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Visible Light Photocatalytic Radical–Radical Cross-Coupling Reactions of Amines and Carbonyls: A Route to 1,2-Amino Alcohols

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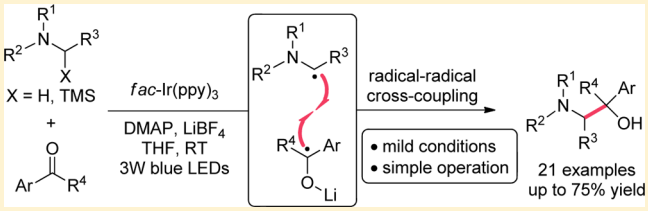
Supporting Information

ABSTRACT: An intermolecular radical–radical cross-coupling reaction of secondary and tertiary amines with aryl ketones and aldehydes has been developed using visible light photoredox catalysis. This reaction provides an efficient and straightforward approach to some useful 1,2-amino alcohols in moderate to good yields under mild conditions.



INTRODUCTION

1,2-Amino alcohols are a type of structural motif found in a variety of bioactive natural products and pharmaceutical agents.[1] In addition, these compounds are important building scaffolds for the synthesis of various chiral ligands, auxiliaries, and bioactive compounds (Scheme 1).[2] Considerable research efforts have been devoted to search for new and more efficient synthetic methods for 1,2-amino alcohols. Traditionally, these scaffolds have been prepared by reduction of amino acids or their derivatives with strong reductants[3] or transition metal-catalyzed aminohydroxylation of olefins.[4−6] However, many of these methods require harsh reaction conditions and result in low atom economy or unsatisfactory regioselectivity. Therefore, the development of more efficient and straightforward protocols for the construction of diverse 1,2-amino alcohol products under mild conditions using readily available starting materials is still highly desirable.[7]

Over the past decade, photoredox catalysis driven by visible light has attracted increasing interest from synthetic chemists due to its inherent green and sustainable features.[8] This strategy has been successfully applied to a wide range of transformations including radical–radical coupling reactions to construct valuable organic molecules.[9] In 2011, MacMillan and co-workers reported the first visible-light-induced C–H arylation of various tertiary amines with cyanoaromatics via a radical–radical cross-coupling process, which afforded an efficient method for the construction of benzylic amines.[9a] Then, this synergistic strategy was successfully expanded to the β-hydroxyalkylation of cyclic ketones with aryl ketones via a combination of photoredox catalysis and organocatalysis (Scheme 2a).[9b] Critical to these successes is the simultaneous activation of the two coupling partners in a single photoredox catalytic cycle: oxidation of intermediate enamines to β-enaminyl radicals and reduction of aryl ketones to ketyl radicals, followed by radical–radical coupling reactions. In 2015, our group reported a novel α-allylation of amines through a cross-coupling reaction of α-amino radical and allylic radical by combining visible light photoredox catalysis and palladium catalysis (Scheme 2b).[10] Therefore, we considered whether the α-amino radical and ketyl radical could be simultaneously generated in a single photoredox catalytic cycle, and the subsequent radical–radical cross-coupling reaction could provide a straightforward synthetic approach to 1,2-amino alcohols. As part of our ongoing efforts to develop novel photocatalytic reactions,[11] we designed and implemented this general methodology for 1,2-amino alcohol construction (Scheme 2c).

RESULTS AND DISCUSSION

During the preparation of this manuscript, Meggers and co-workers reported an elegant example of visible light photocatalytic asymmetric radical–radical coupling of amines and ketones in the presence of a chiral iridium catalyst.[12] In this case, only the tertiary aryl amine and quite electron-deficient heteroaryl trifluoromethyl ketones were suitable substrates for this transformation. Herein, we chose secondary amines **1a** as the model substrate for the reaction with benzophenone **2a** to investigate the feasibility of the proposed reaction. To our delight, the radical–radical cross-coupling reaction occurred smoothly in the presence of *fac*-Ir(ppy)$_3$ (2 mol %; ppy =2-phenylpyridine), 1,4-diazabicyclo[2.2.2]octane (DABCO, 2.0 equiv), and $LiBF_4$ (1.0 equiv) in THF under irradiation with 3 W blue LEDs (Table 1, entry 1),[13] which afforded the desired 1,2-amino alcohol (**3aa**) in 34% yield. Encouraged by this result, we continued to optimize the conditions by varying the reaction parameters to improve the reaction efficiency. A series of other commercially available iridium, ruthenium, and organic dye photocatalysts were evaluated (entries 2–4). We determined that an Ir complex photocatalyst (Ir(ppy)$_2$(dtbbpy)PF_6) could also catalyze this transformation,

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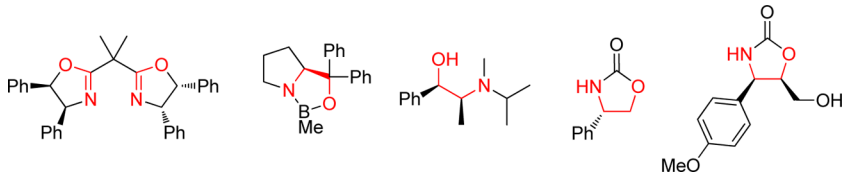
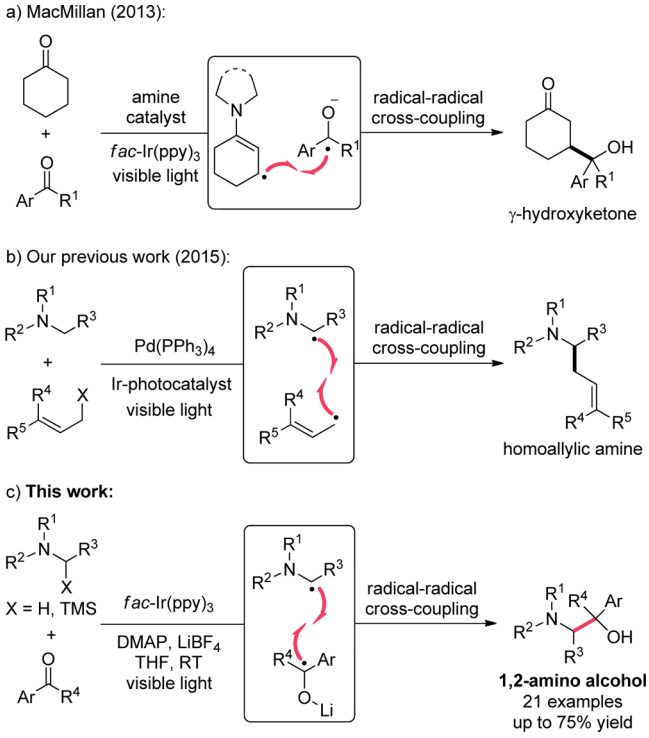
Scheme 1. Representative Chiral Ligands, Auxiliaries, and Bioactive Compounds Containing 1,2-Amino Alcohol Motifs



