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Catalytic Chemo-, *E*/*Z*-, and Enantioselective Cyclizations of *o*-Hydroxybenzyl Alcohols with Dimedone-Derived Enaminones

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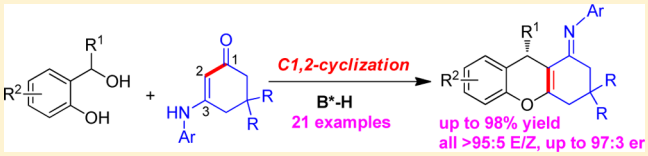
Supporting Information

ABSTRACT: A catalytic chemo-, *E*/*Z*-, and enantioselective cyclization of *o*-hydroxybenzyl alcohols with dimedone-derived enaminones has been established, which not only realized a chemoselective C1,2 cyclization of enaminones but also achieved the catalytic asymmetric construction of the biologically important tetrahydroxanthene framework with high *E*/*Z*- and enantioselectivities (all >95:5 *E*/*Z*, up to 98% yield, 97:3 er). This approach not only represents the first catalytic asymmetric C1,2 cyclization of enaminones with *o*-hydroxybenzyl alcohols but also provides an efficient strategy for constructing oxygenous heterocyclic frameworks with optical purity.



INTRODUCTION

Chiral oxygenous heterocyclic compounds belong to one of the most important family of heterocycles, which exist in many natural products and bioactive molecules.[1a−d] However, the catalytic enantioselective construction of oxygen-containing heterocyclic scaffolds is far less developed than that of nitrogen-containing heterocyclic frameworks because the former is much more challenging than the latter in terms of the activation mode of chiral catalysts to the substrates.[1e−g]

In this context, *o*-hydroxybenzyl alcohols have recently been recognized as a class of versatile building blocks for constructing oxygenous heterocyclic motifs in an enantioselective fashion,[2] because they are able to transform into *o*-quinone methide (*o*-QM) intermediates[3] under the catalysis of chiral Brønsted acids (B*-H), and the *o*-QM intermediates can be activated by B*-H via a hydrogen bond to perform enantioselective reactions. Consequently, elegant developments have been achieved in enantioselective transformations involving *o*-hydroxybenzyl alcohol (Scheme 1), which mainly include conjugate additions with indoles or naphthols (eq 1),[2b−d,3j] tandem cyclizations with 1,3-dicarbonyl compounds or enamides (eq 2),[2e−h] and oxa-Diels−Alder reactions with olefins (eq 3).[2i,j] In spite of these recent advances, the development of catalytic asymmetric reactions based on such alcohols is still in its infancy and therefore is still highly desirable for the construction of oxygenous heterocyclic skeletons with optical purity.

Enaminones are types of competent reactants possessing multiple reactive sites,[4] which should be suitable reaction partners for catalytic asymmetric transformations of *o*-hydroxybenzyl alcohols. However, apart from the challenge in enantioselective control, there is still a chemoselective issue in catalytic asymmetric cyclizations of *o*-hydroxybenzyl alcohols with enaminones. As illustrated in Scheme 2, the C2 position of enaminones is nucleophilic, while the C1 and C3 positions are electrophilic. Thus, the reactions have two orientations to perform cyclizations at the C3 (path A) or C1 (path B) position, which would lead to the generation of C2,3 cyclization product **A** (eq 4) or C1,2 cyclization product **B** (eq 5), respectively.

Normally, however, enaminones are regarded as activated electron-rich olefins, which have a high tendency to perform cyclizations by using the C═C double bond between the C2 and C3 positions (eq 4). Recently, Schneider and co-workers have reported the cyclizations of cyclic enaminones with *o*-hydroxybenzyl alcohols under the catalysis of B*-H (eq 6), which afforded the C2,3-cyclization products in excellent stereoselectivities.[2g,h] In spite of this elegant work, *the utilization of the C−C single bond between the C1 and C2 positions of enaminones in cyclizations has scarcely been reported* (eq 5). As a result, changing the chemoselectivity from C2,3 cyclization to C1,2 cyclization and controlling the enantioselectivity of the reaction have become great challenges in catalytic asymmetric cyclizations of *o*-hydroxybenzyl alcohols with enaminones, which require specific synthetic design.

RESULTS AND DISCUSSION

Spurred by the challenges in catalytic asymmetric cyclizations of *o*-hydroxybenzyl alcohols with enaminones and the great demand for constructing enantioenriched oxygenous heterocyclic frameworks, we decided to employ chiral phosphoric acid (CPA)[5] as a type of competent chrial organocatalyst[6] to catalyze an asymmetric C1,2 cyclization of enaminones with *o*-hydroxybenzyl alcohols. On the basis of our previous works,[2i,7] we envisioned that the electronic nature of the N substituents of enaminones might play a crucial role in the regioselectivity of the reaction. In order to change the chemoselectivity of

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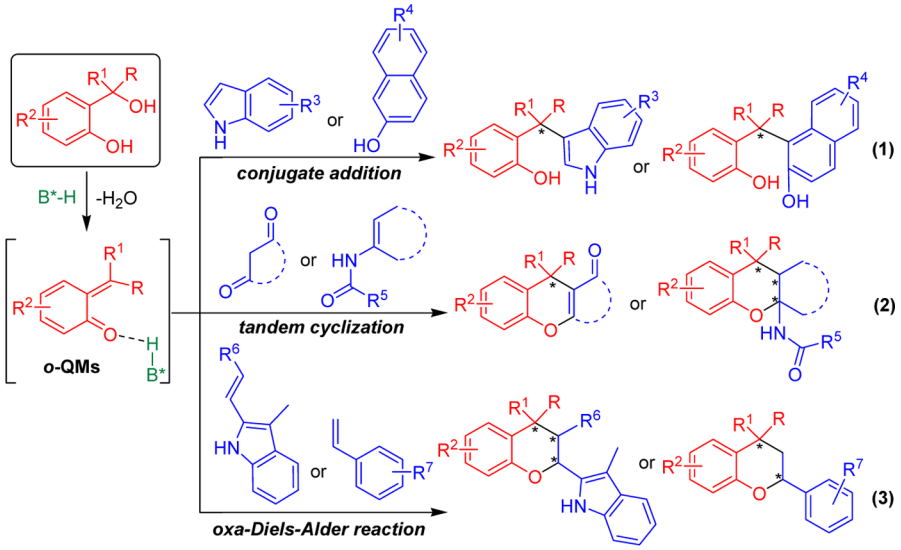
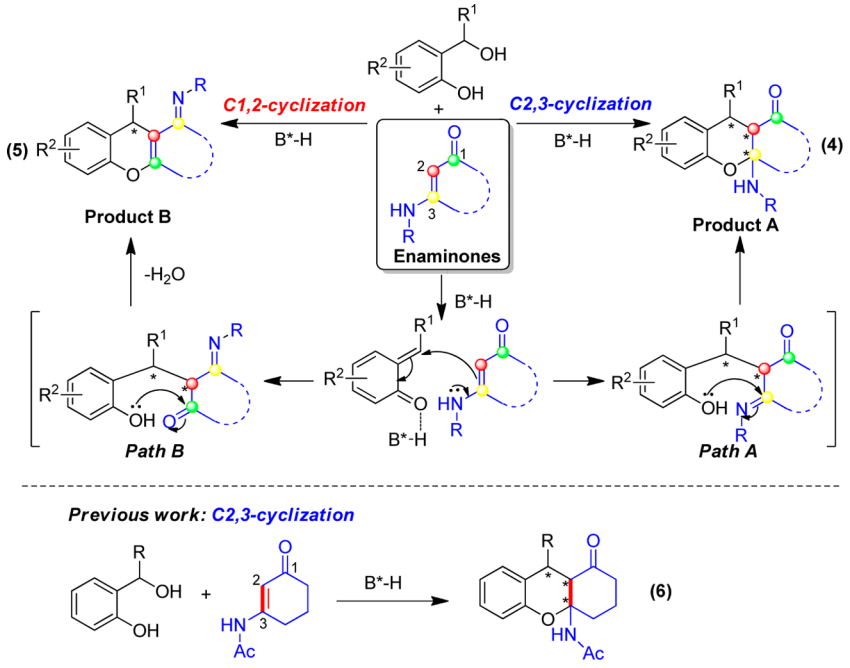
Scheme 1. Profile of *o*-Hydroxybenzyl Alcohol Involved Catalytic Enantioselective Transformations



