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Per-6-amino-β-cyclodextrin as a Chiral Base Catalyst Promoting One-Pot Asymmetric Synthesis of 2-Aryl-2,3-dihydro-4-quinolones

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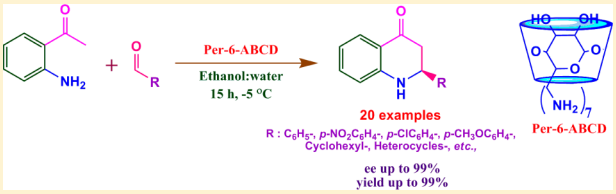
Supporting Information

ABSTRACT: A highly efficient one-pot synthesis of enantiomerically enriched 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones has been carried out for the first time using per-6-ABCD as a supramolecular host, chiral base catalyst, and a reusable promoter to give the corresponding scaffold with high yield (up to 99%) and enantiomeric excess (up to 99%). The catalyst is recovered and reused without loss in its activity.



The demand for chiral compounds often as single enantiomers, which are crucially important to the development of pharmaceutical, agricultural, and fine chemical industries, as well as materials science has escalated sharply in recent years.[1] Among the various approaches employed for this purpose, asymmetric catalysis of organic reactions is one of the most efficient ways to obtain optically pure compounds by utilizing chiral catalysts and auxiliaries.[2] One-pot synthesis is a powerful method for assembling a single molecule from multiple starting materials and for forming several bonds in a one-step process.[3] Consequently, many chiral ligands and their transition-metal complexes have been developed for the homogeneous one-pot asymmetric catalysis of various organic transformations. The main concern in this situation is the need for reusable chiral catalysts for industrial implementation. Due to the high cost of both the metal and the chiral ligands, systems that allow the straightforward separation of expensive chiral catalysts from reaction mixtures and efficient recycling are highly desirable.

The quinolone scaffold is present in many natural products and is regarded as a "privileged building block" for medicinal chemistry, with simple and flexible synthetic routes that allow the production of large chemical libraries of potential bioactive molecules.[4] Consequently, numerous synthetic strategies have been developed to gain access to different varieties of this scaffold. 2-Aryl-2,3-dihydro-4-quinolones represent a new class of antimitotic antitumor agents. Since their two enantiomers were found to display distinctly different activities,[5] a highly enantioselective synthesis of these compounds is desirable. Only four reports are available to date for enantioenriched synthesis of 2-aryl-2,3-dihydro-4-quinolones reported from the groups of Shintani,[6a] Liu,[6b] Lei,[6c] and Feng.[6d] These reports make use of transition-metal-mediated catalytic processes and nonrecoverable chiral catalysts and involve multiple steps for the activation and removal of activating groups and hazardous chemicals. Taking all these into account, the use of multifunctional catalysts which not only generates less waste but also ideally obviates the tedious separation and purification protocols is desirable.

Cyclodextrins (CDs) are macrocyclic oligosaccharides possessing hydrophobic cavities that bind substrates selectively via noncovalent interactions,[7a] and this property enables them to be used in various applications. Native β-CD has been employed as a catalyst[7] for thiol[7b] and aza-Michael addition[7c] in water medium with poor chiral induction. Chemical modification of cyclodextrins is expected to improve the enantioselectivity in asymmetric catalysis[7d] and in chiral NMR analysis.[7e] Selectively modified cyclodextrins are used as sensors as well as catalysts.[8] Peramino-CDs are homogeneous CD derivatives modified by persubstitution at the primary face with amino pendant groups, which display combined hydrophobic and electrostatic binding of guest molecules relative to native CDs. They have been employed as catalysts in various organic transformations[9] and sensors applications.[10] These features prompted us to exploit this catalyst in the efficient one-pot asymmetric cyclization route for the development of quinolone scaffolds starting from *o*-aminoacetophenone and substituted aldehydes via *o*-aminochalcone intermediate (Scheme 1). Herein, we report per-6-ABCD (**1b**) successfully as a reusable multifunctional base catalyst and a chiral host for the one-pot synthesis of 2-aryl-2,3-dihydro-4-quinolones in ethanol/water (1:1,v/v) medium at −5 °C with good to excellent yield and enantiomeric excess. It is also interesting to note that per-6-ABCD can be recovered and reused several times. To the best of our knowledge, this is the first example of a one-pot asymmetric synthesis of 2-aryl-2,3-dihydro-4-quinolones using *o*-aminoacetophenone and substituted aldehyde. A series of six aminocyclodextrin derivatives (Figure 1) were also synthesized and assayed as catalysts for synthesis of 2-aryl-2,3-dihydro-4-quinolones.

Preliminary investigations of the title reaction were carried out using **1b** as the catalyst and *o*-aminoacetophenone (**2**) and benzaldehyde (**3a**) as model substrates to optimize the reaction conditions, and the results are summarized in Table 1. All of the

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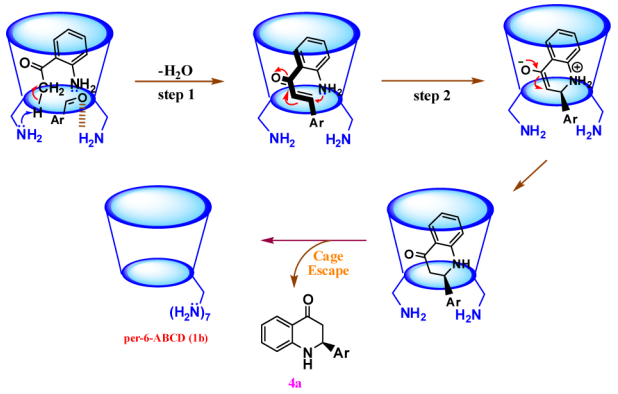
Scheme 1. Proposed Mechanism for One-Pot Asymmetric Synthesis of 2-Aryl-2,3-dihydro-4-quinolone Catalyzed by 1b



reactions are performed in the optimized experimental procedure given in the Experimental Section. The corresponding imine is the major product (Figure S1a, Supporting Information) when the reaction is carried out in β-cyclodextrin in water (entry 1), which indicates the importance of amino groups in this reaction. When diethylamine is employed as an external base along with native β-CD, though moderate conversion is observed, the enantiomeric excess is very poor at room temperature (ee 5.2%) and at 4 °C (ee 6.4%) (entry 2). Interestingly, when the reaction is carried out with **1b** as the catalyst in water the reaction becomes faster with 42% yield of **4a** and 46% ee (entry 3).