Scheme 2. Visible Light Photocatalytic Radical−Radical Coupling Reactions



albeit in lower yield (18% yield). In sharp contrast, no desired coupling product was observed when $Ru(bpy)_3Cl_2$ and eosin Y were employed. A survey of the reaction media for this photoreaction indicated that the transformation was sensitive to the solvent and THF was determined to be the best choice (entries 5−7). The substrate molar ratio on the reaction efficiency has been investigated, and it has been found that utilization of excess amine **1a** substantially improved the reaction efficiency (entry 8 and Table S2). Examination of a range of organic and inorganic bases (Table S2) revealed that 4-dimethylaminopyridine (DMAP), which acts as a base, was the most effective (entries 8−12). Therefore, we defined the reaction of secondary amines **1a** and benzophenone **2a** in the presence of *fac*-$Ir(ppy)_3$ (2 mol %), DMAP (2.0 equiv), and $LiBF_4$ (1.0 equiv)[14] in THF under irradiation with 3 W blue LEDs at room temperature as the standard conditions (entry 9). Finally, control experiments indicated that the photocatalyst, visible light, base, and $LiBF_4$ were all essential for this photochemical transformation (entries 13−16). In this reaction, the 1,2-diamine byproduct can be observed, which was generated by radical−radical homocoupling. We have performed the control experiments using only amine **1a** or ketone **2a** as substrate under the standard conditions. These reactions did not give the 1,2-diamine or 1,2-diol compound, and the substrate can be recovered from the reaction mixture (see section 3 in the Supporting Information for details).

With the optimized conditions in hand, we investigated the substrate scope of this photocatalytic radical−radical coupling reaction. As summarized in Table 2, a wide range of amines **1** and carbonyls **2** were suitable for this reaction. For the arylglycine ester substrates, incorporation of either electron-donating groups (Me and MeO) or electron-withdrawing groups (Br and Cl) on the benzene ring had no obvious impact on the reaction and the corresponding products (**3aa−3ea**) were obtained in 53−65% yields. The substrate bearing the naphthyl group on the nitrogen also tolerated the current conditions, and 1,2-amino alcohol **3fa** was obtained in moderate yield. Moreover, replacement of the ethyl ester group with other functional groups (i.e., methyl ester, cyano group, and cyclic amide) did not significantly affect the reaction efficiency, and the reactions afforded desired products **3ga−3ja** in 56−68% yields. In addition to secondary amines, tertiary amine *N*-phenyl tetrahydroisoquinoline was also suitable for this transformation, with conversion into corresponding product **3ka** in 49% yield. Next, the scope of the carbonyl substrates was investigated for this transformation. A range of substituted benzophenones and 9-fluorenone can serve as efficient coupling partners under our optimized conditions and afforded the vicinal amino alcohol products **3ab−3ad** in good yields. Unfortunately, when aryl-alkyl ketones and dialkyl ketones were used in this coupling protocol, the desired products were not obtained. To further expand the generality of this reaction, we tested more challenging aromatic aldehydes. As highlighted in Table 2, these substrates successfully participated in this transformation and afforded moderate yields of the corresponding products, albeit with low diastereoselectivities (**3ae−3ag**: 47−50% yields, 1.1:1 dr).

To further expand the substrate scope of this reaction, a range of *a*-silylamines were used as sources of *a*-amino radicals.[15] As disclosed in Table 3, the *N*,*N*-diaryl *a*-silylamine proved to be suitable substrates for this transformation, affording the corresponding amino alcohol product **3la** and **3ma** in high yields. The reaction of *N*-methyl-*N*-trimethylsilylmethylaniline and *N*-benzyl-*N*-trimethylsilylmethylaniline also proceeded smoothly to give the desired products in 65% and 67% yield, respectively.

To demonstrate the synthetic utility of this method, a reaction of substrates **1a** and **2a** has been performed on a gram-scale under the optimal conditions. This photocatalytic radical−radical crossing-coupling reaction could proceed well to afford the desired product **3aa** (1.06 g) without loss of the reaction efficiency (Scheme 3a, 57% yield). Additionally, this reaction proceeded well by directly applying sunlight as the light source, delivering the 1,2-amino alcohol product **3aa** in a shorter reaction time and comparable yield (Scheme 3b, 8 h, 58% yield). Perhaps more importantly, a continuous-flow reactor improved significantly the reaction efficiency, achieving the coupling reaction in 40 min (Scheme 3c).

To gain additional insight into the reaction mechanism, radical-trapping experiments were performed under the stand-

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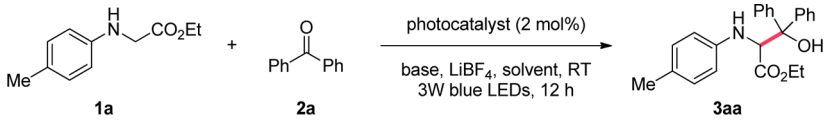
Table 1. Optimization of Reaction Conditions[a]

