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The synthesis of chiral β-aryl-α,β-unsaturated amino alcohols *via* a Pd-catalyzed asymmetric allylic amination†

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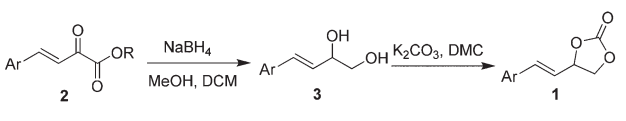
Chiral β-aryl-α,β-unsaturated amino alcohols were synthesized *via* a Pd-catalyzed asymmetric allylic amination of 4-aryl-1,3-dioxolan-2-one using planar chiral 1,2-disubstituted ferrocene-based phosphinooxazolines as ligands. Under the optimized reaction conditions, a series of substrates were examined and the products were obtained in good to excellent yields (up to 92%) and enantioselectivities (up to 98% ee) under mild reaction conditions. The desired products were determined to be of (*R*)-configuration and could subsequently be transformed into compounds with interesting biological activity using simple transformations.

1. Introduction

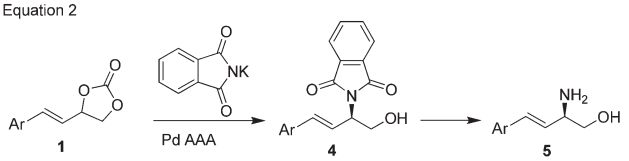
Chiral β-aryl-α,β-unsaturated amino alcohols and their derivatives are important building blocks which can be transformed to a variety of compounds with interesting biological activity, such as JNK3 inhibitors,[1] DNJ analogues,[2] and dopamine D_2 receptor agonists,[3] among others.[4] Over the past twenty years, several methods have been developed to synthesise chiral β-aryl-α,β-unsaturated amino alcohols.[5,6] However, some procedures only yield racemic products[2c,5] and resolution is required to obtain optically pure compounds. Trost and Lennon's groups reported a Pd-catalyzed asymmetric allylic amination of 2-vinyloxirane which provided chiral α,β-unsaturated amino alcohols.[7] A Heck reaction was required in order to obtain products with vinyl substituents. Other synthetic methods require seven to eight steps to achieve this goal from natural valine.[6] Therefore, an efficient synthesis of chiral β-aryl-α,β-unsaturated amino alcohols is greatly desired.

Recently, we reported the efficient organocatalytic asymmetric domino reaction of β,γ-unsaturated α-keto esters to provide multi-substituted, enantiomerically enriched 3,4-dihydro-2*H*-pyran species.[8] We found that β,γ-unsaturated α-keto esters could be reduced to afford the corresponding diols **3**, which could subsequently be reacted with dimethyl carbonate (DMC) to give β-aryl-α,β-unsaturated carbonates **1** (Scheme 1, eqn (1)). Based on our previous work,[9] compounds **1** would be useful substrates for the preparation of chiral β-aryl-α,β-unsaturated amino alcohols *via* a Pd-catalyzed asymmetric allylic amination (Scheme 1, eqn (2)). Here we report the efficient Pd-catalyzed asymmetric allylic amination of 4-aryl-1,3-dioxolan-2-one by using 1,2-disubstituted planar chiral ferrocene-based phosphinooxazoline ligands, which gave good to excellent yields and enantioselectivities.

Equation 1



Equation 2



Scheme 1 The pathway to β-aryl-α,β-unsaturated amino alcohols.

2. Results and discussion

Compound **1a** was used as a substrate to screen solvent effects in the Pd-catalyzed asymmetric allylic amination at 20 °C, using a ruthenocene-based chiral phosphinooxazoline ligand **L1a** recently developed by our group.[10] As shown in Table 1, when toluene and EtOAc were used, the reactions proceeded

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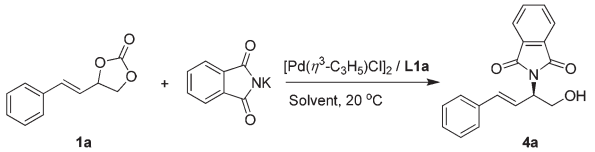
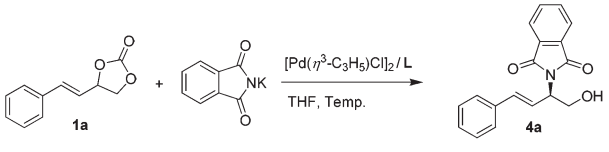
Table 1 Solvent screening[a]



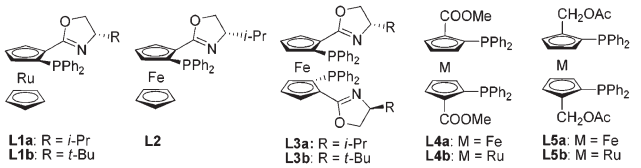
Entry	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	$PhCH_3$	8	82	91
2	EtOAc	8	84	88
3	DCM	12	57	81
4	DMF	12	61	89
5	Dioxane	9	87	91
6	THF	8	89	94

[a] Reactions of **1a** (0.2 mmol) with potassium phthalimide (0.22 mmol) were performed using 6.0 mol% **L1a** and 2.5 mol% $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in a solvent (2 mL). [b] Isolated yield. [c] Determined by HPLC using a chiral AD-H column.

Table 2 Ligand and temperature screening[a]



Entry	Ligand	Temp. (°C)	Time (h)	Yield[b] (%)	ee[c] (%)
1	**L1a**	20	8	91	94
2	**L1b**	20	8	92	50
3	**L2**	20	8	92	95
4	**L3a**	20	10	78	86
5	**L3b**	20	8	80	45
6	**L4a**	20	6	86	50
7	**L4b**	20	6	87	50
8	**L5a**	20	8	82	5
9	**L5b**	20	8	51	13
10	**L2**	0	18	37	97
11	**L2**	10	18	62	95
12	**L2**	30	6	87	78
13	**L2**	40	5	84	64



[a] Reactions of **1a** (0.2 mmol) with potassium phthalimide (0.22 mmol) were performed using a ligand (**L1a–L2:** 6.0 mol%; **L3a–L5b:** 3.0 mol%) and 2.5 mol% $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in a solvent (2 mL). [b] Isolated yield. [c] Determined by HPLC using a chiral AD-H column.

smoothly to give the desired product with good enantioselectivity (entries 1 and 2). However, when the solvent was changed to DCM or DMF, the reaction system became very complex with the formation of many byproducts; thus only moderate yields were obtained (entries 3 and 4). When ether solvents were used, such as dioxane or THF, the reaction proceeded to yield the amino alcohol **2a** with up to 94% ee. Based on the above results, THF was chosen to be the best solvent for subsequent reactions.

