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Diastereoselective Synthesis of *N*-Aryl Tetrahydroquinolines and *N*-Aryl Indolines by the Tandem Reaction of Arynes

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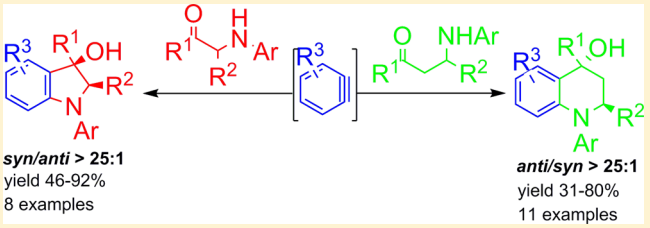
Supporting Information

ABSTRACT: A tandem reaction of arynes with α- or β-amino ketones has been revealed. Arynes react with β-amino ketones through a cascade insertion−cyclization process to afford *N*-aryl tetrahydroquinolines in good yield with excellent *anti*-selectivity. Meanwhile, the coupling of arynes with α-amino ketones produces multisubstituted indolines in high yield with *syn*-selectivity. A quaternary carbon center can be constructed in this process, and the reaction can be easily scaled up.



Tetrahydroquinolines[1] and indolines[2] are two important classes of structural motifs in numerous natural and synthetic compounds with a wide spectrum of biological activities (Figure 1). The significance of these motifs has led to

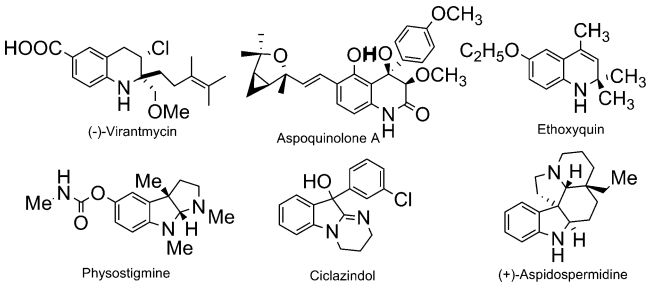


Figure 1. Examples of bioactive tetrahydroquinoline and indoline derivatives.

the development of several efficient methods for the synthesis of tetrahydroquinolines, such as aza-Michael addition,[3] aza-Diels−Alder reaction (Povarov reaction),[4] hydrogenation of quinolines,[5] and other miscellaneous reactions.[6] Different protocols have also been established for the preparation of indolines.[7] However, to the best of our knowledge, information on the synthesis of tetrahydroquinolines and indolines containing a quaternary stereocenter is limited. Such information is essential for studying the bioactivity of these compounds.[8] Therefore, the development of novel and efficient methods for the synthesis of tetrahydroquinolines and indolines with a quaternary center is of high importance.

Arynes are highly active intermediates that can be conveniently generated by the fluoride-induced 1,2-elimination reaction of *o*-(trimethylsilyl)-aryl triflates under very mild conditions, as reported by Kobayashi et al.[9] Their findings paved the way for the dramatic progress of aryne chemistry. Presently, arynes are an important class of building blocks widely applied in organic synthesis.[10] The high electrophilicity of arynes enables them to be used as dienophiles in a series of pericyclic reactions, such as 1,3-dipolar cycloaddition,[11] Diels−Alder reaction,[12] and insertion−cyclization reaction,[13] which facilitate easy access to different types of heterocycles. In particular, the click rection of arynes and amino-carbonyl compounds that is triggered by nitrogen insertion leads to the construction of a large number of pharmaceutically active heterocycles, including acridones,[13a,b] acridines,[13c,d] indolines,[13e,f] polycyclic indolones,[13g,h] isatins,[13i] indoles,[13j,k] and quinazolinones.[13l] Recently, Zhu[13m] and our group[13n] independently reported an efficient method to produce multisubstituted *N*-arylindoles from arynes and α-amino ketones. As a following study, we reasoned that the coupling of arynes with the readily available β-amino ketones can lead to the construction of polysubstituted tetrahydroquinolines. In the present work, we propose a novel approach to the diastereoselective synthesis of *N*-aryl tetrahydroquinolines and indolines involving a tandem insertion−cyclization process of arynes.

We began our studies with the commercially available aryne precursor **1a** and β-amino ketone **2a**. With 3.0 equiv CsF as fluoride source, the cascade reaction smoothly proceeded in acetonitrile at room temperature to furnish the desired tetrahydroquinoline **3a** in 64% yield with excellent diastereoselectivity[14] (*anti*/*syn* > 25:1; Table 1, entry 1), together with a small amount of *N*-phenylation amine **4a**. Considering these successful results, several other fluorides such as KF, NaF, LiF, and Bu_4NF were subsequently tested for the reaction. However, all the fluorides tested above showed lower efficiency, and most of the **2a** was recovered (Table 1, entries 2−5). Interestingly, when 3.0 equiv of 18-crown-6 was added as coadditive, the reaction was finished within a relatively short time, producing the desired product in 72% yield with excellent diastereoselectivity (Table 1, entry 6). A brief screening of the reaction