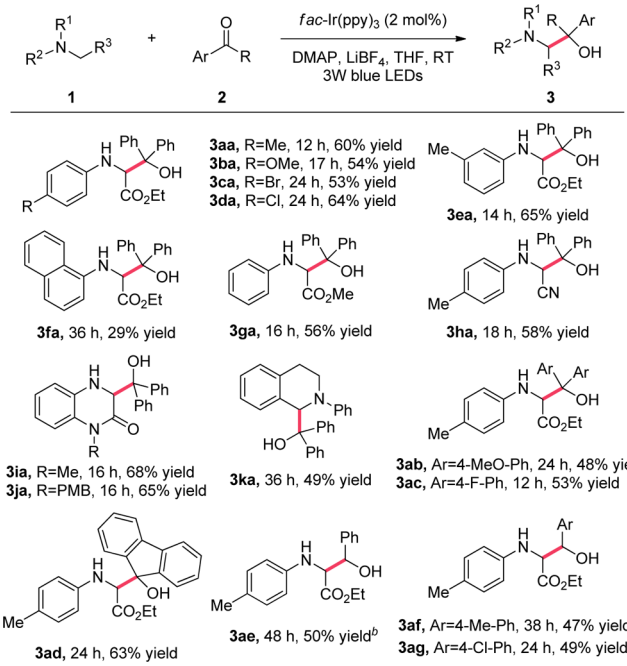


1a 2a 3aa

entry	photocatalyst	base	solvent	yield[b] (%)
1	*fac*-Ir(ppy)$_3$	DABCO	THF	34
2	Ir(ppy)$_2$(dtbbpy)PF$_6$	DABCO	THF	18
3	Ru(bpy)$_3$Cl$_2$	DABCO	THF	0
4	eosin Y	DABCO	THF	0
5	*fac*-Ir(ppy)$_3$	DABCO	DMF	30
6	*fac*-Ir(ppy)$_3$	DABCO	DMSO	15
7	*fac*-Ir(ppy)$_3$	DABCO	CH_3CN	4
8[c]	*fac*-Ir(ppy)$_3$	DABCO	THF	56
9[c]	*fac*-Ir(ppy)$_3$	DMAP	THF	61(60)[d]
10[c]	*fac*-Ir(ppy)$_3$	DBU	THF	5
11[c]	*fac*-Ir(ppy)$_3$	K_2HPO_4	THF	47
12[c]	*fac*-Ir(ppy)$_3$	Na_2CO_3	THF	16
13[c]	none	DMAP	THF	0
14[c,e]	*fac*-Ir(ppy)$_3$	DMAP	THF	0
15[c]	*fac*-Ir(ppy)$_3$	none	THF	0
16[c,f]	*fac*-Ir(ppy)$_3$	DMAP	THF	18

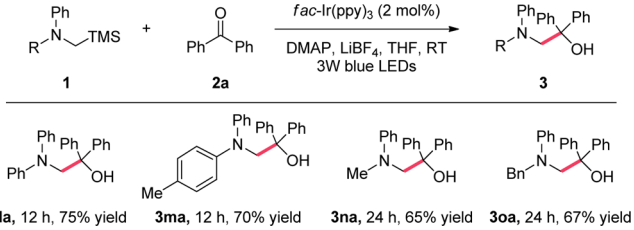
[a]Unless otherwise noted, reactions were performed with **1a** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv), photocatalyst (0.004 mmol, 2 mol %), base (0.4 mmol, 2.0 equiv), $LiBF_4$ (0.2 mmol, 1.0 equiv) and solvent (2.0 mL) under Ar. [b]Determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c]**1a** (0.6 mmol, 3.0 equiv) and **2a** (0.2 mmol) were used. [d]Isolated yield in parentheses. [e]Reaction performed in the dark. [f]Reaction performed without $LiBF_4$.

Table 2. Scope of the Visible Light-Induced Radical−Radical Cross-Coupling Reaction[a]



[a]Reaction conditions: **1** (0.6 mmol, 3.0 equiv), **2** (0.2 mmol), *fac*-Ir(ppy)$_3$ (0.004 mmol, 2 mol %), DMAP (0.4 mmol, 2.0 equiv), $LiBF_4$ (0.2 mmol, 1.0 equiv), THF (2.0 mL) under Ar. Yields of isolated products. [b]The dr values were 1.1:1.

Table 3. Scope of the *a*-Silylamines for the Radical−Radical Cross-Coupling Reaction[a]



[a]Reaction conditions: **1** (0.6 mmol, 3.0 equiv), **2a** (0.2 mmol), *fac*-Ir(ppy)$_3$ (0.004 mmol, 2 mol %), DMAP (0.4 mmol, 2.0 equiv), $LiBF_4$ (0.2 mmol, 1.0 equiv), THF (2.0 mL) under Ar. Yields of isolated products.

ard reaction conditions by adding 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and butylated hydroxytoluene (BHT) as radical scavengers (Scheme 3d,e). No desired product was observed from the reaction mixture, which indicated that the current reaction may occur through a radical pathway. In addition, we performed fluorescence quenching experiments with the *fac*-Ir(ppy)$_3$ as photocatalyst (Figure 1). As expected, the results of a series of Stern−Volmer quenching studies revealed that benzophenone **2a** efficiently quenched the excited state of *fac*-Ir(ppy)$_3$ but amine **1a** did not.

Based on these experimental results and related literature precedents,[9,12,16] a plausible reaction mechanism has been proposed for this transformation as shown in Scheme 4. Initially, irradiation of the Ir(III) photocatalyst with visible light leads to the formation of photoexcited state Ir(III)*, which serves as an efficient reductant to reduce Lewis acid-activated carbonyl **A** by a single electron transfer (SET) process to afford corresponding ketyl radical **B** along with the oxidized Ir(IV) species. Subsequently, amine substrate **1** is oxidized by the Ir(IV) species to regenerate ground-state Ir(III) with the formation of α-amino radical **D** through a single electron transfer process and a base-promoted deprotonation process. α-Amino radical **D** then readily couples with ketyl radical **B** to form intermediate **E**. Finally, 1,2-amino alcohol product **3** is released by the protonation step. Other reaction pathways