The effect of several planar chiral ligands was examined on the reaction. As shown in Table 2, both **L1a** and **L1b** provided excellent yields but ee decreased sharply from 94% to 50% when using **1b** as a ligand (entries 1 and 2). The corresponding ferrocene-based **L2** was examined and also provided excellent yield and enantioselectivity. Subsequently, a number of C_2-symmetric ligands **L3–L5**, which were also developed by our group and showed excellent activities in several asymmetric catalyses, were used in this asymmetric allylic amination reaction. All the reactions provided products with moderate to good yields but only moderate ee (entries 4–9). Thus **L2** was selected for subsequent reactions.

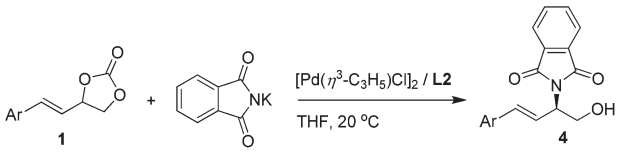
Besides the solvent and the ligand, temperature also had a significant effect on the reaction. When the reaction was carried out at 0 °C, excellent enantioselectivity was observed but the reaction activity decreased substantially. Even after 18 hours, the product was obtained in only 37% yield (entry 10). A similar result was obtained when performing the reaction at 10 °C. The product was obtained in only 62% yield but with excellent enantioselectivity (entry 11). However, when the temperature was increased to 30 °C and 40 °C, the enantioselectivity declined rapidly (entries 12–13, 78% and 64% respectively). The above result indicated that the reaction rate increased but the enantioselectivity was reduced with higher temperatures. Taking these two factors into account, we chose 20 °C as the optimal reaction temperature.

With the optimised conditions in hand, we synthesized a series of 4-aryl-1,3-dioxolan-2-ones **1** using our newly developed methodology (Scheme 1, eqn (1)). Thus, β,γ-unsaturated α-keto esters **2** were reduced with $NaBH_4$ to give the corresponding diols **3**. Subsequently, **3** reacted with dimethyl carbonate (DMC) to give substrates **1** in 48%–78% yield over two steps. Compounds **1** were then subjected to the Pd-catalyzed asymmetric allylic amination reaction, the results of which are shown in Table 3.

The results indicate that no matter whether the substituent is at the *ortho*, *meta* or *para* position of the benzene ring, good yields and excellent ee could be obtained (entries 1–4). Meanwhile, substrates with both electron donating and withdrawing substituent groups also gave good to excellent yields and enantioselectivities when the reaction was performed in THF (entries 5–10). When the aryl group was changed to naphthyl, good ees were also observed but with moderate enantioselectivities, perhaps due to the steric hindrance of the naphthyl group (entries 11 and 12).

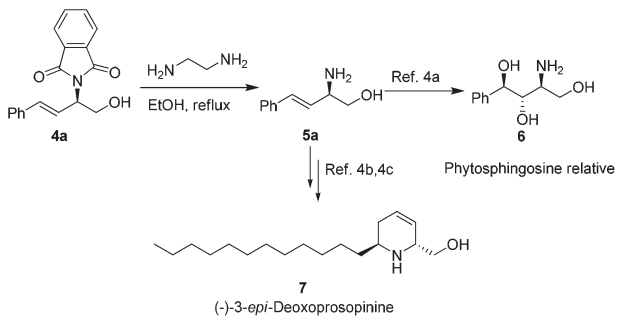
After examining the substrate scope, **4a** was used to synthesise the β-phenyl-α,β-unsaturated amino alcohol **5a** according to a procedure reported by Trost and co-workers (Scheme 2).[7a] Thus, the phthalimide group of **4a** was removed *via* treatment with ethylene diamine in refluxing toluene, to give the desired product **5a** in 91% yield with no loss of enantioselectivity. Additionally, the absolute configuration of the product **4a** was determined to be *R* by comparison of the optical rotation of **5a** with the reported literature value.[2d] The

Table 3 Substrate scope[a]



Entry	1	Ar	Time (h)	Yield[b] (%)	ee[c] (%)
1	**1a**	C_6H_5	8	92	95
2	**1b**	2-$CH_3C_6H_4$	12	78	91
3	**1c**	3-$CH_3C_6H_4$	12	83	92
4	**1d**	4-$CH_3C_6H_4$	12	82	92
5	**1e**	4-$CH_3OC_6H_4$	24	87	87
6	**1f**	2-FC_6H_4	12	92	98
7	**1g**	4-FC_6H_4	12	88	80
8	**1h**	4-ClC_6H_4	12	90	90
9	**1i**	4-BrC_6H_4	12	77	89
10	**1j**	4-$CF_3C_6H_4$	12	91	91
11	**1k**	1-Naphthyl	18	72	88
12	**1l**	2-Naphthyl	18	70	87

[a] Reactions of **1** (0.2 mmol) with potassium phthalimide (0.22 mmol) were performed using 6.0 mol% **L2** and 2.5 mol% $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ in THF (2 mL). [b] Isolated yield. [c] Determined by HPLC using chiral OD-H, AD-H or IE-H columns.



Scheme 2 The application of desired product **4a**.

desired products **5a** have the potential to participate in a variety of transformations. For example, **5a** has the potential to be used as a key intermediate for the synthesis of the phytosphingosine relative (**6**),[4a] a biologically active sphingolipid. It also has the potential to be used for the preparation of the non-natural (−)-3-*epi*-deoxoprosopinine (**7**),[4b,c] an analogue of the *Prosopis* alkaloid family (Scheme 2).

3. Conclusions

To summarize, we have synthesized a series of chiral β-aryl-α,β-unsaturated amino alcohols *via* a Pd-catalyzed asymmetric allylic amination. All the substrates gave good to excellent yields (up to 92%) and enantioselectivities (up to 98% ee value) under mild conditions. Optical rotation tests show that the absolute configuration of the catalytic product **4** is of *R* configuration. The products can potentially be transformed into important compounds with interesting biological activity using simple transformations.

