Introduction

Indane frameworks are found in natural products that possess diverse biological activities and that serve as drug candidates.\(^1\text{-}^3\) Among members of this family, 3-arylindanols and 3-arylindanones are privileged structural components of many pharmaceutical agents and key intermediates in the synthesis of a variety of bioactive compounds (Fig. 1).\(^4\text{-}^7\) Typical examples of this type are (+)-indatraline used for the treatment of depression and cocaine addiction,\(^8\text{-}^{10}\) the antihypertensive agent (+)-irindalone,\(^11\) the neuroprotective agent (+)-quadrangularin A,\(^12\) (+)-isopaciocofural F used for the treatment of osteoporosis\(^13\) and z-diisougenol that has cytotoxic and antioxidant activities.\(^14\) An example of a bioactive indane bearing a 3-alkenyl group is (+)-mulsianthol, which has antitumor activity.\(^14,15\) In addition, 3-arylindanoles and 3-arylindanones are valuable intermediates in routes for the synthesis medicinal agents.

Consequently, the development of methods for convenient and stereoselective syntheses of 3-arylindanol and 3-arylindanones is an important goal in organic synthesis. Typically, enantioenriched 3-aryl-1-indanols are prepared by reduction\(^7\) (NaBH\(_4\) or K-selectride for 1,3-syn indanols) of enantioenriched 3-aryl-1-indanones. Also, Corey’s oxazaborolidine-catalyzed reduction of racemic 3-aryl-1-indanones is known to produce mixtures containing almost equal amount of cis- and trans-3-aryl-1-indanols.\(^16\text{-}^{17}\) Furthermore, resolution of racemic 3-aryl-1-indanol has been accomplished using a commercially available lipase (Novozyme 435\(^\text{®}\)).\(^18\) Previous efforts have shown that enantioenriched 3-aryl-1-indanones can be prepared by intramolecular Friedel-Crafts acylation of enantioenriched 3,3-diaryl propanoic acids under strongly acidic conditions,\(^19\text{-}^{22}\) or by Ir-catalyzed asymmetric hydrogenation of 3-arylinden-1-ones (58-90% ee).\(^23\) Bakers’ yeast-promoted conjugate reduction of 3-arylinden-1-ones to form enantioenriched 3-aryl-1-indanones has also been described.\(^24\text{-}^{26}\) Recent approaches devised to generate enantioenriched 3-aryl-1-indanones rely on metal [Pd or Ni]-catalyzed asymmetric intramolecular reductive Heck reaction of 2′-halochoalones,\(^7,26\text{-}^{28}\) and Rh-catalyzed asymmetric intramolecular 1,4-addition of aryl boronates to enones.\(^29\)

Asymmetric transfer hydrogenation (ATH) reactions, using hydrogen sources other than molecular hydrogen, have proven to be among the most powerful processes for asymmetric reduction of ketones to produce enantioenriched alcohols. These processes have advantages associated with operational simplicity, ready availability of various hydrogen sources, and use of readily accessible and less sensitive catalysts.\(^30\text{-}^{35}\) Indeed, stereoselective ATH of 1-indanones or 2-substituted-1-indanones to produce corresponding 1-indanols or 2-substituted-1-indanols, which utilize chiral transition metal (Ru, Rh) catalysts and a HCO\(_2\)H/Et\(_3\)N mixture as a hydrogen source, have already been described.\(^36\text{-}^{38}\) However, no examples have been reported thus far of ATH promoted transformations of 3-aryl-1-indanones to 3-aryl-indanols having stereogenic...
centers at C-3. This deficiency encouraged us to explore the stereoselective outcome of ATH reactions of 3-aryl-indanones using enantioenriched chiral transition metal catalysts and a HCO₂H/Et₃N mixture as the hydrogen source.

Results and discussion

Previously, it was reported that ATH reaction of 3-methoxycarbonyl-1-indanone (3) with Mohar’s Ru-catalyst (C4, Scheme 1d), containing benzosultam (syn-ULTAM) ligand and HCO₂H/Et₃N (5:2) as hydrogen source (40 °C, 6 h), produces cis-(1R,3S)-3-methoxycarbonyl-1-indanol with high levels of diastereoselectivity and enantioselectivity, owing to dynamic kinetic resolution (DKR) resulting from rapid racemization of the dually stereochemical outcome of ATH reactions of 3-aryl-indanones.

Examples of biologically active 3-(aryl)-substituted indanes.

Fig. 1 Examples of biologically active 3-(aryl)-substituted indanes.

Contrary to expectation, subjection of 3-(3,4-dichlorophenyl)-1-indanone (1s) to the same conditions used for reduction of 3-methoxycarbonyl-1-indanone (3) (C3 as catalyst, FA/TEA = 5:2, 40 °C) leads to incomplete reaction (72%) and formation of a 76:24 mixture of cis (99% ee) and trans indanol 2s, and 28% of enantioenriched indanone 1s (99% ee) (Scheme 1c). In an attempt to find ATH reaction conditions which induce DKR, we employed stronger base of DBU (pKₐ = 24.3) instead of Et₃N (pKₐ = 18.8) in the ATH reaction of 1s. However, ATH of 1s with FA/DBU (5:2) for 24 h, otherwise under the same reaction conditions, is still incomplete (60% conversion) affording 87:13 mixture of cis (87% ee) and trans indanol 2s, and 40% of unreacted indanone 1s (99% ee) (Scheme 1d). When the reaction temperature of ATH reaction of 1s with FA/DBU (5:2) was increased to 60 °C for 24 h, the conversion of the ATH reaction was increased to 81% but, dr (cis-2s: trans 2s = 73:27) and ee of cis-2s (67% ee) was rapidly decrease. Therefore, since ATH reaction of 1s in the presence of (R,R)-Ts-DENEB (C3) and FA/Et₃N (5:2) as hydrogen source provided cis-indanol 2s (99% ee) and of enantioenriched indanone 1s (99% ee) in a single step we changed our attention to ATH accompanying kinetic resolution using FA/Et₃N rather than attempted ATH-DKR employing FA/DBU (Scheme 1c).

To uncover conditions that would make this process more selective, ATH reaction of 1s was conducted under the same reaction conditions but at 23 °C rather than 40 °C for 24 h. Interestingly, the process was found to generate a 92:8 mixture of cis (99% ee) and trans indanol 2s in 56% yield along with 44% of enantioenriched 3-arylindanone 1s (99% ee). These results show that ATH reaction of 1s is not accompanied by DKR and that it proceeds with kinetic resolution (KR) to generate near equal amounts of enantioenriched 3-arylindanol 2s and 3-arylindanone 1s with excellent stereoselectivities for both of the cis-3-arylindanol 2s (99% ee) and recovered 3-arylindanone 1s (99% ee). Thus, the nature of 3-substituent governed lability of the
proton at C-3 center controls whether or not the ATH process is attended by DKR. This is further demonstrated by the observation that treatment of enantioenriched \((S)-3\)-methoxycarbonyl-1-indanone (\((S)-3, 99\% \text{ ee}\)) with a 5:2 FA/TEA mixture in the absence of C3, as expected, does not promote formation of the reduction product 4 but instead leads to quantitative recovery of almost completely racemized indanone 3 (1.3\% ee) (Scheme 2a). In contrast, reaction of
enantoenriched (S)-3-arylindanone ([S]-1S) (99% ee) under the same conditions generates (S)-1S quantitatively without a noticeable decrease in enantiomeric purity (99% ee) (Scheme 2b).

Because enantoenriched forms of variously substituted 3-arylindanols 2 and 3-arylindanones 1 are core motifs in many bioactive natural product and important intermediates in stereoselective syntheses of pharmaceuticals and biologically active compounds, we extended our study to uncover optimal conditions for ATH reactions of racemic 3-arylindanones 1 to produce 3-arylindanols and 3-arylindanones with high levels of stereoselectivity. In the first phase of this investigation, we explored the use of different commercially available chiral Ru-catalysts to promote ATH reaction of racemic 3-arylindanone 1S. ATH reaction of 1S (FA : TEA = 5 : 2) using Noyori catalyst (R,R)-RuCl[TsDPEN](cymene) (C1) or (R,R)-RuCl[TsDPEN](mesitylene) (C2) was found to occur for 6 h to form 3-arylindanol 2S with 53–56% conversions (entries 1 and 2, Table 1), and slightly higher conversions take place when the reaction time is extended to 24 h (65–77% conversion, entries 4 and 5). These processes produce slightly lower cis/trans ratios of 2S compared with those catalyzed by (R,R)-Ts-DENEB (C3) but the conversions of 1S to 2S in ATH reactions using C3 are nearly time independent (6 h, 24 h).