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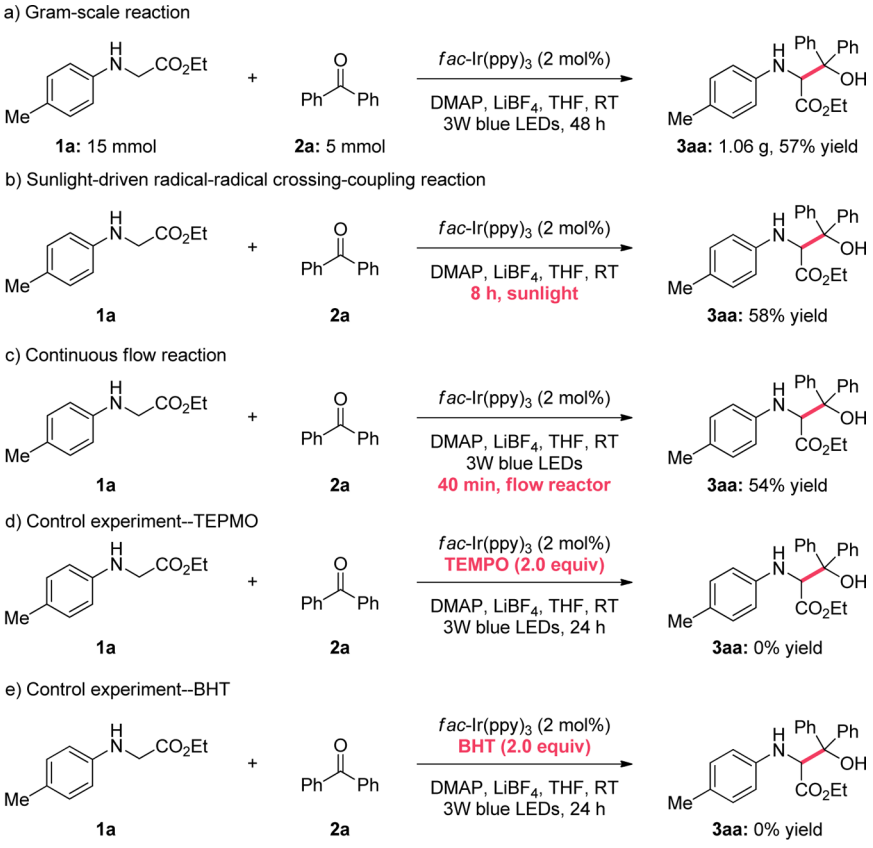
Scheme 3. Demonstration of Synthetic Utility and Control Experiments



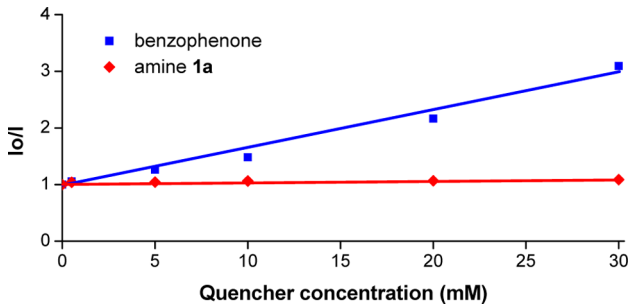
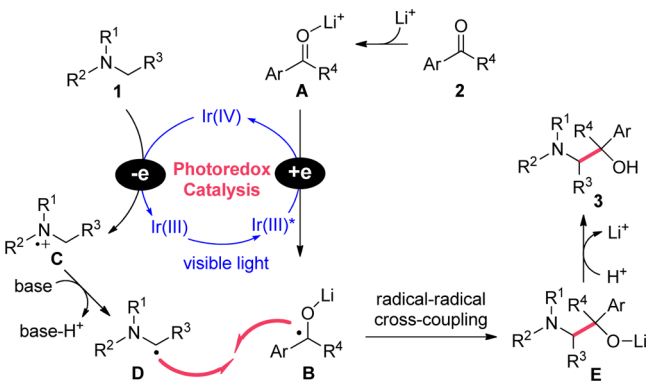


Figure 1. *fac*-Ir(ppy)$_3$ emission quenching with amine **1a** and benzophenone **2a**.

Scheme 4. Plausible Reaction Mechanism



involving addition of α-amino radical to the Lewis acid-activated carbonyl species or coordination of α-amino radical and ketyl radical by Li^+ might be possible and could not be ruled out at the current stage (see section 5 in the Supporting Information for details).

CONCLUSIONS

In summary, we have developed a visible-light-induced photocatalytic radical−radical crossing-coupling reaction of amines and carbonyls. This protocol provides rapid and efficient access to synthetically useful 1,2-amino alcohols. This novel method features a broad substrate scope, mild conditions, and simple operation.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, the materials were purchased from commercial suppliers and used without further purification. All of the amine substrates were prepared according to the literature procedures[17] and determined by ^{1}H NMR analysis. All of the solvents were treated according to general methods. Flash column chromatography was performed using 200−300 mesh silica gel. The ^{1}H NMR spectra were recorded on 400/600 MHz spectrophotometers. The chemical shifts (δ) are reported in ppm using the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). The data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q= quartet, dd = doublet of doublets, m = multiplet), coupling constants (Hz), and integration. The ^{13}C NMR spectra were recorded on 400 (100) MHz with complete proton decoupling spectrophotometer ($CDCl_3$: 77.0 ppm). High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. The IR spectra were recorded on an IR spectrophotometer. The melting points were measured with digital melting point detector.

General Procedure for the Radical−Radical Coupling Reaction of Amines with Carbonyls. To an oven-dried 10 mL Schleck flask equipped with a magnetic stir bar, substrate amines **1** (0.6

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mmol), carbonyls **2** (0.2 mmol), *fac*-Ir(ppy)$_3$ (2 mol %, 0.004 mmol), DMAP (0.4 mmol, 48.9 mg), $LiBF_4$ (0.2 mmol, 18.8 mg), and THF (2 mL) were added. The resulting mixture was degassed using a freeze−pump−thaw procedure (3 times). Then, the solution was stirred under argon and irradiated with 3 W blue LEDs (400−500 nm) (distance app. 5 cm) at room temperature. After the reaction was completed (monitored by TLC analysis), the solvent was removed under reduced pressure, and then the residue was purified by flash column chromatography (petroleum ether/acetone) to afford desired product **3**.

*Ethyl 3-Hydroxy-3,3-diphenyl-2-(p-tolylamino)propanoate (**3aa**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3aa** (45.2 mg, 60% yield) as a white solid. Mp 163−164 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.49 (m, 2H), 7.46 (dd, J = 7.5, 1.8 Hz, 2H), 7.30 (t, J = 7.6 Hz, 2H), 7.25−7.20 (m, 3H), 7.16 (t, J = 7.3 Hz, 1H), 6.96 (d, J = 8.0 Hz, 2H), 6.59 (d, J = 8.3 Hz, 2H), 4.96 (d, J = 8.6 Hz, 1H, N−H), 4.64 (d, J = 8.6 Hz, 1H), 4.53 (s, 1H, O−H), 3.89 (q, J = 7.2 Hz, 2H), 2.21 (s, 3H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 144.2, 143.8, 142.6, 129.7, 128.3, 128.2, 127.5, 127.4, 127.2, 125.8, 125.4, 113.5, 79.3, 62.0, 61.2, 20.4, 13.7; IR (in KBr) 3531, 3469, 3405, 3027, 2983, 1718, 1618, 1522, 1448, 1371, 1309, 1215, 1150, 1022, 812, 756, 697, 529 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{26}NO_3$ [M + H$^+$] 376.1907, found 376.1897.

