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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02287 • Publication Date (Web): 06 Oct 2017

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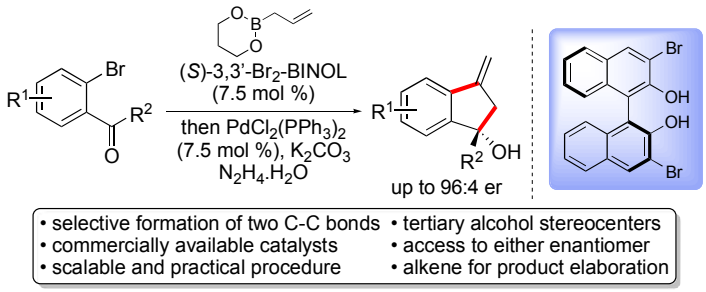


Abstract: A one-pot catalytic enantioselective allylboration/Mizoroki-Heck reaction of 2-bromoaryl ketones has been developed for the asymmetric synthesis of 3-methyleneindanes bearing a tertiary alcohol center. Brønsted acid catalyzed allylboration with a chiral BINOL derivative was followed by a palladium-catalyzed Mizoroki-Heck cyclization, resulting in selective formation of the *exo*-alkene. This novel protocol provides a concise and scalable approach to 1-alkyl-3-methyleneindan-1-ols in high enantiomeric ratios (up to 96:4 er). The potential of these compounds as chiral building blocks was demonstrated with efficient transformation to optically active diol and amino alcohol scaffolds.

INTRODUCTION

Chiral indan-1-ols are an important structural motif,[1] used as key intermediates for the synthesis of biologically active substances, including anistatin (**1**, Figure 1),[2] a sesquiterpene toxin from the seeds of the Japanese star anise and, dopamine reuptake blockers for the treatment of cocaine abuse.[3] Chiral indan-1-ols are also found as core components of natural products, such as tripartin (**2**), a demethylase inhibitor, isolated from a *Streptomyces* species associated with dung beetle larva.[4]

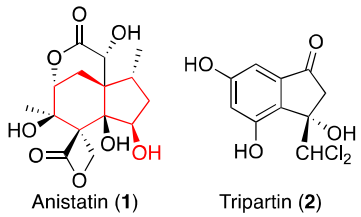


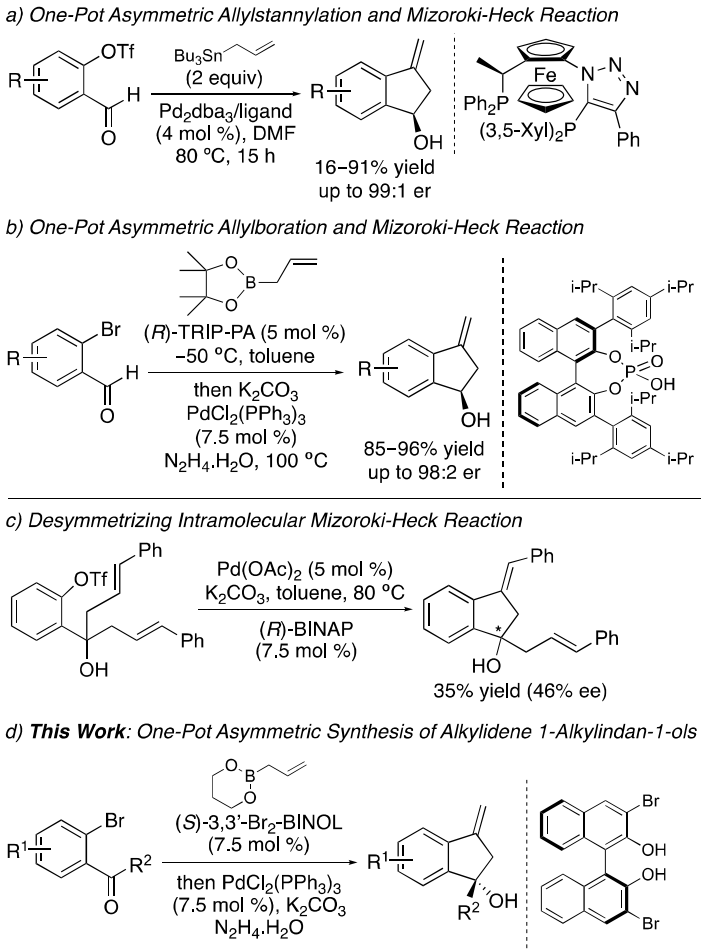
Figure 1. Structures of anistatin (**1**) and tripartin (**2**).

Due to their importance, a number of approaches have been developed for the preparation of chiral indan-1-ol derivatives.[1] Recent efforts have focused on the synthesis of optically active alkylidene indan-1-ols bearing a secondary alcohol center. These have been prepared from benzaldehyde derivatives using asymmetric allylation reactions followed by a metal-catalyzed C–C bond forming reaction.[5] One-pot methods have also been reported. For example, the groups of Schmalz[6] and Fukuzawa[7] described a one-pot asymmetric synthesis of 3-methyleneindan-1-ols from *o*-formylaryl iodides and triflates by sequential Sakurai-type allylstannylation and Mizoroki-Heck reaction in the presence of chiral *P*,*P*-ligands (e.g. Scheme 1a). More recently, we reported the one-pot synthesis of optically active 3-methyleneindan-1-ols from benzaldehydes using allyboration, catalyzed by a chiral binaphthyl-derived phosphoric acid, followed by a Mizoroki-Heck reaction (Scheme 1b).[8] This process was found to be general for both electron-deficient and electron-rich benzaldehydes, giving 3-methyleneindan-1-ols in excellent yields and high enantioselectivity.

While there are numerous methods for the synthesis of 3-methyleneindan-1-ols from benzaldehydes, the more challenging analogous synthesis of 3-methyleneindan-1-ols with a tertiary alcohol center is

less-well known.[9] Only two general methods for the racemic synthesis of these compounds have been reported. A multistep approach has been described involving the preparation of allyl substituted tertiary bromobenzyl alcohols, followed by a Mizoroki-Heck reaction,[10] while Grigg and co-workers developed a one-pot synthesis of tertiary-substituted 3-methyleneindan-1-ols by the palladium-catalyzed reaction of 2-bromoaryl ketones with allene.[11] There is only one example of an asymmetric synthesis of a 1-alkyl-3-methyleneindan-1-ol, described by Oestreich and co-workers, who used a desymmetrizing intramolecular Mizoroki-Heck reaction of an *ortho*-triflate derived diallylated benzyl alcohol (Scheme 1c).[12,13] This gave the tertiary-substituted 3-methyleneindan-1-ol in 35% yield and 46% ee.