Table 1 Optimization of conditions for ATH-KR reactions of 3-arylindanone 1S

| Entry | Cat. | F/T ratio | Solvent | Rxn time (h) | Conv. (%) | cis : trans | ee (%) of cis-2S | ee (%) of trans-2S | ee (%) of recovered 1S |
|-------|------|-----------|---------|--------------|-----------|-------------|-------------------|----------------------|------------------------|
| 1     | C1   | 5 : 2     | DCE     | 6            | 53        | 93 : 7      | 99                | 47                   | 97                     |
| 2     | C2   | 5 : 2     | DCE     | 6            | 56        | 92 : 8      | >99               | 15                   | 99                     |
| 3     | C3   | 5 : 2     | DCE     | 6            | 56        | 92 : 8      | >99               | 40                   | >99                    |
| 4     | C1   | 5 : 2     | DCE     | 24           | 65        | 80 : 20     | >99               | 58                   | 96                     |
| 5     | C2   | 5 : 2     | DCE     | 24           | 77        | 76 : 24     | 98                | 29                   | 91                     |
| 6     | C3   | 5 : 2     | DCE     | 24           | 57        | 88 : 12     | >99               | 42                   | >99                    |
| 7     | C3   | 1 : 1     | DCE     | 53           | 53        | 83 : 17     | >99               | 51                   | 57                     |
| 8     | C3   | 1 : 1     | DCE     | 24           | 58        | 87 : 13     | >99               | 50                   | 93                     |
| 9     | C3   | 1 : 1     | DCE     | 6            | 53        | 89 : 11     | >99               | 53                   | 83                     |
| 10    | C3   | 1 : 1     | DCE     | 24           | 55        | 91 : 9      | >99               | 58                   | 95                     |
| 11    | C3   | 1 : 1     | CH3CN   | 32           | 32        | 100 : 0     | 99                | —                    | 48                     |
| 12    | C3   | 1 : 1     | CH3Cl   | 28           | 99 : 1     | >99         | —                 | 36                   | —                      |
| 13    | C3   | 1 : 1     | THF     | 31           | 31        | 100 : 0     | 99                | —                    | 46                     |
| 14    | C3   | 1 : 1     | EtOAc   | 44           | 99 : 1     | >99         | —                 | 80                   | —                      |
| 15    | C3   | 1 : 1     | DMF     | 46           | 100 : 0    | 99          | —                 | 83                   | —                      |
| 16    | C3   | 1 : 1     | Neat    | 50           | 95 : 5     | 99          | —                 | 96                   | —                      |
| 17    | C3   | 1 : 1     | MeOH    | 6            | 50        | 100 : 0     | 99                | —                    | 99                     |
| 18    | C3   | 1 : 5     | MeOH    | 20           | 50        | 100 : 0     | 99                | —                    | 99                     |

*a Reaction conditions: substrate (1 eq., 0.25 mmol), Cat. (1 mol%); FA : TEA = 10 eq. : 4 eq. (5 : 2), 4 eq. : 4 eq. (1 : 1), or 3 eq. : 15 eq. (1 : 5); solvent (0.2 M); rt, under N2 atmosphere. *b Determined by using 1H-NMR. *c Determined by using chiral HPLC.
56% and 24 h, 57%) (entries 3 and 6). Because longer time (>24 h) ATH reactions of 1s under acidic conditions provided by 5 : 2 FA : TEA are accompanied by formation of small quantities of undesired side-products (e.g., indenes resulting from dehydronation of indanol 2s), the process was carried out under non-acidic conditions using 1 : 1 or 1 : 5 FA : TEA mixtures and C3 as catalyst. ATH reaction using 1 : 5 FA : TEA occurs in a conversion of 53% after 6 h, which remains almost after 24 h (55%, entries 9 and 10). Moreover, no indene side-products are detected in the crude product mixture using 1H-NMR analysis. An investigation of the influence of solvents on the ATH reaction of 1s (entries 11–17) shows that reactions in the CH₃CN, CH₂Cl₂, THF and EtOAc produce cis-indanol 2s in high ee (99% ee), but that the conversion of 1s to 2s is less than 50% after 6 h and the % ee of the recovered indanone 1s is not high (36–83% ee). However, reaction in MeOH for 6 h using 1 : 5 FA/TEA and C3 as the catalyst (entry 17) leads to reduction of only (3R)-1s to form (1R,3R)-2s (50%, 99% ee) and recovery of unreacted (3S)-1s (50%, 99% ee). In addition, when the time for reaction in MeOH is extended to 20 h, the yields and % ee’s of (1R,3R)-2s (50%, 99% ee) and (3S)-1s (50%, 99% ee) remain the same (entry 18).

Having identified optimal conditions (C3 catalyst, 1 : 5 mixture of FA/TEA, in MeOH at rt for 6 h), the scope and limitations of the ATH-KR reaction were explored using variously substituted 3-aryl-indanones. The requisite racemic 3-aryl-indanones used for this purpose were prepared by triflic acid-catalyzed condensation reactions between the requisite of cinchonic acids and arenes (Scheme 3, Method A), or Pd-catalyzed intramolecular reductive Heck cyclization of the corresponding 2’-bromochalcones (Method B).

The results show that 3-arylindanones 1, containing an assortment of electron-donating and withdrawing substituents, undergo ATH-KR reactions under the optimized conditions within 10 h to generate in most cases the corresponding cis-3-aryl-1-indanols (R,R)-2 and unreacted 3-aryl-1-indanones (S)-1 with excellent stereoselectivities (Table 2).

Most reactions reach to 50% conversion within 10 h at room temperature and produce almost equal amounts of the corresponding indanols and indanones. Moreover, extending the reaction times to more than 10 h does not affect the conversion ratios and stereoselectivities (Table 1, entries 17 and 18).

However, in contrast to that of the unsubstituted analog, reactions of 3-arylindanones, containing electron-donating substituents such as Me or OMe on the indanone aromatic ring (Table 2, entries 2–5 and 7), require slightly longer reaction times to attain 50% conversions but the stereoselectivities for both 3-aryl-1-indanol and unreacted 3-aryl-1-indanone formation are excellent. Moreover, ATH-KR reactions of 4-Me-3-phenylindanone (1b, Table 2, entry 2) and 7-Me-3-phenylindanone (1e, Table 2, entry 5) which have Me substituents near to carbonyl moiety or 3-phenyl substituent are not complete (<50% conversion) even after 20 h. However, by carrying out these reactions using 2 mol% of C3 as catalyst, 50% conversions are attained after 6 h for 1b and 1e (entries 2 and 5). These observations suggest that not only electronic nature but also steric factor of substituents on the indanone ring have an influence on the ATH-KR process, perhaps by affecting formation of the catalyst–substrate complex.

Unlike substituents on the indanone ring, the electronic nature and position of substituents on the 3-aryl ring do not noticeably affect the times required to reach 50% conversion, and stereoselectivities of the 3-arylindanols 2 and recovered 3-arylindanones 1 products remain high. For example, ATH-KR reactions of 3-(2-Cl-phenyl), 3-(3-Cl-phenyl), or 3-(4-Cl-phenyl)-1-indanones (1h–1j) and 3-(2-Me-phenyl), 3-(3-Me-phenyl)-, or 3-(4-Me-phenyl)-1-indanones (1k–1m) reach 50% conversion after 7–8 h and produce the corresponding 3-arylindanols and 3-arylindanones with excellent stereoselectivities (entries 8–13). ATH-KR reactions of 3-arylindanones containing diverse electron-rich or electron-deficient 3-aryl groups (1n–1q) proceed in a similar manner to form the corresponding 3-aryl-indanols and unreacted 3-aryl-indanones after 6–8 h with good stereoselectivities (entries 14–17). 3-Arylindanones possessing various substituents on both the indanone and 3-phenyl rings also are suitable substrates for the ATH-KR reaction (entries 20–24). The results show that ATH-KR reactions of 3-arylindanones containing 3-furan (1y) and 3-thiophene (1z) substituents also produce the corresponding 3-arylindanols and unreacted 3-arylindanones with similar efficiencies and stereoselectivities (entries 25 and 26). In addition, ATH-KR reaction of 1c under the same conditions, except employing (S,S)-Ts-DENEB instead of (R,R)-Ts-DENEB as catalyst, yields the antipodal (S,S)-3-arylindanol 2c (45%, 98% ee) and unreacted (R)-3-arylindanone 1c (47%, 99% ee) with excellent levels of stereoselectivity (entry 3). Similarly, ATH-KR reaction of 1s under the same conditions using (S,S)-Ts-DENEB as catalyst forms (S,S)-3-arylindanol 2s (47%, >99% ee) and unreacted (R)-3-arylindanone 1s (47%, 98% ee) (entries 19 and 27).

The absolute configurations of resulting 2a as (1R,3R) and recovered 1a as (S) were determined by comparison of optical rotations and NMR data with those of the known compounds.²²⁻²⁷ The stereochemical outcomes of the ATH reaction can be rationalized by the well-known attractive C–H/π interaction in the transition state between η₆ of (R,R)-Ts-DENEB catalyst (C3) and the aromatic ring moiety of indanone 1a as shown in Fig. 2. The cis product of 2a might be favored as a consequence of 3-phenyl substituent of 1a keeping away from the reaction site in the transition state.⁴¹
### Table 2  ATH-KR reactions of 3-arylindanones

| Entry | Substrate | Time (h) | Conv\(^b\) (%) | Indanol (2)\(^c\) | Recovered indanone\(^c\) |
|-------|-----------|----------|----------------|-------------------|-------------------------|
| 1     | 1a        | 9        | 50             | 45% (97% ee)      | (S)-1a (cis:trans=99:1) |
| 2     | 1b        | 6\(^d\)  | 50             | 43% (95% ee)      | (S)-1b (cis:trans=99:1) |
| 3\(^e\) | 1c       | 10       | 50             | 45% (97% ee)      | (R)-1c (cis:trans=99:1) |
| 4     | 1d        | 10       | 50             | 45% (98% ee)      | (S)-1d (cis:trans=99:1) |
| 5     | 1e        | 6\(^d\)  | 50             | 42% (>99% ee)     | (S)-1e (cis:trans=>99:1) |
| 6     | 1f        | 10       | 50             | 41% (94% ee)      | (S)-1f (cis:trans=>99:1) |

\(^a\) Reaction conditions: 1 mol% (R,R)-TA-DBNEB, HCO\(_2\)H/Et\(_3\)N, MeOH, 25 \(^\circ\)C.

\(^b\) Conv: Conversion.

\(^c\) Indanol (2): cis:trans.

\(^d\) Reaction time at 65 \(^\circ\)C.

\(^e\) Reaction time at 10 \(^\circ\)C.