4. Experimental section

4.1. General information

Unless stated otherwise, all reactions were performed under a nitrogen atmosphere using freshly distilled solvents, and workups were carried out in air. Toluene, EtOAc, DCM, DMF, dioxane and THF were distilled over dehydrating reagents. Commercially available reagents were used without further purification. Melting points were obtained using a Haacke-Buchler variable temperature melting point apparatus (model: SGW X-4) and are uncorrected. Infrared spectra were recorded using a PerkinElmer Spectrum 100 FTIR. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using a Varian MERCURY plus-400 spectrometer with TMS as an internal standard. High resolution mass spectra (HMRS) were performed at the Shanghai Jiao Tong University Analytical Center. High performance liquid chromatography (HPLC) was performed on a Shimadzu LC-2010A liquid chromatograph using Chiralcel OD-H, AD-H and IE-H columns.

4.2. General procedure for the reduction of 2 to 3

The α-keto esters **2** (26.3 mmol) was dissolved in a mixed solvent of dichloromethane (75 mL) and MeOH (75 mL) and the solution was cooled to 0 °C. $NaBH_4$ (1.50 g, 39.6 mmol) was added in three portions over 1 h while the solution was allowed to warm to room temperature. After 2.5 h the reaction was completed according to TLC (EtOAc–DCM = 1 : 2). The mixture was cooled to 0 °C. Acetone was added and stirring was continued for 15 min. The solvent was evaporated *in vacuo* and the solid residue was dissolved in water (75 mL). The solution was acidified to pH 4 with citric acid. The solution was extracted with DCM (75 mL × 4) and dried with Na_2SO_4, and the solvent was evaporated *in vacuo*. After most of the solvent was removed, petroleum ether was added into it, and diol **3** was recrystallised and filtered. A second crop could be obtained *via* the silica gel of the residue of the filtrate (EtOAc–DCM–PE = 1 : 1 : 1.5).

(*E*)-4-Phenylbut-3-ene-1,2-diol (3a).[7a] White pale crystal (3.45 g, yield: 80%). Mp: 77–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27 (br, 2H), 3.60 (dd, J = 7.2, 11.2 Hz, 1H), 3.76 (dd, J = 7.2, 11.2 Hz, 1H), 4.39–4.47 (m, 1H), 6.20 (dd, J = 2.4, 16.0 Hz, 1H), 6.70 (d, J = 16.0 Hz, 1H), 7.25–7.45 (m, 5H).

(*E*)-4-*o*-Tolylbut-3-ene-1,2-diol (3b). White pale crystal (4.03 g, yield: 86%). Mp: 77–79 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 2.71 (br, 2H), 3.61 (dd, J = 8.0, 11.2 Hz, 1H), 3.73–3.78 (m, 1H), 4.35–4.60 (m, 1H), 6.07 (dd, J = 6.4, 16.0 Hz, 1H), 6.90 (d, J = 16.4 Hz, 1H), 7.12–7.44 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.0, 66.8, 73.9, 125.9, 126.4, 128.0, 129.2, 130.2, 130.6, 135.6, 135.8; IR (ν/cm^{-1}): 3267, 2925, 1807, 1645, 1602, 1486, 1461, 1354, 1084, 1064, 968, 892, 750, 683; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 179.1067, found: 179.1072.

(*E*)-4-*m*-Tolylbut-3-ene-1,2-diol (3c).[11] Transparent ointment (3.75 g, yield: 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.03 (t, J = 5.2 Hz, 1H), 2.26 (d, J = 4.0 Hz, 1H), 2.34 (s, 3H), 3.58–3.63 (m, 1H), 3.75–3.77 (m, 1H), 4.42–4.47 (m, 1H), 6.19 (dd, J = 6.4,

16.0 Hz, 1H), 6.66 (dd, J = 0.6, 16.0 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 7.17–7.23 (m, 3H).

(*E*)-4-*p*-Tolylbut-3-ene-1,2-diol (3d). White pale crystal (4.17 g, yield: 89%). Mp: 108–109 °C. ^{1}H NMR δ (400 MHz, DMSO-d_6): δ 2.26 (s, 3H), 3.45 (dd, J = 0.8, 5.6 Hz, 2H), 4.07–4.11 (m, 1H), 4.52 (br, 2H), 6.21 (dd, J = 6.0, 16.0 Hz, 1H), 6.52 (dd, J = 0.8, 16.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 21.4, 66.7, 72.9, 126.7, 129.5, 129.8, 131.1, 134.8, 137.1; IR (ν/cm^{-1}): 3307, 3215, 2926, 2866, 1673, 1513, 1426, 1404, 1301, 1056, 1019, 975, 892, 803, 655; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 179.1067, found: 179.1072.

(*E*)-4-(4-Methoxyphenyl)but-3-ene-1,2-diol (3e).[12] White pale crystal (4.60 g, yield: 90%). Mp: 87–89 °C.

(*E*)-4-(2-Fluorophenyl)but-3-ene-1,2-diol (3f). White pale crystal (4.12 g, yield: 86%). Mp: 54–56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02 (br, 1H), 2.30 (br, 1H), 3.62 (dd, J = 7.6, 14.8 Hz, 1H), 3.78 (d, J = 10.8 Hz, 1H), 4.43–4.47 (m, 1H), 6.30 (dd, J = 6.0, 16.4 Hz, 1H), 6.85 (d, J = 16.0 Hz, 1H), 7.04 (ddd, J = 1.2, 8.0, 10.8 Hz, 1H), 7.09 (td, J = 1.2, 8.0 Hz, 1H), 7.19–7.26 (m, 1H), 7.44 (td, J = 1.2, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 66.6, 73.6, 115.8, 116.0, 124.3 (d, J = 2.9 Hz), 124.6 (d, J = 3.6 Hz), 127.8 (d, J = 3.2 Hz), 129.3 (d, J = 8.4 Hz), 130.6 (d, J = 4.3 Hz), 160.5 (d, J = 247.9 Hz); IR (ν/cm^{-1}): 3447, 2928, 2880, 1676, 1504, 1475, 1460, 1441, 1427, 1404, 1301, 1264, 1114, 985, 763, 657; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 183.0816, found: 183.0821.