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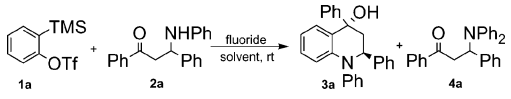
Table 1. Optimization of Reaction Conditions[a]



entry	additives	solvent	*t*/h	3a[b]	*anti*/*syn*[c]	4a[b]
1	CsF (3.0 equiv)	CH_3CN	6	64	>25:1	12
2	KF (3.0 equiv)	CH_3CN	30	6 (90)[d]	–	–
3	NaF (3.0 equiv)	CH_3CN	30	4 (91)[d]	–	–
4	LiF (3.0 equiv)	CH_3CN	30	0 (93)[d]	–	–
5	Bu_4NF (3.0 equiv)	THF	30	10 (67)[d]	>25:1	–
6	KF+18-C-6 (3.0 equiv)	CH_3CN	2	72	>25:1	11
7	KF+18-C-6 (3.0 equiv)	THF	4	30	>25:1	51
8	KF+18-C-6 (3.0 equiv)	CH_2Cl_2	4	31	>25:1	54
9	KF+18-C-6 (3.0 equiv)	toluene	4	0 (44)[d]	–	26
10	KF+18-C-6 (3.0 equiv)	Et_2O	4	0 (43)[d]	–	31
11	KF+18-C-6 (2.0 equiv)	CH_3CN	2	55	>25:1	25
12	KF+18-C-6 (1.0 equiv)	CH_3CN	30	57	>25:1	23
13	no additives	CH_3CN	30	0 (94)[d]	–	–

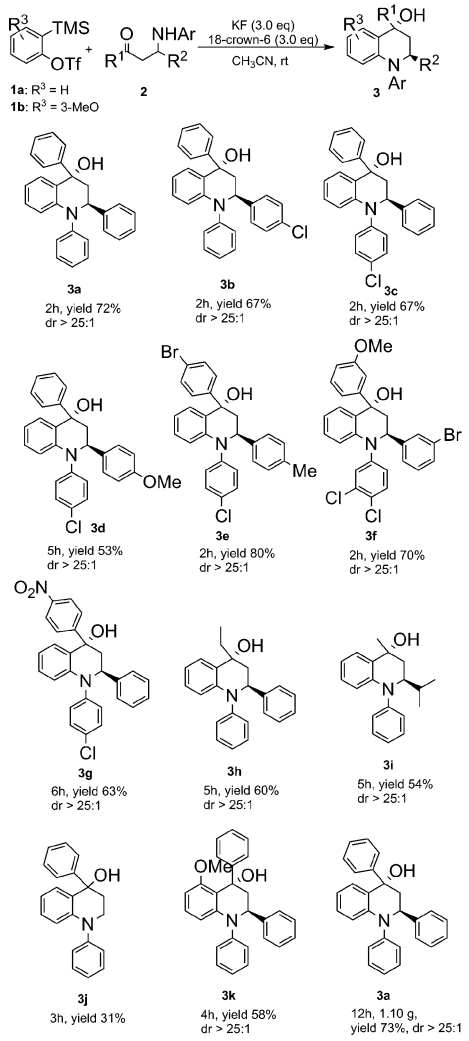
[a]**1a** (0.15 mmol), **2a** (0.10 mmol), solvent: 2.0 mL, rt. [b]Isolated yields. [c]Determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Recovery yield of **2a**.

media proved that acetonitrile was still the best choice with respect to yields and selectivities (Table 1, entries 6−10). Reducing the loading of additive reversed the outcomes of **3a** and **4a** (Table 1, entries 11 and 12). Finally, the control experiment indicated that no product was produced in the absence of additives (Table 1, entry 13).

With the optimized reaction conditions in hand, the scope of the reaction was subsequently examined, and the results are summarized in Scheme 1. A range of differently substituted *β*-amino ketones underwent the tandem reaction smoothly to afford the corresponding tetrahydroquinolines with excellent diastereoselectivity. The electronic properties and varied positions of the substituted groups on the aromatic ring had no evident effects on the reaction yields and selectivities (Scheme 1, **3b** to **3g**). Aliphatic *β*-amino ketones were also proved to be good candidates for the coupling reaction, producing the corresponding alkyl-substituted tetrahydroquinolines in good yield (Scheme 1, **3h** and **3i**). Surprisingly, when *β*-unsubstituted *β*-amino ketone **2j** was employed, a diminished yield was observed (Scheme 1, **3j**). In addition, the unsymmetrical aryne derived from the 3-methoxy substituted triflate precursor **1b** smoothly underwent the cascade reaction to yield 58% of the corresponding tetrahydroquinoline with nearly complete regioselectivity and diastereoselectivity (Scheme 1, **3k**).[15] More interestingly, the reaction can be easily scaled up without losing the reaction yield and diastereoselectivity.

To further demonstrate the utility of this protocol, the tandem insertion−cyclization of arynes and *α*-amino ketones was next investigated. In our previous studies of these similar cascade reactions,[13n] we showed that the direct acidic workup of the crude products led to the formation of dehydrated indoles. However, in this current research, after filtration of the crude reaction mixture through a basic pad of anhydrous potassium carbonate, the hydroxy group can be retained, and indolines were isolated as the major products (Scheme 2). *α*-

Scheme 1. Synthesis of *N*-Aryl Tetrahydroquinolines



Amino ketones substituted with both electron-donating and electron-withdrawing groups efficiently coupled with arynes, producing the corresponding indolines in high yield with excellent diastereoselectivity[14] (Scheme 2, **6a**−**6d**). Additionally, different positions of the substituents only very slightly affected the reaction. Alkyl-substituted *α*-amino ketones were also suitable reactants for the tandem reaction, producing the corresponding alkyl-substituted indolines in moderate yields (Scheme 2, **6e** and **6f**). The symmetric naphthalene can also undergo annulation with *α*-amino ketone to yield 75% of benzindoline **6g** (Scheme 2, **6g**). The unsymmetric aryne again reacted with *α*-amino ketone to afford indoline **6h** with nearly complete regioselectivity (Scheme 2, **6h**).[15]

Two feasible transition states were proposed for current transformation based on experiment outcomes (see Scheme 3). For the reaction of *β*-amino ketones, a six-membered chair model **A** was proposed. The bulky phenyl groups sitting at the equatorial position are more stable than those at the axial position, which would lead to *anti*-selectivity of tetrahydroquinolines. On the other hand, a five-membered envelope model **B** was proposed for the reaction of *α*-amino ketones. Two adjacent phenyl groups adopt *anti*-positions preferentially, which can minimize the van der Waals repulsions and lead to the *syn*-selectivity of indolines.