\(^f\) Reaction time at 50 \(^\circ\)C.
Table 2 (Contd.)

| Entry | Substrate | Time (h) | Conv\(^b\) (%) | Indanol (2)\(^c\) | Recovered indanone\(^c\) | Entry | Substrate | Time (h) | Conv\(^b\) (%) | Indanol (2)\(^c\) | Recovered indanone\(^c\) |
|-------|-----------|----------|----------------|------------------|--------------------------|-------|-----------|----------|----------------|------------------|--------------------------|
| 7     | \(\text{1g}\) | 17       | 50             | \(47\%\) (97\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1g}\) | 48\% (98\% ee) | 21     | \(\text{1u}\) | 11       | 52             | \(42\%\) (95\% ee) \(\text{cis:trans=98:2}\) | \((\text{S})\text{-1u}\) | 45\% (98\% ee) |
| 8     | \(\text{1h}\) | 7        | 50             | \(42\%\) (92\% ee) \(\text{cis:trans=99:1}\) | \((\text{R})\text{-1h}\) | 43\% (97\% ee) | 22     | \(\text{1v}\) | 10       | 52             | \(43\%\) (92\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1v}\) | 43\% (99\% ee) |
| 9     | \(\text{1i}\) | 7        | 50             | \(38\%\) (99\% ee) \(\text{cis:trans=98:2}\) | \((\text{S})\text{-1i}\) | 41\% (92\% ee) | 23     | \(\text{1w}\) | 5        | 51             | \(50\%\) (98\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1w}\) | 45\% (99\% ee) |
| 10    | \(\text{1j}\) | 7        | 50             | \(44\%\) (98\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1j}\) | 45\% (90\% ee) | 24     | \(\text{1x}\) | 10       | 51             | \(42\%\) (98\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1x}\) | 46\% (99\% ee) |
| 11    | \(\text{1k}\) | 8        | 50             | \(43\%\) (98\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1k}\) | 43\% (97\% ee) | 25     | \(\text{1y}\) | 7        | 51             | \(40\%\) (98\% ee) \(\text{cis:trans=99:1}\) | \((\text{R})\text{-1y}\) | 41\% (95\% ee) |
| 12    | \(\text{1l}\) | 7        | 50             | \(43\%\) (94\% ee) \(\text{cis:trans=99:1}\) | \((\text{S})\text{-1l}\) | 41\% (96\% ee) | 26     | \(\text{1z}\) | 8        | 50             | \(43\%\) (98\% ee) \(\text{cis:trans=99:1}\) | \((\text{R})\text{-1z}\) | 50\% (94\% ee) |
Highly enantiomerically enriched 3-aryl-1-indanols and 3-aryl-1-indanones produced in the ATH-KR reactions are valuable intermediates for the synthesis of medicinally important compounds such as (+)-indatraline or (R)-tolterodine. To demonstrate this assertion, (S,S)-3-(3,4-dichlorophenyl)-1-indanol (2s), formed by ATH-KR reaction of 1s, was converted to (+)-indatraline via mesylation and subsequent reaction of the formed mesylate with methylamine in the same one-pot procedure (Scheme 4a). In a route for the synthesis of (R)-tolterodine, a potent and competitive muscarinic antagonist that is currently used for the treatment of urinary urge incontinence, (R)-5-methyl-3-phenyl-1-indanone (1c) obtained from ATH-KR reaction of 1c was transformed to (R)-6-methyl-4-phenylcoumarine (5) via Baeyer-Villiger oxidation without deterioration of optical purity (Scheme 4b). Because the conversion of (R)-5 to (R)-tolterodine via DIBAL-H reduction to a lactol and subsequent reductive amination with disopropylamine has been reported, this route constitutes a formal synthesis of (R)-tolterodine (Scheme 4b). Finally, to demonstrate applications to the synthesis of quinoline derivatives, treatment of (S)-3-(3,4-dichlorophenyl)-1-indanone oxime tosylate (6), obtained from (S)-1s, using 1.5 equiv. of AlCl₃ at room temperature produces the readily separable mixture of (S)-4-aryl-3,4-dihydroquinoline-2(1H)-one (7) and (S)-4-aryl-3,4-dihydroisoquinoline-1(2H)-one (8).

**Conclusions**

In summary, this effort demonstrates that efficient kinetic resolution (KR) attains asymmetric transfer hydrogenation...
(ATH) reactions of diverse racemic 3-aryl-1-indanones when commercial \((\text{R}, \text{R})\)- or \((\text{S}, \text{S})\)-Ts-DENEB is employed as catalyst, a 1 : 5 mixture of HCO₂H and Et₃N is used as a hydrogen source and MeOH is utilized as solvent. These processes, carried out at room temperature, produce near equal amounts of the corresponding cis-3-arylindanols and unreacted 3-arylindanones with excellent levels of diastereo- and enantio-selectivity. The key merit of the process is that it forms both highly enantiomerically enriched cis-3-arylindanols and 3-arylindanones in a single step. In addition, selected stereoselective transformations of 3-arylindanol and 3-arylindanones generated by the ATH-KR process, demonstrate the usefulness of this method in producing key intermediates for the preparation of \((+)\)-indatraline, \((\text{R})\)-tolterodine, \((\text{S})\)-4-aryl-3,4-dihydroquinoline-2(1H)-one and \((\text{S})\)-4-aryl-3,4-dihydroisoquinoline-1(2H)-one.

**Experimental section**

**General**

Synthetic procedure and characterization data of starting 3-aryl-1-indanones 1a–1z are included in the ESI.† All reactions were conducted under an inert atmosphere of nitrogen using anhydrous solvents. Mixtures of HCO₂H/Et₃N (5 : 2 and 1 : 1) are commercially available and 1 : 5 mixture of HCO₂H/Et₃N was prepared by adding 1 equiv. of Et₃N to 5 equiv. of HCO₂H at 0 °C under a nitrogen atmosphere and used as such. Chiral transition metal catalysts C1–C3 were purchased from commercial vendors. The progress of reactions was monitored using thin layer chromatography (TLC) and visualized using UV light and by staining with ethanolic phosphomolybdic acid (PMA) solution or ninhydrin solution followed by heating. Flash column chromatography was carried out on silica gel (38–75 μm). Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F 254 plates. Preparative thin layer chromatography (PLC) was performed on Merck silica gel 60 F 254 2 mm plates. Syntheses under microwave system were conducted by using CEM Discover SP. Nuclear magnetic resonance (NMR) spectra were recorded using Bruker 500 MHz NMR instrument (1H NMR at 500 MHz and 13C NMR at 125 MHz) or Bruker 400 MHz NMR instrument (1H NMR at 400 MHz and 13C NMR at 101 MHz). 1H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constants (Hz). Data for 13C NMR are reported in terms of chemical shift (δ, ppm). High performance liquid chromatography (HPLC) was carried out on a Young Lin HPLC system (7725i Injector,
**Representative procedure for the ATH of 3-phenyl-1-indanone (1a) accompanying kinetic resolution**

To a solution of 3-phenyl-1-indanone (1a, 104 mg, 0.5 mmol) and triethylamine (1.06 mL, 7.5 mmol) dissolved in methanol (1.5 mL) was added formic acid (63.4 µL, 1.5 mmol) followed by (R,R)-Ts-DENEB catalyst (3.2 mg, 0.005 mmol dissolved in 1.0 mL of methanol). The reaction mixture was stirred at 25 °C under N2 atmosphere. After the reaction time specified in the Table 2 (6–14 h), the reaction mixture was diluted with chloroform (30 mL) and washed with water and brine (20 mL) successively. The organic layer was dried with MgSO4, filtered and concentrated by rotary evaporation. The resulting mixture of 3-phenyl-1-indanol (2a) and unreacted remaining indanone 1a were easily separated by flash column chromatography (ethyl acetate : n-hexane 1 : 7). dr and ee’s of the resulting indanol 2a and unreacted remaining indanone 1a were determined by chiral HPLC. (Racemic cis- and trans-3-phenyl-1 indanols (2a) were obtained by NaBH4 reduction of 1a in MeOH.) Absolute configurations were determined by comparison of optical rotations and NMR data with those of the known compounds.

**((1R,3R)-3-Phenyl-2,3-dihydro-1H-inden-1-ol (2a))**

Yield 43% (48.2 mg as white solid); mp 123.3 °C; 97% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, tR(major) = 16.6 min, tR(minor) = 25.4 min; [α]D29 = +5.6 (c 2.4, CH2Cl2); 1H NMR (CDCl3, 500 MHz): δ 7.35 (d, 1H, J = 7.5 Hz), 7.30–7.23 (m, 3H), 7.18 (t, 1H, J = 7.3 Hz), 7.13 (d, 2H, J = 7.1 Hz), 7.09 (d, 1H, J = 7.3 Hz), 5.21 (s, 1H), 4.29 (dd, 1H, J = 8.6, 5.3 Hz), 3.00 (dt, 1H, J = 13.8, 8.6, 7.3 Hz), 1.97 (dt, 1H, J = 13.8, 4.8 Hz), 1.89 (s, 3H), 1.81 (s, 1H); 13C{1H} NMR (101 MHz, CDCl3) δ 145.8, 145.4, 143.4, 135.5, 130.4, 128.6, 127.9, 127.8, 126.2, 121.9, 75.6, 48.4, 46.3, 19.1; HRMS (EI, double focusing) m/z: [M]+ calcd for C16H16O 224.1191; found 224.1201.

**((S)-3-Phenyl-2,3-dihydro-1H-inden-1-one, (S)-1a)**

Yield 35% (36.4 mg as white solid); 98% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, tR(major) = 15.0 min, tR(minor) = 16.2 min; [α]D29 = +72.8 (c 1.5, CH2Cl2); Literature values: [α]D29 = +64.9 (c 0.4, CH2Cl2 for 86% ee)21 [α]D33 = −49 (c 1.0, CHCl3) for 91% ee of ((R)-1a); 1H NMR (CDCl3, 500 MHz): δ 7.82 (d, 1H, J = 7.7 Hz), 7.57 (t, 1H, J = 7.4 Hz), 7.42 (t, 1H, J = 7.4 Hz), 7.32 (t, 2H, J = 7.4 Hz), 7.29–7.24 (m, 2H), 7.2–7.09 (m, 2H), 4.58 (dd, 1H, J = 8.1, 3.9 Hz), 3.24 (dd, 1H, J = 19.2, 8.1 Hz), 2.70 (dd, 1H, J = 19.2, 3.9 Hz); 13C{1H} NMR (CDCl3,101 MHz) δ 206.0, 158.0, 143.7, 136.7, 135.1, 128.9, 127.9, 127.6, 127.0, 126.9, 123.4, 46.8, 44.5; HRMS (EI, double focusing) m/z: [M]+ calcd for C15H14O 210.1045; found 210.1054.