Scheme 2. Chemoselective Issue in Catalytic Asymmetric Cyclizations of *o*-Hydroxybenzyl Alcohols with Enaminones



enaminone-involved cyclizations, we considered that the alteration of the N substituent from the strongly electron withdrawing acyl group to the aryl group might make the C═N bond of the intermediate become less electrophilic than the C═O bond, thus facilitating the nucleophilic addition of the hydroxyl group to the C═O bond and the completion of C1,2 cyclization (Scheme 3).

Herein, we report the catalytic chemo-, *E*/*Z*-, and enantioselective cyclizations of *o*-hydroxybenzyl alcohols with dimedone-derived enaminones, which not only established a chemoselective C1,2 cyclization of enaminones but also achieved the catalytic asymmetric construction of the biologically important tetrahydroxanthene[1c,d] framework with high *E*/*Z*- and enantioselectivities (all >95:5 *E*/*Z*, up to 98% yield, 97:3 er).

At the outset, the reaction of *o*-hydroxybenzyl alcohol **1a** and dimedone-derived enaminone **2a** was employed as a model reaction to test our hypothesis in the presence of CPA **4a** in chloroform at 50 °C (Scheme 4). However, the initial experiment was very frustrating, because this type of enaminone showed low reactivity under the current reaction conditions and only a small amount of product was obtained. Nevertheless, this product was identified as C1,2 cyclization product **3aa**, albeit with an extremely low yield of 7% and a poor enantioselectivity of 53:47 er. This result indicated that the utilization of *N*-aryl-substituted enaminones could indeed lead to C1,2 cyclization with high chemoselectivity as we designed. Thus, encouraged by this preliminary result, we performed a series of experiments on condition optimization such as screening of chiral catalysts **4**–**6**, solvents, additives, reagent ratios, and catalyst loadings (see the Supporting Information

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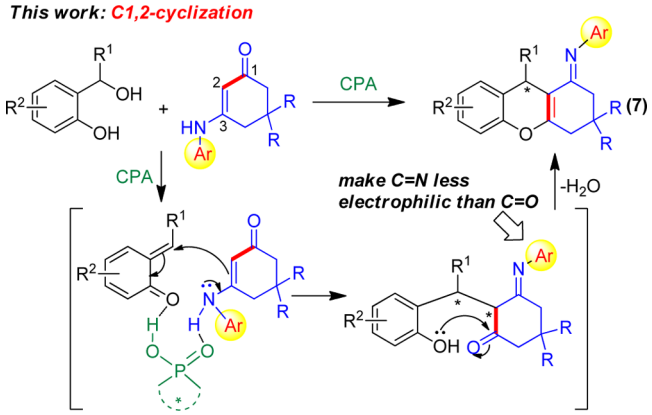
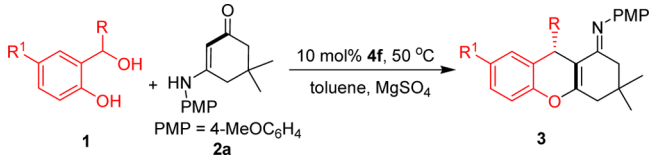
Scheme 3. Design of the Chemo- and Enantioselective C1,2 Cyclization of Enaminones with *o*-Hydroxybenzyl Alcohols



for details). Finally, the optimal reaction conditions were set by using CPA **4f** as catalyst, anhydrous magnesium sulfate as additive, and toluene as solvent, which afforded the product **3aa** in a high yield of 73% and a good enantioselectivity of 89:11 er. Notably, during the process of condition optimization, only a *E* isomer of product **3aa** was observed, which implied the excellent *E*/*Z* selectivity of the reaction.

After establishing the optimal conditions, we investigated the applicability of *o*-hydroxybenzyl alcohols **1** to the catalytic asymmetric C1,2 cyclizations with enaminone **2a**. As displayed in Table 1, a variety of *o*-hydroxybenzyl alcohols **1** bearing different R/R^1 groups served as suitable substrates in the reaction, which offered the chemoselective C1,2 cyclization products **3** in generally good yields with high *E*/*Z*- and enantioselectivities. In detail, the R^1 group could be altered from an electron-neutral hydrogen atom to electron-rich or electron-poor substituents with enhanced enantioselectivity (entry 1 vs entries 2−4), although the electron-withdrawing R^1 group decreased the reactivity of substrate **1** to some extent (entry 4 vs 1−3). In addition, a wide range of electronically different aromatic R groups with ortho, para, or meta substituents could be successfully employed in the reaction, delivering the products **3** in overall excellent enantioselectivities (entries 5−10). It seemed that the position or the electronic nature of the substituents

Table 1. Applicability of *o*-Hydroxybenzyl Alcohols 1[a]



1 **2a** **3**

Entry	3	R/R^1 (1)	yield (%)[b]	*E*/*Z*[c]	er[d]
1	**3aa**	Ph/H (**1a**)	73	>95:5	89:11
2	**3ba**	Ph/MeO (**1b**)	72	>95:5	95:5
3	**3ca**	Ph/Me (**1c**)	98	>95:5	93:7
4	**3da**	Ph/Cl (**1d**)	56	>95:5	95:5
5	**3ea**	2-MeOC$_6$H$_4$/H (**1e**)	51	>95:5	91:9
6	**3fa**	4-MeC$_6$H$_4$/MeO (**1f**)	83	>95:5	95:5
7	**3ga**	4-FC$_6$H$_4$/MeO (**1g**)	60	>95:5	94:6
8	**3ha**	4-ClC$_6$H$_4$/ MeO (**1h**)	43	>95:5	95:5
9	**3ia**	3-MeOC$_6$H$_4$/MeO (**1i**)	94	>95:5	95:5
10[e]	**3ja**	3-FC$_6$H$_4$/MeO (**1j**)	51	>95:5	95:5
11	**3ka**	Me/MeO (**1k**)	58	>95:5	93:7

[a]Unless otherwise indicated, the reaction was carried out on a 0.1 mmol scale and catalyzed by 10 mol % of **4f** in toluene (4 mL) with $MgSO_4$ (100 mg) at 50 °C for 48 h. The **1**:**2a** molar ratio was 4:1. [b]Isolated yield. [c]The *E*/*Z* ratio was determined by ^{1}H NMR. [d]The er value was determined by HPLC. [e]The **1j**:**2a** molar ratio was 6:1.