Scheme 1. Methods for the Asymmetric Synthesis of 3-Methyleneindan-1-ols

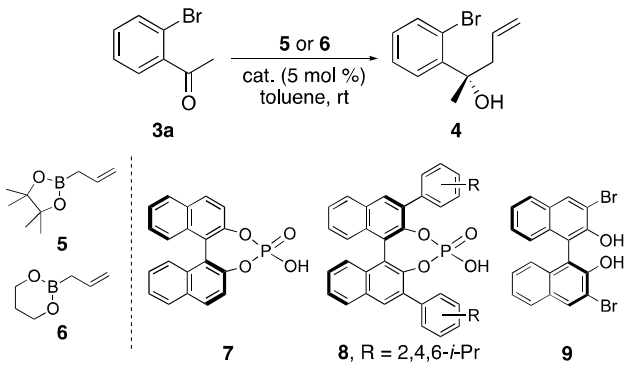


Due to a lack of methods to access optically active 1-alkyl-3-methyleneindan-1-ols, we were interested in developing a general and concise approach for the synthesis of these compounds from readily available 2-bromoaryl ketones. Herein, we now report the one-pot synthesis of 1-alkyl-3-methyleneindan-1-ols from 2-bromoaryl ketones using a combination of an asymmetric allylboration, followed by a Mizoroki-Heck reaction (Scheme 1d). The ease of synthesis has also allowed the investigation of these compounds as synthetic intermediates for the preparation of more functionalized diol and amino alcohol-derived indane scaffolds.

RESULTS AND DISCUSSION

There are relatively few methods for the efficient catalytic asymmetric allylation of aryl ketones[14–19] and thus, our initial studies began by screening various allylboronic esters and chiral Brønsted acids that would allow the effective allylation of 2-bromoaryl ketones. Crucially, conditions were required that would be compatible with a Mizoroki-Heck reaction. As we had previously shown that chiral binaphthyl-derived phosphoric acids could promote asymmetric allylation of 2-bromobenzaldehydes,[8] these were initially investigated for the catalytic allylation of 2-bromoacetophenone (**3a**) using allylboronic acid pinacol ester (**5**) (Table 1). However, neither unsubstituted phosphoric acid **7** or sterically congested (*R*)-TRIP-PA **8**[20] promoted allylation (entries 1 and 2). The 3,3'-dibrominated (*S*)-BINOL catalyst **9**, developed by Schaus and co-workers for asymmetric allylation of aryl ketones was next investigated.[15b,c] While allylation with **5** showed no reaction (entry 3), a 21% yield was obtained using allyldioxaborinane **6** and *t*-BuOH as the solvent (entry 4). To achieve the same result in toluene (required for the one-pot process), an increase in catalyst loading of **9** to 7.5 mol % was required (entry 5). Further optimization, involving longer reaction times and an increase in temperature eventually yielded the allylated product in quantitative yield (entry 7). Analysis of **4** by chiral HPLC indicated an enantiomeric ratio (er) of 98:2.

Table 1. Asymmetric Allylation of 2-Bromoacetophenone (3a)

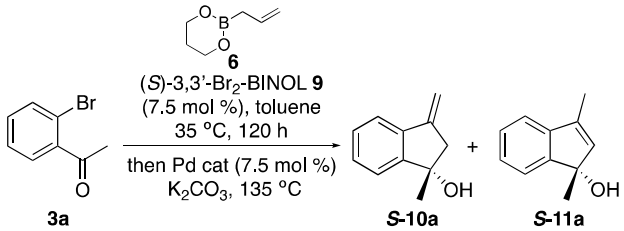


entry	allylborane	chiral ligand	time (h)	yield (%)[a]
1	**5**	**7**	20	0
2	**5**	**8**	20	0
3	**5**	**9**	24	0
4[b]	**6**	**9**	24	21
5[c]	**6**	**9**	24	25
6[c]	**6**	**9**	72	67
7[c,d]	**6**	**9**	120	100

[a]Isolated yield of **4**. [b]*t*-BuOH was used as the solvent. [c]7.5 mol % of **9** was used. [d]Reaction temperature was raised to 35 °C.

Conditions were then investigated for the one-pot, two-step synthesis of (1*S*)-2,3-dihydro-1-methyl-3-(methylene)indan-1-ol (***S*-10a**) from 2-bromoacetophenone (**3a**) using the (*S*)-3,3'-Br_2-BINOL catalyzed allylation, followed by a Mizoroki-Heck reaction (Table 2). The first attempt involved the use of $Pd(PPh_3)_4$ to catalyze the Mizoroki-Heck reaction. While this gave indanol ***S*-10a** as the major product, *endo*-alkene isomer ***S*-11a** was also formed (entry 1).[21] An improvement in the overall yield of the one-pot, two-step process was achieved using $PdCl_2$(dppf), however, this resulted in a lower ratio of ***S*-10a** and ***S*-11a** (entry 2). The most selective catalyst was found to be $PdCl_2(PPh_3)_2$ (entry 3). In combination with the reductant hydrazine hydrate, this led to a 5:1 ratio of ***S*-10a** and ***S*-11a**, respectively, in 90% overall yield. Analysis of the products by chiral HPLC showed a 96:4 er. Purification by column chromatography allowed the isolation of ***S*-10a** in 75% overall yield.

Table 2. Optimization of the One-Pot Procedure

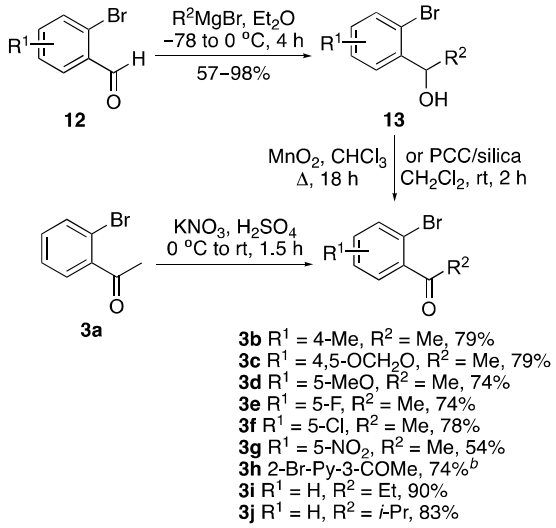


entry	palladium catalyst	time (h)	yield (%)[a]	***S*-10a**:***S*-11a**[b]
1	$Pd(PPh_3)_4$	24	57	2:1
2	$PdCl_2$(dppf)	24	77	1.5:1
3[c]	$PdCl_2(PPh_3)_2$	18	90	5:1

[a]Combined yield of ***S*-10a** and ***S*-11a**. [b]Ratio determined by analysis of ^{1}H NMR spectrum of crude reaction mixture. [c]$N_2H_4.H_2O$ (0.4 equiv) was added with Pd cat.