**((1R,3R)-4-Methyl-3-phenyl-2,3-dihydro-1H-inden-1-ol (2b))**

Yield 45% (46.7 mg as white solid); mp 95.2–95.9 °C; 97% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, tR(major) = 23.2 min, tR(minor) = +16.9 min; [α]D24 = −15.6 (c 1.13, CH2Cl2); Literature values: [α]D23 = −11 (c 1, CHCl3 for 95% ee).27 [α]D23 = +16.1 (c 0.1, CH2Cl2 for 86% ee)23 for (1S,3S)-2a; 1H NMR (CDCl3, 500 MHz): δ 7.48 (d, 1H, J = 7.5 Hz), 7.36–7.27 (m, 3H), 7.27–7.18 (m, 4H), 6.95 (d, 1H, J = 7.5 Hz), 5.34–5.23 (m, 1H), 4.19 (t, 1H, J = 8.4 Hz), 3.03 (dt, 1H, J = 12.9, 7.2 Hz), 2.07–1.90 (m, 2H); 13C{1H} NMR (101 MHz, CDCl3) δ 145.6, 145.2, 144.2, 128.6, 128.4, 128.3, 127.2, 126.6, 125.1, 123.7, 75.1, 48.3, 47.2; HRMS (EI, double focusing) m/z: [M]+ calcd for C15H14O 210.1045; found 210.1054.

**((S)-4-Methyl-3-phenyl-2,3-dihydro-1H-inden-1-one, (S)-1b)**

Yield 45% (48.2 mg as white solid); mp 122.6–123.3 °C; 95% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, tR(major) = 16.6 min, tR(minor) = 25.4 min; [α]D29 = +5.6 (c 2.4, CH2Cl2); 1H NMR (CDCl3, 500 MHz): δ 7.35 (d, 1H, J = 7.5 Hz), 7.30–7.23 (m, 3H), 7.18 (t, 1H, J = 7.3 Hz), 7.13 (d, 2H, J = 7.1 Hz), 7.09 (d, 1H, J = 7.3 Hz), 5.21 (s, 1H), 4.29 (dd, 1H, J = 8.6, 5.3 Hz), 3.00 (dt, 1H, J = 13.8, 8.6, 7.3 Hz), 1.97 (dt, 1H, J = 13.8, 4.8 Hz), 1.89 (s, 3H), 1.81 (s, 1H); 13C{1H} NMR (101 MHz, CDCl3) δ 145.8, 145.4, 143.4, 135.5, 130.4, 128.6, 127.9, 127.8, 126.2, 121.9, 75.6, 48.4, 46.3, 19.1; HRMS (EI, double focusing) m/z: [M]+ calcd for C15H14O 224.1201; found 224.1191.
Yield 47% (52.1 mg as white solid); 94% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 14.6 min, t₀(minor) = 16.1 min); [α]D²⁵ = +36.3 (c 2.77, CH₂Cl₂); ¹H NMR (CDCl₃, 500 MHz): δ 7.69 (d, 1H, J = 6.6 Hz), 7.41–7.34 (m, 2H), 7.29–7.25 (m, 2H), 7.21 (t, 1H, J = 7.3 Hz), 7.02 (d, 2H, J = 7.1 Hz), 4.58 (dd, 1H, J = 8.3, 2.6 Hz), 3.24 (dd, 1H, J = 19.2, 8.3 Hz), 2.60 (dd, 1H, J = 19.2, 2.6 Hz), 2.02 (s, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 128.9, 128.4, 127.4, 126.7, 121.0, 47.6, 43.9, 18.4; HRMS (EI, double focusing) m/z: [M⁺]+ calcd for C₁₆H₁₄O 222.1045; found 222.1038.

(1R,3R)-6-Methyl-3-phenyl-2,3-dihydro-1H-inden-1-ol (2d)

Yield 45% (49.9 mg as white solid); mp 130.1–130.7 °C; 98% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 24.3 min, t₀(minor) = 16.3 min); [α]D²⁵ = −32.7 (c 1.3, CH₂Cl₂); ¹H NMR (CDCl₃, 500 MHz): δ 7.35–7.27 (m, 3H), 7.27–7.20 (m, 3H), 7.05 (d, 1H, J = 7.7 Hz), 6.84 (d, 1H, J = 7.7 Hz), 5.29–5.21 (m, 1H), 4.15 (t, 1H, J = 8.3 Hz), 3.01 (dt, 1H, J = 12.9, 7.2 Hz), 2.38 (s, 3H), 2.01–1.89 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 145.4, 144.5, 144.2, 137.0, 129.3, 128.6, 128.2, 126.5, 124.8, 124.2, 75.1, 48.0, 47.4, 21.3; HRMS (EI, double focusing) m/z: [M⁺]+ calcd for C₁₆H₁₆O 224.1201; found 224.1192.

(S)-6-Methyl-3-phenyl-2,3-dihydro-1H-inden-1-one, (S)-1d

Yield 39.4% (43.7 mg, white solid); mp 92.8–92.9 °C; 96% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 14.4 min, t₀(minor) = 15.4 min); [α]D²⁵ = +60.1 (c 1.7, CH₂Cl₂); ¹H NMR (CDCl₃, 500 MHz): δ 7.61 (s, 1H), 7.39 (d, 1H, J = 7.8 Hz), 7.30 (t, 2H, J = 7.4 Hz), 7.24 (t, 1H, J = 7.4 Hz), 7.16 (d, 1H, J = 7.8 Hz), 7.11 (d, 2H, J = 7.1 Hz), 4.53 (dd, 1H, J = 7.9, 3.7 Hz), 3.22 (dd, 1H, J = 19.2, 8.0 Hz), 2.68 (dd, 1H, J = 19.2, 3.8 Hz), 2.42 (s, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 206.1, 155.4, 143.9, 137.9, 137.0, 136.4, 128.9, 127.6, 126.9, 126.5, 123.3, 47.2, 44.1, 21.1; HRMS (EI, double focusing) m/z: [M⁺]+ calcd for C₁₆H₁₄O 222.1045; found 222.1038.

(1R,3R)-7-Methyl-3-phenyl-2,3-dihydro-1H-inden-1-ol (2e)

Yield 47% (52.2 mg as white solid); >99% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 16.0 min, t₀(minor) = 15.1 min); [α]D²⁵ = −29.4 (c 1.7, CH₂Cl₂). Literature values for (S)-1c: [α]D²⁵ = +28.9° (c 1.0, CHCl₃ for 97% ee). [α]D²⁵ = +20.3 (c 0.1, CH₂Cl₂ for 86% ee).
(S)-5-Fluoro-3-phenyl-2,3-dihydro-1H-inden-1-one, (S)-1f

Yield 45% (50.8 mg, yellow solid); mp 107.5–108.3 °C; >99% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, [α]D²⁵ = +17.1 (c 2.0, CH₂Cl₂), [M]+ calcd for C₁₆H₁₆O₂ 240.1150; found 240.1148.

(1R,3R)-5-Methoxy-3-phenyl-2,3-dihydro-1H-inden-1-ol (2g)

Yield 48% (57 mg as white solid); mp 127.9–128.3 °C; 97% ee (Chiralpak IB, 0 to 6% IPA for 9 min in n-hexane, 0.9 mL min⁻¹, 270 nm, [α]D²⁵ = +17.4 (c 2.9, CH₂Cl₂), [M]+ calcd for C₁₅H₁₅NO 225.1030; found 225.1032.

(S)-5-Methoxy-3-phenyl-2,3-dihydro-1H-inden-1-one, (S)-1g
(1R,3R)-3-(3-Chlorophenyl)-2,3-dihydro-1H-inden-1-ol (2h)

Yield 42% (51 mg as white solid); mp 103.2–104.3 °C; 92% ee (Chiralpak IB, 0 to 3% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, ̂νₖ(major) = 27.5 min, ̂νₖ(minor) = 19.8 min); [α]D²⁷ = +42.8 (c 1.4, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.90 (d, 1H, J = 7.4 Hz), 7.44–7.38 (m, 1H), 7.35–7.25 (m, 2H), 7.21–7.14 (m, 2H), 7.14–7.07 (m, 1H), 7.02 (d, 1H, J = 7.5 Hz), 5.31 (s, 1H), 4.77 (t, 1H, J = 8.1 Hz), 3.09 (dt, 1H, J = 13.1, 7.4 Hz), 2.01–1.79 (m, 2H); ¹⁃C{¹H} NMR (101 MHz, CDCl₃) δ 145.4, 144.4, 142.1, 134.1, 129.4, 129.1, 128.5, 127.7, 127.4, 127.2, 125.2, 124.1, 75.1, 45.3, 44.5; HRMS (EI, double focusing) m/z: [M⁺]⁺ calcd for C₁₅H₁₃ClO₂ 242.0655; found 242.0660.

(S)-3-(3-Chlorophenyl)-2,3-dihydro-1H-inden-1-one, (S)-1i

Yield 41.4% (50.2 mg, white solid); mp 108.5–109.1 °C; 92% ee (Chiralpak IB, 0 to 3% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, ̂νₖ(major) = 17.2 min, ̂νₖ(minor) = 19.1 min); [α]D²⁸ = +66.7 (c 2.33, CH₂Cl₂); Literature value: [α]D²⁸ = +41.4 (c 0.6, CH₂Cl₂) for 84% ee); ¹H NMR (CDCl₃, 400 MHz): δ 7.82 (d, 1H, J = 7.7 Hz), 7.60 (t, 1H, J = 7.5 Hz), 7.51 (t, 1H, J = 7.5 Hz), 7.30–7.26 (m, 1H), 7.25–7.21 (m, 2H), 7.12 (s, 1H), 7.04–6.97 (m, 1H), 4.56 (dd, 1H, J = 8.1, 3.9 Hz), 3.23 (dd, 1H, J = 19.2, 8.1 Hz), 2.66 (dd, 1H, J = 19.2, 3.9 Hz); ¹⁃C{¹H} NMR (101 MHz, CDCl₃) δ 205.3, 157.0, 145.7, 136.8, 135.3, 134.7, 130.2, 128.2, 127.8, 127.2, 126.8, 125.8, 123.6, 46.6, 44.1; HRMS (EI, double focusing) m/z: [M⁺]⁺ calcd for C₁₅H₁₁ClO 240.0650; found 240.0655.
(S)-3-(4-Chlorophenyl)-2,3-dihydro-1H-inden-1-one, (S)-1j

Yield 44.6% (54.1 mg, white solid); mp 75.9-76.5 °C; 90% ee (Chiralpak IB, 0 to 3% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, \( t_0 \) (major) = 17.5 min, \( t_0 \) (minor) = 18.4 min; [\( \alpha \) \( D \)] = +37.9 (c 2.6, CH₂Cl₂). Literature values: [\( \alpha \) \( D \)] = +34.2 (c 0.6, CHCl₃ for 77% ee). [\( \alpha \) \( D \)] = +48.5 (c 0.4, CH₂Cl₂ for 90% ee). [\( \alpha \) \( D \)] = +7.82 (d, 1H, J = 7.7 Hz), 7.59 (t, 1H, J = 7.7, 1.1 Hz), 7.34 (t, 1H, J = 7.5 Hz), 3.71-7.21 (m, 3H), 7.06 (d, 2H, J = 8.3 Hz), 4.56 (dd, 1H, J = 8.1, 3.8 Hz), 3.23 (dd, 1H, J = 19.2, 8.1 Hz), 2.63 (dd, 1H, J = 19.2, 3.8 Hz); [\( \alpha \) \( D \)] = +20.5 (m, 1H, 100 MHz, CDCl₃) δ 125.3, 123.5, 121.8, 129.0, 128.1, 126.8, 123.5, 46.7, 43.8; HRMS (EI, double focusing) \( m/z \) [\( M \)] calcd for C₁₈H₁₄ClO; found 242.0498; found 242.0501.