affected the reactivity to some extent, since electronically rich R groups delivered higher yields than their electronically poor counterparts (entry 6 vs entries 7 and 8, entry 9 vs entry 10). More importantly, an aliphatic R group as exemplified by a methyl group could also be utilized in the reaction, giving the cyclization product **3ja** in an acceptable yield and good enantioselectivity (entry 11), which greatly increases the applicability of this protocol in constructing an enantioenriched tetrahydroxanthene scaffold because aliphatic R groups have seldom been employed with *o*-hydroxybenzyl alcohols in previous catalytic asymmetric transformations.[2h,i]

Next, an investigation on the generality of *N*-aryl-substituted enaminones **2** was carried out by reactions with *o*-hydroxybenzyl alcohol **1b** under the optimal conditions. As shown in Table 2, a series of dimedone-derived enaminones **2** bearing electronically different *N*-aromatic groups proved to be

Scheme 4. Catalysts and Model Reaction Employed To Optimize the Conditions

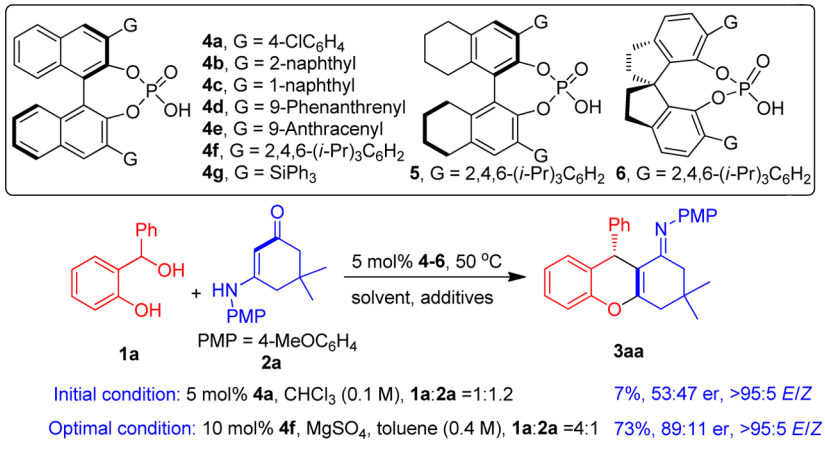


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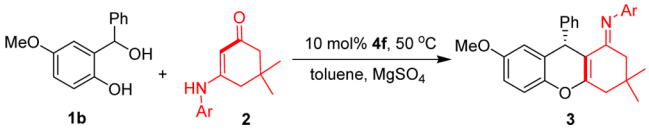
Table 2. Generality of *N*-Aryl-Substituted Enaminones 2[a]



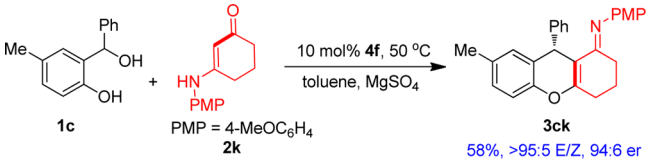
entry	3	Ar (2)	yield (%)[b]	*E*/*Z*[c]	er[d]
1	**3bb**	4-EtOC$_6$H$_4$ (**2b**)	90	>95:5	96:4
2	**3bc**	4-^{t}BuC$_6$H$_4$ (**2c**)	89	>95:5	95:5
3	**3bd**	4-^{i}PrOC$_6$H$_4$ (**2d**)	96	>95:5	95:5
4	**3be**	4-PhOC$_6$H$_4$ (**2e**)	62	>95:5	95:5
5	**3bf**	4-FC$_6$H$_4$ (**2f**)	70	>95:5	96:4
6	**3bg**	4-ClC$_6$H$_4$ (**2g**)	51	>95:5	97:3
7	**3bh**	Ph (**2h**)	65	>95:5	94:6
8	**3bi**	3,4-(MeO)$_2$C$_6$H$_3$ (**2i**)	84	>95:5	96:4
9	**3bj**	3,4,5-(MeO)$_3$C$_6$H$_2$ (**2j**)	87	>95:5	97:3

[a]Unless otherwise indicated, the reaction was carried out on the 0.01 mmol scale and catalyzed by 10 mol % of **4f** in toluene (4 mL) with $MgSO_4$ (100 mg) at 50 °C for 48 h. The **1b**:**2** molar ratio was 4:1. [b]Isolated yield. [c]The *E*/*Z* ratio was determined by ^{1}H NMR. [d]The er value was determined by HPLC.

competent reactants, which smoothly performed the chemo- and enantioselective C1,2 cyclizations in overall high yields (51%−96%) and with excellent *E*/*Z*- and enantioselectivities (all >95:5 *E*/*Z*, 94:6 to 97:3 er). It seemed that the electronic nature of the substituents did not impose any evident effect on the enantioselectivity, but it obviously influenced the reactivity, due to the fact that electron-rich phenyl groups delivered higher yields than electron-poor or electron-neutral groups in most cases (entries 1−3 vs entries 5−7). Moreover, enaminones **2i**,**j** bearing multiply substituted aromatic groups could also take part in the desired C1,2 cyclization reaction to give the corresponding products in excellent yields and satisfying enantioselectivities (entries 8 and 9).

In addition, this protocol could be extended to other types of enaminones instead of dimedone-derived enaminones. For example, cyclohexane-1,3-dione-derived enaminone **2k** was employed as a substrate to the reaction with *o*-hydroxybenzyl alcohol **1c** under the standard conditions, which smoothly afforded the corresponding C1,2 cyclization product **3ck** in a moderate yield, excellent *E*/*Z* selectivity, and good enantioselectivity (Scheme 5).

Scheme 5. Use of Cyclohexane-1,3-dione-Derived Enaminone 2k as a Substrate



The reaction pathway mainly included conjugate addition of enaminones **2** to *o*-hydroxybenzyl alcohols **1** and a subsequent intramolecular cyclization (Scheme 6). The chemoselectivity of the reaction stems from the step of intramolecular cyclization. In our case, the *N*-aryl group of enaminones **2** enabled the C═N bond of intermediate **A** to become less electrophilic than the C═O bond, thus facilitating the regioselective intramolecular nucleophilic attack of OH group at the C═O bond, which led to the generation of C1,2 cyclization products **3** after dehydration. In contrast, in previous reports,[2g,h] the N substituent of enaminones was an acetyl group (Ac). The strongly electron withdrawing property of the Ac group made the C═N bond of intermediate **A** more electrophilic than the C═O bond, which led to the regioselective nucleophilic addition of the OH group to C═N bond and thus the formation of C2,3 cyclization products. Therefore, the regioselectivity in the intramolecular cyclization of intermediate **A** should be largely ascribed to the electronic nature of the N substituents of enaminones.