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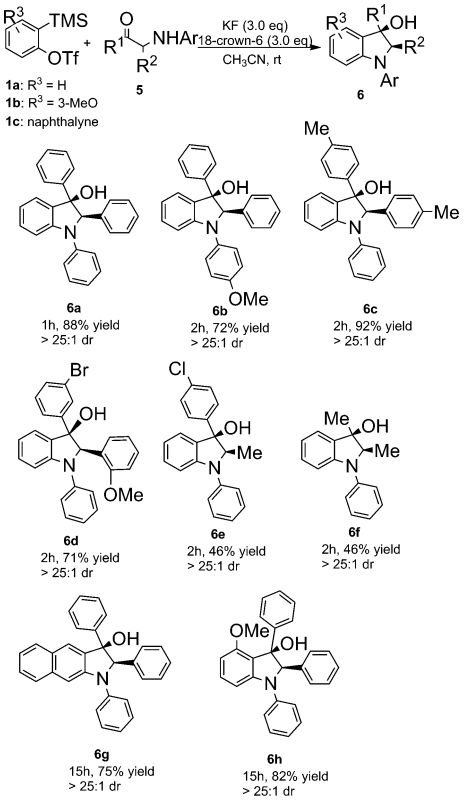
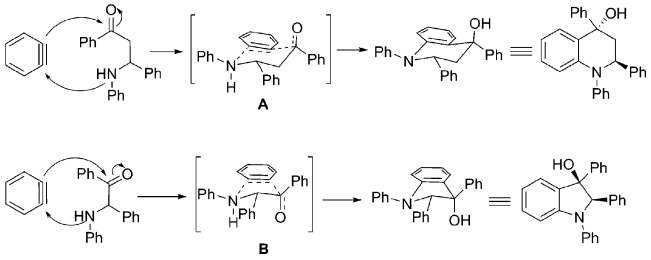
Scheme 2. Synthesis of *N*-Aryl Indolines



Scheme 3. Proposed Mechanism



In summary, we have described an insertion−cyclization reaction of arynes with α- or β-amino ketones. The mild reaction conditions, simple procedure, and excellent diastereoselectivity provided a novel approach to the synthesis of these versatile nitrogen-containing heterocycles.

EXPERIMENTAL SECTION

All reactions were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring bar. Anhydrous THF, ether, and toluene were distilled from sodium, anhydrous CH_2Cl_2 and CH_3CN were distilled from calcium hydride. ^1H NMR (400 MHz), ^{13}C NMR (100 MHz, $CDCl_3$) spectra were recorded using tetramethylsilane as an internal standard and reported in ppm (δ). α-Aminoketones[16] and β-aminoketones[17] were prepared according to the literature.

General Procedure for the Tandem Reaction of Aryne with β-Aminoketone (or α-Aminoketone). To a mixture of aminoketone **2** (or **5**) (0.3 mmol), KF (52 mg, 0.9 mmol), 18-crown-6 (238 mg, 0.9 mmol) in anhydrous acetonitrile (2.0 mL) was added 2-(trimethylsilyl) aryl triflate **1** (0.45 mmol) under N_2 atmosphere. The mixture was stirred at room temperature until full consumption of the starting aminoketone as indicated by TLC. The reaction mixture was then diluted with ethyl acetate, filtered through a short pad of anhydrous K_2CO_3, and concentrated. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc, 15:1−10:1) to give the desired product.

Scale-up Experiment. To a solution of β-aminoketone **2a** (1.204 g, 4.0 mmol), KF (232 mg, 4.0 mmol), 18-crown-6 (1.06 g, 4.0 mmol) in anhydrous acetonitrile (8.0 mL) was added 2-(trimethylsilyl)-aryl triflate **1a** (1.2 mL, 5 mmol). The mixture was stirred for 12 h at room temperature under a nitrogen atmosphere. The reaction mixture was then filtered through a short pad of anhydrous K_2CO_3, washed with ethyl acetate, and concentrated. The crude product was purified by flash column chromatography on silica gel (PE/EtOAc, 15:1−10:1) to give **3a** in 73% yield (1.10 g).

*1,2,4-Triphenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3a**).* Reaction time: 2 h; 81.5 mg, 72% yield; white solid; mp 58.7−60.4 °C; IR (KBr, cm^{-1}) ν 3449, 1631, 1599, 1485, 1449, 1352, 1120, 1095, 1044, 889, 758, 698, 507; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57−7.53 (m, 2H), 7.36−7.32 (m, 2H), 7.29−7.25 (m, 3H), 7.23−7.18 (m, 2H), 7.15−7.04 (m, 6H), 7.01−6.96 (m, 1H), 6.84−6.81 (m, 1H), 6.64−6.59 (m, 1H), 6.46−6.43 (m, 1H), 5.06 (dd, J = 3.3, 12.1 Hz, 1H), 2.66−2.57 (m, 1H), 2.39−2.32 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.71, 147.07, 146.67, 142.21, 129.36, 129.30, 129.05, 128.94, 128.43, 128.14, 128.10, 127.96, 127.14, 126.88, 126.39, 125.92, 118.04, 116.79, 73.51, 60.98, 48.51; HRMS (EI, TOF): m/z calcd for $C_{27}H_{23}NO$ $[M]^+$ 377.1780, found: 377.1776.