(1R,3R)-3-(m-Tolyl)-2,3-dihydro-1H-inden-1-ol (2l)

Yield 43% (47 mg as white solid); mp 77.0-77.3 °C; 94% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, \( t_0 \) (major) = 30.0 min, \( t_0 \) (minor) = 19.4 min; [\( \alpha \) \( D \)] = -22.0 (c 0.7, CH₂Cl₂). [\( \alpha \) \( D \)] = -7.47 (d, 1H, J = 7.4 Hz), 7.29 (t, 1H, J = 7.4 Hz), 7.26-7.17 (m, 2H), 7.09-6.99 (m, 3H), 6.95 (d, 1H, J = 7.5 Hz), 5.27 (t, 1H, J = 7.2 Hz), 4.14 (t, 1H, J = 8.4 Hz), 3.01 (dt, 1H, J = 12.8, 7.2 Hz), 2.32 (s, 3H), 2.11-1.87 (m, 2H); [\( \alpha \) \( D \)] = +145.7, 145.2, 144.2, 138.2, 129.0, 128.5, 128.3, 127.4, 127.1, 125.3, 125.1, 123.6, 75.1, 48.2, 47.2, 21.4; HRMS (EI, double focusing) \( m/z \) [\( M \)] calcd for C₁₆H₁₄O; found 222.1036.

(5)-3-(o-Toly)-2,3-dihydro-1H-inden-1-one, (S)-1k

Yield 43.4% (48.2 mg, yellow solid); mp 55.7-56.5 °C; 97% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, \( t_0 \) (major) = 15.8 min, \( t_0 \) (minor) = 16.9 min; [\( \alpha \) \( D \)] = -72.5 (c 2.8, CH₂Cl₂). Literature value for (S)-1k: [\( \alpha \) \( D \)] = +56 (c 1.0, CHCl₃ for 98% ee). [\( \alpha \) \( D \)] = -7.83 (d, 1H, J = 7.7 Hz), 7.60 (t, 1H, J = 7.5 Hz), 7.44 (t, 1H, J = 7.5 Hz), 7.30 (d, 1H, J = 7.7 Hz), 7.22 (d, 1H, J = 7.4 Hz), 7.15 (t, 1H, J = 7.4 Hz), 7.08 (t, 1H, J = 7.4 Hz), 6.77 (d, 1H, J = 7.0 Hz), 4.84 (dd, 1H, J = 8.1, 3.9 Hz), 3.25 (dd, 1H, J = 19.1, 8.1 Hz), 2.57 (dd, 1H, J = 19.1, 3.9 Hz), 2.43 (s, 3H); [\( \alpha \) \( D \)] = +206.0, 157.8, 142.0, 137.3, 135.9, 135.0, 130.6, 127.0, 126.8, 126.6, 123.5, 45.8, 29.7, 19.9; HRMS (EI, double focusing) \( m/z \) [\( M \)] calcd for C₁₆H₁₄O; found 222.1036.
Yield 41.2% (45.8 mg, pale yellow solid); mp 62.7–63.7 °C; 96% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, \( t_R \) (major) = 15.8 min, \( t_R \) (minor) = 16.3 min); \([\alpha]_D^{28} = +74.2\) (c 2.1, CH₂Cl₂). Literature value for (R)-H: \([\alpha]_D^{28} = +33.2\) (c 0.9, CHCl₃ for 95% ee)¹; \(^1\)H NMR (CDCl₃, 400 MHz): \( \delta 7.81 \) (d, 1H, \( J = 7.7 \) Hz), 7.57 (t, 1H, \( J = 7.5 \) Hz), 7.42 (t, 1H, \( J = 7.5 \) Hz), 7.28 (d, 1H, \( J = 7.5 \) Hz), \( J = 6.96–6.88 \) (m, 2H), 4.54 (dd, 1H, \( J = 8.0, 3.9 \) Hz), 3.22 (dd, 1H, \( J = 19.2, 8.0 \) Hz), 2.69 (dd, 1H, \( J = 19.2, 3.9 \) Hz), 2.31 (s, 3H); \(^13\)C{¹H} NMR (101 MHz, CDCl₃) \( \delta 21.0; \) HRMS (EI, double focusing) n/z: [M⁺] calc'd for C₁₆H₁₄O₂ 222.1045; found 222.1032.

(1R,3R)-3-(p-Tolyl)-2,3-dihydro-1H-inden-1-ol (2m)

Yield 42% (47 mg as white solid); mp 97.7–98.0 °C; 95% ee (Chiralpak IB, 6% IPA in n-hexane, 1 mL min⁻¹, 270 nm, \( t_R \) (major) = 12.4 min, \( t_R \) (minor) = 7.1 min); \([\alpha]_D^{28} = -21.7\) (c 1.5, CH₂Cl₂); \(^1\)H NMR (CDCl₃, 400 MHz): \( \delta 7.47 \) (d, 1H, \( J = 7.4 \) Hz), 7.29 (t, 1H, \( J = 7.4 \) Hz), 7.22 (t, 1H, \( J = 7.3 \) Hz), 7.17–7.10 (m, 4H), 6.95 (d, 1H, \( J = 7.5 \) Hz), 5.28 (s, 1H), 4.16 (d, 1H, \( J = 8.2 \) Hz), 3.01 (dt, 1H, \( J = 12.8, 7.2 \) Hz), 2.34 (s, 3H), 2.00–1.85 (m, 2H); \(^13\)C{¹H} NMR (101 MHz, CDCl₃) \( \delta 145.8, 145.2, 141.2, 136.2, 129.3, 128.3, 128.1, 127.1, 125.1, 123.6, 75.1, 47.9, 47.3, 21.0; \) HRMS (EI, double focusing) n/z: [M⁺] calc'd for C₁₆H₁₄O₂ 224.1201; found 224.1190.

(1R,3R)-3-(4-Methoxyphenyl)-2,3-dihydro-1H-inden-1-ol (2n)

Yield 45.0% (53.6 mg as white solid); mp 110.8–111.3 °C; 99% ee (Chiralpak IB, 7% IPA in n-hexane, 1 mL min⁻¹, 270 nm, \( t_R \) (major) = 43.4 min, \( t_R \) (minor) = 45.7 min); \([\alpha]_D^{28} = -20.6\) (c 2.5, CH₂Cl₂); \(^1\)H NMR (CDCl₃, 400 MHz): \( \delta 7.5 \) (d, 1H, \( J = 7.4 \) Hz), 7.3–7.3 (m, 1H), 7.3–7.2 (m, 1H), 7.1 (d, 2H, \( J = 8.7 \) Hz), 6.9 (d, 1H, \( J = 7.4 \) Hz), 6.9 (d, 2H, \( J = 8.7 \) Hz), 5.3 (q, 1H, \( J = 6.9, 5.9 \) Hz), 4.1 (t, 1H, \( J = 8.4 \) Hz), 3.8 (s, 3H), 3.0 (dt, 1H, \( J = 12.9, 7.2 \) Hz), 2.0–1.8 (m, 2H) ppm; \(^13\)C{¹H} NMR (101 MHz, CDCl₃) \( \delta 165.6, 160.9, 143.7, 130.2, 128.9, 127.0, 125.1, 116.0, 109.8, 55.7, 47.1, 44.5, 29.7; \) HRMS (EI, double focusing) n/z: [M⁺] calc'd for C₁₆H₁₄O₂ 240.1150; found 240.1161.
Yield 45.2% (53.8 mg, yellow solid); mp 72.7–73.1 °C; >99% (Chiralpak IB, 7% IPA in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 41.8 min, t₀(minor) = 49.9 min); [α]D²⁰ = +69.7 (c 2.1, CH₂Cl₂). Literature values: [α]D²⁰ = +41.1 (c 0.6, CHCl₃ for 70% ee) )); [α]D²⁰ = +59.1 (c 0.6, CH₂Cl₂ for 84% ee)); [α]D²⁰ = −17.7 (c 1.4, CHCl₃); [α]D²⁰ = −19.2, 8.0 Hz), 2.64 (dd, 1H, J = 19.2, 3.9 Hz); 13C{¹H} NMR (101 MHz, CDCl₃) δ 205.7, 163.0–160.6 (dd, JF = 245.6 Hz), 157.7, 139.5–139.4 (JDF = 3.4 Hz), 136.7, 135.2, 129.2–129.1 (dd, JDF = 8.0 Hz), 128.0, 126.8, 123.5, 115.9–115.7 (JDF = 21.5 Hz), 46.9, 43.7; HRMS (EI, double focusing) m/z: [M⁺] cale for C₁₂H₂₂FO₂ 226.0794; found 226.0791.