Following optimization of the one-pot process for the preparation of indanol ***S*-10a**, we wanted to explore the scope of the one-pot method with a range of 2-bromoaryl ketones. These were prepared in a straightforward manner from commercially available 2-bromobenzaldehydes (Scheme 2). Addition of a Grignard reagent gave the corresponding secondary alcohols that were then oxidized to the 2-bromoaryl ketones using either manganese oxide or a PDC/silica mixture. This allowed the scalable synthesis of a wide range of 2-bromoaryl ketones in good yields over the two steps. An additional substrate bearing a 5-nitro group (**3g**) was prepared in 54% yield by direct nitration of 2-bromoacetophenone (**3a**).[22]

Scheme 2. Synthesis of 2-Bromoaryl Ketones[a]

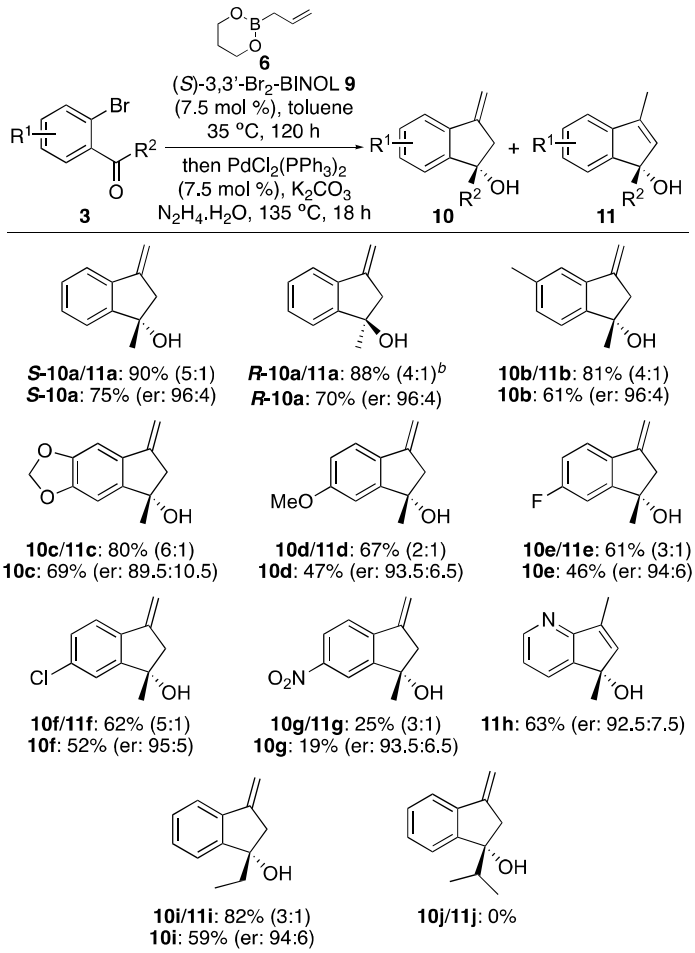


[a]Isolated yields are shown. [b]PDC was used to prepare ketone **3h**.

Having produced a series of 2-bromoaryl ketones, these were then applied to the one-pot allylboration and Mizoroki-Heck process (Scheme 3). Initially, we wanted to demonstrate that either indanol enantiomer could be prepared using either (*S*)- or (*R*)-3,3'-Br_2-BINOL. Therefore, the one-pot process with 2-bromoacetophenone (**3a**) was repeated using (*R*)-3,3'-Br_2-BINOL. As expected, this gave similar results, with indanol ***R*-10a** produced with a 96:4 er and isolated in 70% overall yield. 2-Bromoaryl methyl ketones with various aryl substituents were then subjected to the one-pot process using (*S*)-3,3'-Br_2-BINOL. Substrates with electron-rich aryl substituents gave the two isomeric indanols in high yields over the two-steps, with the major (1*S*)-3-methyleneindanols **10a**–**10c** produced with high er (from 89.5:10.5 to 96:4) and easily isolated in good yields (61–75%). The exception to these general results was observed for methoxy-derived indanols **10d/11d**. While the (1*S*)-3-methyleneindanol **10d** was formed with high er and isolated in a reasonable 47% overall yield, a modest 2:1 ratio of alkene isomers was generated from the one-pot process. In this case, we believe the methoxy substituent facilitates isomerization in the presence of the Pd(0)-catalyst following completion of the Mizoroki-Heck reaction. It should be noted that other studies which have prepared electron-rich, racemic 1-alkyl-3-

methyleneindan-1-ols by a single step Mizoroki-Heck reactions have been complicated by the formation of an indene by-product, formed via dehydration.[10] In this study, using the asymmetric one-pot process, no dehydration was observed with analogous substrates (e.g. **3c**). Electron-deficient 2-bromoaryl ketones were then investigated and also found to be substrates for this process. While halogenated analogues **10e** and **10f** were formed with high er and isolated in good overall yields, the nitro-substituted (1*S*)-3-methyleneindanol **10g** was formed in only 19% yield, demonstrating a limitation of this approach. Interestingly, pyridine analogue **11h** was isolated solely as the *endo*-alkene isomer, in 63% yield. In this case, isomerization of the *exo*-alkene is likely facilitated by coordination of the Pd(0)-catalyst with the adjacent nitrogen atom. This study also briefly investigated the scope of the ketone side-chain. Use of the one-pot process with 2-bromoaryl ethyl ketone **3i** gave a high overall yield of the indanol products with (1*S*)-3-methyleneindanol **10i** produced with 94:6 er and isolated in 59% yield. However, increasing the bulk of the side-chain with an isopropyl group (**3j**) completely inhibited the allylation step. While (*S*)-3,3'-Br_2-BINOL-catalyzed allylations have been performed with a range of alkyl-substituted aryl ketones,[15b,c] compounds with both a bulky alkyl group and a 2-bromoaryl substituent are not substrates for this reaction.

Scheme 3. Scope of the One-Pot Two-Step Process[a]

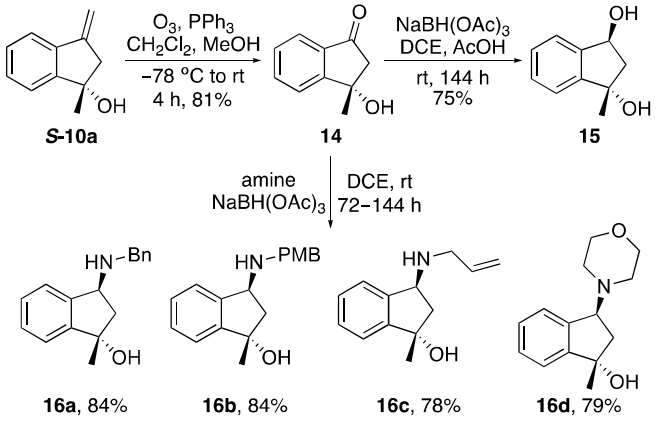


[a]Ratio of isomers **10** and **11** determined by analysis of ^{1}H NMR spectrum of crude reaction mixture. Enantiomeric ratio determined by chiral HPLC. [b]The one-pot process was performed using (*R*)-3,3'-Br_2-BINOL.

