:15, UV detection at 254 nm, flow rate = 1.0 mL/min), retention time: (−)-*cis*-**3b** = 10.86 min, (+)-*cis*-**3b** = 12.21 min.

4.3.4. *trans*-(1*S*,2*S*)-5-Methoxy-acenaphthene-1,2-diol *trans*-3b

^{1}H NMR (400 MHz, DMSO-d_6): 7.83 (d, J = 8.4 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.2 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 6.98 (d, J = 7.6 Hz, 1H), 5.75 (d, J = 6.8 Hz, 1H), 5.64 (d, J = 6.8 Hz, 1H), 5.14 (d, J = 6.8 Hz, 1H), 5.10 (d, J = 6.8 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): 157.4, 137.0, 131.0, 127.4, 124.5, 123.8, 123.3, 122.8, 122.2, 103.4, 85.3, 83.5, 56.3; IR (KBr, cm^{-1}): 3296; HRMS-EI (70 eV) *m/z*, calcd for $C_{13}H_{12}O_3$ 216.0786, found 216.0788; mp: 158.5–160.5 °C (Lit.[25] 155–156 °C). $[\alpha]_D^{20} = -24.2$ (c 0.26, $CHCl_3$). The anantiomeric excess was determined by HPLC with a chiral AD-H column, (*n*-hexane/isopropyl alcohol = 90:10, UV detection at 254 nm, flow rate = 1.0 mL/min), retention time: (*S*,*S*)-*trans*-**3b** = 19.50 min, (*R*,*R*)-*trans*-**3b** = 20.58 min.

4.3.5. *cis*-5-Bromo-acenaphthene-1,2-diol *cis*-3c

^{1}H NMR (400 MHz, DMSO-d_6): 7.87 (d, J = 7.2 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.59 (d, J = 6.8 Hz, 1H), 7.42 (d, J = 7.2 Hz, 1H), 5.39–5.25 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): 145.2, 144.8, 136.3, 131.3, 129.8, 129.3, 122.7, 122.0, 121.9, 117.6, 72.2, 72.1; IR (KBr, cm^{-1}): 3335; HRMS-EI (70 eV) *m/z*, calcd for $C_{12}H_9BrO_2$ 263.9786, found 263.9783; mp: 180.0–183.2 °C. $[\alpha]_D^{20} = +3.4$ (c 0.38, EtOAc). The anantiomeric excess was determined by HPLC with a chiral AD-H column, (*n*-hexane/isopropyl alcohol = 90:10, UV detection at 254 nm, flow rate = 1.0 mL/min), retention time: (+)-racemic-*cis*-**3c** = 12.34 min, (−)-racemic-*cis*-**3c** = 14.03 min.

4.3.6. *trans*-(1S,2S)-Bromo-acenaphthene-1,2-diol *trans*-3c

^{1}H NMR (400 MHz, DMSO-d_6): 7.87 (d, J = 7.6 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.55 (d, J = 6.8 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 6.00 (d, J = 6.0 Hz, 2H), 5.18 (s, 1H), 5.13 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): 144.8, 144.5, 136.6, 131.8, 130.4, 129.7, 123.1, 121.7, 121.6, 118.0, 82.6, 82.1. IR (KBr, cm^{-1}): 3333; HRMS-EI (70 eV) *m/z*, calcd for $C_{12}H_9BrO_2$ 263.9786, found 263.9783; mp: 165.0–170.2 °C (Lit.[26] 216–217 °C); $[\alpha]_D^{20} = +15.1$ (c 0.35, EtOAc). The anantiomeric excess was determined by HPLC with a chiral AD-H column, (*n*-hexane/isopropyl alcohol = 90:10, UV detection at 254 nm, flow rate = 1.0 mL /min), retention time: (*S*,*S*)-*trans*-**3c** = 12.66 min, (*R*,*R*)-*trans*-**3c** = 14.52 min.