(*E*)-4-(4-Fluorophenyl)but-3-ene-1,2-diol (3g). White pale crystal (4.12 g, yield: 86%). Mp: 61–63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.06 (br, 2H), 3.59 (dd, J = 7.2, 11.2 Hz, 1H), 3.76 (dd, J = 3.6, 10.8 Hz, 1H), 4.42 (d, J = 3.6 Hz, 1H), 6.12 (dd, J = 6.4, 16.0 Hz, 1H), 6.66 (d, J = 16.0 Hz, 1H), 6.98–7.03 (t, J = 8.4 Hz, 2H), 7.33–7.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 66.7, 73.4, 115.8 (d, J = 21.4 Hz), 127.6 (d, J = 2.0 Hz), 128.3 (d, J = 8.0 Hz), 131.1, 132.7 (d, J = 3.0 Hz); IR (ν/cm^{-1}): 3388, 2925, 2871, 1658, 1602, 1509, 1457, 1408, 1384, 1229, 1093, 1074, 1031, 972, 849, 810; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 183.0816, found: 183.0821.

(*E*)-4-(4-Chlorophenyl)but-3-ene-1,2-diol (3h). White pale crystal (4.28 g, yield: 82%). Mp: 96–98 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.35 (d, J = 6.4 Hz, 2H), 4.09–4.13 (m, 1H), 4.68 (br, 1H), 4.98 (br, 1H), 6.33 (dd, J = 5.6, 16.0 Hz, 1H), 6.55 (dd, J = 1.2, 16.0 Hz, 1H), 7.33–7.44 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.5, 72.8, 128.3, 128.5, 129.2, 132.2, 133.3, 136.5; IR (ν/cm^{-1}): 3387, 2926, 2873, 1667, 1505, 1491, 1474, 1459, 1441, 1426, 1405, 1302, 1262, 1114, 1090, 1030, 1013, 973, 806, 658; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 199.0520, found: 199.0526.

(*E*)-4-(4-Bromophenyl)but-3-ene-1,2-diol (3i). White powder (4.99 g, yield: 78%). Mp: 110–111 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.35 (dd, J = 1.2, 6.0 Hz, 2H), 4.08–4.13 (m, 1H), 4.76 (br, 2H), 6.34 (dd, J = 5.6, 16.0 Hz, 1H), 6.53 (dd, J = 1.6, 16.0 Hz, 1H), 7.34–7.49 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.5, 72.8, 120.7, 128.3, 128.9, 132.1, 133.5, 136.9. IR (ν/cm^{-1}): 3421, 2927, 2878, 1677, 1504, 1488, 1474, 1460, 1440, 1427, 1403, 1300, 1263, 1113, 1071, 984, 657. HR-ESI-MS: $[M + H]^+$ m/z calcd for: 243.0015, found: 243.0021.

(*E*)-4-(4-(Trifluoromethyl)phenyl)but-3-ene-1,2-diol (3j). White pale crystal (4.52 g, yield: 74%). Mp: 67–69 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.03 (br, 1H), 2.39 (br, 1H), 3.61 (dd, J = 7.2, 11.2 Hz, 1H), 3.79 (dd, J = 3.6, 10.4 Hz, 1H), 4.45–4.49 (m, 1H), 6.31 (dd, J = 6.4, 16.0 Hz, 1H), 6.74 (d, J = 16.0 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 66.6, 73.1, 125.7, 125.7, 125.8, 126.8, 130.5, 130.7, 139.9; IR (ν/cm^{-1}): 3378, 2929, 2875, 1666, 1615, 1506, 1460, 1443, 1427, 1409, 1327, 1305, 1164, 1119, 1068, 864, 817, 655, 600; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 233.0784, found: 233.0789.

(*E*)-4-(Naphthalen-1-yl)but-3-ene-1,2-diol (3k). White pale crystal (4.85 g, yield: 86%). Mp: 116–118 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.34 (br, 2H), 3.44 (d, J = 6.0 Hz, 1H), 4.24–4.25 (m, 1H), 6.32 (dd, J = 16.0, 5.2 Hz, 1H), 7.35 (d, J = 16.0 Hz, 1H), 7.45–7.55 (m, 3H), 7.62 (d, J = 5.8 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.90–7.92 (m, 1H), 8.15 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.7, 73.1, 123.9, 124.2, 126.3, 126.4, 126.5, 126.8, 128.1, 129.1, 131.2, 134.0, 135.0, 135.5; IR (ν/cm^{-1}): 3453, 2928, 2880, 1676, 1505, 1474, 1460, 1440, 1427, 1404, 1301, 1264, 1114, 985, 657; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 214.1109, found: 215.1072.

(*E*)-4-(Naphthalen-2-yl)but-3-ene-1,2-diol (3l). White pale crystal (4.62 g, yield: 82%). Mp: 146–148 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.31 (d, J = 8.0 Hz, 1H), 3.39 (t, J = 6.0 Hz, 1H), 4.15–4.18 (m, 1H), 4.69 (t, J = 6.0 Hz, 1H), 5.01 (d, J = 4.4 Hz, 1H), 6.45 (dd, J = 16.0, 5.6 Hz, 1H), 6.73 (d, J = 16.0 Hz, 1H), 7.43–7.47 (m, 2H), 7.65–7.67 (m, 1H), 7.81–7.86 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 66.7, 73.0, 124.3, 126.3, 126.4, 127.0, 128.2, 128.4, 128.7, 129.6, 132.9, 133.0, 133.9, 135.2; IR (ν/cm^{-1}): 3470, 2928, 2881, 1678, 1505, 1474, 1460, 1440, 1427, 1404, 1300, 1264, 1113, 985, 657; HR-ESI-MS: $[M + Na]^+$ m/z calcd for: 237.0852, found: 237.0891.

4.3. General method for the preparation of the substrates 1

K_2CO_3 (2.0 g) was added to a solution of diol **3** (20 mmol) in dimethyl carbonate (35 mL). The mixture was stirred at 100 °C for 4 hours and monitored by TLC (EtOAc–PE = 1/6). The remaining K_2CO_3 was filtered off. The filtrate was evaporated *in vacuo*. The residue was redissolved in DCM and filtered through a pad of silica gel. The crude product was obtained through the evaporation of DCM and the pure product **1** was obtained *via* recrystallization in DCM and PE.