During solvent optimization, the reaction studied in various solvents such as water, dimethylformamide, dimethyl sulfoxide, acetonitrile, methanol and ethanol affords only modest yield and low enantioselectivity (entries 4–8). On the other hand, the ethanol/water (1:1,v/v) mixture is identified as the most suitable solvent with respect to both yield and enantioselectivity (entry 12). Under these optimized conditions, to enhance enantioselectivity, the effect of temperature is also recorded (entry 13). At low temperature (−5 °C), the enantioselectivity in **4a** increases drastically (ee up to 98%) with a decrease in the yield (up to 71%) (entry 13). The absolute configuration of the predominant enantiomer was assigned as *S* (Supporting Information) by comparison with literature data.[6a−d]

The reaction was studied in the presence of the more sterically demanding **1a** and less sterically demanding **1c** under the optimized conditions, and they display low reactivity and enantioselectivity compared to **1b** (entry 14). The reaction was also studied with monoamino-CDs under the optimized conditions. Poor reactivity and enantioselectivity were noticed with **1d** (yield 42%, ee 31%), **1e** (yield 75%, ee 84%), and **1f** (yield 67%, ee 62%) (entry 15). The reaction was also examined with different molar ratios of host and guest. Though very good conversions were observed, the ee was excellent only when the H/G ratio was ≥1 (entries 16–20). These observations clearly indicate that optimum results are found (yield 98%, ee 98%) when the reaction is carried out in ethanol/water (1:1, v/v) at −5 °C with **1b** for 15 h (entry 13).

To test the generality of the reaction, various substituted aldehydes were subjected to the above optimized reaction conditions, and the results are given in Table 2. Good to excellent yields and enantioselectivities were obtained for a wide range of *para*-substituted aromatic aldehydes. Cyclic and heterocyclic aldehydes provided products in high yield (81–99%) with excellent enantioselectivity (82–99%). A variety of functional groups, including methoxy, nitro, chloro, and methyl groups, are well-tolerated. Substitution on the aryl ring of the aldehyde at different positions also influences the reactivity. Among the *ortho*-, *meta*-, and *para*-substituted aldehydes examined, *para*-substituted aldehydes provide excellent yields (93–99%) with high enantioselectivities (94–99%) when compared to the *ortho*- and *meta*-substituted aldehydes. When more than one substituent is present in the phenyl ring and the distance between the carbonyl carbon and phenyl ring increases (entries 13 and 14), the yield as well as ee decrease considerably. These results clearly suggest that electronic factors play a limited role, but the position and size (steric factors) of substituents play a major role in enhancing the ee. *Para*-substituted aldehydes (which ensure a stronger binding and deeper inclusion into the CD cavity) show higher ee. A gram scale experiment was also performed using **1b** and gave excellent isolated yield (99%) with high ee (99%) (entry 3), and the results are comparable to those obtained for a small-scale reaction.

Per-6-ABCD (**1b**) was also recovered and reused up to seven times with only a marginal decrease in yield and ee (Supporting Information, Table S2). To evaluate in more detail the cavity size effect of the catalyst's architecture in this system, we extended our study with **1a** and **1c** to selected aliphatic and highly substituted aromatic aldehydes under optimized reaction conditions (Supporting Information, Table S3). The reaction was catalyzed by **1a** smoothly for aliphatic aldehydes to afford the corresponding product (**4t** and **4u**) with good yield and reasonable enantioselectivities (entries 3 and 4) compared to aromatic aldehydes (entries 1 and 2). With its large cavity, **1c** is found to be useful for disubstituted (in different positions)-aldehydes also resulting in excellent yield and enantiopurity (entries 5–9).

On the basis of the above results based on reactivity and stereochemical outcome and also in accordance with previous literature reports,[11] a plausible reaction pathway is proposed as shown in Scheme 1.The first step involves formation of

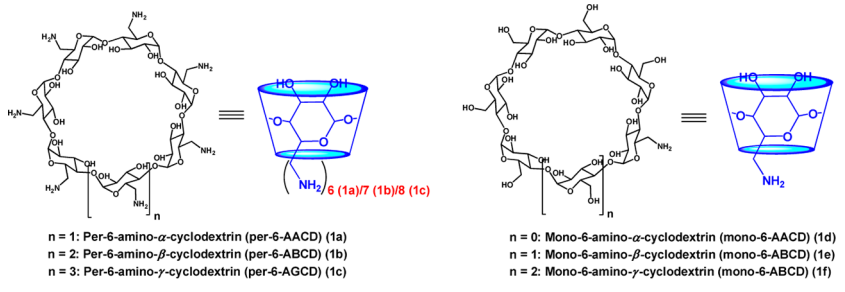


Figure 1. Aminocyclodextrin catalysts employed in this study.

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Table 1. Optimization of Reaction Conditions for the Synthesis of 2-Aryl-2,3-dihydro-4-quinolones[a]

entry	medium	catalyst[b]	T (°C)	yield[c] (%)	ee[d] (%)
1	water	β-CD	rt	imine (78)	
2	water	β-CD:diethylamine[e]	rt (4 °C)	54 (50)	5.2 (6.4)
3	water	**1b**	rt	42	46
4	dimethylformamide	**1b**	rt	56	31
5	dimethylsulfoxide	**1b**	rt	61	37
6	acetonitrile	**1b**	rt	66	52
7	methanol	**1b**	rt	72	60
8	ethanol	**1b**	rt	86	71
9	dimethylformamide/water	**1b**	rt	80	66
10	acetonitrile/water	**1b**	rt	86	71
11	methanol/water	**1b**	rt	94	76
12	ethanol/water	**1b**	rt	99	84
13	ethanol/water	**1b**	10/0/−5/−10/−15	99/99/98/90/71	86/95/98/98/98
14	ethanol/water	**1a**	−5	99	62
15	ethanol/water	**1c**	−5	89	78
16	ethanol/water	**1d**	−5	42	31
17	ethanol/water	**1e**	−5	75	84
18	ethanol/water	**1f**	−5	67	62
19	ethanol/water	**1b**(0.25:1)[f]	−5	85	36
20	ethanol/water	**1b**(0.50:1)[g]	−5	92	67
21	ethanol/water	**1b**(0.75:1)[h]	−5	96	86
22	ethanol/water	**1b**(1:1)[i]	−5	98	98
23	ethanol/water	**1b**(2:1)[j]	−5	99	99

[a]All reactions were performed with catalyst **1b** (0.1 mmol), *o*-aminoacetophenone (0.1 mmol), aldehyde (0.1 mmol) in ethanol/water (1:1,v/v) stirred at −5 °C for 15 h, unless otherwise noted. [b]Catalyst used as mole ratio of 1:1 catalyst/aldehyde, unless otherwise noted. [c]Isolated yield. [d]ee value was determined by HPLC analysis on a chiral stationary phase (AD-H column). Absolute configurations of products were assigned by comparison with the HPLC retention time of the corresponding product reported in the literature (ref 6a−d.). [e]β-CD as chiral host, diethylamine as the external base. [f]Mole ratio of **1b**/aldehyde is 0.25:1. [g]Mole ratio of **1b**/aldehyde is 0.50:1. [h]Mole ratio of **1b**/aldehyde is 0.75:1. [i]Mole ratio of **1b**/aldehyde is 1:1. [j]Mole ratio of **1b**/aldehyde is 2:1.