In the next stage of this project, we wanted to demonstrate that the optically active 1-alkyl-3-methyleneindanols that can now be accessed using our concise one-pot approach, could be further functionalized to generate chiral synthetic building blocks. In a preliminary study, we have shown that the methylene unit of the indanols can be used to incorporate a second stereogenic center through an oxidation and reduction sequence (Scheme 4). Initially, multigram quantities of ***S*-10a** were produced by scale-up of the one-pot process. During these reactions it was found that the catalyst loading of both

(*S*)-3,3'-Br_2-BINOL **9** and $PdCl_2(PPh_3)_2$ could be lowered to 5 mol %, while still maintaining er (96:4) and high yield (72%) of ***S*-10a**. Ozonolysis of ***S*-10a** under standard conditions gave indanone **14** in 81% yield. Indanone **14** is a structural analogue of tripartin (**2**, Figure 1), a natural product from bacteria associated with the dung beetle *Copris tripartitus*.[4] Various borohydride reagents were next investigated for reduction of **14**. The most selective was sodium triacetoxyborohydride and while the use of this required a prolonged reaction time, diol **15** was isolated as a single diastereomer in 75% yield. The highly selective nature of sodium triacetoxyborohydride was used for reductive amination of indanone **14**. With various amines this gave the corresponding 3-aminoindanols **16a–d** as single diastereomers in high yields (78–84%). It was proposed that reduction of indanone **14** and the corresponding imines was achieved via a directed mechanism, involving coordination of the reducing agent to the 1-hydroxyl group, followed by reduction of the same face of the ketone/imine. This was confirmed by X-ray crystallographic analysis of diol **15** and morpholine derivative **16d**, which clearly show the *anti*-relationship of the C-1 hydroxyl and C-3 hydroxyl/amine groups.[23]

Scheme 4. Synthesis of 3-Hydroxy and 3-Aminoindanols[a]



[a]Isolated yields are shown.

CONCLUSIONS

In summary, a one-pot asymmetric allylboration and Mizoroki-Heck reaction of 2-bromoaryl ketones has been developed for the concise synthesis of optically active 1-alkyl-3-methyleneindanes bearing a tertiary alcohol center. As well as generating these compounds with high enantiomeric ratios, the method is scalable and can be used to access either enantiomer. Now that a general procedure for the preparation of these compounds has been established, the synthetic utility of these highly functional scaffolds can be realized. We have shown that these compounds can be readily converted to hydroxyl and amine chiral building blocks in a highly diastereoselective manner. Investigation of further applications of these chiral 3-methyleneindanes is currently underway.

EXPERIMENTAL SECTION

All reagents and starting materials were obtained from commercial sources and used as received. All dry solvents were purified using a solvent purification system. All reactions were performed in oven-dried glassware under an atmosphere of argon unless otherwise stated. Brine refers to a saturated solution of sodium chloride. Flash column chromatography was performed using silica gel 60 (40–63 μm). Aluminium-backed plates pre-coated with silica gel $60F_{254}$ were used for thin layer chromatography and were visualized with a UV lamp or by staining with potassium permanganate. ^{1}H NMR spectra were recorded on a NMR spectrometer at either 400 or 500 MHz and data are reported as follows: chemical shift in ppm relative to tetramethylsilane or the solvent as the internal standard ($CDCl_3$, δ 7.26 ppm or CD_3OD, δ 3.31 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of nonequivalent resonances, integration). ^{13}C NMR spectra were recorded on a NMR spectrometer at either 101 or 126 MHz and data are reported as follows: chemical shift in ppm relative to tetramethylsilane or the solvent as internal standard ($CDCl_3$, δ 77.0 ppm or CD_3OD, δ 49.0 ppm), multiplicity with respect to hydrogen (deduced from DEPT experiments, C, CH, CH_2 or CH_3). IR spectra were recorded on a FTIR spectrometer; wavenumbers are indicated in cm^{-1}.

Mass spectra were recorded using electron impact, chemical ionization or electrospray techniques. HRMS spectra were recorded using a dual-focusing magnetic analyzer mass spectrometer. Melting points are uncorrected. Optical rotations were determined as solutions irradiating with the sodium D line (λ = 589 nm) using a polarimeter. $[\alpha]_D$ values are given in units 10^{-1} deg cm^2 g^{-1}. Chiral HPLC methods were calibrated with the corresponding racemic mixtures.

General procedure for the synthesis of secondary alcohols (13). To a stirred solution of a 2-bromobenzaldehyde (1 equiv.) in dry diethyl ether (2 mL/mmol) at –78 °C, under an argon atmosphere was added dropwise, a solution of methylmagnesium bromide (1 M in dibutyl ether, 2 equiv.), ethylmagnesium bromide (1 M in THF, 2 equiv.) or isopropylmagnesium bromide (1 M in THF, 2 equiv.). After addition, the reaction mixture was allowed to warm to 0 °C and stirred for 3 h. The reaction mixture was then quenched with a saturated solution of aqueous ammonium chloride (10–15 mL/mmol). The product was extracted using diethyl ether (3 × 20 mL/mmol). The combined organic layers were washed with brine (2 × 20 mL/mmol), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude material using silica gel flash column chromatography, eluting with diethyl ether in petroleum ether gave the secondary alcohols.

1-(2'-Bromo-4'-methylphenyl)ethan-1-ol (13b). The reaction was performed according to the general procedure using 2-bromo-4-methylbenzaldehyde (**12b**) (0.40 g, 2.0 mmol) and methylmagnesium bromide solution (4.0 mL, 4.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-4'-methylphenyl)ethan-1-ol (**13b**) (0.42 g, 98%) as a colorless oil. IR (neat) 3335, 2974, 1609, 1488 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 6.5 Hz, 3H), 1.95 (d, J = 3.5 Hz, 1H), 2.31 (s, 3H), 5.21 (qd, J = 6.5, 3.5 Hz, 1H), 7.15 (br d, J = 8.0 Hz, 1H), 7.35 (br d, J = 0.9 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 20.7 (CH_3), 23.6 (CH_3), 69.0 (CH), 121.6 (C), 126.4 (CH), 128.7 (CH), 133.1 (CH), 138.9 (C), 141.5 (C); MS (ESI) *m/z* 237 (MNa^+, 100); HRMS (ESI) calcd for $C_9H_{11}{}^{79}BrNaO$ (MNa^+), 236.9885, found 236.9882.