(*E*)-4-Styryl-1,3-dioxolan-2-one (1a).[3b] White crystal (3.39 g, yield: 89%). Mp: 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (t, J = 8.0 Hz, 1H), 4.65 (t, J = 8.0 Hz, 1H), 5.30 (q, J = 8.0 Hz, 1H), 6.18 (dd, J = 8.0, 16.0 Hz, 1H), 6.78 (d, J = 16.0 Hz, 1H), 7.33–7.43 (m, 5H).

(*E*)-4-(2-Methylstyryl)-1,3-dioxolan-2-one (1b). White crystal (3.19 g, yield: 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H), 4.25 (t, J = 8.0 Hz, 1H), 4.67 (t, J = 8.0 Hz, 1H), 5.32 (q, J = 8.0 Hz, 1H), 6.08 (dd, J = 8.0, 16.0 Hz, 1H), 7.02 (d, J = 16.0 Hz, 1H), 7.18–7.25 (m, 3H), 7.43–7.46 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.9, 69.7, 78.3, 123.9, 126.2, 126.6, 129.1, 130.8, 134.1, 135.0, 136.4, 155.1; IR (ν/cm^{-1}): 3552, 3455, 2968, 2911, 2360, 2344, 1860, 1758, 1648, 1489, 1480, 1400, 1385, 1360,

1312, 1164, 1073, 1049, 974, 784, 777, 768, 709; HRMS (FAB) Calcd for $(M + H)^+$ $C_{12}H_{13}O_3$: 205.0859; Found: 205.0865.

(*E*)-4-(3-Methylstyryl)-1,3-dioxolan-2-one (1c). White crystal (3.10 g, yield: 76%). Mp: 46–47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H), 4.23 (t, J = 8.0 Hz, 1H), 4.65 (t, J = 8.4 Hz, 1H), 5.29 (q, J = 8.0 Hz, 1 H), 6.17 (dd, J = 8.0, 16.0 Hz, 1H), 6.75 (d, J = 15.6 Hz, 1H), 7.11–7.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 69.5, 78.2, 122.3, 124.4, 127.9, 129.0 (d, J = 16.7 Hz), 130.2, 134.9, 137.3, 138.7, 155.1; IR (ν/cm^{-1}): 1807, 1783, 1653, 1474, 1394, 1359, 1323, 1176, 1070, 1041, 981, 881, 780, 710, 690, 513; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 205.0859, found: 205.0865.

(*E*)-4-(4-Methylstyryl)-1,3-dioxolan-2-one (1d). White crystal (3.51 g, yield: 86%). Mp: 94–95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (s, 3H), 4.22 (t, J = 8.4 Hz, 1H), 4.63 (t, J = 8.4 Hz, 1H), 5.28 (q, J = 8 Hz, 1H), 6.12 (dd, J = 8.0, 16.0 Hz, 1H), 6.74 (d, J = 16.0 Hz, 1H), 7.17 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 69.6, 78.4, 121.4, 127.2, 129.8, 132.2, 137.2, 139.5, 155.2; IR (ν/cm^{-1}): 1792, 1655, 1513, 1393, 1358, 1320, 1207, 1188, 1073, 1050, 973, 896, 801, 770, 716, 511, 483; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 205.0859, found: 205.0865.

(*E*)-4-(4-Methoxylstyryl)-1,3-dioxolan-2-one (1e). White crystal (3.79 g, yield: 86%). Mp: 73–74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (s, 3H), 4.21 (t, J = 8.0 Hz, 1H), 4.62 (t, J = 8.0 Hz, 1H), 5.26 (q, J = 8.0 Hz, 1H), 6.02 (dd, J = 8.0, 16.0 Hz, 1H), 6.71 (d, J = 16.0 Hz, 1H), 6.87 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8,0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.6, 69.7, 78.6, 114.4, 120.1, 127.7, 128.6, 136.9, 155.3, 160.6; IR (ν/cm^{-1}): 1808, 1780, 1651, 1606, 1513, 1369, 1328, 1301, 1253, 1178, 1137, 1074, 1040, 983, 889, 851, 812, 775, 709; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 221.0808, found: 221.0814.

(*E*)-4-(2-Fluorostyryl)-1,3-dioxolan-2-one (1f). White crystal (3.41 g, yield: 82%). Mp: 49–50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25 (t, J = 8.0 Hz, 1H), 4.67 (t, J = 8.0 Hz, 1H), 5.31 (q, J = 7.6 Hz, 1H), 6.30 (dd, J = 7.6, 16.0 Hz, 1H), 6.91 (d, J = 16.0 Hz, 1H), 7.01–7.19 (m, 2H), 7.26–7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.5, 78.1, 116.2, 116.4, 124.6 (d, J = 2.8 Hz), 125.3 (d, J = 5.9 Hz), 128.3 (d, J = 3.7 Hz), 129.7 (d, J = 2.9 Hz), 130.8 (d, J = 8.7 Hz), 155.0, 161.0 (d, J = 248.8 Hz); IR (ν/cm^{-1}): 1789, 1652, 1610, 1578, 1493, 1478, 1402, 1366, 1334, 1230, 1176, 1073, 1049, 975, 935, 865, 768, 710, 490, 471; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 209.0608, found: 209.0614.

(*E*)-4-(4-Fluorostyryl)-1,3-dioxolan-2-one (1g). White crystal (3.80 g, yield: 91%). Mp: 56–57 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (t, J = 8.0 Hz, 1H), 4.65 (t, J = 8.4 Hz, 1H), 5.29 (q, J = 8.0 Hz, 1H), 6.10 (dd, J = 8.0, 16.0 Hz, 1H), 6.75 (d, J = 16.0 Hz, 1H), 7.02–7.07 (m, 2H), 7.37–7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.6, 78.0, 116.1 (d, J = 21.9 Hz), 122.3 (d, J = 2.3 Hz), 128.9 (d, J = 8.5 Hz), 131.2 (d, J = 4.0 Hz) 135.9, 155.0; IR (ν/cm^{-1}): 1809, 1780, 1603, 1511, 1240, 1179, 1041, 982, 855, 818, 774; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 209.0608, found: 209.0614.