chalcone by the condensation between *o*-aminoacetophenone and aldehyde. In the second step, isomerization of chalcone, via aza-Michael addition[12] (nucleophilic attack of the 2′-amino group to β-carbon) takes place followed by tautomerization to afford 2-aryl-2,3-dihydro-4-quinolone with high enantioselectivity (ee > 99%). Aza-Michael addition takes place inside the per-6-ABCD cavity, through its *Si* face, which is activated by amino groups of **1b**. Thus, it is clear that the mode of binding of substance plays a crucial role[9b,e] for the stereochemical outcome in this study. Control experiments also indicate clearly that mode of addition of reactants and the amount of catalyst plays a major role. Upon addition of **3a** instead **2** to **1b** the corresponding imine is obtained as sole product and using catalytic amount of **1b** as catalyst and reaction is completed within 6 h at room temperature in ACN as solvent with higher yield and less ee (Supporting Information, Table S1).

The phenyl ring along with the olefinic double bond is deeply penetrating inside the cavity, and the benzoyl moiety of chalcone stays out/near of the wider rim of **1b** (Scheme 1 and Supporting Information, Figure S5). This type of inclusion (mode A, Supporting Information, Figure S7) with a lower complexation energy (ΔE = −42.61 kcal·M^{-1}) is preferred more than other modes (mode B, Supporting Information, Figure S8), in which the benzoyl moiety penetrates inside the cavity and the phenyl group with olefinic double bond of the chalcone stays outside (ΔE = −38.92 kcal·M^{-1}). Mode A is stabilized by hydrogen bonding between the carbonyl group and amino group of chalcone and amino groups of **1b**. During the addition of **3a**, a ternary complex of **2** and **3a** with **1b** is formed (2328 M^{-2} with a relative error 1.17% for n = 3), which is more stable than a binary complex (1635 M^{-1} with relative error 1.08% for n = 3) of **1b** and **2**, which is also evident from molecular modeling studies. Formation of the binary and ternary complexes and then the intermediate is also evident from ESI-MS data. The molecular ion peaks (m/z found 1369.5998, calcd 1369.6012; m/z found 1263.5579, calcd 1263.5798; Supporting Information, Figures S12 and S11, respectively) correspond to ternary complex of **2** and **3a** with **1b** and the binary complex of **3a** and **1b**, respectively. During the course of reaction, the reaction mixture is also analyzed by ESI-MS, which shows the molecular ion peak (m/z found 1351.5989, calcd 1351.5892), and it is confirmed that the reaction proceeds via *o*-aminochalcone (^{1}H and ^{13}C NMR) as the intermediate (2651 M^{-1} with relative error 0.98% for n = 3).

In the proposed mechanism (Scheme 1), primary amino groups present in the narrow rim of **1b** acting as an internal base (pK_a 6.5−8.9)[13]activate the acetyl group of **2** by abstracting a proton (reddish orange color, observed λ_{max} = 356 nm, Supporting Information, Figure S1b(b)), producing additional support for inclusion of *o*-aminoacetophenone (Supporting Information, binary complex structure Figure S11). This is followed by nucleophilic attack on the included aldehyde and subsequent dehydration to generate chalcone (yellow color). Simultaneously, isomerization of chalcone via aza-Michael addition[12] to the β-carbon of chalcone and tautomerization afford the 2-aryl-2,3-dihydro-4-quinolones with high enantioselectivity (ee > 99%). This occurs from the amino-functionalized narrow rim side of **1b** leading to the formation of the major (*S*)-isomer, which is confirmed from the

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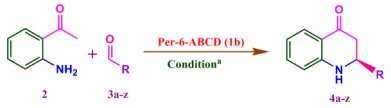
Table 2. Asymmetric One-Pot Synthesis of 2-Aryl-2,3-dihydro-4-quinolones Catalyzed by Per-6-ABCD with Various Substituted Aldehydes[a]



entry	R	product	yield[b] (%)	ee[c] (%)
1	C_6H_5–	**4a**	98	98
2	*p*-$NO_2C_6H_4$–	**4b**	97	98
3[d]	*p*-ClC_6H_4–	**4c**	99	99
4	*m*-ClC_6H_4–	**4d**	90	90
5	*o*-ClC_6H_4–	**4e**	86	82
6	*p*-$OCH_3C_6H_4$–	**4f**	98	97
7	*m*-$OCH_3C_6H_4$–	**4g**	95	92
8[e]	*p*-OHC_6H_4–	**4h**	20	88
9[e]	*o*-OHC_6H_4–	**4i**	18	72
10	*p*-$CH_3C_6H_4$–	**4j**	94	94
11	*p*-*i*-PrC_6H_4–	**4k**	93	99
12	*p*-$NMe_2C_6H_4$–	**4l**	96	99
13[f]	$C_6H_5CH{=}CH$–	**4m**	79	86
14[f]	$C_6H_5CH_2$–	**4n**	85	91
15	2′-pyrrolyl–	**4o**	98	98
16	2′-furanyl–	**4p**	95	95
17	2′-thiophene-yl–	**4q**	91	98
18	2′-pyridinyl–	**4r**	99	99
19	cyclohexyl–	**4s**	81	88
20[f]	CH_3–	**4t**	59	69
21	$(CH_3)_2CH$-CH_2–	**4u**	64	74
22	*m*,*p*-$Cl_2C_6H_3$–	**4v**	93	80
23[f]	*p*-Cl,*m*-$NO_2C_6H_3$–	**4w**	98	78
24	*m*-OCH_3-*p*-OH-C_6H_3–	**4x**	86	87
25	*m*,*m*′-$(OCH_3)_2$-*p*-OHC_6H_2–	**4y**	81	72
26	6-nitropiperonal	**4z**	82	91

[a]All reactions were performed with **1b** (0.1 mmol), *o*-aminoacetophenone (0.1 mmol), aldehyde (0.1 mmol) in ethanol/water (1:1,v/v) stirred at −5 °C for 15 h, unless otherwise noted. [b]Isolated yield. [c]ee value was determined by HPLC analysis on a chiral stationary phase (AD-H column). Absolute configurations of products were assigned by comparison with the HPLC retention time of the corresponding product reported in literature (ref 6a−d). [d]Gram scale. [e]Reaction carried for 48 h; the other product is the corresponding chalcone. [f]Reaction carried for 24 h.

specific rotation[6] of the adduct (**4a**). If the attack takes place from the wider rim of CD (a *Re* face attack), it may lead to formation of the (*R*)-enantiomer, which is obtained in small excess in the *β*-CD-diethylamine system (Table 1, entry 2) and not observed with **1b**. The complexation energies of two enantiomers of 2-aryl-2,3-dihydro-4-quinolones **4a** with **1b** are also calculated and confirm that the (*S*)-enantiomer forms a more stable complex (ΔE = −48.92 kcal·M^{-1}, mode C, Supporting Information, Figure S9) than the corresponding (*R*)-enantiomer (ΔE = −40.28 kcal·M^{-1}, mode D, Supporting Information, Figure S10).