*Ethyl 3-Hydroxy-2-((4-methoxyphenyl)amino)-3,3-diphenylpropanoate (**3ba**).* Purification by chromatography (petroleum ether/acetone = 30:1) afforded **3ba** (42.2 mg, 54% yield) as a white solid. Mp 135−136 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, J = 7.8 Hz, 2H), 7.47 (d, J = 7.8 Hz, 2H), 7.34−7.27 (m, 3H), 7.25−7.14 (m, 3H), 6.74 (d, J = 8.4 Hz, 2H), 6.63 (d, J = 8.4 Hz, 2H), 4.91 (s, 1H, N−H), 4.53 (s, 1H, O−H), 4.50 (s, 1H), 3.90 (q, J = 7.2 Hz, 2H), 3.73 (s, 3H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 152.6, 144.2, 142.6, 140.3, 128.3, 128.2, 127.4, 127.2, 125.8, 125.4, 115.0, 114.7, 79.2, 62.9, 61.2, 55.7, 13.7; IR (in KBr) 3526, 3458, 3405, 2992, 2834, 1712, 1516, 1452, 1374, 1224, 1030, 821, 756, 696, 523 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{26}NO_4$ [M + H$^+$] 392.1856, found 392.1856.

*Ethyl 2-((4-Bromophenyl)amino)-3-hydroxy-3,3-diphenylpropanoate (**3ca**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3ca** (46.9 mg, 53% yield) as a white solid. Mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.9 Hz, 2H), 7.44 (d, J = 7.9 Hz, 2H), 7.36−7.26 (m, 3H), 7.25−7.14 (m, 5H), 6.56 (d, J = 8.4 Hz, 2H), 4.93 (d, J = 8.7 Hz, 1H, N−H), 4.81 (d, J = 8.7 Hz, 1H), 4.52 (s, 1H, O−H), 3.93 (q, J = 7.1 Hz, 2H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.7, 145.2, 143.9, 142.3, 131.9, 128.4, 128.3, 127.6, 127.3, 125.6, 125.3, 115.0, 110.0, 79.2, 61.6, 61.5, 13.7; IR (in KBr) 3524, 3453, 3417, 3027, 2980, 1713, 1595, 1499, 1373, 1314, 1213, 1147, 1066, 1019, 815, 755, 697, 505 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{23}BrNO_3$ [M + H$^+$] 440.0856, found 440.0861.

*Ethyl 2-((4-Chlorophenyl)amino)-3-hydroxy-3,3-diphenylpropanoate (**3da**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3da** (50.9 mg, 64% yield) as a white solid. Mp 181−182 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, J = 7.7 Hz, 2H), 7.44 (d, J = 7.7 Hz, 2H), 7.36−7.26 (m, 3H), 7.25−7.14 (m, 3H), 7.09 (d, J = 8.3 Hz, 2H), 6.60 (d, J = 8.4 Hz, 2H), 4.94 (d, J = 8.7 Hz, 1H, N−H), 4.79 (d, J = 8.7 Hz, 1H), 4.52 (s, 1H, O−H), 3.93 (q, J = 7.1 Hz, 2H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 144.9, 144.0, 142.4, 129.1, 128.4, 128.3, 127.6, 127.3, 125.6, 125.3, 123.0, 114.6, 79.3, 62.0, 61.5, 13.7; IR (in KBr) 3527, 3457, 3415, 3028, 2980, 1714, 1599, 1501, 1447, 1373, 1313, 1211, 1147, 1018, 817, 756, 696, 506 cm^{-1}; HRMS (ESI) m/z calcd for $C_{23}H_{23}ClNO_3$ [M + H$^+$] 396.1361, found 396.1353.

*Ethyl 3-Hydroxy-3,3-diphenyl-2-(m-tolylamino)propanoate (**3ea**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3ea** (48.8 mg, 65% yield) as a white solid. Mp 157−158 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 (d, J = 7.9 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.36−7.26 (m, 3H), 7.25−7.14 (m, 3H), 7.04 (t, J = 7.7 Hz, 1H), 6.55 (d, J = 7.4 Hz, 1H), 6.50 (d, J = 7.4 Hz, 2H), 5.00 (d, J = 8.7 Hz, 1H, N−H), 4.73 (d, J = 8.7 Hz, 1H), 4.53 (s, 1H, O−H), 3.91 (q, J = 7.1 Hz, 2H), 2.25 (s, 3H), 0.91 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 146.2, 144.3, 142.6, 139.0, 129.1, 128.3, 128.2, 127.4, 127.2, 125.8, 125.5, 119.3, 114.3, 110.5, 79.3, 61.8, 61.3, 21.5, 13.7; IR (in KBr) 3526, 3479, 3419, 2984, 1712, 1599, 1494, 1447, 1367, 1326, 1214, 1186, 763, 694, 515 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{26}NO_3$ [M + H$^+$] 376.1907, found 376.1916.

*Ethyl 3-Hydroxy-2-(naphthalen-1-ylamino)-3,3-diphenylpropanoate (**3fa**).* Purification by chromatography (petroleum ether/acetone = 30:1) afforded **3fa** (23.8 mg, 29% yield) as a white solid. Mp 181−182 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.58 (d, J = 7.7 Hz, 2H), 7.52 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.5 Hz, 1H), 7.39−7.30 (m, 4H), 7.26−7.21 (m, 4H), 7.14 (t, J = 7.4 Hz, 1H), 6.82 (d, J = 7.5 Hz, 1H), 5.59 (d, J = 7.3 Hz, 1H, N−H), 5.17 (d, J = 7.3 Hz, 1H), 4.61 (s, 1H, O−H), 3.93 (q, J = 7.1 Hz, 2H), 0.92 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 144.1, 142.6, 141.5, 134.3, 132.4, 130.0, 128.4, 128.32, 128.27, 127.6, 127.3, 126.2, 125.5, 124.9, 123.4, 120.1, 118.3, 105.2, 79.5, 61.8, 61.4, 13.7; IR (in KBr) 3527, 3480, 3418, 3060, 2986, 1719, 1582, 1525, 1477, 1409, 1369, 1218, 1146, 1019, 761, 698, 554 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{26}NO_3$ [M + H$^+$] 412.1907, found 412.1910.