(1R,3R)-3-(4-Bromophenyl)-2,3-dihydro-1H-inden-1-ol (2p)

Yield 40% (58 mg as white solid); mp 132.2–132.7 °C; 99% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 20.2 min, t₀(minor) = 21.5 min); [α]D²⁰ = −17.7 (c 1.4, CHCl₃); 1H NMR (CDCl₃, 400 MHz): δ 7.54–7.37 (m, 3H), 7.27–7.20 (m, 1H), 7.10 (d, 1H, J = 8.4 Hz), 6.92 (d, 1H, J = 7.4 Hz), 5.36–5.20 (m, 1H), 4.15 (t, 1H, J = 8.3 Hz), 3.00 (dt, 1H, J = 13.0, 7.3 Hz), 2.08 (s, 1H), 1.89 (dt, 1H, J = 13.0, 3.0 Hz); 13C{¹H} NMR (101 MHz, CDCl₃) δ 145.2, 145.0, 143.3, 131.7, 130.0, 128.5, 127.4, 125.0, 123.8, 120.4, 75.0, 47.8, 46.9; HRMS (EI, double focusing) m/z: [M⁺] cale for C₁₃H₁₂BrO 288.0150; found 288.0147.

(S)-3-(4-Bromophenyl)-2,3-dihydro-1H-inden-1-one, (S)-1p

Yield 42.3% (60.7 mg, pale yellow solid); mp 60.1–60.5 °C; 94% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t₀(major) = 17.3 min, t₀(minor) = 18.2 min); [α]D²⁰ = +47.1 (c 2.9, CHCl₃). Literature value: [α]D²⁰ = +44.0 (c 0.4, CH₂Cl₂ for 90% ee)); 1H NMR (CDCl₃, 400 MHz): δ 7.82 (d, 1H, J = 7.5 Hz), 7.59 (d, 1H, J = 7.8 Hz), 7.49–7.39 (m, 3H), 7.24 (d, 1H, J = 7.8 Hz), 7.00 (d, 2H, J = 8.4 Hz), 4.55 (dd, 1H, J = 8.1, 3.8 Hz), 3.23 (dd, 1H, J = 19.2, 8.1 Hz), 2.63 (dd, 1H, J = 19.2, 3.8 Hz); 13C{¹H} NMR (101 MHz, CDCl₃) δ 205.4, 157.2, 142.7, 136.8, 135.2, 132.0, 129.4, 128.1, 126.8, 123.6, 123.0, 46.7, 43.9; HRMS (EI, double focusing) m/z: [M⁺] cale for C₁₃H₁₂BrO 285.9993; found 285.9991.
(1R,3R)-3-(4-(Trifluoromethyl)phenyl)-2,3-dihydro-1H-inden-1-ol (2q)

Yield 34% (47 mg as white solid); mp 98.5–99.7 °C; 97% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, ²⁰σ(major) = 20.7 min, ²⁰σ(minor) = 18.8 min); [α]D²⁹ = −8.7 (c 3.8, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.58 (d, 2H, J = 8.2 Hz), 7.49 (d, 1H, J = 7.5 Hz), 7.40–7.29 (m, 3H), 7.29–7.21 (m, 1H), 6.92 (d, 1H, J = 7.5 Hz), 5.37–5.29 (m, 1H), 4.26 (d, 1H, J = 8.9 Hz), 3.04 (dt, 1H, J = 13.0, 7.3 Hz), 2.04 (s, 1H), 1.94 (dd, 1H, J = 13.0, 8.9, 7.3 Hz); ¹³C{¹H} NMR (CDCl₃, 101 MHz) δ 148.5, 145.0 (d, J_C-F = 48.4 Hz), 128.9 (q, J_C-F = 32.4 Hz), 128.6, 127.6, 125.6 (t, J_C-F = 3.7 Hz), 125.0, 123.9, 122.9, 75.0, 48.2, 46.8; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₆H₁₄O₂ 278.0918; found 278.0915.

(S)-3-(3,4-Dimethylphenyl)-2,3-dihydro-1H-inden-1-one, (S)-1r

Yield 44% (52 mg as white solid); mp 89.8–90.8 °C; 99% ee (Chiralpak IB, 0 to 2% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, ²⁰σ(major) = 29.7 min, ²⁰σ(minor) = 24.3 min); [α]D²⁹ = −21.3 (c 2.8, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.47 (d, 1H, J = 7.4 Hz), 7.29 (t, 1H, J = 7.4 Hz), 7.22 (d, 1H, J = 7.2 Hz), 7.09 (d, 1H, J = 7.7 Hz), 7.00 (s, 1H), 6.96 (d, 2H, J = 7.5 Hz), 5.27 (d, 1H, J = 7.2 Hz), 4.12 (d, 1H, J = 8.3 Hz), 3.00 (dt, 1H, J = 12.8, 7.2 Hz), 2.25 (s, 3H), 2.24 (s, 3H), 2.01–1.86 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 145.9, 145.2, 141.7, 136.7, 134.8, 129.8, 129.5, 128.3, 127.1, 125.6, 125.1, 123.6, 75.1, 47.9, 47.3, 19.8, 19.4; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₅H₁₄O 238.1358; found 238.1358.

(S)-3-(4-(Trifluoromethyl)phenyl)-2,3-dihydro-1H-inden-1-one, (S)-1q

Yield 42.7% (58.9 mg, pale yellow solid); mp 84.2–84.5 °C; 94% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, ²⁰σ(major) = 16.9 min, ²⁰σ(minor) = 20.9 min); [α]D³⁵ = +30.7 (c 3.2, CH₂Cl₂); Literature value: [α]D³⁵ = +33.0 (c 0.6 CH₂Cl₂ for 88% ee); ¹H NMR (CDCl₃, 400 MHz): δ 7.84 (d, 1H, J = 7.5 Hz), 7.64–7.52 (m, 3H), 7.46 (d, 1H, J = 7.8 Hz), 7.25 (d, 3H, J = 8.1 Hz), 4.65 (dd, 1H, J = 8.1, 3.9 Hz), 3.26 (dd, 1H, J = 19.2, 8.1 Hz), 2.67 (dd, 1H, J = 19.2, 3.9 Hz); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.9, 148.7–147.8 (m), 136.8, 135.3, 129.4 (q, J_C-F = 32.5 Hz), 128.3, 128.0, 126.8, 125.9 (q, J_C-F = 3.8 Hz), 125.4–122.7 (d, J_C-F = 272.0 Hz), 123.7, 46.5, 44.2; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₆H₁₄F₂O 276.0762; found 276.0762.

(1R,3R)-3-(3,4-Dimethylphenyl)-2,3-dihydro-1H-inden-1-ol (2s)

Yield 49.6% (58.6 mg, pale yellow solid); mp 103.9–105.0 °C; >99% ee (Chiralpak IB, 0 to 2% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, ²⁰σ(major) = 17.0 min, ²⁰σ(minor) = 17.8 min); [α]D³⁵ = +58.7 (c 1.1, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.80 (d, 1H, J = 7.7 Hz), 7.55 (t, 1H, J = 7.5 Hz), 7.40 (t, 1H, J = 7.4 Hz), 7.27 (d, 1H, J = 7.7 Hz), 7.07 (d, 1H, J = 7.6 Hz), 6.93–6.81 (m, 2H), 4.50 (dd, 1H, J = 8.0, 3.8 Hz), 3.20 (dd, 1H, J = 19.2, 8.0 Hz), 2.67 (dd, 1H, J = 19.2, 3.8 Hz), 2.23 (s, 3H), 2.21 (s, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 206.3, 158.3, 141.1, 137.1, 136.7, 135.2, 135.0, 130.1, 128.8, 127.7, 126.9, 125.0, 123.3, 46.9, 44.1, 19.8, 19.3; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₇H₁₆O 236.1201; found 236.1201.

(1R,3R)-3-(3,4-Dichlorophenyl)-2,3-dihydro-1H-inden-1-ol (2r)

Yield 42% (58 mg as white solid); mp 91.7–93.1 °C; 99% ee (Chiralpak IB, 0 to 4.5% IPA for 10 min in n-hexane, 0.8 mL min⁻¹,
(S)-3-(3,4-Dichlorophenyl)-2,3-dihydro-1H-inden-1-one, (S)-1s

Yield 46.8% (64.8 g, white solid); mp 114.1–114.5 °C; >99% ee (Chiralpak IB, 0 to 4.5% IPA for 10 min in n-hexane, 0.8 mL min⁻¹, 270 nm, tᵣₘ(major) = 23.7 min, tᵣₘ(minor) = 22.8 min); [α]D²⁵ = +35.5 (c 2.4, CH₂Cl₂). Literature values: [α]D²⁵ = +48 (c 1.0, CHCl₃ for 92% ee).[a] [α]D²⁵ = +38.2 (c 0.5, CH₂Cl₂ for 90% ee).[b] [1H NMR (CDCl₃, 400 MHz): δ 7.83 (d, 1H, J = 7.7 Hz), 7.61 (t, 1H, J = 7.4 Hz), 7.46 (t, 1H, J = 7.4 Hz), 7.38 (d, 1H, J = 8.3 Hz), 7.26 (d, 1H, J = 7.7 Hz), 7.23 (d, 1H, J = 2.1 Hz), 6.95 (dd, 1H, J = 8.3, 2.1 Hz), 4.55 (dd, 1H, J = 8.1, 3.8 Hz), 3.23 (dd, 1H, J = 19.2, 8.1 Hz), 2.62 (dd, 1H, J = 19.2, 3.8 Hz); [13C]¹H NMR (CDCl₃, 101 MHz, C14D): δ 204.1, 167.4 (d, JCF = 256.8 Hz), 161.1 (d, JCF = 9.6 Hz), 139.9, 137.0, 133.1 (d, JCF = 1.8 Hz), 129.7, 127.4, 125.7 (d, JCF = 10.4 Hz), 116.3 (d, JCF = 24.0 Hz), 113.4 (d, JCF = 22.4 Hz), 47.0, 43.9, 21.0; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₅H₁₂Cl₂O 278.0265; found 278.0263.