Active participation and catalysis by the amino groups of **1b** are also supported by the fact that per-6-amino-*β*-cyclodextrin hydrochloride fails to catalyze the addition of **3a** to **2** and aza-Michael addition of *o*-aminochalcone. A control experiment carried out with **1b**/adamantanol complex as the catalyst (2248 M^{-1} with relative error 1.20% for n = 3) gives a good yield of **4a** without any ee, which confirms active participation of the chiral cavity of **1b** in inducing enantiometric excess. We believe that the cooperative binding and tighter fit of guest inside the CD cavity ensure their proximity to the chiral centers in CD, which may have contributed to the high enantioselectivities. Though the bulk of the reaction and induction of ee takes place inside the cavity of **1b**, occurrence of the reaction outside the cavity to a smaller extent is also likely (particularly at room temperature and in polar solvents (Table 1, entries 4−6)) in view of the dynamic equilibrium between the free and complexed guest.

In summary, we have presented a highly efficient and enantioselective (92−99% ee) one-pot synthesis of 2-aryl-2,3-dihydro-4-quinolone scaffolds for the first time using **1b**, which simultaneously acts as a multifunctional base to promote the reaction as well as chiral promoter to provide the enantiomerically enriched **4a**. It is relevant to note here that when evaluated for interactions with tubulin and for cytotoxic activity against a panel of various human tumor cell lines the optically pure (*S*)-isomer exhibits greater biological activity than the racemates or (*R*)-isomer.[5] This protocol has provided broad substrate scope for various substituted aldehydes in the synthesis of **4a** under much simpler experimental conditions to give good yields and excellent enantiomeric excesses. The catalyst can be easily recovered by simple filtration and reused several times without significant loss in its activity.

EXPERIMENTAL SECTION

General Procedure for Per-6-ABCD (1b)-Promoted One-Pot Asymmetric Synthesis of 2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones. Aminocyclodextrins (**1a−f**) were synthesized and purified according to the procedure described in the literature, and their characterization data are accordance with the literature.[14]

Per-6-ABCD (**1b**) (0.112 g, 0.1 mmol) was suspended in ethanol/water (1:1 v/v; 2 mL). *o*-Aminoacetophenone (**2**) (13.51 mg, 0.1 mmol) dissolved in ethanol (0.5 mL) was added dropwise to the per-6-ABCD (**1b**) suspension with constant stirring and continued for 30 min to complete complexation (appeared as a reddish orange color, λ_{max} = 365 nm). Then aldehyde **3a−z** (0.1 mmol) was added and the mixture allowed to stir at −5 °C for 10 h. After completion of the reaction, products were extracted with ethyl acetate, dried with sodium sulfate, and concentrated under reduced pressure. The resulting crude product was purified by passing over a column of siliga gel 60−120 mesh using petroleum ether/ethyl acetate (8/2 ratio as an eluent) to afford 2-aryl-2,3-dihydro-4-quinolones **4a−z** as a light yellow−dark yellow solid which was analyzed by NMR spectroscopy (300 MHz, $CDCl_3$, T = 300 K, TMS = 0 ppm), ESI-MS and CSP (chiral stationary phase) HPLC. Percent ee was determined by HPLC at 214 nm using a Chiralpak AD-H column with *n*-hexane and 2-propanol mixtures at a flow rate 0.5−1.0 mL/min (or it otherwise noted). After extraction of the product, per-6-ABCD (**1b**) is washed three times with ethyl acetate, filtered, dried in vacuo, and reused (Supporting Information).

Determination of Absolute Configurations of the Products. The ^{1}H NMR spectrum of **4a** was consistent with the literature data.[7] The enantiomers of **4a** were analyzed by chiral-phase HPLC using a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 26.6 min [(*R*)-enantiomer], major enantiomer t_{major} = 30.0 min [(*S*)-enantiomer], 98% ee, $[\alpha]^{20}_D$ = +27.1 (*c* 0.42, $CHCl_3$) [lit.[6c] $[\alpha]^{20}_D$ = +27.3 (*c* 0.35, $CHCl_3$)], [lit.[6a] Daicel Chiralpak AD-H column with 50:50 *n*-hexane−2-propanol, 0.3 mL/min: major enantiomer t_{major} = 14.5 min [(*R*)-enantiomer], minor enantiomer t_{minor} = 15.7 min [(*S*)-enantiomer], 98% ee, $[\alpha]^{20}_D$ −28.4 (*c* 0.77, $CHCl_3$)]. The configuration of **4a** (*S*) was assigned accordingly, and the configurations of other products were assigned by analogy.[6]

*(S)-2-Phenyl-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 1, **4a**):* pale yellow solid (21.86 mg, 98% yield); mp 150−152 °C [lit.[11m] mp 149−150 °C); $[\alpha]^{20}_D$ = +27.1 (*c* 0.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.72 (dd, J = 4.5, 15.3 Hz, 1H), 2.97 (dd, J = 3.6, 15.3 Hz, 1H), 5.17 (dd, J = 8.4, 3.3 Hz, 1H), 5.57 (br s, 1H),

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6.79−6.83 (m, 2H), 7.26−7.32 (m, 4H), 7.42−7.43 (m, 2H), 7.94−7.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 45.9, 57.9, 115.5, 117.9, 118.5, 126.2, 127.1, 128.0, 128.5, 135.0, 140.6, 151.2, 192.9; ESI-MS m/z calcd for $C_{15}H_{13}NO$ $[M + H]^+$ 224.1076, found 224.2500 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 26.6 min, major enantiomer t_{major} = 30.0 min, 98% ee.

(S)-2-(4-Nitrophenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 2, ***4b****):* orange solid (26.00 mg, 97% yield); mp 200−202 °C (lit.[11m] mp 200−202 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.79 (dd, J = 5.4, 15.6 Hz, 1H), 2.96 (dd, J = 3.6, 15.6 Hz, 1H), 5.23 (dd, J = 9.3, 4.2 Hz, 1H), 5.81 (br s, 1H), 6.78−6.81 (m, 2H), 7.25−7.27 (m, 1H), 7.82−7.84 (m, 2H), 7.95−7.97 (m, 1H), 8.16−8.19 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 47.1, 57.2, 115.9, 117.4, 118.4, 123.8, 124.1, 128.6, 134.8, 139.6, 141.5, 151.3, 190.5; ESI-MS m/z calcd for $C_{15}H_{12}N_2O_3$ $[M + H]^+$ 269.0927, found 269.0833 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (20:80 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 32.6 min, major enantiomer t_{major} = 40.0 min, 98% ee.