*Methyl 3-Hydroxy-3,3-diphenyl-2-(phenylamino)propanoate (**3ga**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3ga** (38.6 mg, 56% yield) as a white solid. Mp 157−159 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, J = 7.2 Hz, 2H), 7.45 (d, J = 7.3 Hz, 2H), 7.32 (t, J = 7.6 Hz, 2H), 7.26−7.20 (m, 3H), 7.20−7.11 (m, 3H), 6.73 (t, J = 7.4 Hz, 1H), 6.66 (d, J = 8.0 Hz, 2H), 5.01 (d, J = 8.5 Hz, 1H, N−H), 4.77 (d, J = 8.5 Hz, 1H), 4.49 (s, 1H, O−H), 3.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 146.0, 144.1, 142.3, 129.3, 128.4, 128.3, 127.5, 127.3, 125.7, 125.2, 118.3, 113.3, 79.2, 61.6, 52.2; IR (in KBr) 3523, 3394, 3058, 2956, 1719, 1600, 1503, 1441, 1357, 1312, 1216, 805, 756, 697, 537 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{22}NO_3$ [M + H$^+$] 348.1594, found 348.1597.

*3-Hydroxy-3,3-diphenyl-2-(p-tolylamino)propanenitrile (**3ha**).* Purification by chromatography (petroleum ether/acetone = 30:1) afforded **3ha** (37.8 mg, 58% yield) as a white solid. Mp 173−174 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 2H), 7.49−7.38 (m, 4H), 7.38−7.30 (m, 3H), 7.30−7.25 (m, 1H), 7.06 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 8.1 Hz, 2H), 4.99 (d, J = 10.8 Hz, 1H, N−H), 4.04 (d, J = 10.8 Hz, 1H), 3.32 (s, 1H, O−H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 141.9, 141.3, 130.1, 130.0, 128.9, 128.5, 128.5, 128.2, 126.3, 126.0, 118.0, 115.1, 79.1, 56.1, 20.5; IR (in KBr) 3524, 3377, 3021, 2924, 1607, 1520, 1449, 1387, 1310, 1183, 1054, 872, 805, 751, 697, 507 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{21}N_2O$ [M + H$^+$] 329.1648, found 329.1651.

*3-(Hydroxydiphenylmethyl)-1-methyl-3,4-dihydroquinoxalin-2(1H)-one (**3ia**).* Purification by chromatography (petroleum ether/acetone = 20:1) afforded **3ia** (46.9 mg, 68% yield) as a white solid. Mp 143−145 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, J = 6.5 Hz, 2H), 7.41−7.34 (m, 4H), 7.30−7.27 (m, 3H), 7.19−7.16 (m, 1H), 6.87 (d, J = 7.8 Hz, 2H), 6.80 (t, J = 7.7 Hz, 1H), 6.43 (d, J = 7.9 Hz, 1H), 5.74 (s, 1H, N−H), 4.67 (s, 1H), 3.67 (s, 1H, O−H), 3.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 143.7, 142.9, 133.5, 128.5, 128.4, 128.0, 127.9, 127.5, 127.34, 127.27, 124.1, 119.2, 114.6, 113.7, 79.5, 64.1, 28.7; IR (in KBr) 3368, 3060, 1655, 1599, 1511, 1448, 1416, 1376, 1304, 1135, 1040, 745, 705, 641 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{20}N_2NaO_2$ [M + Na$^+$] 367.1417, found 367.1412.

*3-(Hydroxydiphenylmethyl)-1-(4-methoxybenzyl)-3,4-dihydroquinoxalin-2(1H)-one (**3ja**).* Purification by chromatography (petroleum ether/acetone = 20:1) afforded **3ja** (58.7 mg, 65% yield) as a white solid. Mp 145−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92−7.83 (m, 2H), 7.45−7.30 (m, 8H), 6.92 (d, J = 8.0 Hz, 2H), 6.85−6.73 (m, 4H), 6.64 (t, J = 7.7 Hz, 1H), 6.41 (d, J = 7.4 Hz, 1H), 5.87 (s, 1H, N−H), 5.22 (d, J = 15.8 Hz, 1H), 4.85 (s, 1H), 4.79 (d, J = 15.8 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 1H, O−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 158.7, 143.5, 142.6, 133.4, 128.5, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 125.7, 124.2, 119.0, 115.5, 114.1, 113.7, 79.8, 64.4, 55.2, 44.7; IR (in KBr) 3444, 3363, 3063, 1655, 1601, 1511, 1447, 1400, 1304, 1251, 1171, 1034, 817, 753, 701, 634, 587 cm-1; HRMS (ESI) m/z calcd for $C_{29}H_{26}N_2NaO_3$ [M + Na$^+$] 473.1836, found 473.1825.

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*Diphenyl(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methanol (**3ka**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3ka** (38.3 mg, 49% yield) as a white solid. Mp 158−159 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, J = 7.4 Hz, 2H), 7.36−7.31 (m, 2H), 7.31−7.27 (m, 1H), 7.27−7.21 (m, 5H), 7.21−7.17 (m, 2H), 7.13 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 8.2 Hz, 2H), 7.02 (d, J = 7.6 Hz, 1H), 6.90 (t, J = 7.3 Hz, 1H), 6.85 (t, J = 7.6 Hz, 1H), 6.21 (d, J = 7.8 Hz, 1H), 5.44 (s, 1H), 4.68 (s, 1H, O−H), 3.36−3.28 (m, 1H), 2.99−2.92 (m, 1H), 2.87−2.87 (m, 1H), 2.30−2.24 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.6, 144.7, 143.4, 136.0, 133.2, 129.3, 129.1, 128.2, 128.0, 127.8, 127.7, 127.6, 127.4, 127.2, 126.9, 125.4, 120.8, 118.7, 80.4, 70.7, 42.9, 24.6; IR (in KBr) 3524, 3443,3352, 3054, 2967, 2911, 1591, 1493, 1336, 1268, 1206, 1140, 1036, 942, 758, 700, 571 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{26}NO$ [M + H$^+$] 392.2009, found 392.2018.