1-(2'-Bromo-4',5'-methylenedioxyphenyl)ethan-1-ol (13c).[24] The reaction was performed according to the general procedure using 2-bromo-4,5-methylenedioxybenzaldehyde (**12c**) (0.69 g, 3.0 mmol) and methylmagnesium bromide solution (6.0 mL, 6.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-4',5'-methylenedioxyphenyl)ethan-1-ol (**13c**) (0.63 g, 86%) as a colorless oil which solidified upon standing to give a white solid. Mp 51–53 °C (lit.[24] 52–53 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (d, J = 6.4 Hz, 3H), 1.87 (d, J = 3.3 Hz, 1H), 5.18 (qd, J = 6.4, 3.3 Hz, 1H), 5.97 (d, J = 1.6 Hz, 1H), 5.98 (d, J = 1.6 Hz, 1H), 6.96 (s, 1H), 7.09 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 23.6 (CH_3), 69.1 (CH), 101.7 (CH_2), 106.6 (CH), 111.8 (C), 112.4 (CH), 138.1 (C), 147.4 (C), 147.8 (C); MS (ESI) *m/z* 269 (MNa^+, 100), 267 (98).

1-(2'-Bromo-5'-methoxyphenyl)ethan-1-ol (13d).[10] The reaction was performed according to the general procedure using 2-bromo-5-methoxybenzaldehyde (**12d**) (0.44 g, 3.0 mmol) and methylmagnesium bromide solution (6.0 mL, 6.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-5'-methoxyphenyl)ethan-1-ol (**13d**) (0.63 g, 90%) as a colorless oil. Spectroscopic data were consistent with the literature.[10] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 6.4 Hz, 3H), 1.96 (d, J = 3.4 Hz, 1H), 3.81 (s, 3H), 5.19 (qd, J = 6.4, 3.4 Hz, 1H), 6.69 (dd, J = 8.8, 3.1 Hz, 1H), 7.16 (d, J = 3.1 Hz, 1H), 7.39 (d, J = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 23.6 (CH_3), 55.5 (CH_3), 69.2 (CH), 111.8 (C), 112.0 (CH), 114.7 (CH), 133.2 (CH), 145.8 (C), 159.4 (C); MS (EI) *m/z* 232 (M^+, 39), 230 (40).

1-(2'-Bromo-5'-fluorophenyl)ethan-1-ol (13e). The reaction was performed according to the general procedure using 2-bromo-5-fluorobenzaldehyde (**12e**) (0.61 g, 3.0 mmol) and methylmagnesium bromide solution (6.0 mL, 6.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-5'-fluorophenyl)ethan-1-ol (**13e**) (0.58 g, 88%) as a colorless oil. IR (neat) 3323, 2974, 1580, 1465 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 6.4 Hz, 3H), 2.05 (d, J = 3.5 Hz, 1H), 5.14–5.23 (m, 1H), 6.86 (ddd, J = 8.6, 8.0, 3.2 Hz, 1H), 7.34

(dd, J = 9.8, 3.2 Hz, 1H), 7.46 (dd, J = 8.6, 5.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 23.5 (CH_3), 69.1 (CH), 114.0 (d, $^2J_{C\text{-}F}$ = 24.0 Hz, CH), 115.3 (C), 115.9 (d, $^2J_{C\text{-}F}$ = 22.8 Hz, CH), 133.8 (d, $^3J_{C\text{-}F}$ = 7.8 Hz, CH), 147.0 (d, $^3J_{C\text{-}F}$ = 6.7 Hz, C), 162.5 (d, $^1J_{C\text{-}F}$ = 247.2 Hz, C); MS (EI) *m/z* 218 (M^+, 38), 205 (82), 203 (100), 175 (16), 152 (38), 123 (11), 96 (60); HRMS (EI) calcd for $C_8H_8{}^{79}BrFO$ (M^+), 217.9743, found 217.9731.

1-(2'-Bromo-5'-chlorophenyl)ethan-1-ol (13f). The reaction was performed according to the general procedure using 2-bromo-5-chlorobenzaldehyde (**12f**) (0.66 g, 3.0 mmol) and methylmagnesium bromide solution (6.0 mL, 6.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-5'-chlorophenyl)ethan-1-ol (**13f**) (0.68 g, 96%) as a colorless oil. IR (neat) 3336, 2976, 1449 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 6.4 Hz, 3H), 2.01 (d, J = 3.7 Hz, 1H), 5.18 (qd, J = 6.4, 3.7 Hz, 1H), 7.11 (dd, J = 8.4, 2.6 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 23.6 (CH_3), 69.0 (CH), 119.2 (C), 127.0 (CH), 128.8 (CH), 133.7 (CH), 134.1 (C), 146.5 (C); MS (EI) *m/z* 236 (M^+, 38), 234 (29), 223 (24), 221 (100), 219 (81), 112 (56), 75 (27); HRMS (EI) calcd for $C_8H_8{}^{81}Br^{35}ClO$ (M^+), 235.9425, found 235.9430.

1-(2'-Bromo-3'-pyridyl)ethan-1-ol (13h). The reaction was performed according to the general procedure using 2-bromopyridine-3-carboxaldehyde (**12h**) (1.00 g, 5.40 mmol) and methylmagnesium bromide solution (11.0 mL, 10.8 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-3'-pyridyl)ethan-1-ol (**13h**) (0.94 g, 87%) as a yellow oil. IR (neat) 3410, 2932, 1651, 1389 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (d, J = 6.4 Hz, 3H), 3.76 (br s, 1H), 5.12–5.20 (m, 1H), 7.28 (dd, J = 7.6, 4.8 Hz, 1H), 7.93 (dd, J = 7.6, 2.0 Hz, 1H), 8.16 (dd, J = 4.8, 2.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 23.7 (CH_3), 67.9 (CH), 123.4 (CH), 135.8 (CH), 140.9 (C), 142.6 (C), 148.4 (CH); MS (ESI) *m/z* 224 (MNa^+, 98); HRMS (ESI) calcd for $C_7H_8{}^{79}BrNNaO$ (MNa^+), 223.9681, found 223.9674.

1-(2'-Bromophenyl)propan-1-ol (13i).[25] The reaction was performed according to the general procedure using 2-bromobenzaldehyde (**12a**) (1.0 mL, 8.0 mmol) and ethylmagnesium bromide solution (16 mL, 16 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromophenyl)propan-1-ol (**13i**) (1.40 g, 81%) as a colorless oil. Spectroscopic data were consistent with the literature.[25] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (td, J = 7.4, 0.8 Hz, 3H), 1.65–1.90 (m, 2H), 1.95–2.05 (m, 1H), 5.01 (dt, J = 8.0, 4.0 Hz, 1H), 7.12 (br t, J = 7.5 Hz, 1H), 7.33 (br t, J = 7.5 Hz, 1H), 7.49–7.56 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 10.1 (CH_3), 30.6 (CH_2), 74.2 (CH), 122.2 (C), 127.4 (CH), 127.6 (CH), 128.7 (CH), 132.6 (CH), 143.6 (C); MS (ESI) *m/z* 239 (MNa^+, 95), 237 (100).