(S)-2-(4-Chlorophenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 3, ***4c****):* pale yellow solid (25.44 mg, 99% yield); mp 169−170 °C (lit.[11g] mp 168−170 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.80 (dd, J = 3.9, 14.7 Hz, 1H), 3.15 (dd, J = 4.8, 14.7 Hz, 1H), 5.17 (dd, J = 9.0, 3.0 Hz, 1H), 5.81 (br s, 1H), 6.78−6.81 (m, 2H), 7.38−7.39 (m, 1H), 7.43−7.59 (m, 4H), 7.95−7.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.3, 57.8, 116.0, 118.6, 119.0, 127.5, 127.9, 129.1, 134.1, 135.5, 139.5, 151.4, 192.8; ESI-MS m/z calcd for $C_{15}H_{12}ClNO$ $[M + H]^+$ 258.0686, found 258.1667 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 29.0 min, major enantiomer t_{major} = 33.4 min, 99% ee.

(S)-2-(3-Chlorophenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 4, ***4d****):* pale yellow solid (23.13 mg, 90% yield); mp 143−145 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.83 (dd, J = 3.9, 15.0 Hz, 1H), 3.03 (dd, J = 3.3, 15.0 Hz, 1H), 5.13−5.19 (m, 1H), 5.75 (br s, 1H), 6.79−6.81 (m, 2H), 7.27−7.34 (m, 4H), 7.48 (s, 1H), 7.95−7.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.1, 57.9, 116.0, 118.6, 119.0, 124.7, 126.7, 127.5, 128.5, 130.2, 134.8, 135.4, 143.1, 151.3, 192.5; ESI-MS m/z calcd for $C_{15}H_{12}ClNO$ $[M + H]^+$ 258.0686, found 258.1660 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 *n*-hexane−2-propanol, 0.2 mL/min, 214 nm); minor enantiomer t_{minor} = 60.1 min, major enantiomer t_{minor} = 66.0 min, 90% ee.

(S)-2-(2-Chlorophenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 5, ***4e****):* pale yellow solid (22.10 mg, 86% yield); mp 146−147 °C [lit.[11m] mp 145−147 °C]; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 3.58 (dd, J = 3.9, 13.8 Hz, 1H), 3.02 (dd, J = 4.2, 13.8 Hz, 1H), 5.44−5.59 (m, 1H), 5.95 (br s, 1H), 6.78−6.82 (m, 2H), 7.25−7.27 (m, 3H), 7.52 (d, J = 6.3 Hz, 2H), 7.96−7.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 37.2, 47.4, 109.2, 111.8, 112.3, 120.7, 122.4, 122.5, 123.2, 123.3, 125.9, 128.6, 131.5, 144.8, 186.0; ESI-MS m/z calcd for $C_{15}H_{12}ClNO$ $[M + H]^+$ 258.0686, found 258.2250 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 *n*-hexane-2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 41.9 min, major enantiomer t_{major} = 46.0 min, 82% ee.

(S)-2-(4-Methoxyphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 6, ***4f****):* yellow solid (24.82 mg, 98% yield); mp 145−146 °C (lit.[11m] mp 145−147 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.83 (dd, J = 3.0, 15.3 Hz, 1H), 3.03 (dd, J = 3.6, 15.3 Hz, 1H), 3.82 (s, 3H), 5.19 (dd, J = 8.1, 3.3 Hz, 1H), 5.78 (br s, 1H), 6.77−6.88 (m, 4H), 7.26−7.37 (m, 3H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.2, 55.0, 57.6, 114.0, 115.7, 117.9, 118.6, 127.5, 129.8, 132.8, 135.1, 151.5, 159.3, 193.3; ESI-MS m/z calcd for $C_{16}H_{15}NO_2$ $[M + H]^+$ 254.3037, found 254.2562 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 38.5 min, major enantiomer t_{major} = 46.6 min, 97% ee.

(S)-2-(3-Methoxyphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 7, ***4g****):* brownish yellow solid (24.06 mg, 95% yield); mp 129−131 °C (lit.[11m] mp 129−130 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.72−2.83 (m, 1H), 2.96−3.07 (m, 1H), 3.78 (s, 3H), 5.15−5.18 (m, 1H), 5.70 (br s, 1H), 6.76−6.81 (m, 3H), 6.99−7.06 (m, 2H), 7.20−7.27 (m, 2H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 42.2, 55.6, 55.9, 112.9, 114.4, 116.9, 117.9, 121.3, 123.2, 127.0, 129.5, 130.9, 143.5, 149.6, 159.9, 191.4; ESI-MS m/z calcd for $C_{16}H_{15}NO_2$ $[M + H]^+$ 254.3037, found 254.3104 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (60:40 *n*-hexane−2-propanol, 0.5 mL/min, 214 nm); minor enantiomer t_{minor} = 27.3 min, major enantiomer t_{major} = 30.3 min, 92% ee.

(S)-2-(4-Hydroxyphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 8, ***4h****):* yellow solid (4.78 mg, 20% yield); mp 158−161 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.82 (dd, J = 3.0, 15.3 Hz, 1H), 3.02 (dd, J = 5.4, 15.0 Hz, 1H), 4.61 (br s, 2H), 5.19 (dd, J = 9.6, 3.3 Hz, 1H), 6.78−6.81 (m, 4H), 7.23−7.27 (m, 3H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 42.5, 55.4, 116.0, 117.0, 117.9, 123.2, 127.0, 127.9, 131.0, 135.5, 149.5, 156.2, 192.3; ESI-MS m/z calcd for $C_{15}H_{13}NO_2$ $[M + H]^+$ 240.1025, found 240.1106 (rel int 100%). Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85; O, 13.37. Found: C, 75.31; H, 5.50; N, 5.86; O, 13.39. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.4 mL/min, 214 nm); minor enantiomer t_{minor} = 28.3 min, major enantiomer t_{major} = 30.1 min, 88% ee.