*Ethyl 3-Hydroxy-3,3-bis(4-methoxyphenyl)-2-(p-tolylamino)-propanoate (**3ab**).* Purification by chromatography (petroleum ether/acetone = 30:1) afforded **3ab** (41.7 mg, 48% yield) as a white solid. Mp 154−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 8.9 Hz, 2H), 6.97 (d, J = 8.3 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.78 (d, J = 8.9 Hz, 2H), 6.60 (d, J = 8.4 Hz, 2H), 4.87 (s, 1H), 4.40 (s, 1H, O−H), 3.92 (q, J = 7.1 Hz, 2H), 3.77 (s, 3H), 3.73 (s, 3H), 2.22 (s, 3H), 0.94 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 158.7, 158.5, 143.8, 136.7, 135.2, 132.2, 129.7, 127.5, 127.1, 126.6, 119.6, 113.5, 78.7, 62.2, 61.2, 55.2, 55.1, 20.4, 13.8; IR (in KBr) 3466, 3410, 2835, 1716, 1613, 1517, 1463, 1367, 1300, 1253, 1188, 1030, 818, 534 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{30}NO_5$ [M + H$^+$] 436.2118, found 436.2109.

*Ethyl 3,3-Bis(4-fluorophenyl)-3-hydroxy-2-(p-tolylamino)-propanoate (**3ac**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3ac** (43.6 mg, 53% yield) as a white solid. Mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.44 (m, 2H), 7.44−7.31 (m, 2H), 7.25−7.18 (m, 1H), 7.02−6.85 (m, 5H), 6.58 (d, J = 8.4 Hz, 2H), 4.88 (s, 1H), 4.60 (s, 2H), 3.94 (q, J = 7.1 Hz, 2H), 2.22 (s, 3H), 0.96 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 161.9 (d, J = 240 Hz), 143.7, 139.7, 139.4 (d, J = 170 Hz), 130.3 (d, J = 8 Hz), 129.8, 127.7 (d, J = 8 Hz), 127.4 (d, J = 8 Hz), 115.3 (d, J = 12 Hz), 115.0 (d, J = 12 Hz), 114.3 (d, J = 22 Hz), 113.8, 78.7, 62.4, 61.5, 20.4, 13.8; IR (in KBr) 3534, 3479, 3409, 2970, 1717, 1606, 1513, 1409, 1372, 1302, 1236, 1160, 1015, 834, 597, 530, cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{24}F_2NO_3$ [M + H$^+$] 412.1719, found 412.1719.

*Ethyl 2-(9-Hydroxy-9H-fluoren-9-yl)-2-(p-tolylamino)acetate (**3ad**).* Purification by chromatography (petroleum ether/acetone = 40:1) afforded **3ad** (46.9 mg, 63% yield) as a white solid. Mp 111−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.5 Hz, 1H), 7.62 (d, J = 7.5 Hz, 2H), 7.57 (d, J = 7.5 Hz, 1H), 7.43−7.28 (m, 4H), 7.03 (d, J = 8.3 Hz, 2H), 6.79 (d, J = 8.4 Hz, 2H), 4.49 (s, 1H), 3.76 (q, J = 7.1 Hz, 2H), 2.25 (s, 3H), 0.79 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 145.5, 144.9, 140.2, 140.0, 129.8, 129.5, 129.4, 129.1, 127.9, 127.8, 124.6, 123.7, 120.1, 119.8, 119.6, 115.6, 81.8, 66.3, 61.2, 20.5, 13.5; IR (in KBr) 3530, 3393, 2983, 2905, 1738, 1611, 1521, 1446, 1306, 1191, 1148, 1042, 819, 745, 616, 550, 488 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{24}NO_3$ [M + H$^+$] 374.1751, found 374.1748.

*Ethyl 3-Hydroxy-3-phenyl-2-(p-tolylamino)propanoate (**3ae**).* Purification by chromatography (petroleum ether/acetone = 10:1) afforded **3ae** (29.8 mg, 50% yield) as a white solid (1.1:1 dr). Mp 102−104 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (d, J = 7.6 Hz, 2H, major+minor), 7.38−7.28 (m, 8H, major+minor), 7.00 (d, J = 7.9 Hz, 2H, minor), 6.96 (d, J = 7.9 Hz, 2H, major), 6.65 (d, J = 7.9 Hz, 2H, minor), 6.54 (d, J = 7.9 Hz, 2H, major), 5.16 (d, J = 4.6 Hz, 1H, minor), 4.94 (d, J = 4.3 Hz, 1H, major), 4.38 (d, J = 4.6 Hz, 1H, minor), 4.15 (d, J = 4.3 Hz, 1H, major), 4.07−3.98 (m, 4H, major +minor, N−H+O-H), 3.23 (s, 4H, major+minor), 2.24 (s, 3H, minor), 2.22 (s, 3H, major), 1.12−0.99 (m, 6H, major+minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 171.8, 144.3, 144.2, 139.7, 139.6, 129.8, 129.7, 128.8, 128.6, 128.39, 128.37, 128.2, 128.1, 126.4, 125.8, 114.8, 114.6, 74.6, 73.8, 64.8, 63.3, 61.4, 61.2, 20.5, 20.4, 14.0, 13.9; IR (in KBr) 3467, 3400, 2983, 2914, 1699, 1614, 1521, 1450, 1303, 1262, 1194, 1025, 814, 752, 702, 572, 503 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{22}NO_3$ [M + H$^+$] 300.1594, found 300.1598.

*Ethyl 3-Hydroxy-3-(p-tolyl)-2-(p-tolylamino)propanoate (**3af**).* Purification by chromatography (petroleum ether/acetone = 10:1) afforded **3af** (29.6 mg, 47% yield) as a white solid (1.1:1 dr). Mp 109−110 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (d, J = 8.0 Hz, 2H, major), 7.21 (d, J = 7.9 Hz, 2H, minor), 7.19−7.11 (m, 4H, major +minor), 6.99 (d, J = 8.0 Hz, 2H, minor), 6.96 (d, J = 8.0 Hz, 2H, major), 6.65 (d, J = 8.4 Hz, 2H, minor), 6.55 (d, J = 8.4 Hz, 2H, major), 5.12 (d, J = 4.6 Hz, 1H, minor), 4.91 (d, J = 5.7 Hz, 1H, major), 4.36 (d, J = 4.6 Hz, 1H, minor), 4.13 (d, J = 5.7 Hz, 1H, major), 4.10−3.99 (m, 4H, major+minor), 3.14 (s, 2H, major+minor, O−H), 2.34 (s, 6H, major+minor), 2.24 (s, 3H, minor), 2.22 (s, 3H, major), 1.16−1.00 (m, 6H, major+minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 171.9, 144.4, 144.3, 137.9, 137.8, 136.61, 136.60, 129.8, 129.7, 129.1, 129.0, 128.7, 128.5, 126.3, 125.7, 114.8, 114.7, 74.4, 73.7, 64.7, 63.3, 61.3, 61.2, 21.14, 21.13, 20.5, 20.4, 14.0, 13.9; IR (in KBr) 3323, 2980, 2917, 1735, 1690, 1616, 1519, 1308, 1264, 1195, 1069, 1023, 812, 508 cm^{-1}; HRMS (ESI) m/z calcd for $C_{19}H_{24}NO_3$ [M + H$^+$] 314.1751, found 314.1755.