1-(2'-Bromophenyl)-2-methylpropan-1-ol (13j).[26] The reaction was performed according to the general procedure using 2-bromobenzaldehyde (**12a**) (1.0 mL, 8.0 mmol) and isopropylmagnesium bromide solution (16 mL, 16 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromophenyl)-2-methylpropan-1-ol (**13j**) (0.91 g, 57%) as a colorless oil. Spectroscopic data were consistent with the literature.[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, J = 6.8 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H), 1.85 (br s, 1H), 2.00–2.14 (m, 1H), 4.86 (d, J = 6.0 Hz, 1H), 7.09–7.15 (m, 1H), 7.29–7.36 (m, 1H), 7.50 (td, J = 7.6, 1.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.8 (CH_3), 19.5 (CH_3), 34.0 (CH), 77.6 (CH), 122.7 (C), 127.4 (CH), 128.3 (CH), 128.6 (CH), 132.6 (CH), 142.9 (C); MS (EI) *m/z* 230 (M^+, 8), 228 (10), 187 (81), 185 (100), 172 (17), 157 (9), 105 (9), 84 (23), 77 (43).

General procedure A for oxidation to 2-bromoaryl ketones (3). To a stirred solution of a secondary alcohol (1 equiv.) in chloroform (3 mL/mmol) at room temperature was added manganese(IV) oxide (10 equiv.). The reaction mixture was stirred for 18 h under reflux. After cooling to room temperature, the mixture was filtered through a pad of Celite®, which was washed with diethyl ether (2 × 15 mL/mmol). The filtrate was then concentrated. The crude product was purified using silica

gel flash column chromatography, eluting with diethyl ether in petroleum ether to give the corresponding ketone derivatives.

General procedure B for oxidation to 2-bromoaryl ketones (3). To a stirred solution of a secondary alcohol (1 equiv.) in dichloromethane (5 mL/mmol) at room temperature was added a homogeneous mixture of PCC and silica gel (1:1 by mass) (3 equiv.). The resulting suspension was stirred for 2 h. The mixture was filtered through a pad of silica gel, which was washed with dichloromethane (2 × 30 mL/mmol). The filtrate was then concentrated. The crude product was purified using silica gel flash column chromatography, eluting with diethyl ether in petroleum ether to give the corresponding ketone derivatives.

1-(2'-Bromo-4'-methylphenyl)ethan-1-one (3b).[27] The reaction was performed according to general procedure A using 1-(2'-bromo-4'-methylphenyl)ethan-1-ol (**13b**) (0.42 g, 2.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-4'-methylphenyl)ethan-1-one (**3b**) (0.33 g, 79%) as a yellow oil. Spectroscopic data were consistent with the literature.[27] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.62 (s, 3H), 7.17 (dd, J = 8.0, 0.8 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 0.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.0 (CH_3), 30.2 (CH_3), 119.3 (C), 128.2 (CH), 129.4 (CH), 134.5 (CH), 138.1 (C), 142.9 (C), 200.7 (C); MS (CI) *m/z* 215 (MH^+, 48), 213 (51), 136 (100), 71 (33), 69 (35).

1-(2'-Bromo-4',5'-methylenedioxyphenyl)ethan-1-one (3c).[28] The reaction was performed according to general procedure B using 1-(2'-bromo-4',5'-methylenedioxyphenyl)ethan-1-ol (**13c**) (0.50 g, 2.0 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-4',5'-methylenedioxyphenyl)ethan-1-one (**3c**) (0.39 g, 79%) as a colorless oil. Spectroscopic data were consistent with the literature.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61 (s, 3H), 6.04 (s, 2H), 7.03 (s, 1H), 7.05 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.3 (CH_3), 102.5

(CH_2), 109.3 (CH), 112.0 (C), 113.9 (CH), 134.3 (C), 147.4 (C), 150.4 (C), 199.5 (C); MS (ESI) *m/z* 267 (MNa^+, 100), 265 (99).

1-(2'-Bromo-5'-methoxyphenyl)ethan-1-one (3d).[10] The reaction was performed according to general procedure A using 1-(2'-bromo-5'-methoxyphenyl)ethan-1-ol (**13d**) (0.62 g, 2.7 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-5'-methoxyphenyl)ethan-1-one (**3d**) (0.46 g, 74%) as a colorless oil. Spectroscopic data were consistent with the literature.[10] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 3.81 (s, 3H), 6.85 (dd, J = 8.8, 3.1 Hz, 1H), 6.98 (d, J = 3.1 Hz, 1H), 7.48 (d, J = 8.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.3 (CH_3), 55.6 (CH_3), 109.1 (C), 114.2 (CH), 117.9 (CH), 134.6 (CH), 142.3 (C), 158.9 (C), 201.3 (C); MS (EI) *m/z* 230 (M^+, 54), 228 (55), 215 (99), 213 (100), 187 (17), 185 (17), 172 (14), 157 (15), 78 (18), 63 (35).

1-(2'-Bromo-5'-fluorophenyl)ethan-1-one (3e).[10] The reaction was performed according to general procedure A using 1-(2'-bromo-5'-fluorophenyl)ethan-1-ol (**13e**) (0.55 g, 2.5 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-5'-fluorophenyl)ethan-1-one (**3e**) (0.40 g, 74%) as a colorless oil. Spectroscopic data were consistent with the literature.[10] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64 (s, 3H), 7.04 (ddd, J = 8.8, 7.6, 3.1 Hz, 1H), 7.18 (dd, J = 8.4, 3.1 Hz, 1H), 7.58 (dd, J = 8.8, 4.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.1 (CH_3), 113.1 (d, $^4J_{C\text{-}F}$ = 3.2 Hz, C), 116.1 (d, $^2J_{C\text{-}F}$ = 24.1 Hz, CH), 119.1 (d, $^2J_{C\text{-}F}$ = 22.5 Hz, CH), 135.4 (d, $^3J_{C\text{-}F}$ = 7.8 Hz, CH), 142.9 (d, $^3J_{C\text{-}F}$ = 5.8 Hz, C), 161.4 (d, $^1J_{C\text{-}F}$ = 250.3 Hz, C), 199.9 (C); MS (EI) *m/z* 218 (M^+, 35), 216 (36), 203 (98), 201 (100), 175 (33), 173 (34), 94 (58), 86 (38), 84 (60).

1-(2'-Bromo-5'-chlorophenyl)ethan-1-one (3f).[24] The reaction was performed according to general procedure A using 1-(2'-bromo-5'-chlorophenyl)ethan-1-ol (**13f**) (0.43 g, 1.8 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromo-5'-chlorophenyl)ethan-1-one (**3f**) (0.33 g, 78%) as a yellow oil. Spectroscopic data were

consistent with the literature.[24] ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.63 (s, 3H), 7.28 (dd, J = 8.5, 2.5 Hz, 1H), 7.43 (d, J = 2.5 Hz, 1H), 7.55 (d, J = 8.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.2 (CH_3), 116.8 (C), 128.9 (CH), 131.8 (CH), 133.8 (C), 135.0 (CH), 142.7 (C), 199.9 (C); MS (EI) *m/z* 234 (M^+, 45), 232 (33), 219 (100), 217 (77), 191 (39), 189 (24), 110 (16), 84 (12), 75 (33).