*2-(4-Chlorophenyl)-1,4-diphenyl-1,2,3,4-tetrahydroquinolin-4-ol(**3b**).* Reaction time: 2 h; 82.8 mg, 67% yield; light-yellow solid; mp 65.3−66.2 °C; IR (KBr, cm^{-1}) ν 3437, 2912, 2830, 1632, 1593, 1489, 1449, 1350, 1090, 1063, 1043, 1013, 891, 827, 752, 700, 511; ^1H NMR (400 MHz, $CDCl_3$) δ 7.57−7.50 (m, 2H), 7.39−7.32 (m, 2H), 7.31−7.27 (m, 1H), 7.25−7.19 (m, 4H), 7.14−7.05 (m, 5H), 7.02−6.96 (m, 1H), 6.86−6.81 (m, 1H), 6.66−6.60 (m, 1H), 6.45−6.40 (m, 1H), 5.05 (dd, J = 2.7, 12.0 Hz, 1H), 2.56 (dd, J = 13.1, 13.1 Hz, 1H), 2.35−2.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.55, 146.88, 146.46, 140.78, 132.65, 129.43, 129.40, 129.34, 128.96, 128.26, 127.96, 126.93, 126.31, 126.16, 118.21, 116.74, 73.37, 60.39, 48.31; HRMS (MALDI, TOF): m/z calcd for $C_{27}H_{22}{}^{35}ClNO$ $[M + H - H_2O - H_2]^+$ 392.1201, found: 392.1203.

*1-(4-Chlorophenyl)-2,4-diphenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3c**).* Reaction time: 2 h; 82.7 mg, 67% yield; white solid; mp 60.5−61.8 °C; IR (KBr, cm^{-1}) ν 3447, 2832, 2716, 1631, 1598, 1489, 1450, 1363, 1215, 1090, 1043, 895, 827, 750, 700, 569; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56−7.51 (m, 2H), 7.38−7.32 (m, 2H), 7.30−7.24 (m, 3H), 7.21−7.08 (m, 5H), 7.05−6.98 (m, 3H), 6.86−6.81 (m, 1H), 6.68−6.62 (m, 1H), 6.45−6.39 (m, 1H), 5.00 (dd, J = 2.8, 12.0 Hz, 1H), 2.60 (dd, J = 13.3, 13.3 Hz, 1H), 2.38−2.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.29, 146.83, 145.39, 141.87, 131.31, 130.57, 129.50, 129.03, 128.97, 128.73, 128.25, 128.01, 127.96, 127.33, 126.93, 126.29, 118.45, 116.80, 73.40, 61.04, 48.39; HRMS (MALDI, TOF): m/z calcd for $C_{27}H_{22}{}^{35}ClNO$ $[M + H - H_2O - H_2]^+$ 392.1201, found: 392.1205.

*1-(4-Chlorophenyl)-2-(4-methoxyphenyl)-4-phenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3d**).* Reaction time: 5 h; 70.2 mg, 53% yield; light-yellow solid; mp 73.5−74.8 °C; IR (KBr, cm^{-1}) ν 3447, 3028, 2930, 2835, 1601, 1512, 1489, 1452, 1352, 1311, 1246, 1170, 1089, 978, 829, 756, 700; ^1H NMR (400

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MHz, $CDCl_3$) δ 7.55−7.51 (m, 2H), 7.37−7.32 (m, 2H), 7.30−7.26 (m, 1H), 7.21−7.13 (m, 4H), 7.02−6.97 (m, 3H), 6.84−6.80 (m, 1H), 6.71−6.67 (m, 2H), 6.66−6.60 (m, 1H), 6.37 (d, J = 8.3 Hz, 1H), 4.94 (dd, J = 2.8, 12.1 Hz, 1H), 3.71 (s, 3H), 2.58 (dd, J = 13.5, 13.5 Hz, 1H), 2.34−2.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.65, 147.43, 146.97, 145.40, 133.79, 131.35, 130.79, 129.51, 129.10, 129.08, 128.92, 128.55, 127.94, 126.88, 126.28, 118.28, 116.68, 113.57, 73.49, 60.34, 55.12, 48.35; HRMS (MALDI, TOF): m/z calcd for $C_{28}H_{24}{}^{35}ClNO_2$ $[M + H - H_2O - H_2]^+$ 422.1306, found: 422.1308.

*4-(4-Bromophenyl)-1-(4-chlorophenyl)-2-(p-tolyl)-1,2,3,4-tetrahydroquin-olin-4-ol (**3e**).* Reaction time: 2 h; 121.2 mg, 80% yield; light-yellow solid; mp 124.4−124.7 °C; IR (KBr, cm^{-1}) ν 3439, 2832, 1632, 1601, 1489, 1450, 1352, 1215, 1090, 1069, 1045, 1011, 816, 756; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.38 (m, 4H), 7.21−7.17 (m, 2H), 7.14−7.09 (m, 2H), 7.03−6.94 (m, 5H), 6.82−6.77 (m, 1H), 6.68−6.62 (m, 1H), 6.42−6.37 (m, 1H), 4.93 (dd, J = 2.6, 11.9 Hz, 1H), 2.52 (dd, J = 13.3, 13.3 Hz, 1H), 2.32−2.26 (m, 2H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.31, 146.16, 145.18, 138.49, 137.01, 131.37, 131.00, 130.60, 129.53, 129.17, 128.99, 128.92, 128.25, 127.97, 127.84, 120.87, 118.43, 116.77, 73.28, 60.57, 48.30, 21.06; HRMS (MALDI, TOF): m/z calcd for $C_{28}H_{23}{}^{79}Br^{35}ClNO$ $[M + H - H_2O - H_2]^+$ 484.0462, found: 484.0436.