4.3.7. *cis*-5-thiomorpholin-acenaphthene-1,2-diol *cis*-3d

^{1}H NMR (400 MHz, DMSO-d_6): 7.80 (d, J = 8.4 Hz, 1H), 7.55 (t, J = 6.8 Hz, 1H), 7.45 (d, J = 6.8 Hz, 1H), 7.38 (d, J = 7.2 Hz, 1H), 7.11 (d, J = 7.2 Hz, 1H), 5.28–5.14 (m, 4H), 3.29 (t, J = 4.4 Hz 4H), 2.90 (t, J = 4.4 Hz, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): 148.4, 145.0, 139.3, 136.9, 127.5, 125.6, 121.0, 120.8, 120.7, 116.6, 73.1, 72.0, 55.0, 27.7. IR (KBr, cm^{-1}): 3412; HRMS-EI (70 eV) *m/z*, calcd for $C_{16}H_{17}NO_2S$ 287.0980, found 287.0990; mp: 153.5–154.5 °C. $[\alpha]_D^{20} = +5.5$ (c 0.36, EtOAc). The enantiomeric excess was determined by HPLC with a chiral AD-H column, (*n*-hexane/isopropyl alcohol = 80:20, UV detection at 254 nm, flow rate = 1.0 mL/min), retention time: (−)-*cis*-**3d** = 15.22 min, (+)-*cis*-**3d** = 16.32 min.

4.3.8. *trans*-(1S,2S)-5-thiomorpholin-acenaphthene-1,2-diol *trans*-3d

^{1}H NMR (400 MHz, DMSO-d_6): 7.80 (d, J = 8.4 Hz, 1H), 7.55 (t, J = 6.8 Hz, 1H), 7.41 (d, J = 6.8 Hz, 1H), 7.34 (d, J = 7.6 Hz, 1H),

7.11 (d, J = 7.6 Hz, 1H), 5.77 (d, J = 6.8 Hz, 1H), 5.69 (d, J = 6.8 Hz, 1H), 5.13 (d, J = 6.8 Hz, 1H), 5.09 (d, J = 6.4 Hz, 1H), 3.29 (t, J = 3.6 Hz, 4H), 2.89 (t, J = 3.6 Hz, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): 148.3, 144.2, 138.7, 136.7, 127.5, 125.5, 120.6, 120.2, 120.1, 116.6, 82.8, 81.8, 54.9, 27.7; IR (KBr, cm^{-1}): 3294, 1019; HRMS-EI (70 eV) m/z, calcd for $C_{16}H_{17}NO_2S$ 287.0980, found 287.0987; mp: 144.4–147.4 °C. $[\alpha]_D^{20} = -29.6$ (c 0.24, $CHCl_3$) The anantiomeric excess was determined by HPLC with a chiral AD-H column, (n-hexane/isopropyl alcohol = 80:20, UV detection at 254 nm, flow rate = 1.0 mL /min), retention time: (*R*,*R*)-*trans*-**3d** = 10.96 min, (*S*,*S*)-*trans*-**3d** = 12.83 min.

4.4. Experimental procedure for 4a–4d

4.4.1. *trans*-(1S,2S)-Bis-*p*-*N*,*N*-dimethylaminobenzoyloxy-1,2-dihydroacenaphthene *trans*-4a

A mixture of *trans*-**3a** (18 mg, 0.1 mmol), *p*-*N*,*N*-dimethylaminobenzoyl chloride (73 mg, 0.4 mmol) and AgCN (60 mg, 0.4 mmol) in toluene (10 mL) was stirred at rt for 48 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and filtered. The filter was dried by anhydrous $MgSO_4$. Evaporation of the solvent gave a yellow solid which was purified by silica gel column chromatography using a mixture of n-hexane and EtOAc (4:1) as eluent. The pure *trans*-**4a** was afforded as the white solid (25 mg) in 52% yield; ^{1}H NMR (400 MHz, $CDCl_3$): 7.95 (d, J = 8.8 Hz, 4H), 7.82 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 7.2 Hz, 2H), 7.57 (t, J = 6.8 Hz, 2H), 6.99 (s, 2H), 6.61 (d, J = 8.8 Hz, 4H), 3.00 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.7, 153.4, 139.5, 137.7, 131.6, 130.8, 128.4, 125.4, 122.5, 116.4, 110.6, 81.2, 40.0; IR (KBr, cm^{-1}): 1695, 1610, 1276, 1183, 1091; HRMS-ESI (M+H)$^+$ m/z, calcd for $C_{30}H_{29}N_2O_4$ 481.2127, found 481.2147; mp: 168.5–170.7 °C. $[\alpha]_D^{20} = +672$ (c 0.10, $CHCl_3$).