(*E*)-4-(4-Chlorostyryl)-1,3-dioxolan-2-one (1h). White crystal (3.95 g, yield: 88%). Mp: 75–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (t, J = 8.0 Hz, 1H), 4.66 (t, J = 8.4 Hz, 1H), 5.29 (q, J = 8.0 Hz, 1H), 6.16 (dd, J = 8.0, 16.0 Hz, 1H), 6.74 (d, J = 16.0 Hz, 1H), 7.30–7.35 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.5, 77.8, 123.2, 128.4, 129.3, 133.5, 135.1, 135.7, 155.0; IR (ν/cm^{-1}): 1779, 1652, 1591, 1494, 1396, 1368, 1191, 1071, 1053, 1009, 975, 807, 776; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 225.0313, found: 225.0318.

(*E*)-4-(4-Bromostyryl)-1,3-dioxolan-2-one (1i). White crystal (4.95 g, yield: 92%). Mp: 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (dd, J = 7.6, 8.8 Hz, 1H), 4.65 (t, J = 8.4 Hz, 1H), 5.29 (qd, J = 0.8, 8.0 Hz, 1 H), 6.17 (dd, J = 8.0, 16.0 Hz, 1H), 6.72 (d, J = 8.0 Hz 1H), 7.24–7.30 (m, 2H), 7.45–7.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.5, 77.7, 123.3, 123.4, 128.7, 132.2, 133.9, 135.7, 154.9; IR (ν/cm^{-1}): 1789, 1488, 1392, 1362, 1326, 1183, 1169, 1075, 1049, 1010, 975, 807, 776; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 268.9808, found: 268.9813.

(*E*)-4-(4-(Trifluoromethyl)styryl)-1,3-dioxolan-2-one (1j). White crystal (4.80 g, yield: 93%). Mp: 52–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (t, J = 8.0 Hz, 1H), 4.68 (t, J = 8.0 Hz, 1H), 5.33 (q, J = 8.0 Hz, 1H), 6.28 (dd, J = 8.0, 16.0 Hz, 1H), 6.83 (d, J = 16.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.4, 77.4, 125.3, 126.1 (q, J = 3.6 Hz), 127.4, 130.8, 131.2, 135.1, 138.4, 154.8; IR (ν/cm^{-1}): 1813, 1782, 1367, 1331, 1176, 1131, 1108, 1072, 1041, 977, 865, 824, 775, 710, 599; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 259.0577, found: 259.0582.

(*E*)-4-(2-(Naphthalen-1-yl)vinyl)-1,3-dioxolan-2-one (1k). White crystal (2.69 g, yield: 56%). Mp: 124–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.29 (t, J = 8.0 Hz, 1H), 4.70 (t, J = 8.0 Hz, 1H), 5.41 (q, J = 8.0 Hz, 1H), 6.21 (dd, J = 8.0, 16.0 Hz, 1H), 7.40–8.15 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.6, 78.1, 123.5, 124.8, 125.7, 125.8, 126.4, 126.9, 129.0, 129.6, 131.2, 132.7, 133.8, 134.4, 155.1; IR (ν/cm^{-1}): 1797, 1652, 1470, 1328, 1168, 1051, 973, 935, 803, 783, 775; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 241.0859, found: 241.0865.

(*E*)-4-(2-(Naphthalen-2-yl)vinyl)-1,3-dioxolan-2-one (1l). White crystal (3.36 g, yield: 70%). Mp: 141–142 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.29 (t, J = 8.0 Hz, 1H), 4.69 (t, J = 8.0 Hz, 1H), 5.36 (q, J = 8.0 Hz, 1H), 6.30 (dd, J = 8.0, 16.0 Hz, 1H), 6.94 (d, J = 16.0 Hz, 1H), 7.48–7.61 (m, 3H), 7.79–7.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.6, 78.2, 122.7, 123.4, 126.9, 127.0, 128.0, 128.2, 128.5, 128.9, 132.4, 133.5, 133.8, 137.2, 155.1. IR (ν/cm^{-1}): 1804, 1781, 1650, 1472, 1368, 1324, 1175, 1137, 1072, 1039, 983, 879, 815, 742, 709, 478; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 241.0859, found: 241.0865.

4.4. General procedure for Pd-catalyzed asymmetric allylic amination

Ferrocene based phosphinooxazoline ligand (5.8 mg, 0.012 mmol) and π-allylpalladium chloride dimer (1.8 mg, 0.005 mmol) in a 10 mL flask were purged of air for 5 min. The procedure was repeated two more times before THF (1.0 mL, degassed by a freeze–pump–thaw method) was added and the resulting solution was allowed to stir for 60 min. Substrates **1** (0.20 mmol) and potassium phthalimide (41.7 mg, 0.225 mmol) were added to a separated flask, and the air was purged with nitrogen. Degassed THF (1 mL, degassed by a

freeze–pump–thaw method) was added. The catalyst solution was then added to the suspension of the substrate. After stirring for the corresponding time (see Table 3) at 20 °C, the solvent was removed *in vacuo* and the reaction mixture was quenched by the addition of an ammonium chloride saturated solution and extracted with EtOAc. The organic layer (20 mL × 2) was dried with Na_2SO_4, and the solvent was removed *in vacuo*. The residue was purified by column chromatography on silica gel (gradient, 5% to 25% EtOAc–PE) to afford the corresponding product **4**.

(*E*)-2-(1-Hydroxy-4-phenylbut-3-en-2-yl)isoindoline-1,3-dione (4a).[13] Light yellow solid (54.0 mg, yield: 92%). Mp: 89–90 °C. The enantiomeric excess was determined by HPLC (Chiralcel AD-H, hexane–i-PrOH = 70 : 30, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 19.4 min (minor) and t_{R2} = 20.5 min (major); ee = 95%.

(*E*)-2-(1-Hydroxy-4-*o*-tolylbut-3-en-2-yl)isoindoline-1,3-dione (4b). White ointment (48.0 mg, yield: 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 4.03 (dd, J = 5.2, 11.6 Hz, 1H), 4.22 (dd, J = 8.0, 11.2 Hz, 1H), 5.07–5.14 (m, 1H), 6.43 (dd, J = 8.0, 15.2 Hz, 1H), 6.90 (d, J = 15.2 Hz, 1H), 7.09–7.16 (m, 3H), 7.42–7.47 (m, 1H), 7.70–7.78 (m, 1H), 7.82–7.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.0, 56.2, 63.5, 123.6, 123.8, 124.3, 126.1, 126.3, 128.3, 130.5, 132.1, 132.8, 134.4, 134.5, 135.3, 135.9, 168.8; IR (ν/cm^{-1}): 3458, 3212, 3061, 2927, 1714, 1607, 1485, 1467, 1377, 1307, 1261, 1172, 1047, 968, 875, 799, 752, 719, 645, 530; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 308.1287, found: 308.1276. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 55.9 min (minor) and t_{R2} = 63.6 min (major); ee = 91%; $[\alpha]_D^{25}$: −18.9 (c 0.28, $CHCl_3$).