(S)-2-(2-Hydroxyphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 9, ***4i****):* yellow solid (4.30 mg, 18% yield); mp 164−168 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.89 (dd, J = 3.6, 15.6 Hz, 1H), 3.04 (dd, J = 3.6, 15.6 Hz, 1H), 4.97 (br s, 2H), 5.52 (dd, J = 9.3, 3.3 Hz, 1H), 6.79−6.91 (m, 3H), 6.91 (m, 1H), 7.07 (m, 1H), 7.08 (m, 1H), 7.27 (m, 1H), 7.95−7.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 42.4, 51.8, 116.2, 116.8, 117.5, 122.7, 123.2, 126.3, 126.5, 126.9, 128.2, 131.2, 150.1, 156.6, 192.7; ESI-MS m/z calcd for $C_{15}H_{13}NO_2$ $[M + H]^+$ 240.1025, found 240.1092 (rel int 100%). Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85; O, 13.37. Found: C, 75.31; H, 5.51; N, 5.85; O, 13.38. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (70:30 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 26.2 min, major enantiomer t_{minor} = 31.3 min, 72% ee.

(S)-2-p-Tolyl-2,3-dihydroquinolin-4(1H)-one (Table 2, Entry 10, ***4j****):* glittering pale yellow solid (22.28 mg, 94% yield); mp 148−149 °C (lit.[11g,m] mp 148−149 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.21 (s, 3H), 2.80 (dd, J = 3.3, 16.2 Hz, 1H), 3.04 (dd, J = 4.2, 16.2 Hz, 1H), 5.11−5.28 (m, 1H), 5.81 (br s, 1H), 6.78−6.81 (m, 2H), 7.12 (d, J = 6.9 Hz, 2H), 7.17−7.38 (m, 3H), 7.95−7.98 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 20.7, 46.0, 57.8, 115.5, 117.9, 118.6, 126.1, 127.2, 129.2, 134.9, 137.7, 137.8, 151.3, 193.0; ESI-MS m/z calcd for $C_{16}H_{15}NO$ $[M + H]^+$ 238.1233, found 238.1695 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (60:40 *n*-hexane−2-propanol, 0.4 mL/min, 214 nm); minor enantiomer t_{minor} = 14.2 min, major enantiomer t_{major} = 17.7 min, 94% ee.

(S)-2-(4-Isopropylphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 11, ***4k****):* glittering yellow solid (24.65 mg, 93% yield); mp 156−158 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 1.22 (s, 6H), 2.78−2.88 (m, 2H), 2.96−3.00 (m, 1H), 5.14−5.19 (m, 1H), 5.75 (br s, 1H), 6.78−6.81 (m, 2H), 7.20−7.27 (m, 3H), 7.39 (d, J = 4.8 Hz, 2H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 24.3, 34.3, 46.8, 58.6, 116.2, 118.7, 119.5, 127.0, 127.4, 128.0, 135.7, 138.8, 149.7, 152.0, 193.7; ESI-MS m/z calcd for $C_{18}H_{19}NO$ $[M + H]^+$ 266.1546, found 266.1673 (rel int 100%). Anal. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28; O, 6.03. Found: C, 81.48; H, 7.22; N, 5.30; O, 6.04. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (70:30 *n*-hexane-2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 16.8 min, major enantiomer t_{major} = 19.0 min, 99% ee.

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*(S)-2-(4-(Dimethylamino)phenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 12, **4l**):* glittering yellow solid (25.54 mg, 96% yield); mp 183−184 °C (lit.[11m] mp 182−184 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.80 (dd, J = 3.3, 15.3 Hz, 1H), 3.02 (dd, J = 3.6, 15.6 Hz, 1H), 3.52 (s, 6H), 5.15 (dd, J = 9.6, 3.9 Hz, 1H), 5.78 (br s, 1H), 6.606−6.63 (m, 2H), 6.78−6.81 (m, 2H), 7.17 (d, J = 4.2 Hz, 2H), 7.25−7.28 (m, 1H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 40.5, 46.4, 57.9, 112.5, 115.9, 118.0, 118.9, 127.48, 127.51, 128.4, 135.2, 150.6, 151.8, 193.9; ESI-MS m/z calcd for $C_{17}H_{18}N_2O$ $[M + H]^+$ 267.1498, found 267.3333 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (50:50 n-hexane−2-propanol, 0.2 mL/min, 214 nm); minor enantiomer t_{minor} = 27.5 min, major enantiomer t_{major} = 34.1 min, 99% ee.

*(S,E)-2-Styryl-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 13, **4m**):* brownish yellow solid (19.68 mg, 79% yield); mp 117−118 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.49 (dd, J = 5.1, 14.7 Hz, 1H), 2.63 (dd, J = 4.8, 14.7 Hz, 1H), 4.67−4.72 (m, 1H), 5.47 (br s, 1H), 6.36−6.40 (m, 1H), 6.51−6.54 (m, 1H), 6.78−6.81 (m, 2H), 7.20−7.28 (m, 6H), 7.94−7.96 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 47.3, 52.0, 113.6, 115.7, 117.2, 128.2, 128.7, 128.8, 128.9, 129.2, 129.6, 130.4, 132.0, 134.4, 137.3, 150.3, 196.2; ESI-MS m/z calcd for $C_{17}H_{15}NO$ $[M + H]^+$ 250.1233, found 250.1253 (rel int 100%). Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62; O, 6.42. Found: C, 81.90; H, 6.07; N, 5.63; O, 6.44. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (70:30 n-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 19.8 min, major enantiomer t_{major} = 21.6 min, 86% ee.

*(R)-2-Benzyl-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 14, **4n**):* brown solid (20.15 mg, 85% yield); mp 105−108 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.30−2.37 (m, 1H), 2.61−2.66 (m, 1H), 2.89−2.92 (m, 1H), 3.02−3.08 (m, 1H), 4.33−4.39 (m, 1H), 5.54 (br s, 1H), 6.70−6.82 (m, 2H), 7.25−7.28 (m, 6H), 7.92−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 39.5, 42.0, 48.8, 116.5, 116.8, 121.9, 126.4, 127.2, 128.4, 129.6, 130.7, 136.9, 150.8, 192.2; ESI-MS m/z calcd for $C_{16}H_{15}NO$ $[M + H]^+$ 238.1233, found 238.2603 (rel int 100%). Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90; O, 6.74. Found: C, 80.98; H, 6.38; N, 5.91; O, 6.74. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (40:60 n-hexane−2-propanol, 0.4 mL/min, 214 nm); major enantiomer t_{major} = 19.9 min, minor enantiomer t_{minor} = 22.9 min, 91% ee.

*(S)-2-(1H-Pyrrol-2-yl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 15, **4o**):* pale yellow sticky liquid (20.78 mg, 98% yield); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.89 (dd, J = 3.0, 13.8 Hz, 1H), 3.02 (dd, J = 3.3, 13.8 Hz, 1H), 5.00 (br s, 2H), 5.31 (dd, J = 10.2, 3.6 Hz, 1H), 6.06−6.08 (m, 1H), 6.16−6,19 (m, 1H), 6.65−6.67 (m, 1H), 6.79−6.81 (m, 2H), 7.25−7.28 (m, 1H), 7.94−8.16 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 44.0, 48.5, 102.5, 107.6, 117.0, 117.9, 118.1, 123.2, 127.2, 128.9, 131.2, 149.9, 192.0; ESI-MS m/z calcd for $C_{13}H_{12}N_2O$ $[M + H]^+$ 213.1028, found 213.1012 (rel int 100%). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20; O, 7.54. Found: C, 73.57; H, 5.72; N, 13.21; O, 7.54. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (70:30 n-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 17.5 min, major enantiomer t_{major} = 20.8 min, 98% ee.