(1R,3R)-5-Fluoro-3-(4-methoxyphenyl)-2,3-dihydro-1H-inden-1-ol (2t)

Yield 42% (53 mg as white solid); mp 87.3–88.1 °C; 99% ee (Chiralpak IB, 0 to 3% IPA for 8 min in n-hexane, 1 mL min⁻¹, 270 nm, tᵣₘ(major) = 25.2 min, tᵣₘ(minor) = 22.4 min); [α]D²⁵ = −33.7 (c 1.4, CH₂Cl₂); [3H NMR (CDCl₃, 400 MHz): δ 7.40 (dd, 1H, J = 8.3, 5.2 Hz), 7.14 (d, 2H, J > 8.1 Hz), 7.10 (d, 2H, J = 8.1 Hz), 6.96 (t, 1H, J = 8.7 Hz), 6.62 (d, 1H, J = 9.0 Hz), 5.23 (t, 1H, J = 7.2 Hz), 4.11 (t, 1H, J = 8.4 Hz), 3.01 (dt, 1H, J = 12.9, 7.3 Hz), 2.34 (s, 3H), 2.13–1.88 (m, 2H); [13C]¹H NMR (CDCl₃, 101 MHz, C14): δ 163.4 (d, JCF = 245.5 Hz), 158.5, 148.4 (d, JCF = 7.9 Hz), 140.7 (d, JCF = 2.2 Hz), 135.6, 129.1, 125.0 (d, JCF = 9.1 Hz), 114.4 (d, JCF = 22.8 Hz), 114.1, 111.8 (d, JCF = 22.3 Hz), 74.4, 55.3, 47.6, 47.4; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₆H₁₅FO 242.1107; found 242.1116.
(S)-5-Fluoro-3-(4-methoxyphenyl)-2,3-dihydro-1H-inden-1-one, (S)-1u

Yield 44.8% (57.4 mg, pale brown solid); mp 112.3 – 112.9 °C; 98% ee (Chiralpak IB, 0 to 6% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, tₘajor = 18.2 min, tₘinor = 17.7 min); [α] D²⁰¹⁺ = +55.5 (c 2.5, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.80 (dd, 1H, J = 8.5, 5.3 Hz), 7.10 (td, 1H, J = 8.5, 1.8 Hz), 7.04 (d, 2H, J = 8.7 Hz), 6.91 (dd, 1H, J = 8.5, 1.8 Hz), 6.86 (d, 2H, J = 8.7 Hz), 4.50 (dd, 1H, J = 8.0, 3.9 Hz), 3.80 (s, 3H), 3.23 (dd, 1H, J = 19.2, 8.1 Hz), 2.68 (dd, 1H, J = 19.2, 3.9 Hz); ¹³C (¹H) NMR (101 MHz, CDCl₃) δ 204.1, 167.4 (d, JCF = 256.8 Hz), 161.2 (d, JCF = 96.9 Hz), 158.8, 134.9, 133.1 (d, JCF = 1.8 Hz), 128.6, 125.7 (d, JCF = 10.3 Hz), 116.3 (d, JCF = 24.0 Hz), 114.4, 113.4 (d, JCF = 22.4 Hz), 55.3, 47.1, 43.6; HRMS (EI, double focusing) m/z: [M⁺] calculated for C₁₆H₁₃FO₂ 256.0900; found 256.0903.

(1R,3R)-5-Fluoro-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-inden-1-ol (2v)

Yield 43% (48 mg as white solid); mp 86.1 – 86.5 °C; 92% ee (Chiralpak IB, 0 to 2% IPA for 60 min in n-hexane, 0.6 mL min⁻¹, 270 nm, tₘajor = 48.3 min, tₘinor = 46.1 min); [α] D²⁰¹⁺ = −21.9 (c 2.6, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.59 (d, 2H, J = 8.1 Hz), 7.44 (dd, 1H, J = 8.3, 5.2 Hz), 7.35 (d, 2H, J = 8.1 Hz), 7.01 (t, 1H, J = 8.6 Hz), 6.60 (d, 1H, J = 8.8 Hz), 5.29 (s, 1H), 4.24 (t, 1H, J = 8.3 Hz), 3.06 (dt, 1H, J = 13.1, 7.3 Hz), 1.98 (dd, 2H, J = 13.1, 8.9, 7.1 Hz); ¹³C (¹H) NMR (101 MHz, CDCl₃) δ 163.4 (d, JCF = 246.4 Hz), 147.7 – 147.6 (m), 147.0 (d, JCF = 7.9 Hz), 140.8 (d, JCF = 2.4 Hz), 129.2 (d, JCF = 32.4 Hz), 128.6, 125.7 (q, JCF = 3.8 Hz), 125.4, 125.3, 114.9 (d, JCF = 22.9 Hz), 111.8 (d, JCF = 22.4 Hz), 74.3, 48.1, 47.1; HRMS (EI, double focusing) m/z: [M⁺] calculated for C₁₆H₁₃FO₂ 278.0265; found 278.0268.

Yield 49.6% (68.7 mg as a white solid); mp 100.5 – 101.1 °C; 98% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, tₘajor = 21.8 min, tₘinor = 20.1 min); [α] D²⁰¹⁺ = −42.4 (c 3.4, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.45 (d, 1H, J = 1.8 Hz), 7.30 (d, 2H, J = 8.4 Hz), 7.21 (dd, 1H, J = 8.1, 1.8 Hz), 7.14 (d, 2H, J = 8.4 Hz), 6.84 (d, 1H, J = 8.1 Hz), 5.26 (q, 1H, J = 7.0 Hz), 4.12 (d, 1H, J = 8.3 Hz), 3.03 (dt, 1H, J = 13.0, 7.2 Hz), 2.0 – 1.8 (m, 2H) ppm; ¹³C (¹H) NMR (CDCl₃, 101 MHz): δ 147.1, 143.5, 142.2, 133.3, 132.6, 129.5, 128.9, 128.7, 126.2, 124.2, 47.3, 47.3; HRMS (EI, double focusing) m/z: [M⁺] calculated for C₁₅H₁₂Cl₂O 278.0265; found 278.0268.

(S)-5-Fluoro-3-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1H-inden-1-one, (S)-1v

(1R,3R)-6-Chloro-3-(4-chlorophenyl)-2,3-dihydro-1H-inden-1-ol (2w)

Yield 43.2% (63.5 mg, pale brown solid); mp 112.0 – 112.4 °C; 99% ee (Chiralpak IB, 0 to 2% IPA for 60 min in n-hexane, 0.6 mL min⁻¹, 270 nm, tₘajor = 44.6 min, tₘinor = 43.7 min); [α] D²⁰¹⁺ = +29.9 (c 2.9, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.84 (dd, 1H, J = 8.5, 5.3 Hz), 7.60 (d, 2H, J = 8.1 Hz), 7.25 (d, 2H, J = 8.1 Hz), 7.15 (td, 1H, J = 8.6, 2.1 Hz), 6.89 (dd, 1H, J = 8.4, 1.7 Hz), 4.62 (dd, 1H, J = 8.2, 3.9 Hz), 3.28 (dd, 1H, J = 19.3, 8.2 Hz), 2.69 (dd, 1H, J = 19.2, 3.9 Hz); ¹³C (¹H) NMR (101 MHz, CDCl₃) δ 203.1, 168.7, 166.2, 159.7 (d, JCF = 9.5 Hz), 146.9, 133.2 (d, JCF = 1.9 Hz), 129.7 (q, JCF = 32.6 Hz), 128.0, 126.1 (q, JCF = 3.8 Hz), 124.0 (d, JCF = 271.9 Hz), 116.8 (d, JCF = 23.9 Hz), 113.4 (d, JCF = 22.5 Hz), 46.7, 44.0; HRMS (EI, double focusing) m/z: [M⁺] calculated for C₁₆H₁₀Cl₂O 294.0668; found 294.0674.

(S)-6-Chloro-3-(4-chlorophenyl)-2,3-dihydro-1H-inden-1-one, (S)-1w
Yield: 45.3% (62.7 mg, white solid); mp 81.6–82.1 °C; >99% ee (Chiralpak IB, 0 to 4% IPA for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, t_R(major) = 17.9 min, t_R(minor) = 16.9 min); [α]_D^20 = +44.9 (c 2.9, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.77 (d, 1H, J = 2.0 Hz), 7.54 (dd, 1H, J = 8.2, 2.0 Hz), 7.29 (d, 2H, J = 8.4 Hz), 7.19 (d, 1H, J = 8.2 Hz), 7.04 (d, 2H, J = 8.4 Hz), 4.53 (dd, 1H, J = 19.3, 3.9 Hz), 3.26 (dd, 1H, J = 19.3, 3.9 Hz) ppm; ¹³C{¹H} NMR (CDCl₃, 101 MHz): δ 203.9, 155.3, 141.6, 138.2, 135.2, 134.7, 133.1, 129.2, 128.9, 128.0, 123.4, 47.0, 43.4 ppm; HRMS (EI, double focusing) m/z: [M]⁺ calecd for C₁₅H₁₀Cl₂O 276.0109; found 276.0108.

(1R,3R)-6-Methyl-3-(p-toly)-2,3-dihydro-1H-inden-1-ol (2x)

Yield: 42.3% (50.0 mg, white solid); mp 100.8–101.8 °C; 98% ee (Chiralpak IB, 0 to 3% IPA for 8 min in n-hexane, 1 mL min⁻¹, 270 nm, t_R(major) = 18.8 min, t_R(minor) = 15.4 min); [α]_D^20 = −39.6 (c 1.8, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.48 (d, 1H, J = 6.8 Hz), 7.36–7.26 (m, 3H), 7.23–7.17 (m, 1H), 6.31 (t, 1H, J = 3.0, 1.8 Hz), 6.13 (d, 1H, J = 3.1 Hz), 5.24 (t, 1H, J = 6.3 Hz), 4.34 (t, 1H, J = 7.5 Hz), 2.91 (ddt, 1H, J = 1350.7, 13.4, 7.9, 6.9 Hz), 2.21–2.03 (m, 2H); ¹³C{¹H} NMR (CDCl₃, 101 MHz): δ 156.9, 144.7, 143.0, 141.7, 128.6, 127.7, 124.9, 124.4, 110.2, 105.3, 75.1, 42.3, 41.5; HRMS (EI, double focusing) m/z: [M]⁺ calecd for C₁₃H₁₂O₂ 200.0837; found 200.0846.