1-(2'-Bromo-3'-pyridyl)ethan-1-one (3h). To a stirred solution of 1-(2'-bromo-3'-pyridyl)ethan-1-ol (**13h**) (0.940 g, 4.70 mmol) in DMF (5 mL) at room temperature was added a solution of PDC (2.65 g, 7.05 mmol) in DMF (5 mL). The resulting suspension was stirred for 18 h then filtered through a pad of Celite®, washed with diethyl ether (2 × 30 mL) and concentrated *in vacuo*. The crude product was then purified using silica gel flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) to give 1-(2'-bromo-3'-pyridyl)ethan-1-one (**3h**) (0.69 g, 74%) as a yellow oil. IR (neat) 1697, 1566, 1389, 1273 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 3H), 7.36 (dd, J = 7.6, 4.7 Hz, 1H), 7.75 (dd, J = 7.6, 2.0 Hz, 1H), 8.45 (dd, J = 4.7, 2.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.3 (CH_3), 122.7 (CH), 137.4 (CH), 138.1 (C), 138.5 (C), 151.4 (CH), 199.8 (C); MS (ESI) *m/z* 200 (MH^+, 100); HRMS (ESI) calcd for $C_7H_7{}^{79}BrNO$ (MH^+), 199.9706, found 199.9710.

2'-Bromopropiophenone (3i).[25] The reaction was performed according to general procedure B using 1-(2'-bromophenyl)propan-1-ol (**13i**) (1.30 g, 6.00 mmol). Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 2'-bromopropiophenone (**3i**) (1.15 g, 90%) as a yellow oil. Spectroscopic data were consistent with the literature.[25] δ_H (400 MHz, $CDCl_3$) δ 1.21 (t, J = 7.2 Hz, 3H), 2.93 (q, J = 7.2 Hz, 2H), 7.25–7.31 (m, 1H), 7.33–7.39 (m, 2H), 7.57–7.62 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 8.1 (CH_3), 36.1 (CH_2), 118.5 (C), 127.4 (CH), 128.2 (CH), 131.3 (CH), 133.6 (CH), 142.0 (C), 205.1 (C); MS (ESI) *m/z* 237 (MNa^+, 98) 235 (100).

1-(2'-Bromophenyl)-2-methylpropan-1-one (3j).[26] The reaction was performed according to general procedure B using 1-(2'-bromophenyl)-2-methylpropan-1-ol (**13j**) (0.90 g, 3.9 mmol).

Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave 1-(2'-bromophenyl)-2-methylpropan-1-one (**3j**) (0.73 g, 83%) as a yellow oil. Spectroscopic data were consistent with the literature.[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (d, J = 7.0 Hz, 6H), 3.32 (sept, J = 7.0 Hz, 1H), 7.25–7.31 (m, 2H), 7.33–7.39 (m, 1H), 7.57–7.62 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 18.1 (2 × CH_3), 40.2 (CH), 118.7 (C), 127.2 (CH), 128.1 (CH), 131.0 (CH), 133.4 (CH), 142.1 (C), 208.7 (C); MS (ESI) *m/z* 251 (MNa^+, 98) 249 (100).

1-(2'-Bromo-5'-nitrophenyl)ethan-1-one (3g).[22] 1-(2'-Bromophenyl)ethan-1-one (**3a**) (0.54 mL, 4.0 mmol) was added to a solution of potassium nitrate (0.50 g, 5.0 mmol) in concentrated sulfuric acid (4 mL) at 0 °C. The reaction mixture was then allowed to warm to room temperature and was stirred for 1.5 h. The mixture was quenched with water (5 mL) and extracted with dichloromethane (2 × 15 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel flash chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) yielded 1-(2'-bromo-5'-nitrophenyl)ethan-1-one (**3g**) (0.53 g, 54%) as a white powder. Mp 86–87 °C (lit.[22] 85–87 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.69 (s, 3H), 7.83 (d, J = 8.7 Hz, 1H), 8.15 (dd, J = 8.7, 2.7 Hz, 1H), 8.31 (d, J = 2.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 30.1 (CH_3), 123.8 (CH), 125.9 (CH), 126.2 (C), 135.2 (CH), 142.4 (C), 147.1 (C), 198.7 (C); MS (EI) *m/z* 245 (M^+, 27), 243 (27), 230 (100), 182 (22), 151 (28), 105 (17), 75 (44).

***B*-Allyl-1,3,2-dioxaborinane (6).**[15c] Trimethylborate (5.6 mL, 50 mmol) was dissolved in dry diethyl ether (50 mL) under an argon atmosphere and cooled to –78 °C. Allylmagnesium bromide solution (50 mL, 1 M in diethyl ether) was added dropwise over 0.5 h. After addition, the reaction mixture was stirred for 2 h at –78 °C, then acidified at 0 °C with a 3 M aqueous solution of hydrochloric acid (60 mL). The organic phase was separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to approximately 100 mL. To this solution was added 1,3-propanediol (3.6 mL, 50 mmol) as well as oven dried 4Å molecular sieves (10 g) and the resulting mixture was stirred for 16 h at room temperature. The

molecular sieves were filtered and washed with diethyl ether (2 × 50 mL). The solvent was removed *in vacuo*, and the crude product was then dissolved in *n*-pentane (100 mL). The resulting cloudy suspension was filtered through a pad of Celite®, washed and concentrated *in vacuo*. Purification by silica gel flash chromatography, eluting with 35% diethyl ether in *n*-pentane gave a pale yellow oil. Further purification by short-path Kugelrohr distillation gave *B*-allyl-1,3,2-dioxaborinane (**6**) (4.0 g, 63%) as a colorless oil. Spectroscopic data were consistent with the literature.[15c] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (br d, J = 7.6 Hz, 2H), 1.93 (quin, J = 5.5 Hz, 2H), 3.98 (t, J = 5.5 Hz, 4H), 4.88 (ddt, J = 10.0, 2.4, 1.2 Hz, 1H), 4.92 (ddt, J = 15.2, 2.4, 1.2 Hz, 1H), 5.85 (ddt, J = 15.2, 10.0, 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 22.0 (d, $^1J_{C\text{-}B}$ = 64.6 Hz, CH_2), 27.3 (CH_2), 61.9 (2 × CH_2), 113.9 (CH_2) 135.5 (CH); MS (CI) *m/z* 127 (MH^+, 12), 113 (32), 103 (44), 97 (40), 85 (83), 71 (100), 69 (71).