*(S)-2-(Furan-2-yl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 16, **4p**):* pale yellow semisolid (20.24 mg, 95% yield); mp 92−93 °C (lit.[11d] mp 92 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.81−2.89 (m, 1H), 3.01−3.06 (m, 1H), 5.45−5.56 (m, 1H), 5.87 (br s, 1H), 6.36−6.50 (m, 2H), 6.78−6.86 (m, 2H), 7.25−7.27 (m, 1H), 7.55−7.58 (m, 1H), 7.94−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 39.3, 47.5, 104.8, 111.4, 117.0, 117.9, 123.2, 127.0, 131.0, 142.1, 149.6, 152.4, 192.4; ESI-MS m/z calcd for $C_{13}H_{11}NO_2$ $[M + H]^+$ 214.0869, found 214.0988 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 n-hexane−2-propanol, 0.4 mL/min, 214 nm); minor enantiomer t_{minor} = 20.5 min, major enantiomer t_{major} = 23.7 min, 95% ee.

*(S)-2-(Thiophene-2-yl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 17, **4q**):* brownish yellow solid (20.84 mg, 91% yield); mp 135−137 °C (lit.[11m] mp 135−137 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.83 (dd, J = 7.5, 16.2 Hz, 1H), 3.07 (dd, J = 7.2, 16.2 Hz, 1H), 5.25 (br s, 1H), 5.48−5.53 (m, 1H), 6.78−6.81 (m, 2H), 6.82−6.98 (m, 2H), 7.18−7.27 (m, 2H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.9, 53.6, 116.0, 118.7, 119.2, 126.8, 127.5, 128.9, 130.5, 132.5, 135.4, 150.8, 192.6; ESI-MS m/z calcd for $C_{13}H_{11}NOS$ $[M + H]^+$ 230.0640, found 230.1657 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (50:50 n-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 15.5 min, major enantiomer t_{major} = 17.4 min, 98% ee.

*(S)-2-(Pyridin-2-yl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 18, **4r**):* brownish yellow solid (22.18 mg, 99% yield); mp 128−130 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.75 (dd, J = 3.9, 15.6 Hz, 1H), 3.14 (dd, J = 4.2, 15.3 Hz, 1H), 4.46 (br s, 1H), 5.14 (dd, J = 9.0, 3.3 Hz, 1H), 6.78−6.88 (m, 2H), 7.16−7.35 (m, 3H), 7.62 (m, 1H), 7.86−7.88 (m, 1H), 8.58 (d, J = 3.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.2, 52.1, 115.8, 117.1, 124.0, 125.0, 126.9, 131.5, 134.5, 136.8, 140.9, 150.0, 153.5, 191.6; ESI-MS m/z calcd for $C_{14}H_{12}N_2O$ $[M + H]^+$ 225.1029, found 225.1381 (rel int 100%). Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49; O, 7.13. Found: C, 74.99; H, 5.42; N, 12.51; O, 7.13. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 n-hexane−2-propanol, 0.4 mL/min, 214 nm); minor enantiomer t_{minor} = 26.4 min, major enantiomer t_{major} = 32.2 min, 99% ee.

*(S)-2-Cyclohexyl-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 19, **4s**):* brown solid (18.56 mg, 81% yield); mp 140−141 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 1.31−1.62 (m, 11H), 2.25−2.29 (m, 1H), 2.64−2.69 (m, 1H), 3.65−3.70 (m, 1H), 5.28 (br s, 1H), 6.75−6.81 (m, 2H), 7.25−7.27 (m, 1H), 7.92−7.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 25.4, 27.6, 31.8, 43.1, 46.3, 53.0, 115.4, 117.1, 117.9, 131.8, 134.2, 150.4, 194.7; ESI-MS m/z calcd for $C_{15}H_{19}NO$ $[M + H]^+$ 230.1546, found 230.1467 (rel int 100%). Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11; O, 6.98. Found: C, 78.58; H, 8.37; N, 6.11; O, 6.99. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (40:60 n-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 34.5 min, major enantiomer t_{major} = 37.7 min, 88% ee.

*(R)-2-Methyl-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 20, **4t**):* brownish yellow semisolid (9.50 mg, 59% yield); mp 49−50 °C (lit.[111] mp 49−51 °C); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 1.28 (d, J = 3.6 Hz, 3H), 2.28−2.35 (m, 1H), 2.56−2.65 (m, 1H), 4.04−4.10 (m, 1H), 5.58 (br s, 1H), 6.73−6.82 (m, 2H), 7.25−7.28 (m, 1H), 7.92−7.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 18.6, 44.6, 46.9, 116.9, 119.9, 121.6, 127.3, 130.5, 151.8, 192.7; ESI-MS m/z calcd for $C_{10}H_{11}NO$ $[M + H]^+$ 162.0919, found 162.0992 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 n-hexane−2-propanol, 0.4 mL/min, 214 nm); major enantiomer t_{major} = 18.5 min, minor enantiomer t_{minor} = 20.7 min, 69% ee.

*(R)-2-Isobutyl-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 21, **4u**):* brownish yellow sticky liquid (13.00 mg, 64% yield); ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 0.86 (s, 6H), 1.34−1.54 (m, 3H), 2.81−2.32 (m, 1H), 2.55−2.28 (m, 1H), 3.95−4.04 (m, 1H), 5.47 (br s, 1H), 6.74−6.81 (m, 2H), 7.25−7.27 (m, 1H), 7.92−7.94 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 22.1, 24.9, 43.0, 43.9, 46.4, 116.4, 116.7, 121.9, 127.2, 131.7, 150.8, 192.3; ESI-MS m/z calcd for $C_{13}H_{17}NO$ $[M + H]^+$ 204.1388, found 204.1402 (rel int 100%). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89; O, 7.87. Found: C, 76.81; H, 8.44; N, 6.89; O, 7.88. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (70:30 n-hexane−2-propanol, 0.3 mL/min, 214 nm); major enantiomer t_{major} = 26.8 min, minor enantiomer t_{minor} = 29.9 min, 74% ee.