*2-(3-Bromophenyl)-1-(3,4-dichlorophenyl)-4-(3-methoxyphenyl)-1,2,3,4-tetrahydroquinolin-4-ol (**3f**).* Reaction time: 2 h; 116.6 mg, 70% yield; light-yellow solid; mp 72.9−75.2 °C; IR (KBr, cm^{-1}) ν 3452, 2832, 1593, 1450, 1383, 1352, 1215, 1130, 1043, 764, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.43−7.38 (m, 2H), 7.30−7.26 (m, 1H), 7.24−7.17 (m, 2H), 7.14−7.04 (m, 2H), 6.96−6.92 (m, 1H), 6.88−6.79 (m, 3H), 6.74−6.66 (m, 2H), 6.54−6.49 (m, 1H), 4.92 (dd, J = 3.1, 11.6 Hz, 1H), 3.73 (s, 3H), 2.51 (dd, J = 13.5, 13.5 Hz, 1H), 2.40−2.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.61, 149.03, 146.32, 146.28, 143.03, 132.96, 130.83, 130.20, 130.14, 129.57, 129.52, 129.49, 129.45, 129.37, 128.86, 128.60, 128.03, 125.11, 122.33, 120.13, 119.32, 117.31, 113.42, 112.93, 73.04, 60.87, 55.19, 48.20; HRMS (MALDI, TOF): m/z calcd for $C_{28}H_{22}{}^{79}Br^{35}Cl_2NO_2$ $[M + H - H_2O - H_2]^+$ 534.0022, found: 534.0003.

*1-(4-Chlorophenyl)-4-(4-nitrophenyl)-2-phenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3g**).* Reaction time: 6 h; 86.4 mg, 63% yield; light-yellow solid; mp 79.2−80.3 °C; IR (KBr, cm^{-1}) ν 3422, 2816, 1599, 1490, 1450, 1350, 1086, 1015, 853, 756; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22−8.18 (m, 2H), 7.75−7.71 (m, 2H), 7.25−7.17 (m, 5H), 7.16−7.10 (m, 2H), 7.05−7.01 (m, 3H), 6.75−6.71 (m, 1H), 6.70−6.64 (m, 1H), 6.45−6.41 (m, 1H), 4.99 (dd, J = 3.1, 11.9 Hz, 1H), 2.56 (dd, J = 12.2, 13.9 Hz, 1H), 2.46 (s, 1H), 2.35 (dd, J = 3.2, 13.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.70, 147.30, 146.99, 144.78, 141.10, 131.70, 130.68, 129.64, 129.59, 128.91, 128.38, 128.03, 127.61, 127.51, 127.02, 123.24, 118.70, 116.89, 73.57, 60.75, 48.01; HRMS (MALDI, TOF): m/z calcd for $C_{27}H_{21}{}^{35}ClN_2O_3$ $[M + H - H_2O - H_2]^+$ 437.1051, found: 437.1043.

*4-Ethyl-1,2-diphenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3h**).* Reaction time: 5 h; 59.5 mg, 60% yield; brown oil; IR (KBr, cm^{-1}) ν 3429, 3031, 2967, 2879, 1728, 1593, 1573, 1487, 1452, 1367, 1302, 1214, 1125, 1068, 1008, 961, 876, 752, 699; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.40 (m, 1H), 7.30−7.26 (m, 2H), 7.21−7.16 (m, 4H), 7.15−7.10 (m, 1H), 7.05−6.98 (m, 4H), 6.81−6.76 (m, 1H), 6.51−6.47 (m, 1H), 4.88 (dd, J = 3.8, 11.3 Hz, 1H), 2.36−2.17 (m, 2H), 2.09−1.97 (m, 2H), 1.92 (s, 1H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.04, 146.83, 142.96, 129.19, 128.58, 128.49, 128.17, 127.92, 127.30, 127.06, 125.56, 125.42, 118.36, 117.36, 70.16, 60.48, 42.78, 33.43, 8.91; HRMS (MALDI, TOF): m/z calcd for $C_{23}H_{23}NO$ $[M + H - H_2O - H_2]^+$ 310.1590, found: 310.1587.

*2-Isopropyl-4-methyl-1-phenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3i**).* Reaction time: 5 h; 45.5 mg, 54% yield; brown oil; IR (KBr, cm^{-1}) ν 3554, 3433, 3062, 2961, 2872, 1598, 1562, 1492, 1457, 1367, 1300, 1281, 1215, 1164, 1125, 1082, 1023, 945, 886, 859, 746, 699, 512; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.39 (m, 3H), 7.30−7.25 (m, 1H), 7.22−7.18 (m, 2H), 6.96−6.90 (m, 1H), 6.73−6.68 (m, 1H), 6.26−6.22 (m, 1H), 3.67 (dt, J = 12, 3.2 Hz, 1H), 2.01−1.96 (m, 1H), 1.94 (s, 1H), 1.88−1.81 (m, 1H), 1.80−1.73 (m, 1H), 1.72 (s, 3H), 0.87 (d, J = 7.0 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.18, 146.58, 129.78, 129.27, 128.55, 127.85, 126.32, 125.62, 117.80, 117.30, 67.23, 59.04, 36.25, 29.02, 28.18, 19.54, 15.18; HRMS (MALDI, TOF): m/z calcd for $C_{19}H_{23}NO$ $[M + H - H_2O - H_2]^+$ 262.1590, found: 262.1600.