As illustrated in Scheme 7, the absolute and *E*/*Z* configuration of compound **3aa** was identified to be *S*,*E* by single-crystal X-ray diffraction analysis (98:2 er after recrystallization).[8] The absolute and *E*/*Z* configurations of other compounds **3** were designated by analogy. According to the experimental results, we suggested a possible transition state to explain the stereochemistry of this C1,2 cyclization of enaminones. Initially, the *o*-QM intermediate was generated in situ from *o*-hydroxybenzyl alcohol **1a** in the presence of CPA **4f**, which then simultaneously activated both *o*-QM and enaminone **2a** via a hydrogen-bonding interaction to facilitate a *E*/*Z*- and enantioselective conjugate addition. The rigid (*R*)-BINOL backbone and the two bulky 2,4,6-triisopropylphenyl groups at the 3,3′-positions of chiral phosphoric acid **4f** contributed greatly to the experimentally observed *S* configuration. The repulsion between the phenyl group linked to the chiral center and the PMP group linked to the imine functionality resulted in the exclusive formation of the *E* configuration. Then, a chemoselective C1,2-cyclization occurred via the nucleophilic addition of a hydroxyl group to a carbonyl group instead of an imine group, again under the catalysis of CPA **4f**, to afford the final product **3aa** with *E* configuration.

In order to get some insight into the reaction pathway, some control experiments were carried out (Scheme 8). First, *o*-methoxybenzyl alcohol **1l** was employed in the reaction in place of *o*-hydroxybenzyl alcohols under the standard conditions (eq 8). However, no reaction (N. R.) occurred, which indicated that the free phenolic hydroxyl group of substrates **1** played a crucial role in the reaction via forming the key intermediate of *o*-QM. In the presence of this methoxyl group, the *o*-QM intermediate could hardly be generated, thus resulting in the failure of the reaction. Second, substrate **1a** was subjected to the reaction with enaminone **2a** (0.6 equiv) under the standard conditions to see whether a kinetic resolution of substrate **1a** took place during the reaction process (eq 9). After the reaction was complete, the recovered substrate **1a** was obtained in an almost racemic form (52:48 er), although the cyclization product **3aa** was generated in a good enantioselectivity of 87:13 er. This phenomenon implied that no evident kinetic resolution occurred during the reaction process.

CONCLUSIONS

In summary, we have established catalytic chemo-, *E*/*Z*-, and enantioselective cyclizations of *o*-hydroxybenzyl alcohols with dimedone-derived enaminones, which not only realized a chemoselective C1,2 cyclization of enaminones but also achieved the catalytic asymmetric construction of the biologically important tetrahydroxanthene framework with high *E*/*Z*- and enantioselectivities (all >95:5 *E*/*Z*, up to 98% yield, 97:3 er). This approach not only represents the first catalytic asymmetric C1,2 cyclization of enaminones with *o*-hydroxybenzyl alcohols but also provides an efficient strategy for

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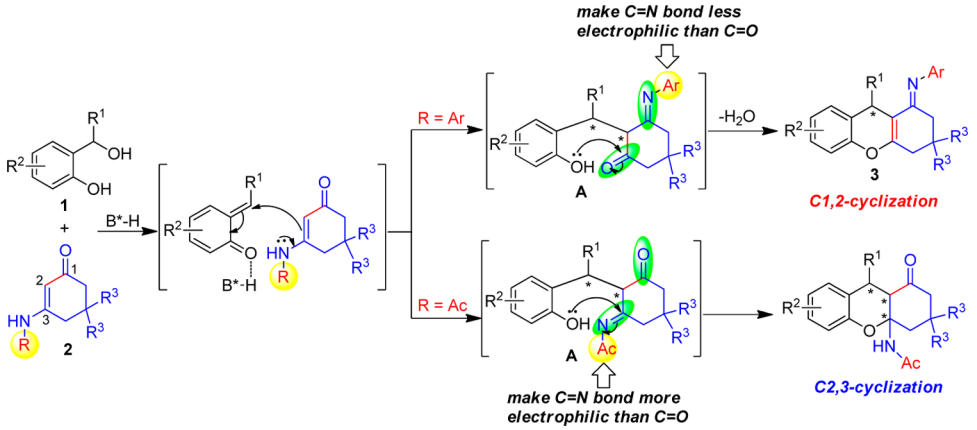
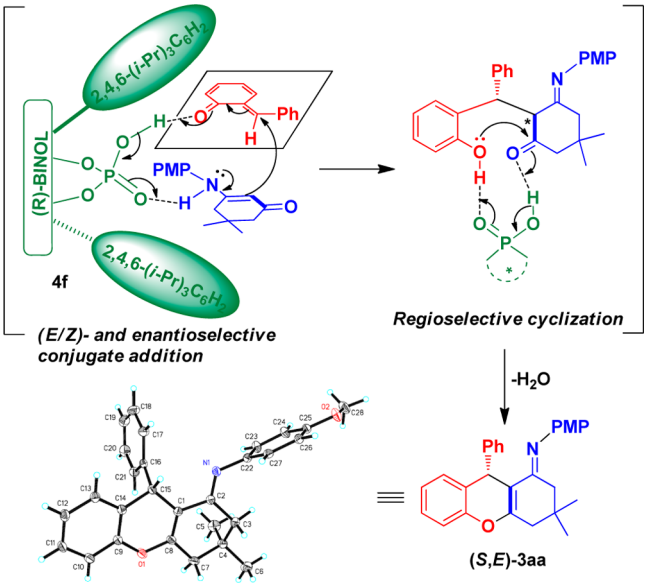
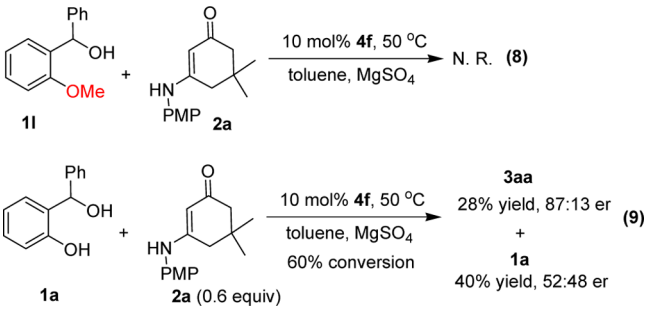
Scheme 6. Suggested Reaction Pathway To Explain the Chemoselectivity



Scheme 7. Suggested Transition State To Explain the Stereochemistry



Scheme 8. Control Experiments



constructing oxygenous heterocyclic frameworks with optical purity.

EXPERIMENTAL SECTION

General Information. ^{1}H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively. The solvent used for NMR spectroscopy was $CDCl_3$, using tetramethylsilane as the internal reference. HRMS spectra were recorded on a LTQ-Orbitrap mass spectrometer. Enantiomeric ratios (er) were determined by chiral high-performance liquid chromatography (chiral HPLC). The chiral columns used for the determination of enantiomeric excesses by chiral HPLC were Chiralpak AD-H and IA columns. Optical rotation values were measured with instruments operating at λ 589 nm, corresponding to the sodium D line at the temperatures indicated. The X-ray source used for the single-crystal X-ray diffraction analysis of compound **3aa** was Cu Kα (λ = 1.54178), and the structure was drawn with thermal ellipsoids at the 30% probability level. Analytical grade solvents for column chromatography and commercially available reagents were used as received. All starting materials commercially available were used directly. Substrates **1** and **2** were synthesized according to the literature methods.[2e,9]

Typical Procedure for the Catalytic Asymmetric Synthesis of Products 3. Anhydrous toluene (4 mL) was added to the mixture of *o*-hydroxybenzyl alcohols **1** (0.4 mmol), enaminones **2** (0.1 mmol), anhydrous magnesium (100 mg), and the catalyst **4f** (0.01 mmol) under a dry argon atmosphere. After it was stirred at 50 °C for 48 h, the reaction mixture was directly purified by flash column chromatography on silica gel (flushed by 10% Et_3N/petroleum ether in advance) to afford pure products **3**.