(R)-3-(Furan-2-yl)-2,3-dihydro-1H-inden-1-one, (R)-1y

tYield 41.3% (41.0 mg, brown oil); 95% ee (Chiralpak IB, 0 to 5% EtOH for 3 min in n-hexane, 0.8 mL min⁻¹, 270 nm, t_R(major) = 14.1 min, t_R(minor) = 14.4 min); [α]_D^20 = −7.8 (c 1.5, CH₂Cl₂) Literature values: [α]_D^20 = −4.3 (c 0.6, CHCl₃) for 50% ee); [α]_D^20 = −7.4 (c 0.3, CHCl₃ for 58% ee); ¹H NMR (CDCl₃, 400 MHz): δ 7.80 (d, 1H, J = 7.6 Hz), 7.65–7.59 (m, 2H), 7.52 (d, 1H, J = 7.8 Hz), 7.44 (t, 1H, J = 7.4 Hz), 7.35 (d, 1H, J = 1.8 Hz), 6.31 (t, 1H, J = 3.2, 1.8 Hz), 6.11 (d, 1H, J = 3.2 Hz), 4.69 (dd, 1H, J = 8.1, 4.1 Hz), 3.13 (dd, 1H, J = 19.0, 8.1 Hz), 2.88 (dd, 1H, J = 19.0, 4.1 Hz); ¹³C{¹H} NMR (CDCl₃, 101 MHz): δ 205.0, 155.6, 154.7, 142.2, 136.4, 135.0, 128.3, 126.6, 123.7, 110.3, 105.8, 42.8, 37.7; HRMS (EI, double focusing) m/z: [M]⁺ calecd for C₁₅H₁₄O₂ 198.0681; found 198.0677.
(1R,3S)-3-(Thiophen-2-yl)-2,3-dihydro-1H-inden-1-ol (2z)

Yield 42% (50 mg, pale brown solid); mp 75.9–76.2 °C; 98% ee (Chiralpak IB, 0 to 5% EtOH for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, $t_\text{R}(\text{major}) = 14.7$ min, $t_\text{R}(\text{minor}) = 14.2$ min; $[\alpha]_D^{22} = -5.2$ (c 2.3, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz): δ 7.46 (d, 1H, $J = 7.3$ Hz), 7.34–7.24 (m, 2H), 7.18 (dd, 1H, $J = 5.1, 1.2$ Hz), 7.14 (d, 1H, $J = 7.4$ Hz), 6.96 (dd, 1H, $J = 5.1, 3.5$ Hz), 6.92 (d, 1H, $J = 3.1$ Hz), 5.23 (t, 1H, $J = 7.0$ Hz), 4.49 (t, 1H, $J = 8.2$ Hz), 3.06 (dt, 1H, $J = 14.7, 7.2$ Hz), 2.15–1.96 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 148.0, 144.9, 144.6, 128.5, 127.6, 126.8, 124.9, 124.6, 123.9, 123.9, 74.8, 47.5, 43.1; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₅H₁₃OS 214.0457; found 214.0452.

Yield 49.7% (53.2 mg, brown solid); mp 54.8–55.0 °C; 94% ee (Chiralpak IB, 0 to 5% EtOH for 7 min in n-hexane, 1 mL min⁻¹, 270 nm, $t_\text{R}(\text{major}) = 34.5$ min, $t_\text{R}(\text{minor}) = 16.4$ min; $[\alpha]_D^{21} = -3.0$ (c 2.4, CH₂Cl₂). Literature value for [S]-Iz: $[\alpha]_D^{25} = +8$ (c 1.0, CHCl₃ for 93% ee); ¹H NMR (CDCl₃, 400 MHz): δ 7.80 (d, 1H, $J = 7.6$ Hz), 7.61 (t, 1H, $J = 7.5$ Hz), 7.51–7.40 (m, 2H), 7.19 (d, 1H, $J = 5.1$ Hz), 6.95 (dd, 1H, $J = 5.1, 3.5$ Hz), 6.88 (d, 1H, $J = 3.5$ Hz), 4.89 (dd, 1H, $J = 8.0, 4.0$ Hz), 3.27 (dd, 1H, $J = 19.1, 8.0$ Hz), 2.80 (dd, 1H, $J = 19.1, 4.0$ Hz); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 204.8, 156.7, 146.8, 136.1, 135.1, 128.3, 126.9, 126.7, 124.7, 124.3, 123.5, 47.2, 39.4; HRMS (EI, double focusing) m/z: [M⁺] calcd for C₁₅H₁₀OS 214.0452; found 214.0457.

Synthesis of (1R,3S)-3-(3,4-dichlorophenyl)-N-methyl-2,3-dihydro-1H-inden-1-amine, (+)-indatraline†

A solution of (1S,3S)-3-(3,4-dichlorophenyl)-2,3-dihydro-1H-inden-1-ol (2s) (87 mg, 0.3 mmol) and triethylamine (210 µL, 1.5 mmol) dissolved in anhydrous THF (3.0 mL) was cooled to −20 °C and methanesulfonyl chloride (70 µL, 0.9 mmol) was added dropwise. The reaction mixture was stirred at −20 °C for 1 h. Then 2 M solution of methylamine in THF (3.75 mL 7.5 mmol) was added slowly over 30 min. The reaction mixture was allowed to warm to rt and stirred 18 hours. The solvent was removed by rotary evaporation, and EtOAc (10 mL) and water (10 mL) were added. The phases were separated and the aqueous layer was re-extracted with EtOAc (20 mL × 3) and the combined organic layers were washed with brine (40 mL), dried over anhydrous MgSO₄, and concentrated by rotary evaporation. The crude residue was purified by flash column chromatography (EtOAc : Et₂O = 95 : 5) to give (+)-indatraline (56.6 mg, 65%) as a yellow oil.

Synthesis of (R)-6-methyl-4-phenylchroman-2-one [(R)-3]†

To a solution of (R)-1c (90 mg, 0.4 mmol) and p-toluenesulfonic acid (19.5 mg, 0.09 mmol) in CH₂Cl₂ (6 mL) was added m-CPBA (443 mg 1.76 mmol) portionwise. The solution was heated to reflux for 24 hours. After cooling to room temperature, the reaction mixture was quenched with saturated aqueous NaHCO₃ (10 mL) and Na₂S₂O₃ (10 mL) and extracted with EtOAc (20 mL × 3). The combined organic layers were dried over anhydrous MgSO₄ and concentrated by rotary evaporator. The crude residue was purified by flash column chromatography on silica-gel (EtOAc : n-hexane 1 : 10) to provide (R)-5 as a white solid (65%, 65 mg).
A suspension of hydroxylamine hydrochloride (144 mg, 2.1 mmol) and NaOAc (212 mg, 2.6 mmol) in 80% aqueous EtOH (20 mL) was stirred at rt for 30 min. (S)-3-(3,4-dichlorophenyl)-2,3-dihydro-1H-inden-1-one ((S)-7) (360 mg, 1.3 mmol) was added and the reaction mixture was heated gently to reflux for 2 h. After cooling to rt, the solvent was evaporated under vacuum and the residue was diluted with EtOAc (60 mL) and washed with water (30 mL) and brine successively. The organic layer was dried over anhydrous MgSO4, and concentrated by rotary evaporation. The crude residue was purified by flash chromatography (EtOAc : hexane 1 : 3) to give (S)-7 (26.8 mg, 35% yield). Rf for (S)-7 = 0.2 and Rf for (S)-8 = 0.1 (EtOAc : n-hexane 1 : 2).

(S)-4-(3,4-Dichlorophenyl)-3,4-dihydroisoquinolin-1(2H)-one (S-8).

Yield 41% (26.4 mg, as white solid); mp 131.1–131.9 °C; 99% ee (Chiralpak IA, 10% EtOH in n-hexane, 1 mL min−1, 270 nm, tR[major] = 19.6 min, tR[minor] = 25.1 min; [α]D 0B = −21.2 (c 0.9, CH2Cl2); 1H NMR (CDCl3, 400 MHz): δ = 8.2 (d, 1H, J = 7.1 Hz), 7.5–7.4 (m, 3H), 7.0–7.0 (m, 3H), 6.7 (s, 1H), 4.3–4.2 (m, 1H), 3.8 (ddd, 1H, J = 12.5, 5.2, 2.7 Hz), 3.7 (ddd, 1H, J = 12.5, 7.1, 3.1 Hz); 13C{H} NMR (CDCl3, 101 MHz): δ = 166.0, 141.0, 140.0, 132.9, 132.8, 131.6, 130.7, 130.4, 128.8, 128.4, 128.0, 127.9, 127.6, 46.9, 43.3; HRMS [EI, double focusing] m/z: [M]+ calcd for C13H11Cl2NO 291.0218; found 291.0218.

Yield 35% (23.1 mg, as white solid); mp 176.8–177.2 °C; 98% ee (Chiralpak IA, 10% EtOH in n-hexane, 1 mL min−1, 270 nm, tR[major] = 19.6 min, tR[minor] = 25.1 min; [α]D 0B = −21.2 (c 0.9, CH2Cl2); 1H NMR (CDCl3, 400 MHz): δ = 8.2 (d, 1H, J = 7.1 Hz), 7.5–7.4 (m, 3H), 7.0–7.0 (m, 3H), 6.7 (s, 1H), 4.3–4.2 (m, 1H), 3.8 (ddd, 1H, J = 12.5, 5.2, 2.7 Hz), 3.7 (ddd, 1H, J = 12.5, 7.1, 3.1 Hz); 13C{H} NMR (CDCl3, 101 MHz): δ = 166.0, 141.0, 140.0, 132.9, 132.8, 131.6, 130.7, 130.4, 128.8, 128.4, 128.0, 127.9, 127.6, 46.9, 43.3; HRMS [EI, double focusing] m/z: [M]+ calcd for C13H11Cl2NO 291.0218; found 291.0218.

Conflicts of interest

There are no conflicts to declare.

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