(*E*)-2-(1-Hydroxy-4-*m*-tolylbut-3-en-2-yl)isoindoline-1,3-dione (4c). Light yellow oil (51.0 mg, yield: 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31(s, 3H), δ 4.03 (dd, J = 4.8, 11.2 Hz, 1H), 4.21 (dd, J = 8.0, 11.2 Hz, 1H), 5.04–5.12 (m, 1H), 6.56 (dd, J = 7.6, 16.0 Hz, 1H), 6.64 (d, J = 15.6 Hz, 1H), 7.02–7.24 (m, 4H), 7.69–7.79 (m, 2H), 7.81–7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 56.0, 63.5, 122.8, 123.7, 123.8, 124.2, 127.5, 128.7, 129.2, 132.1, 134.4, 135.0, 136.1, 168.8; IR (ν/cm^{-1}): 3436, 2929, 2881, 1772, 1711, 1669, 1504, 1387, 1325, 1302, 1164, 1117, 1067, 723, 659; HR-ESI-MS: $[M + Na]^+$ m/z calcd for: 330.1123, found: 330.1106; The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 54.0 min (minor) and t_{R2} = 58.0 min (major); ee = 92%; $[\alpha]_D^{25}$: −15.2 (c 0.20, $CHCl_3$).

(*E*)-2-(1-Hydroxy-4-*p*-tolylbut-3-en-2-yl)isoindoline-1,3-dione (4d). Light yellow oil (50.4 mg, yield: 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 4.02 (dd, J = 4.8, 11.6 Hz, 1H), 4.20 (dd, J = 8.0, 11.6 Hz, 1H), 5.03–5.11 (m, 1H), 6.54 (dd, J = 8.0, 16.0 Hz, 1H), 6.64 (d, J = 16.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 11.2 Hz, 2H), 7.70–7.77 (m, 2H), 7.83–7.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.5, 52.2, 59.5, 118.0, 119.7, 119.9, 122.9, 125.5, 128.1, 130.4, 130.6, 130.9, 164.9; IR (ν/cm^{-1}): 3427, 2926, 1772, 1709, 1668, 1467, 1387, 1303, 1053, 971, 875, 802, 721, 530; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 308.1297, found: 308.1287; The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 53.4 min (minor) and t_{R2} = 64.8 min (major); ee = 92%; $[\alpha]_D^{25}$: −25.6 (c 0.20, $CHCl_3$).

(*E*)-2-(1-Hydroxy-4-(4-methoxyphenyl)but-3-en-2-yl)isoindoline-1,3-dione (4e).[13] White ointment (56.3 mg, yield: 87%). IR (ν/cm^{-1}): 3439, 2931, 1771, 1708, 1666, 1607, 1512, 1387, 1334, 1071, 1009, 970, 875, 806, 719, 530. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 86.8 min (minor) and t_{R2} = 110.6 min (major); ee = 87%; $[\alpha]_D^{25}$: −18.2 (c 0.20, $CHCl_3$).

(*E*)-2-(4-(2-Fluorophenyl)-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (4f). White ointment (57.3 mg, Yield: 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (dd, J = 4.4, 11.2 Hz, 1H), 4.21 (dd, J = 8.0, 11.6 Hz, 1H), 5.05–5.13 (m, 1H), 6.64 (dd, J = 8.0, 16.0 Hz, 1H), 6.81 (d, J = 16.0 Hz, 1H), 6.94–7.52 (m, 4H), 7.66–7.88 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.1, 63.4, 115.8, 116.1, 123.7, 124.3, 125.7, 127.1, 127.8, 129.6, 129.7, 132.0, 134.4, 168.8; IR (ν/cm^{-1}): 3401, 2933, 2880, 1772, 1710, 1668, 1487, 1388, 1371, 1302, 1229, 1108, 1065, 971, 875, 760, 722, 530; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 312.1044, found: 312.1036; The enantiomeric excess was determined by HPLC (Chiralcel IE-H, hexane–i-PrOH = 70 : 30, UV = 254 nm, flow rate = 1.0 mL min^{-1}): t_{R1} = 14.5 min (minor) and t_{R2} = 15.9 min (major); ee = 98%; $[\alpha]_D^{25}$: −1.2 (c 0.20, $CHCl_3$).

(*E*)-2-(4-(4-Fluorophenyl)-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (4g). White ointment (54.8 mg, yield: 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (dd, J = 4.8, 11.2 Hz, 1H), 4.18–4.22 (m, 1H), 5.03–5.08 (m, 1H), 6.54 (dd, J = 8.0, 16.0 Hz, 1H), 6.61 (d, J = 16.0 Hz, 1H), 6.70–6.95 (m, 2H), 7.24–7.32 (m, 4H) 7.70–7.74 (m, 2H), 7.83–7.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.9, 63.3, 115.6, 115.8, 122.9, 123.7, 128.4, 128.5, 132.0, 133.6, 134.4; IR (ν/cm^{-1}): 3439, 2927, 1771, 1707, 1601, 1509, 1388, 1369, 1334, 1228, 1159, 1088, 1045, 970, 818, 721, 529; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 312.1023, found: 312.1036. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 64.1 min (minor) and t_{R2} = 68.2 min (major); ee = 80%; $[\alpha]_D^{25}$: −4.1 (c 0.20, $CHCl_3$).