*(S,E)-N-(3,3-Dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)-4-methoxyaniline (**3aa**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 73% (29.9 mg); >95:5 *E*/*Z*; pale yellow solid; mp 127−128 °C; $[\alpha]_D^{20}$ = −208.8 (*c* 1.36, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.3 Hz, 2H), 7.24−7.06 (m, 6H), 7.01 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 8.7 Hz, 2H), 6.47 (d, *J* = 8.7 Hz, 2H), 5.34 (s, 1H), 3.78 (s, 3H), 2.51−2.39 (m, 2H), 2.17−2.05 (m, 2H), 1.03 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, CDCl3) δ 163.8, 156.3, 155.4, 150.2, 146.9, 145.1, 129.9, 128.2, 127.8, 127.2, 125.9, 125.8, 124.3, 120.7, 116.2, 114.1, 112.6, 55.5, 44.4, 41.4, 39.0, 31.4, 29.0, 27.5; IR (KBr) 2953, 2925, 2865, 2833, 1659, 1615, 1501, 1380, 1232, 1186, 1118, 1035, 839, 762, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{27}NO_2 + H)^+$ requires *m*/*z* 410.2115, found *m*/*z* 410.2110; enantiomeric ratio 89:11, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 6.533 min (minor), t_R = 5.437 min (major).

*(S,E)-4-Methoxy-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3ba**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 72% (31.6 mg); >95:5 *E*/*Z*; pale yellow solid; mp 130−131 °C; $[\alpha]_D^{20}$ = −231.6 (*c* 0.59, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.85−6.78 (m, 2H), 6.77−6.70 (m, 1H), 6.65 (d, *J* = 2.9 Hz, 1H), 6.54−6.42 (m, 2H), 5.30 (s, 1H), 3.78 (s, 3H), 3.70 (s, 3H), 2.49−2.37 (m, 2H), 2.17−2.04 (m, 2H), 1.02 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 156.5, 156.1, 155.4, 146.8, 145.2, 144.4, 128.2, 127.9, 126.6, 125.9, 120.7, 117.0, 114.1, 113.7, 113.5, 111.8, 55.5, 55.4, 41.5, 41.4, 39.5, 31.4, 29.1, 27.4; IR

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(KBr) 3411, 2955, 2832, 1666, 1626, 1500, 1377, 1212, 1033, 847, 715, 695 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{29}NO_3 + H)^+$ requires m/z 440.2220, found m/z 440.2226; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol =85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 6.657 min (minor), t_R = 5.447 min (major).

*(S,E)-4-Methoxy-N-(3,3,7-trimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3ca**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 98% (41.5 mg); >95:5 *E/Z*; pale yellow solid; mp 134−135 °C; $[\alpha]_D^{20}$ = −173.2 (*c* 0.64, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 7.4 Hz, 2H), 7.22 (t, J = 7.6 Hz, 2H), 7.12 (t, J = 7.3 Hz, 1H), 6.95 (d, J = 9.7 Hz, 3H), 6.85−6.78 (m, 2H), 6.51−6.42 (m, 2H), 5.29 (s, 1H), 3.78 (s, 3H), 2.50−2.38 (m, 2H), 2.23 (s, 3H), 2.16−2.04 (m, 2H), 1.02 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 156.3, 155.4, 148.2, 147.1, 145.2, 133.7, 130.1, 128.3, 127.9, 127.8, 125.8, 125.5, 120.6, 115.9, 114.1, 112.5, 55.4, 41.4, 41.3, 39.1, 31.4, 29.0, 27.4, 20.7; IR (KBr) 3446, 2961, 2828, 2359, 1654, 1614, 1499, 1376, 1210, 1028, 810, 720, 677 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{29}NO_2 + H)^+$ requires m/z 424.2271, found m/z 424.2289; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 85/15, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 5.200 min (minor), t_R = 4.097 min (major).

*(S,E)-N-(7-Chloro-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)-4-methoxyaniline (**3da**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 56% (24.8 mg); >95:5 *E/Z*; yellow solid; mp 105−106 °C; $[\alpha]_D^{20}$ = −131.7 (*c* 0.42, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 7.2 Hz, 2H), 7.23 (t, J = 7.5 Hz, 2H), 7.16−7.10 (m, 3H), 7.02−6.98 (m, 1H), 6.83−6.77 (m, 2H), 6.47−6.41 (m, 2H), 5.27 (s, 1H), 3.78 (s, 3H), 2.49−2.37 (m, 2H), 2.16−2.04 (m, 2H), 1.02 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 156.0, 155.5, 148.7, 146.3, 144.9, 129.5, 128.9, 128.2, 128.1, 127.5, 127.4, 126.1, 120.6, 117.7, 114.1, 112.3, 55.5, 41.3, 41.2, 39.1, 31.4, 29.0, 27.4; IR (KBr) 2960, 1652, 1597, 1500, 1376, 1230, 1101, 1026, 801, 755, 693, 528 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{26}ClNO_2 + H)^+$ requires m/z 444.1725, found m/z 444.1724; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 90/10, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 5.770 min (minor), t_R = 4.960 min (major).

*(S,E)-4-Methoxy-N-(9-(2-methoxyphenyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3ea**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 51% (22.4 mg); >95:5 *E/Z*; pale yellow sticky oil; $[\alpha]_D^{20}$ = −218.9 (*c* 0.40, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.27 (m, 1H), 7.25−7.21 (m, 1H), 7.13−7.07 (m, 2H), 7.00−6.92 (m, 2H), 6.86−6.81 (m, 2H), 6.79−6.74 (m, 2H), 6.37 (d, J = 8.6 Hz, 2H), 5.70 (s, 1H), 3.81 (s, 3H), 3.76 (s, 3H), 2.53−2.40 (m, 2H), 2.18−2.03 (m, 2H), 1.04 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 156.8, 155.2, 150.1, 145.2, 135.7, 129.6, 129.2, 127.0, 126.9, 126.1, 123.9, 120.8, 120.5, 115.8, 113.8, 111.7, 111.4, 56.1, 55.4, 41.5, 41.3, 33.0, 31.4, 29.0, 27.7; IR (KBr) 2956, 2831, 2359, 1662, 1616, 1501, 1377, 1232, 1177, 1032, 837, 750 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{29}NO_3 + H)^+$ requires m/z 440.2220, found m/z 440.2220; enantiomeric ratio 91:9, determined by HPLC (Daicel Chirapak IA, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 5.647 min (minor), t_R = 8.360 min (major).

*(S,E)-4-Methoxy-N-(7-methoxy-3,3-dimethyl-9-(p-tolyl)-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3fa**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 83% (37.6 mg); >95:5 *E/Z*; pale yellow solid; mp 121−122 °C; $[\alpha]_D^{20}$ = −200.6 (*c* 0.65, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 8.0 Hz, 2H), 7.01 (t, J = 8.6 Hz, 3H), 6.85−6.79 (m, 2H), 6.72 (dd, J = 8.9, 3.0 Hz, 1H), 6.65 (d, J = 2.9 Hz, 1H), 6.50 (d, J = 8.7 Hz, 2H), 5.27 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 2.47−2.37 (m, 2H), 2.28 (s, 3H), 2.17−2.04 (m, 2H), 1.02 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 156.4, 156.1, 155.4, 145.2, 144.4, 143.8, 135.2, 128.7, 128.0, 126.9, 120.7, 117.0, 114.0, 113.5, 113.4, 111.9, 55.5, 55.4, 41.4, 41.3, 39.0, 31.4, 29.1, 27.4, 21.1; IR (KBr) 3552, 3412, 2951, 2359, 1654, 1616, 1499, 1378, 1211, 1033, 847, 740 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{31}NO_3 + H)^+$ requires m/z 454.2378, found m/z 454.2372; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 9.453 min (minor), t_R = 7.093 min (major).