*Ethyl 3-(4-Chlorophenyl)-3-hydroxy-2-(p-tolylamino)propanoate (**3ag**).* Purification by chromatography (petroleum ether/acetone = 10:1) afforded **3ag** (32.5 mg, 49% yield) as a white solid (1.1:1 dr). Mp 89−91 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.31 (m, 6H, major+minor), 7.29 (d, J = 8.3 Hz, 2H, minor), 7.01 (d, J = 8.0 Hz, 2H, minor), 6.97 (d, J = 8.1 Hz, 2H, major), 6.65 (d, J = 8.1 Hz, 2H, minor), 6.55 (d, J = 8.1 Hz, 2H, major), 5.14 (s, 1H, minor), 4.92 (d, J = 5.6 Hz, 1H, major), 4.35 (d, J = 4.6 Hz, 1H, minor), 4.10 (d, J = 5.6 Hz, 1H, major), 4.09−3.97 (m, 4H, major+minor), 3.23 (d, J = 26.3 Hz, 2H, major+minor, O−H), 2.24 (s, 3H, minor), 2.23 (s, 3H, major), 1.14−1.05 (m, 6H, major+minor); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 171.4, 144.0, 143.8, 138.3, 138.2, 134.0, 133.8, 129.9, 129.8, 129.1, 129.0, 128.53, 128.50, 127.9, 127.3, 114.9, 114.8, 73.9, 73.1, 64.6, 63.4, 61.5, 61.4, 20.5, 20.4, 14.1, 14.0; IR (in KBr) 3525, 3441, 3391, 3318, 2981, 1736, 1687, 1597, 1520, 1406, 1262, 1193, 1018, 813, 506 cm^{-1}; HRMS (ESI) m/z calcd for $C_{18}H_{21}ClNO_3$ [M + H$^+$] 334.1204, found 334.1206.

*2-(Diphenylamino)-1,1-diphenylethanol (**3la**).* Purification by chromatography (petroleum ether/diethyl ether = 50:1) afforded **3la** (54.8 mg, 75% yield) as a white solid. Mp 138−139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.32 (m, 4H), 7.19−7.07 (m, 10H), 6.88 (t, J = 7.3 Hz, 2H), 6.76 (d, J = 8.0 Hz, 4H), 4.63 (s, 2H), 3.26 (s, 1H, O−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 145.0, 129.2, 128.0, 126.8, 126.1, 122.2, 122.0, 78.5, 64.0; IR (in KBr) 3472, 3026, 2946, 1591, 1492, 1448, 1331, 1234, 1178, 1062, 1021, 835, 775, 748, 696, 579 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{24}NO$ [M + H$^+$] 366.1852, found 366.1857. This compound is known.[18]

*1,1-Diphenyl-2-(phenyl(p-tolyl)amino)ethanol (**3ma**).* Purification by chromatography (petroleum ether/diethyl ether = 50:1) afforded **3ma** (53.1 mg, 70% yield) as a white solid. Mp 145−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.28 (m, 4H), 7.21−7.04 (m, 8H), 6.91 (d, J = 8.0 Hz, 2H), 6.81 (t, J = 7.3 Hz, 1H), 6.73 (d, J = 8.0 Hz, 2H), 6.66 (d, J = 8.3 Hz, 2H), 4.59 (s, 2H), 3.28 (s, 1H, O−H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 146.4, 145.0, 132.7, 129.7, 128.8, 127.8, 126.6, 126.0, 124.0, 120.8, 119.8, 78.5, 64.1, 20.8; IR (in KBr) 3649, 3323, 2922, 2852, 1689, 1594, 1494, 1447, 1259, 1184, 750, 698, 591 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{26}NO$ [M + H$^+$] 380.2009, found 380.2002.

*2-(Methyl(phenyl)amino)-1,1-diphenylethanol (**3na**).* Purification by chromatography (petroleum ether/diethyl ether = 50:1) afforded **3na** (39.4 mg, 65% yield) as a white solid. Mp 82−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.49 (m, 3H), 7.34−7.26 (m, 4H), 7.24−7.16 (m, 4H), 7.15−7.11 (m, 2H), 6.90 (d, J = 8.2 Hz, 1H), 6.78 (t, J = 7.3 Hz, 1H), 4.13 (s, 2H), 3.62 (s, 1H, O−H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.9, 128.4, 128.1, 127.1, 126.8, 125.7, 118.6, 114.3, 76.6, 66.2, 39.6; IR (in KBr) 3484, 3058, 3025, 2814, 1600, 1503, 1446, 1362, 1263, 1179, 1060, 1027, 952, 751, 699, 648, 604 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{22}NO$ [M + H$^+$] 304.1696, found 304.1700. This compound is known.[18]

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*2-(Benzyl(phenyl)amino)-1,1-diphenylethanol (**3oa**).* Purification by chromatography (petroleum ether/diethyl ether = 50:1) afforded **3oa** (50.9 mg, 67% yield) as a white solid. Mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.46 (m, 3H), 7.30−7.25 (m, 5H), 7.21−7.17 (m, 3H), 7.16−7.10 (m, 5H), 6.90 (d, J = 7.9 Hz, 3H), 6.73 (t, J = 7.2 Hz, 1H), 4.31 (s, 2H), 4.09 (s, 2H), 3.41 (s, 1H, O−H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.9, 128.4, 128.3, 128.1, 127.1, 126.9, 126.8, 126.7, 126.5, 125.7, 118.2, 114.4, 77.4, 62.2, 53.7; IR (in KBr) 3564, 3059, 3027, 2926, 1598, 1498, 1448, 1197, 1160, 1027, 749, 699, 651, 605 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{26}NO$ [M + H$^+$] 380.2009, found 380.2010.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01217.

Details for conditions optimization, luminescence quenching experiments, quantum yield mensuration, and copies of ^{1}H NMR and ^{13}C NMR spectra of products **3** (PDF)

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Notes

The authors declare no competing financial interest.

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