(*E*)-2-(4-(4-Chlorophenyl)-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (4h). White ointment (59.0 mg, yield: 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (dd, J = 4.8, 11.6 Hz, 1H), 4.20 (dd, J = 8.0, 12.0 Hz, 1H), 5.03–5.09 (m, 1H), 6.54 (dd, J = 7.2, 16.0 Hz, 1H), 6.61 (d, J = 16.0 Hz, 1H), 7.20–7.34 (m, 4H), 7.70–7.76 (m, 1H), 7.82–7.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.9, 63.3, 123.7, 123.9, 128.1, 129.0, 132.0, 133.5, 134.0, 134.5, 134.7, 168.8; IR (ν/cm^{-1}): 3441, 2928, 1771, 1708, 1668, 1491, 1467, 1387, 1370, 1089, 1064, 1039, 1013, 970, 809, 720; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 328.0727, found: 328.0740. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 71.4 min (minor) and t_{R2} = 78.3 min (major); ee = 90%; $[\alpha]_D^{25}$: −8.0 (c 0.23, $CHCl_3$).

(*E*)-2-(4-(4-Bromophenyl)-1-hydroxybut-3-en-2-yl)isoindoline-1,3-dione (4i). White ointment (57.3 mg, yield: 77%). ^{1}H NMR

(400 MHz, $CDCl_3$): δ 4.02 (dd, J = 4.8, 11.6 Hz, 1H), 4.20 (dd, J = 8.0, 12.0 Hz, 1H), 5.02–5.09 (m, 1H), 6.54–6.61 (m, 2H), 7.20–7.28 (m, 2H), 7.37–7.44 (m, 2H), 7.69–7.77 (m, 2H), 7.81–7.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.9, 63.3, 123.7, 124.0, 128.4, 131.9, 132.0, 133.6, 134.5, 134.6, 135.2, 168.8; IR (ν/cm^{-1}): 3453, 2927, 1771, 1708, 1487, 1467, 1387, 1334, 1071, 1009, 970, 875, 806, 719, 530; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 372.0249, found: 372.0235. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 76.0 min (minor) and t_{R2} = 83.3 min (major); ee = 89%; $[\alpha]_D^{25}$: −8.9 (c 0.23, $CHCl_3$).

(*E*)-2-(1-Hydroxy-4-(4-(trifluoromethyl)phenyl)but-3-en-2-yl)-isoindoline-1,3-dione (4j). White ointment (65.8 mg, yield: 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.05 (dd, J = 4.4, 11.6 Hz, 1H), 4.22 (dd, J = 7.2, 12.0 Hz, 1H), 5.06–5.14 (m, 1H), 6.65–6.69 (m, 2H), 7.44–7.57 (m, 4H), 7.70–7.77 (m, 2H), 7.84–7.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.7, 63.4, 123.8, 123.8, 125.7, 125.7, 125.8, 125.8, 126.0, 127.1, 132.0, 133.2, 134.6, 139.6, 168.8; IR (ν/cm^{-1}): 3421, 2926, 1772, 1711, 1686, 1671, 1467, 1386, 1301, 1053, 780, 722; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 362.0972, found: 362.1004. The enantiomeric excess was determined by HPLC (Chiralcel AD-H, hexane–i-PrOH = 80 : 20, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 30.2 min (major) and t_{R2} = 32.2 min (minor); ee = 91%; $[\alpha]_D^{25}$: −11.0 (c 0.20, $CHCl_3$).

(*E*)-2-(1-Hydroxy-4-(naphthalen-1-yl)but-3-en-2-yl)isoindoline-1,3-dione (4k). White ointment (49.4 mg, yield: 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.11 (dd, J = 5.2, 11.6 Hz, 1H), 4.28 (dd, J = 8.0, 11.6 Hz, 1H), 5.19–5.26 (m, 1H), 6.60 (dd, J = 7.6, 15.6 Hz, 1H), 7.38–7.64 (m, 6H), 7.70–8.07 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 63.6, 123.8, 123.9, 124.6, 125.8, 126.1, 126.4, 126.5, 128.8, 128.8, 131.3, 132.1, 133.8, 134.0, 134.6, 168.9; IR (ν/cm^{-1}): 3442, 2927, 1771, 1708, 1666, 1467, 1387, 1067, 969, 798, 777, 720; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 344.1271, found: 344.1287; The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 101.0 min (minor) and t_{R2} = 110.3 min (major); ee = 88%; $[\alpha]_D^{25}$: −23.3 (c 0.60, $CHCl_3$).

(*E*)-2-(1-Hydroxy-4-(naphthalen-2-yl)but-3-en-2-yl)isoindoline-1,3-dione (4l). White ointment (48.1 mg, yield: 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (dd, J = 5.6, 10.8 Hz, 1H), 4.26 (dd, J = 8.0, 11.6 Hz, 1H), 5.10–5.18 (m, 1H), 6.70 (dd, J = 7.6, 15.6 Hz, 1H), 6.83 (d, J = 16.0 Hz, 1H), 7.40–7.62 (m, 3H), 7.67–7.80 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 63.5, 123.5, 123.7, 123.8, 126.4, 126.6, 127.2, 127.9, 128.3, 128.5, 132.1, 133.5, 133.7, 133.7, 134.5, 135.0, 168.9; IR (ν/cm^{-1}): 3393, 2930, 2879, 1772, 1709, 1669, 1505, 1467, 1426, 1386, 1301, 1264, 1114, 1066, 970, 874, 816, 749, 723; HR-ESI-MS: $[M + H]^+$ m/z calcd for: 344.1278, found: 344.1287. The enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane–i-PrOH = 95 : 5, UV = 254 nm, flow rate = 0.5 mL min^{-1}): t_{R1} = 106.6 min (minor) and t_{R2} = 162.9 min (major); ee = 87%; $[\alpha]_D^{25}$: −8.1 (c 0.30, $CHCl_3$).

4.5. The synthesis of (*E*)-2-amino-4-phenylbut-3-en-1-ol (5a)[7a]

A mixture of **4a** (200 mg, 0.669 mmol) and ethylenediamine (178 μL, 2.67 mmol) in 15 mL of absolute ethanol was stirred at reflux for 12 h. The white precipitate was filtered and the filtrate was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (20% EtOAc–PE) to afford the corresponding product **5a** as a white crystal (99.1 mg, yield: 91%). Mp: 96–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.45 (dd, J = 7.6, 11.4 Hz, 1H), 3.59–3.69 (m, 2H), 6.15 (dd, J = 7.2, 16.0 Hz, 1H), 6.55 (d, J = 16.0 Hz, 1H), 7.15–7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 55.6, 66.6, 126.6, 127.9, 128.8, 130.6, 131.1, 136.9; $[\alpha]_D^{20}$: −24.8 (c 0.31, $CHCl_3$).

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