*(S,E)-N-(9-(4-Fluorophenyl)-7-methoxy-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)-4-methoxyaniline (**3ga**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 60% (27.4 mg); >95:5 *E/Z*; white solid; mp 144−145 °C; $[\alpha]_D^{20}$ = −189.8 (*c* 0.49, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.25 (m, 2H), 7.01 (d, J = 8.9 Hz, 1H), 6.93−6.86 (m, 2H), 6.84−6.79 (m, 2H), 6.74 (dd, J = 8.9, 3.0 Hz, 1H), 6.60 (d, J = 2.9 Hz, 1H), 6.49−6.43 (m, 2H), 5.27 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 2.41 (s, 2H), 2.16−2.03 (m, 2H), 1.01 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 161.1 (J = 242.0 Hz) 156.4, 156.1, 155.4, 145.1, 144.3, 142.6, 129.7 (J = 7.8 Hz), 126.4, 120.6, 117.1, 114.6 (J = 21.0 Hz), 114.1, 113.6, 111.7, 55.6, 55.5, 41.4, 41.3, 38.8, 31.4, 29.1, 27.2; IR (KBr) 3552, 3413, 2955, 2359, 1617, 1500, 1378, 1220, 1031, 851, 744, 627 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{28}FNO_3 + H)^+$ requires m/z 458.2126, found m/z 458.2119; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 12.317 min (minor), t_R = 7.913 min (major).

*(S,E)-N-(9-(4-Chlorophenyl)-7-methoxy-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)-4-methoxyaniline (**3ha**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 43% (20.3 mg); >95:5 *E/Z*; white solid; mp 164−165 °C; $[\alpha]_D^{20}$ = −208.0 (*c* 0.36, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.22 (m, 2H), 7.20−7.14 (m, 2H), 7.01 (d, J = 8.9 Hz, 1H), 6.84−6.78 (m, 2H), 6.73 (dd, J = 8.9, 3.0 Hz, 1H), 6.58 (d, J = 2.9 Hz, 1H), 6.46 (d, J = 8.7 Hz, 2H), 5.26 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 2.41 (s, 2H), 2.15−2.03 (m, 2H), 1.01 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 156.6, 156.1, 155.5, 145.4, 144.9, 144.3, 131.5, 129.6, 128.1, 126.0, 120.7, 117.2, 114.1, 113.7, 113.6, 111.6, 55.5, 55.4, 41.4, 41.3, 38.9, 31.4, 29.1, 27.2; IR (KBr) 3552, 3413, 2953, 2359, 1616, 1499, 1377, 1220, 1032, 850, 743, 627 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{28}ClNO_3 + H)^+$ requires m/z 474.1830, found m/z 474.1822; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 11.320 min (minor), t_R = 7.397 min (major).

*(S,E)-4-Methoxy-N-(7-methoxy-9-(3-methoxyphenyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3ia**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 94% (44.1 mg); >95:5 *E/Z*; pale yellow sticky oil; $[\alpha]_D^{20}$ = −171.7 (*c* 0.70, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (t, J = 8.1 Hz, 1H), 7.00 (d, J = 8.9 Hz, 1H), 6.93−6.87 (m, 2H), 6.84−6.79 (m, 2H), 6.75−6.64 (m, 3H), 6.52−6.45 (m, 2H), 5.28 (s, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 3.70 (s, 3H), 2.48−2.37 (m, 2H), 2.18−2.05 (m, 2H), 1.02 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 159.3, 156.6, 156.1, 155.4, 148.3, 145.1, 144.4, 128.9, 126.5, 120.7, 117.1, 114.0, 113.9, 113.6, 113.5, 111.7, 111.3, 55.6, 55.5, 55.1, 41.4, 41.3, 39.4, 31.4, 29.1, 27.4; IR (KBr) 3552, 3413, 2954, 2831, 2359, 1617, 1500, 1377, 1213, 1034, 838, 756, 617 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{31}NO_4 + H)^+$ requires m/z 470.2326, found m/z 470.2322; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 14.293 min (minor), t_R = 11.920 min (major).

*(S,E)-N-(9-(3-Fluorophenyl)-7-methoxy-3,3-dimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)-4-methoxyaniline (**3ja**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h;

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yield, 51% (23.3 mg); >95:5 *E/Z*; pale yellow solid; mp 100−101 °C; $[\alpha]_D^{20}$ = −163.4 (*c* 0.35, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.13 (m, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 3H), 6.76−6.71 (m, 1H), 6.62 (d, *J* = 2.7 Hz, 1H), 6.47 (d, *J* = 8.5 Hz, 2H), 5.30 (s, 1H), 3.78 (s, 3H), 3.71 (s, 3H), 2.48−2.37 (m, 2H), 2.17−2.05 (m, 2H), 1.02 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 162.6 (*J* = 211.5 Hz), 156.7, 156.1, 155.5, 145.0, 144.3, 129.3 (*J* = 8.1 Hz), 125.9, 123.9, 120.7, 117.2, 115.0 (*J* = 21.4 Hz), 114.1, 113.7, 113.6, 112.8 (*J* = 21.1 Hz), 111.4, 55.6, 55.5, 41.4, 41.3, 39.3, 31.4, 29.1, 27.3; IR (KBr) 3552, 3413, 2959, 2360, 1616, 1500, 1377, 1220, 1030, 814, 739, 668 cm^{-1}; ESI FTMS exact mass calcd for $(C_{29}H_{28}FNO_3 + H)^+$ requires *m*/*z* 458.2126, found *m*/*z* 458.2126; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 98/2, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 21.050 min (minor), t_R = 18.033 min (major).

*(S,E)-4-Methoxy-N-(7-methoxy-3,3,9-trimethyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3ka**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 58% (21.9 mg); >95:5 *E/Z*; pale yellow sticky oil; $[\alpha]_D^{20}$ = −262.4 (*c* 0.37, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, *J* = 8.5 Hz, 1H), 6.88−6.84 (m, 2H), 6.74−6.69 (m, 2H), 6.67−6.63 (m, 2H), 4.15−4.09 (m, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 2.32 (s, 2H), 2.23 (d, *J* = 15.5 Hz, 1H), 2.09 (d, *J* = 15.5 Hz, 1H), 1.40 (d, *J* = 6.8 Hz, 3H), 1.01 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 156.8, 156.1, 155.5, 145.2, 144.5, 128.9, 120.9, 116.6, 114.1, 113.0, 112.7, 112.6, 55.6, 55.4, 41.5, 41.4, 31.3, 29.3, 28.4, 26.9, 24.8; IR (KBr) 3552, 3413, 2957, 2360, 1616, 1500, 1382, 1222, 1036, 803, 729, 618 cm^{-1}; ESI FTMS exact mass calcd for $(C_{24}H_{27}NO_3 + H)^+$ requires *m*/*z* 378.2064, found *m*/*z* 378.2070; enantiomeric ratio 93:7, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 9.660 min (minor), t_R = 5.633 min (major).