*1,4-Diphenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3j**).* Reaction time: 3 h; 36.8 mg, 31% yield; light-brown oil; IR (KBr, cm^{-1}) ν 3552, 3441, 3060, 3031, 2944, 2857, 1593, 1569, 1494, 1446, 1319, 1271, 1220, 1164, 1120, 1065, 1025, 980, 755, 695, 560; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.44 (m, 2H), 7.41−7.31 (m, 4H), 7.30−7.23 (m, 3H), 7.19−7.13 (m, 1H), 7.02−6.92 (m, 2H), 6.77−6.72 (m, 1H), 6.67−6.61 (m, 1H), 3.92−3.83 (m, 1H), 3.52−3.44 (m, 1H), 2.40−2.32 (m, 1H), 2.31 (s, 1H), 2.24−2.16 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.83, 147.70, 144.78, 129.65, 129.23, 128.72, 128.48, 127.97, 126.92, 126.48, 125.62, 124.68, 118.26, 115.31, 73.40, 47.43, 39.35; HRMS (MALDI, TOF): m/z calcd for $C_{21}H_{19}NO$ $[M + H - H_2O - H_2]^+$ 282.1277, found: 282.1277.

*5-Methoxy-1,2,4-triphenyl-1,2,3,4-tetrahydroquinolin-4-ol (**3k**).* Reaction time: 4 h; 71.0 mg, 58% yield; white solid; mp 164.8−167.4 °C; IR (KBr, cm^{-1}) ν 3572, 3447, 2926, 2833, 1736, 1601, 1592, 1493, 1466, 1435, 1352, 1234, 1107, 1080, 1055, 986, 910, 889, 761, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.24 (m, 2H), 7.21−7.14 (m, 5H), 7.13−7.07 (m, 4H), 7.05−6.96 (m, 5H), 6.30 (d, J = 8.0 Hz, 1H), 6.19 (d, J = 8.5 Hz, 1H), 4.86−4.81 (m, 1H), 3.86 (s, 1H), 3.36 (s, 3H), 2.54−2.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.43, 150.83, 148.90, 146.61, 141.19, 129.02, 128.73, 128.63, 128.14, 127.78, 127.52, 126.73, 125.71, 125.43, 124.47, 117.01, 110.39, 102.20, 72.50, 61.00, 55.29, 49.68; HRMS (MALDI, TOF): m/z calcd for $C_{28}H_{25}NO_2$ $[M + H - H_2O - H_2]^+$ 388.1696, found: 388.1700.

*3-(Diphenylamino)-1,3-diphenylpropan-1-one (**4a**).* yellow solid; mp 139.5−140.6 °C; IR (KBr, cm^{-1}) ν 3061, 3030, 1685, 1587, 1496, 1446, 1355, 1272, 1211, 989, 751, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.72 (m, 2H), 7.53−7.47 (m, 1H), 7.39−7.29 (m, 4H), 7.28−7.19 (m, 3H), 7.19−7.13 (m, 4H), 6.96−6.87 (m, 6H), 6.19 (t, J = 6.8 Hz, 1H), 3.80−3.72 (m, 1H), 3.59−3.50 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.83, 146.74, 141.83, 136.87, 133.15, 129.13, 128.51, 128.48, 128.01, 127.22, 127.10, 123.01, 121.90, 58.20, 41.86; HRMS (EI, TOF): m/z calcd for $C_{27}H_{23}NO$ $[M]^+$ 377.1780, found: 377.1778.

*1,2,3-Triphenylindolin-3-ol (**6a**).* Reaction time: 1 h; 95.9 mg, 88% yield; white solid; mp 66.7−68.1 °C; IR (KBr, cm^{-1}) ν 3542, 3058, 3019, 2860, 1587, 1500, 1474, 1361, 1302, 1268, 1169, 1030, 917, 751, 698, 652, 513; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.39 (m, 2H), 7.37−7.29 (m, 3H), 7.27−7.20

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(m, 6H), 7.19−7.10 (m, 5H), 7.07 (d, J = 7.4 Hz, 1H), 6.97 (t, J = 7.2 Hz, 1H), 6.85 (t, J = 7.3 Hz, 1H), 5.30 (s, 1H), 1.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 148.82, 144.33, 142.55, 134.30, 133.97, 129.66, 129.03, 128.42, 128.39, 128.17, 127.98, 127.30, 126.50, 125.64, 122.94, 121.52, 120.26, 108.85, 82.05, 80.05; HRMS (MALDI, TOF): m/z calcd for $C_{26}H_{21}NO$ [M + H − H_2O]$^+$ 346.1590, found: 346.1582.

*1-(4-Methoxyphenyl)-2,3-diphenylindolin-3-ol (**6b**).* Reaction time: 2 h; 85.9 mg, 72% yield; light-yellow solid; mp 146.6−149.3 °C; IR (KBr, cm^{-1}) ν 3485, 2835, 1599, 1510, 1462, 1354, 1240, 1028, 830, 750, 696, 592, 572, 522; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.40 (m, 2H), 7.38−7.31 (m, 3H), 7.25−7.17 (m, 4H), 7.15−7.10 (m, 4H), 7.05 (d, J = 7.4 Hz, 1H), 6.89 (m, J = 8.1 Hz, 1H), 6.85−6.78 (m, 3H), 5.22 (s, 1H), 3.73 (s, 3H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.12, 150.63, 144.00, 135.95, 134.09, 133.32, 129.73, 128.68, 128.19, 128.11, 127.86, 127.24, 126.80, 125.50, 124.65, 119.78, 114.44, 108.79, 82.06, 81.03, 55.34; HRMS (MALDI, TOF): m/z calcd for $C_{27}H_{23}NO_2$ [M + H − H_2O]$^+$ 376.1696, found: 376.1699.