*(S)-2-(3,4-Dichlorophenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 22, **4v**):* yellow semisolid (27.06 mg, 93% yield); mp 205−208 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.86 (dd, J = 7.8, 16.2 Hz, 1H), 3.05 (dd, J = 7.2, 16.2 Hz, 1H), 5.15 (dd, J = 9.9, 3.3 Hz, 1H), 5.76 (br s, 1H), 6.78−6.81 (m, 2H), 7.25−7.27 (m, 2H), 7.40−7.42 (m, 1H), 7.52 (s, 1H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 43.2, 56.9, 117.0, 117.9, 123.1, 126.7, 126.9, 127.0,

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129.3, 129.8, 130.3, 130.9, 143.0, 149.6, 191.4; ESI-MS m/z calcd for $C_{15}H_{11}Cl_2NO$ $[M + H]^+$ 292.0297, found 292.0357 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (70:30 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 28.6 min, major enantiomer t_{major} = 30.8 min, 80% ee.

*(S)-2-(4-Chloro-3-nitrophenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 23, **4w**):* brownish yellow soild (29.60 mg, 98% yield); mp 186−188 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.87 (dd, J = 7.2, 15.3 Hz, 1H), 3.03 (dd, J = 7.8, 15.3 Hz, 1H), 5.21 (dd, J = 9.9, 4.8 Hz, 1H), 5.59 (br s, 1H), 6.77−6.81 (m, 2H), 7.25−7.27 (m, 1H), 7.60−7.72 (m, 2H), 7.91−7.97 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 42.2, 56.0, 117.0, 117.9, 121.0, 123.2, 127.0, 128.1, 131.2, 131.5, 131.9, 143.5, 148.2, 149.9, 192.3; ESI-MS m/z calcd for $C_{15}H_{11}ClN_2O_3$ $[M + H]^+$ 303.0536, found 303.0612 (rel int 100%). Anal. Calcd for $C_{15}H_{11}ClN_2O_3$: C, 59.52; H, 3.66; Cl, 11.71; N, 9.25; O, 15.86. Found: C, 59.52; H, 3.68; Cl, 11.72; N, 9.25; O, 15.87. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.4 mL/min, 214 nm); minor enantiomer t_{minor} = 27.5 min, major enantiomer t_{major} = 32.1 min, 78% ee.

*(S)-2-(4-Hydroxy-3-methoxyphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 24, **4x**):* yellow solid (23.14 mg, 86% yield); mp 143−144 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.83 (dd, J = 5.4, 16.2 Hz, 1H), 3.01 (dd, J = 6.0, 16.2 Hz, 1H), 3.84 (s, 3H), 5.15−5.20 (m, 1H), 5.52 (br s, 2H), 6.78−6.86 (m, 5H), 7.25−7.28 (m, 1H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.2, 55.5, 57.9, 108.4, 114.1, 115.4, 117.9, 118.5, 119.2, 127.1, 132.5, 134.9, 145.3, 146.4, 151.1, 193.0; ESI-MS m/z calcd for $C_{16}H_{15}NO_3$ $[M + H]^+$ 270.1131, found 270.1667 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (80:20 *n*-hexane−2-propanol, 0.5 mL/min, 214 nm); minor enantiomer t_{minor} = 27.1 min, major enantiomer t_{major} = 29.1 min, 87% ee.

*(S)-2-(4-Hydroxy-3,5-dimethoxyphenyl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 25, **4y**):* yellow solid (24.22 mg, 81% yield); mp 167−168 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.78−2.83 (m, 1H), 2.98−3.05 (m, 1H), 3.73 (s, 6H), 5.12−5.29 (m, 1H), 5.57 (br s, 2H), 6.53 (s, 2H), 6.78−6.81 (m, 2H), 7.25−7.27 (m, 1H), 7.95−7.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 46.5, 56.0, 58.5, 103.0, 115.6, 118.1, 118.7, 127.2, 131.9, 134.4, 135.0, 146.9, 151.2, 192.9; ESI-MS m/z calcd for $C_{17}H_{17}NO_4$ $[M + H]^+$ 300.1237, found 300.1608 (rel int 100%). Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.72; N, 4.68; O, 21.38. Found: C, 68.24; H, 5.73; N, 4.69; O, 21.39. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (50:50 *n*-hexane−2-propanol, 0.3 mL/min, 214 nm); minor enantiomer t_{minor} = 24.1 min, major enantiomer t_{major} = 27.3 min, 72% ee.

*(S)-2-(6-Nitrobenzo[d][1,3]dioxol-5-yl)-2,3-dihydroquinolin-4(1H)-one (Table 2, entry 26, **4z**):* yellow solid (25.59 mg, 82% yield); mp 179−180 °C; ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.87 (dd, J = 7.2, 16.5 Hz, 1H), 3.31 (dd, J = 6.9, 16.5 Hz, 1H), 5.24 (dd, J = 10.2, 6.0 Hz, 1H), 5.76 (br s, 1H), 6.12 (s, 2H), 6.26−6.82 (m, 2H), 7.14 (s, 1H), 7.26−7.29 (m, 2H), 7.93−7.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 39.1, 47.4, 100.1, 110.5, 111.8, 113.3, 121.9, 125.6, 129.1, 130.0, 132.9, 142.0, 146.7, 151.7, 154.9, 193.7; ESI-MS m/z calcd for $C_{16}H_{12}N_2O_5$ $[M + H]^+$ 313.0825, found 313.2591 (rel int 100%). Anal. Calcd for $C_{16}H_{12}N_2O_5$: C, 61.54; H, 3.87; N, 8.97; O, 25.62. Found: C, 61.54; H, 3.90; N, 8.98; O, 25.64. HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (50:50 *n*-hexane−2-propanol, 0.2 mL/min, 214 nm); minor enantiomer t_{minor} = 51.6 min, major enantiomer t_{major} = 42.1 min, 91% ee.

(S)-2-Phenyl-1-tosyl-2,3-dihydroquinolin-4(1H)-one (Scheme S1, Supporting Information): ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm) 2.51 (s, 3H), 2.72 (dd, J = 3.3, 15.6 Hz, 1H), 3.14 (dd, J = 3.6, 15.6 Hz, 1H), 5.98 (dd, J = 9.6, 3.3 Hz, 1H), 7.24−7.36 (m, 8H), 7.61−7.70 (m, 3H), 7.84−7.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm) 22.4, 41.2, 56.6, 125.6, 126.2, 126.5, 126.9, 127.1, 127.4, 128.0, 128.9, 131.4, 135.3, 137.1, 138.1, 140.8, 145.3, 191.8; ESI-MS m/z calcd for $C_{22}H_{19}NO_3S$ $[M + H]^+$ 378.1164, found 378.1321 (rel int 100%). HPLC: enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 *n*-hexane−2-propanol, 0.4 mL/min, 214 nm); minor enantiomer t_{minor} = 38.9 min, major enantiomer t_{major} = 44.6 min, 97% ee.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General methods, experimental procedures, copies of ^{1}H and ^{13}C NMR, HPLC trace, and ESI-MS. 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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