*(S,E)-4-Ethoxy-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bb**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 90% (40.8 mg); >95:5 *E/Z*; pale yellow solid; mp 104−105 °C; $[\alpha]_D^{20}$ = −111.4 (*c* 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.85−6.76 (m, 2H), 6.72 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.64 (d, *J* = 2.9 Hz, 1H), 6.45 (d, *J* = 8.5 Hz, 2H), 5.30 (s, 1H), 4.06−3.91 (m, 2H), 3.70 (s, 3H), 2.51−2.34 (m, 2H), 2.17−2.03 (m, 2H), 1.40 (t, *J* = 7.0 Hz, 3H), 1.01 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 156.4, 156.1, 154.7, 146.8, 145.1, 144.4, 128.2, 127.9, 126.6, 125.9, 120.7, 117.0, 114.7, 113.7, 113.4, 111.8, 63.7, 55.6, 41.4, 41.3, 39.5, 31.4, 29.1, 27.4, 15.0; IR (KBr) 2963, 2926, 2359, 1659, 1594, 1496, 1380, 1209, 1024, 835, 719, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{31}NO_3 + H)^+$ requires *m*/*z* 454.2377, found *m*/*z* 454.2364; enantiomeric ratio 96:4, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 12.003 min (minor), t_R = 9.357 min (major).

*(S,E)-4-(tert-Butyl)-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bc**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 89% (41.4 mg); >95:5 *E/Z*; white sticky oil; $[\alpha]_D^{20}$ = −130.7 (*c* 0.78, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.29 (m, 2H), 7.29−7.26 (m, 1H), 7.26−7.19 (m, 3H), 7.16−7.09 (m, 1H), 7.02 (d, *J* = 8.9 Hz, 1H), 6.76−6.69 (m, 1H), 6.65 (d, *J* = 2.9 Hz, 1H), 6.50−6.40 (m, 2H), 5.30 (s, 1H), 3.70 (s, 3H), 2.50−2.36 (m, 2H), 2.16−2.05 (m, 2H), 1.32 (s, 9H), 1.03 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 156.4, 156.1, 149.2, 146.8, 145.1, 144.4, 128.3, 127.9, 126.6, 125.8, 125.5, 119.1, 117.1, 113.6, 113.5, 111.8, 55.6, 41.5, 41.4, 39.6, 34.2, 31.6, 31.4, 29.0, 27.4; IR (KBr) 3026, 2958, 2360, 1657, 1615, 1495, 1378, 1215, 1024, 802, 727, 697 cm^{-1}; ESI FTMS exact mass calcd for $(C_{32}H_{35}NO_2 + H)^+$ requires *m*/*z* 466.2741, found *m*/*z* 466.2748; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 6.787 min (minor), t_R = 5.317 min (major).

*(S,E)-4-Isopropoxy-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bd**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 96% (44.8 mg); >95:5 *E/Z*; pale yellow solid; mp 107−108 °C; $[\alpha]_D^{20}$ = −193.7 (*c* 0.77, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.4 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.15−7.09 (m, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.83−6.77 (m, 2H), 6.72 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.65 (d, *J* = 2.9 Hz, 1H), 6.49−6.39 (m, 2H), 5.30 (s, 1H), 4.52−4.41 (m, 1H), 3.70 (s, 3H), 2.50−2.36 (m, 2H), 2.18−2.04 (m, 2H), 1.33 (s, 3H), 1.32 (s, 3H), 1.02 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 156.4, 156.1, 153.6, 146.8, 144.4, 128.2, 127.9, 126.6, 125.9, 120.7, 117.0, 116.5, 113.7, 113.4, 111.8, 70.4, 55.6, 41.5, 41.3, 39.5, 31.4, 29.1, 27.4, 22.2; IR (KBr) 2955, 2924, 2359, 1662, 1609, 1498, 1378, 1209, 1119, 1023, 836, 720 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{33}NO_3 + H)^+$ requires *m*/*z* 468.2533, found *m*/*z* 468.2517; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 11.250 min (minor), t_R = 9.163 min (major).

*(S,E)-N-(7-Methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)-4-phenoxyaniline (**3be**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 62% (31.1 mg); >95:5 *E/Z*; white sticky oil; $[\alpha]_D^{20}$ = −161.8 (*c* 0.51, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.29 (m, 4H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 7.03−6.97 (m, 3H), 6.96−6.90 (m, 2H), 6.75−6.70 (m, 1H), 6.65 (d, *J* = 2.9 Hz, 1H), 6.52−6.45 (m, 2H), 5.29 (s, 1H), 3.70 (s, 3H), 2.51−2.38 (m, 2H), 2.17−2.05 (m, 2H), 1.04 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 158.1, 156.8, 156.1, 152.1, 147.7, 146.7, 144.3, 129.6, 128.2, 128.0, 126.6, 125.9, 122.6, 120.8, 119.9, 118.0, 117.1, 113.7, 113.5, 111.7, 55.6, 41.4, 39.5, 31.5, 29.1, 27.4; IR (KBr) 3441, 2975, 2852, 1668, 1636, 1580, 1379, 1222, 1133, 947, 850, 715, 675 cm^{-1}; ESI FTMS exact mass calcd for $(C_{34}H_{31}NO_3 + H)^+$ requires *m*/*z* 502.2377, found *m*/*z* 502.2378; enantiomeric ratio 95:5, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 19.907 min (minor), t_R = 11.760 min (major).

*(S,E)-4-Fluoro-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bf**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 70% (29.9 mg); >95:5 *E/Z*; white solid; mp 105−106 °C; $[\alpha]_D^{20}$ = −117.9 (*c* 0.51, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.28 (m, 2H), 7.25−7.18 (m, 2H), 7.15−7.09 (m, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.98−6.89 (m, 2H), 6.73 (dd, *J* = 8.9, 3.0 Hz, 1H), 6.64 (d, *J* = 2.9 Hz, 1H), 6.50−6.36 (m, 2H), 5.27 (s, 1H), 3.70 (s, 3H), 2.51−2.36 (m, 2H), 2.12−1.99 (m, 2H), 1.02 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 158.8 (*J* = 238.6 Hz), 156.9, 156.1, 147.9, 146.7, 144.3, 128.1 (*J* = 13.6 Hz), 126.5, 125.9, 120.7 (*J* = 7.7 Hz), 117.1, 115.4 (*J* = 22.1 Hz), 113.7, 113.5, 111.6, 55.6, 41.4, 39.5, 31.4, 29.0, 27.4; IR (KBr) 3055, 2957, 2867, 2359, 1657, 1620, 1497, 1378, 1212, 1035, 843, 717, 680 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{26}FNO_2 + H)^+$ requires *m*/*z* 428.2020, found *m*/*z* 428.2028; enantiomeric ratio 96:4, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, *T* = 30 °C, 254 nm), t_R = 8.960 min (minor), t_R = 6.450 min (major).