*1-Phenyl-2,3-di-p-tolylindolin-3-ol (**6c**).* Reaction time: 2 h; 108.1 mg, 92% yield; light-yellow solid; mp 172.6−174.6 °C; IR (KBr, cm^{-1}) ν 3552, 3028, 2850, 1589, 1473, 1358, 1329, 1274, 1207, 1071, 1045, 920, 837, 783, 752, 696, 657, 582; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.27 (m, 2H), 7.24−7.19 (m, 3H), 7.18−7.12 (m, 5H), 7.08−7.00 (m, 5H), 6.96 (t, J = 7.2 Hz, 1H), 6.83 (t, J = 7.3 Hz, 1H), 5.27 (s, 1H), 2.37 (s, 3H), 2.28 (s, 3H), 1.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.81, 142.64, 141.50, 137.81, 136.83, 134.12, 131.13, 129.51, 129.16, 128.97, 128.63, 128.28, 126.45, 125.63, 122.82, 121.56, 120.13, 108.70, 81.81, 79.80, 21.19, 21.08; HRMS (MALDI, TOF): m/z calcd for $C_{28}H_{25}NO$ [M + H − H_2O]$^+$ 374.1903, found: 374.1890.

*3-(3-Bromophenyl)-2-(2-methoxyphenyl)-1-phenylindolin-3-ol (**6d**).* Reaction time: 2 h; 100.6 mg, 71% yield; light-yellow solid; mp 168.7−170.3 °C; IR (KBr, cm^{-1}) ν 3536, 3422, 3055, 2954, 1589, 1491, 1462, 1352, 1275, 1244, 1206, 1177, 1111, 1090, 1038, 947, 923, 800, 767, 700, 615; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.41−7.37 (m, 1H), 7.31−7.25 (m, 4H), 7.24−7.18 (m, 3H), 7.17−7.08 (m, 4H), 6.96−6.91 (m, 1H), 6.89−6.84 (m, 3H), 5.74 (s, 1H), 3.57 (s, 3H), 2.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.73, 147.92, 142.62, 133.94, 130.01, 129.71, 129.37, 129.34, 129.22, 129.04, 128.45, 125.63, 124.94, 123.02, 122.35, 122.10, 120.88, 120.40, 119.88, 110.77, 109.33, 81.86, 73.53, 55.15; HRMS (MALDI, TOF): m/z calcd for $C_{27}H_{22}{}^{79}BrNO_2$ [M + H − H_2O]$^+$ 454.0801, found: 454.0796.

*3-(4-Chlorophenyl)-2-methyl-1-phenylindolin-3-ol (**6e**).* Reaction time: 2 h; 45.9 mg, 46% yield; light-yellow solid; mp 125.7−127.4 °C; IR (KBr, cm^{-1}) ν 3056, 2920, 1594, 1556, 1492, 1458, 1371, 1246, 1212, 1087, 1012, 835, 770, 698, 517, 487; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.53 (m, 2H), 7.44−7.39 (m, 2H), 7.38−7.33 (m, 2H), 7.26−7.13 (m, 4H), 7.02−6.98 (m, 1H), 6.82−6.76 (m, 2H), 4.01 (q, J = 6.5 Hz, 1H), 2.18 (s, 1H), 1.22 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.36, 142.40, 141.91, 133.58, 133.21, 129.96, 129.40, 128.36, 128.06, 124.87, 124.85, 124.79, 119.68, 108.80, 81.40, 71.82, 10.28; HRMS (MALDI, TOF): m/z calcd for $C_{21}H_{18}{}^{35}ClNO$ [M]$^+$ 335.1071, found: 335.1063.

*2,3-Dimethyl-1-phenylindolin-3-ol (**6f**).* Reaction time: 2 h; 65.7 mg, 46% yield; brown oil; IR (KBr, cm^{-1}) ν 3557, 3428, 3047, 2977, 2922, 2859, 1595, 1500, 1477, 1458, 1363, 1285, 1218, 1097, 1015, 919, 724, 698; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.32 (m, 3H), 7.22−7.07 (m, 4H), 6.83−6.77 (m, 1H), 6.72 (d, J = 8.0 Hz, 1H), 3.80 (q, J = 6.5 Hz, 1H), 1.85 (s, 1H), 1.64 (s, 3H), 1.27 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.27, 142.61, 134.01, 129.51, 129.30, 124.36, 124.28, 123.15, 119.19, 108.59, 68.64, 23.96, 11.55; HRMS (MALDI, TOF): m/z calcd for $C_{16}H_{17}NO$ [M + Na]$^+$ 262.1202, found: 262.1191.

*1,2,3-Triphenyl-2,3-dihydro-1H-benzo[f]indol-3-ol (**6g**).* Reaction time: 15 h; 93.1 mg, 75% yield; brown solid; mp 78.8−80.1 °C; IR (KBr, cm^{-1}) ν 3456, 3048, 1631, 1497, 1447, 1381, 1350, 1235, 1096, 1030, 917, 857, 751, 711, 692, 533; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.60 (m, 2H), 7.54 (s, 1H), 7.48−7.44 (m, 3H), 7.41−7.38 (m, 1H), 7.37−7.34 (m, 2H), 7.33−7.30 (m, 2H), 7.30−7.28 (m, 2H), 7.28−7.24 (m, 5H), 7.19−7.15 (m, 2H), 7.04−6.97 (m, 1H), 5.34 (s, 1H), 2.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.12, 144.48, 142.37, 137.35, 135.34, 134.75, 129.37, 129.15, 128.59, 128.33, 128.27, 128.14, 127.47, 126.65, 126.47, 126.19, 125.02, 122.94, 122.91, 120.88, 102.80, 81.56, 79.87; HRMS (EI, TOF): m/z calcd for $C_{30}H_{23}NO$ [M]$^+$ 413.1780, found: 413.1773.