4.4.2. *trans*-(1S,2S)-Bis-*p*-*N*,*N*-dimethylaminobenzoyloxy-1,2-dihydro-5-methoxyacenaphthene *trans*-4b

The same treatment of *trans*-**3b** gave *trans*-**4b** in 44% yield. ^{1}H NMR (400 MHz, $CDCl_3$): 8.05 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.8 Hz, 4H), 7.69 (d, J = 7.2 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 6.97 (s, 1H), 6.87 (d, J = 4.4 Hz, 2H), 6.63(d, J = 8.8 Hz, 4H), 4.01 (s, 3H), 3.02 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.8, 166.6, 155.3, 153.4, 139.2, 138.9, 131.7, 131.6, 131.4, 127.5, 123.2, 123.1, 122.9, 121.0, 116.9, 116.7, 110.8, 106.1, 81.9, 81.0, 55.8, 40.1; IR (KBr, cm^{-1}): 1701, 1607, 1271, 1180, 1092; HRMS-ESI (M+Na)$^+$ m/z, calcd for $C_{31}H_{30}N_2O_5Na$ 533.2052, found 533.2037; mp: 78.8–79.1 °C. $[\alpha]_D^{20} = +480$ (c 0.15, $CHCl_3$).

4.4.3. *trans*-(1S,2S)-Bis-*p*-*N*,*N*-dimethylaminobenzoyloxy-1,2-dihydro-5-bromoacenaphthene *trans*-4c

The same treatment of *trans*-**3c** gave *trans*-**4c** in 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$): 8.01 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.8 Hz, 4H), 7.81 (d, J = 7.2 Hz, 1H), 7.74 (d, J = 6.8 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.55 (d, J = 7.6 Hz, 1H), 6.97 (s, 1H), 6.89 (s, 1H), 6.65 (d, J = 8.4 Hz, 4H), 3.03 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.5, 166.4, 153.3, 139.8, 139.4, 138.6, 131.7, 131.6, 130.3, 129.7, 125.0, 123.5, 123.4, 120.5, 111.1, 81.0, 80.6, 40.3; IR (KBr, cm^{-1}): 1705, 1606, 1271, 1180, 1091; HRMS-ESI (M+H)$^+$ m/z, calcd for $C_{30}H_{28}BrN_2O_4$ 559.1232, found 559.1208; mp: 176.3–176.9 °C. $[\alpha]_D^{20} = +429$ (c 0.27, $CHCl_3$).

4.4.4. *trans*-(1*R*,2*R*)-Bis-*p*-*N*,*N*-dimethylaminobenzoyloxy-1,2-dihydro-5-thiomorpholinacenaphthene *trans*-4d

The same treatment of *trans*-**3d** gave *trans*-**4d** in 39% yield; ^{1}H NMR (400 MHz, $CDCl_3$): 7.94 (d, J = 9.2 Hz, 5H), 7.68 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.18 (s, 1H), 6.96 (s, 1H), 6.89 (s, 1H), 6.65 (d, J = 8.4 Hz, 4H), 3.44 (s, 4H), 3.03 (s, 12H), 2.96 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.8, 166.7, 153.5, 149.9, 140.0, 139.3, 134.6, 131.7, 127.8, 126.4, 123.1, 122.8, 122.2, 117.0, 116.6, 110.8, 81.6, 80.9, 55.3, 40.2, 28.6; IR (KBr, cm^{-1}): 1701, 1607, 1274, 1182, 1100; HRMS-ESI (M+Na)$^+$ m/z, calcd for $C_{34}H_{35}N_3O_4NaS$ 604.2246, found 604.2225; mp: 101.9–103.2 °C. $[\alpha]_D^{20} = +237$ (c 0.19, $CHCl_3$).

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