*(S,E)-4-Chloro-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bg**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 51% (22.6 mg); >95:5 *E/Z*; pale yellow solid; mp 101−102 °C; $[\alpha]_D^{20}$ = −143.3 (*c* 0.42, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 6.9 Hz, 2H), 7.25−7.16 (m, 4H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 6.72 (d, *J* = 8.9 Hz, 1H), 6.63 (s, 1H), 6.42 (d, *J* = 6.3 Hz, 2H), 5.24 (s, 1H), 3.70 (s, 3H), 2.50−2.37 (m, 2H), 2.10−1.97 (m,

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2H), 1.01 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 157.1, 156.1, 150.5, 146.6, 144.2, 128.8, 128.1, 128.0, 127.6, 126.4, 125.9, 120.9, 117.1, 113.7, 113.5, 111.5, 55.6, 41.5, 41.4, 39.5, 31.5, 28.9, 27.4; IR (KBr) 3412, 2959, 1656, 1612, 1481, 1379, 1216, 1089, 1025, 813, 716, 696 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{26}ClNO_2 + H)^+$ requires m/z 444.1725, found m/z 444.1728; enantiomeric ratio 97:3, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 98/2, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 13.753 min (minor), t_R = 10.957 min (major).

*(S,E)-N-(7-Methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bh**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 65% (26.6 mg); >95:5 *E*/*Z*; white solid; mp 107−108 °C; $[\alpha]_D^{20}$ = −138.5 (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 7.4 Hz, 2H), 7.28−7.20 (m, 4H), 7.13 (t, J = 7.3 Hz, 1H), 7.06−6.96 (m, 2H), 6.77−6.71 (m, 1H), 6.66 (d, J = 2.9 Hz, 1H), 6.51 (d, J = 7.3 Hz, 2H), 5.31 (s, 1H), 3.71 (s, 3H), 2.50−2.38 (m, 2H), 2.13−2.01 (m, 2H), 1.02 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 156.7, 156.1, 152.0, 146.7, 144.4, 128.7, 128.2, 127.9, 126.6, 125.9, 122.4, 119.5, 117.1, 113.7, 113.5, 111.7, 55.6, 41.4, 39.5, 31.4, 28.9, 27.4; IR (KBr) 3413, 3005, 2957, 2832, 2360, 1655, 1611, 1494, 1377, 1209, 1035, 830, 729, 674 cm^{-1}; ESI FTMS exact mass calcd for $(C_{28}H_{27}NO_2 + H)^+$ requires m/z 410.2115, found m/z 410.2122; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 7.017 min (minor), t_R = 4.887 min (major).

*(S,E)-3,4-Dimethoxy-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bi**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 84% (39.4 mg); >95:5 *E*/*Z*; white sticky oil; $[\alpha]_D^{20}$ = −171.2 (*c* 0.75, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.29 (m, 2H), 7.22 (t, J = 7.6 Hz, 2H), 7.12 (t, J = 7.3 Hz, 1H), 7.01 (d, J = 8.9 Hz, 1H), 6.78−6.69 (m, 2H), 6.64 (d, J = 2.9 Hz, 1H), 6.10 (d, J = 2.2 Hz, 1H), 6.06−6.00 (m, 1H), 5.29 (s, 1H), 3.85 (s, 3H), 3.79 (s, 3H), 3.69 (s, 3H), 2.49−2.37 (m, 2H), 2.16−2.05 (m, 2H), 1.02 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 156.9, 156.1, 153.4, 148.3, 146.7, 144.3, 133.3, 128.2, 128.0, 126.5, 125.9, 117.1, 113.7, 113.5, 111.5, 96.5, 61.0, 56.0, 55.6, 41.5, 41.4, 39.5, 31.4, 28.9, 27.6; IR (KBr) 3431, 2959, 2830, 1676, 1656, 1540, 1397, 1220, 1040, 850, 710, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{30}H_{31}NO_4 + H)^+$ requires m/z 470.2326, found m/z 470.2332; enantiomeric ratio 96:4, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 70/30, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 5.900 min (minor), t_R = 5.007 min (major).

*(S,E)-3,4,5-Trimethoxy-N-(7-methoxy-3,3-dimethyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3bj**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 87% (43.6 mg); >95:5 *E*/*Z*; pale yellow sticky oil; $[\alpha]_D^{20}$ = −108.4 (*c* 0.74, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.29 (m, 2H), 7.22 (t, J = 7.6 Hz, 2H), 7.12 (t, J = 7.3 Hz, 1H), 7.01 (d, J = 8.9 Hz, 1H), 6.75−6.70 (m, 1H), 6.63 (d, J = 2.9 Hz, 1H), 5.69 (s, 2H), 5.26 (s, 1H), 3.81 (s, 3H), 3.76 (s, 6H), 3.69 (s, 3H), 2.50−2.37 (m, 2H), 2.16−2.05 (m, 2H), 1.04 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 156.6, 156.1, 149.2, 146.8, 145.7, 144.7, 144.4, 128.2, 127.9, 126.6, 125.9, 117.1, 113.7, 113.4, 111.7, 110.6, 104.3, 56.2, 55.8, 55.6, 41.5, 41.4, 39.5, 31.4, 29.0, 27.5; IR (KBr) 2955, 2359, 1655, 1584, 1496, 1378, 1215, 1126, 1028, 832, 733, 698 cm^{-1}; ESI FTMS exact mass calcd for $(C_{31}H_{33}NO_5 + H)^+$ requires m/z 500.2431, found m/z 500.2435; enantiomeric ratio 97:3, determined by HPLC (Daicel Chirapak AD-H, hexane/isopropyl alcohol 80/20, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 8.163 min (minor), t_R = 6.480 min (major).

*(S,E)-4-Methoxy-N-(7-methyl-9-phenyl-2,3,4,9-tetrahydro-1H-xanthen-1-ylidene)aniline (**3ck**):* flash column chromatography eluent (flushed by 10% Et_3N/petroleum ether in advance), petroleum ether/ethyl acetate 30/1; reaction time, 48 h; yield, 58% (22.8 mg); >95:5 *E*/*Z*; pale yellow sticky oil; $[\alpha]_D^{20}$ = −255.1 (*c* 0.27, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 7.5 Hz, 2H), 7.25−7.20 (m, 2H), 7.12 (t, J = 7.3 Hz, 1H), 6.95 (d, J = 10.1 Hz, 3H), 6.83−6.78 (m, 2H), 6.52 (d, J = 8.7 Hz, 2H), 5.33 (s, 1H), 3.78 (s, 3H), 2.67−2.53 (m, 2H), 2.40−2.26 (m, 2H), 2.23 (s, 3H), 1.89−1.84 (m, 1H), 1.80−1.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 158.2, 155.5, 148.2, 147.2, 133.8, 130.0, 128.4, 128.3, 128.0, 127.9, 125.8, 125.6, 120.9, 115.9, 114.1, 113.8, 55.5, 38.9, 28.2, 27.8, 21.0, 20.8; IR (KBr) 3668, 3552, 3418, 3381 2966, 1776, 1616, 1398, 1316, 1273, 1186, 1054, 1015, 862, 771, 622 cm^{-1}; ESI FTMS exact mass calcd for $(C_{27}H_{25}NO_2 + H)^+$ requires m/z 396.1958, found m/z 396.1966; enantiomeric ratio 94:6, determined by HPLC (Daicel Chirapak OD-H, hexane/isopropyl alcohol 95/5, flow rate 1.0 mL/min, T = 30 °C, 254 nm), t_R = 5.483 min (minor), t_R = 4.673 min (major).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01613.

Crystal data of compound **3aa** (CIF)

Optimization of conditions, characterization data (including ^{1}H and ^{13}C NMR and HPLC spectra) for all products **3**, and crystal data of compound **3aa** (PDF)

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Notes

The authors declare no competing financial interest.

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