*4-Methoxy-1,2,3-triphenylindolin-3-ol (**6h**).* Reaction time: 15 h; 96.8 mg, 82% yield; white solid; mp 135.2−136.8 °C; IR (KBr, cm^{-1}) ν 3536, 3062, 3035, 2946, 2834, 1593, 1500, 1485, 1466, 1358, 1261, 1110, 1030, 926, 771, 702, 621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.36 (m, 2H), 7.35−7.29 (m, 2H), 7.29−7.24 (m, 4H), 7.23−7.15 (m, 5H), 7.15−7.09 (m, 2H), 6.96−6.83 (m, 2H), 6.44−6.37 (m, 1H), 5.10 (s, 1H), 3.60 (s, 3H), 2.77 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.22, 149.77, 146.54, 142.90, 135.78, 130.99, 128.96, 128.31, 128.15, 128.05, 127.84, 126.90, 125.39, 122.48, 120.47, 103.19, 102.90, 82.02, 80.75, 55.33; HRMS (EI, TOF): m/z calcd for $C_{27}H_{23}NO_2$ [M + Na] $^+$ 416.1621, found: 416.1632.

*1-(4-Bromophenyl)-3-((4-chlorophenyl)amino)-3-(p-tolyl)-propan-1-one (**2e**).* Reaction time: 20 h; 1.2 g, 70% yield; light-yellow solid; mp 136.5−137.4 °C; IR (KBr, cm^{-1}) ν 3390, 1670, 1629, 1603, 1584, 1506, 1487, 1397, 1352, 1311, 1280, 1213, 1075,992, 812, 734, 505; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 7.7 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 7.02 (d, J = 8.5 Hz, 2H), 6.47 (d, J = 8.5 Hz, 2H), 4.90 (t, J = 6.3 Hz, 1H), 4.66 (s, 1H), 3.45−3.34 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.19, 145.43, 139.14, 137.26, 135.34, 132.00, 129.64, 129.59, 128.92, 128.72, 126.15, 122.49, 114.97, 54.56, 46.09, 21.06; HRMS (MALDI, TOF): m/z calcd for $C_{22}H_{19}{}^{81}Br{}^{35}ClNO$ [M]$^+$ 429.0312, found: 429.0312.

*3-(3-Bromophenyl)-3-((3,4-dichlorophenyl)amino)-1-(3-methoxyphenyl) propan-1-one (**2f**).* Reaction time: 20 h; 1.3 g, 68% yield; light-yellow solid; mp 110.6−111.6 °C; IR (KBr, cm^{-1}) ν 3387, 1669, 1635, 1604, 1506, 1487, 1400, 1351, 1313, 1283, 1214, 1173, 1075, 991, 814, 738, 507; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.70−7.65 (m, 1H), 7.31 (t, J = 7.9 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H), 7.09 (d, J = 8.7 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H), 6.91 (s, 1H), 6.81−6.75 (m, 1H), 6.65−6.60 (m, 1H), 6.41−6.35 (m, 1H), 4.88 (t, J = 6.2 Hz, 1H), 4.82 (s, 1H), 3.77 (s, 3H), 3.40 (d, J = 6.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.57, 160.11, 146.34, 143.42, 138.16, 136.39, 132.61, 131.23, 130.49, 130.28, 130.12, 126.62, 123.08, 120.52, 118.40, 115.10, 113.37, 112.74, 112.15, 55.22, 54.55, 45.98; HRMS (ESI, TOF): m/z calcd for $C_{22}H_{18}{}^{81}Br{}^{35}Cl_2NO_2$ [M + H]$^+$ 479.9950, found: 479.9944.

*5-Methyl-4-(phenylamino)hexan-2-one (**2i**).* Reaction time: 8 h; 319.4 mg, 78%; brown oil; IR (KBr, cm^{-1}) ν 3386, 3053, 2961, 2873, 1711, 1601, 1508, 1468, 1430, 1364,

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1316, 1264, 1180, 1091, 1068, 1031, 991, 869, 750, 691, 502; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−7.11 (m, 2H), 6.69−6.64 (m, 1H), 6.61−6.57 (m, 2H), 3.76−3.71 (m, 1H), 3.66 (s, 1H), 2.65−2.51 (m, 2H), 2.13 (s, 3H), 1.99−1.90 (m, 1H), 0.96 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.23, 147.51, 129.36, 117.33, 113.33, 54.96, 45.31, 31.46, 30.55, 18.74, 18.61; HRMS (MALDI, TOF): m/z calcd for $C_{13}H_{19}NO$ $[M + H]^+$ 206.1539, found: 206.1533.

*1-(3-Bromophenyl)-2-(2-methoxyphenyl)-2-(phenylamino)ethanone (**5d**).* Reaction time: 48 h; 584.9 mg, 82% yield; yellow solid; mp 114.2−116.4 °C; IR (KBr, cm^{-1}) ν 3396, 3056, 3018, 2939, 2840, 1684, 1601, 1566, 1503, 1465, 1431, 1310, 1239, 1092, 1027, 996, 902, 751, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (t, J = 1.8 Hz, 1H), 7.99−7.95 (m, 1H), 7.61−7.57 (m, 1H), 7.24−7.08 (m, 5H), 6.89−6.81 (m, 2H), 6.72−6.63 (m, 3H), 6.43 (s, 1H), 5.41 (s, 1H), 4.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.90, 156.05, 146.06, 136.62, 136.22, 131.84, 130.11, 129.68, 129.23, 128.19, 127.15, 125.73, 122.68, 121.62, 117.73, 113.41, 111.07, 55.66, 55.15; HRMS (MALDI, TOF): m/z calcd for $C_{21}H_{18}{}^{79}BrNO_2$ $[M + H]^+$ 396.0594, found: 396.0604.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for **2e**, **2f**, **2i**, **3a**−**3k**, **4a**, **5d**, **6a**−**6h**; ROESY spectra for **3g** and **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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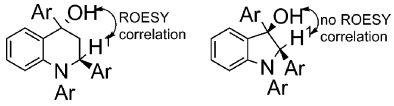

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