(2*S*)-2-(2'-Bromophenyl)pent-4-en-2-ol (4).[10] *B*-Allyl-1,3,2-dioxaborinane (**6**) (0.026 mL, 0.21 mmol) and (*S*)-(–)-3,3'-dibromo-1,1'-bi-2-naphthol (**9**) (0.0050 g, 0.011 mmol) was dissolved in toluene (1 mL) and stirred for 0.1 h at 35 °C in an oven dried microwave vial. A solution of 1-(2'-bromophenyl)ethan-1-one (**3a**) (0.020 mL, 0.15 mmol) in distilled toluene (0.75 mL) was added and the reaction mixture was stirred for 5 days at 35 °C under an argon atmosphere. Purification by flash column chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) gave (2*S*)-2-(2'-bromophenyl)pent-4-en-2-ol (**4**) (0.036 g, 100%) as a colorless oil. Spectroscopic data were consistent with the literature.[10] $[\alpha]_D^{31}$ –34.3 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 3H), 2.62 (s, 1H), 2.64 (br dd, J = 14.0, 8.4 Hz, 1H), 3.29 (ddt, J = 14.0, 6.3, 1.1 Hz, 1H), 5.06–5.19 (m, 2H), 5.55 (dddd, J = 17.0, 10.1, 8.4, 6.3 Hz, 1H), 7.10 (td, J = 7.8, 1.7 Hz, 1H), 7.30 (td, J = 7.8, 1.3 Hz, 1H), 7.58 (dd, J = 7.8, 1.3 Hz, 1H), 7.70 (dd, J = 7.8, 1.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 27.3 (CH_3), 45.1 (CH_2), 74.7 (C), 119.4 (CH_2), 120.0 (C), 127.4 (CH), 128.3 (CH), 128.6 (CH), 133.7 (CH), 135.1 (CH), 145.0 (C); MS (ESI) *m/z* 265 (MNa^+, 100), 263 (97). Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{minor} = 1.78 min, t_{major} = 1.96 min; er = 98:2.

General procedure for the one-pot asymmetric synthesis of 1-alkyl-1-indanols. *B*-Allyl-1,3,2-dioxaborinane (**6**) (1.4 equiv.) and (*S*)-(–)-3,3'-dibromo-1,1'-bi-2-naphthol (**9**) (7.5 mol %) was dissolved in distilled toluene (5 mL/mmol) and stirred for 0.1 h at 35 °C in an oven dried microwave vial. A solution of 2'-bromoaryl ketone (1.0 equiv.) in toluene (5 mL/mmol) was added and the reaction mixture was stirred for 5 days at 35 °C. Bis(triphenylphosphine)palladium(II) dichloride (7.5 mol %), potassium carbonate (2 equiv.) and hydrazine monohydrate (0.4 equiv.) were added to the reaction mixture. The vial was sealed and heated to 135 °C for 18 h. The reaction mixture was cooled to room temperature, diluted with diethyl ether (2 mL/mmol), filtered through a pad of Celite® and concentrated *in vacuo*. Purification of the crude product using silica gel flash chromatography, eluting with diethyl ether or ethyl acetate in petroleum ether or ethyl acetate in hexane gave the corresponding 1-alkyl-1-indenols.

(1*S*)-1,3-Dimethylinden-1-ol [(*S*)-11a] and (1*S*)-2,3-dihydro-1-methyl-3-(methylene)indan-1-ol [(*S*)-10a].[10] The reaction was performed according to the general procedure using 1-(2'-bromophenyl)ethan-1-one (**3a**) (0.067 mL, 0.50 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) to yield first (1*S*)-1,3-dimethylinden-1-ol [**(*S*)-11a**] (0.012 g, 15%), and then (1*S*)-2,3-dihydro-1-methyl-3-(methylene)indan-1-ol [**(*S*)-10a**] (0.060 g, 75%) as colorless oils, which solidified upon standing. Spectroscopic data were consistent with the literature.[10] Data for (1*S*)-1,3-dimethylinden-1-ol [**(*S*)-11a**]: Mp 95–97 °C; $[\alpha]_D^{31}$ +55.9 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.58 (s, 3H), 1.67 (s, 1H), 2.06 (d, J = 1.6 Hz, 3H), 5.99 (q, J = 1.6 Hz, 1H), 7.15 (br d, J = 7.3 Hz, 1H), 7.22 (td, J = 7.3, 1.0 Hz, 1H), 7.28 (td, J = 7.3, 1.0 Hz, 1H), 7.40 (br d, J = 7.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 12.7 (CH_3), 23.8 (CH_3), 81.1 (C), 119.3 (CH), 121.2 (CH), 126.3 (CH), 128.3 (CH), 137.7 (CH), 138.9 (C), 143.0 (C), 150.0 (C); MS (ESI) *m/z* 183 (MNa^+, 100). Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 2.43 min, t_{minor} = 2.80 min; er = 96:4; Data for (1*S*)-2,3-dihydro-1-methyl-3-(methylene)indan-1-ol [**(*S*)-10a**]: Mp 79–81 °C; $[\alpha]_D^{31}$ +10.9 (*c*

1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.59 (s, 3H), 1.95 (s, 1H), 2.88 (dt, J = 16.5, 2.1 Hz, 1H), 2.95 (dt, J = 16.5, 2.1 Hz, 1H), 5.09 (t, J = 2.1 Hz, 1H), 5.52 (t, J = 2.1 Hz, 1H), 7.28–7.34 (m, 2H), 7.39–7.44 (m, 1H), 7.46–7.52 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.1 (CH_3), 49.4 (CH_2), 78.7 (C), 104.5 (CH_2), 120.6 (CH), 122.9 (CH), 128.6 (CH), 129.1 (CH), 139.4 (C), 145.9 (C), 150.4 (C); MS (ESI) *m/z* 183 (MNa^+, 100). Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 2.58 min, t_{minor} = 2.96 min; er = 96:4.

(1*R*)-1,3-Dimethylinden-1-ol [(*R*)-11a] and (1*R*)-2,3-dihydro-1-methyl-3-(methylene)indan-1-ol [(*R*)-10a]. The reaction was performed according to the general procedure using 1-(2'-bromophenyl)ethan-1-one (**3a**) (0.067 mL, 0.50 mmol) and (*R*)-(+)-3,3'-dibromo-1,1'-bi-2-naphthol (0.016 g, 0.040 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) to yield first (1*R*)-1,3-dimethylinden-1-ol [**(*R*)-11a**] (0.014 g, 18%) and then (1*R*)-2,3-dihydro-1-methyl-3-(methylene)indan-1-ol [**(*R*)-10a**] (0.056 g, 70%) as colorless oils, which solidified upon standing. Melting point and spectroscopic data were as recorded for [**(*S*)-11a**] and [**(*S*)-10a**]. Additional data for [**(*R*)-11a**]: $[\alpha]_D^{31}$ –56.2 (*c* 0.5, $CHCl_3$); enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{minor} = 2.38 min, t_{major} = 2.75 min; er = 96:4; Additional data for [**(*R*)-10a**]: $[\alpha]_D^{31}$ –13.0 (*c* 1.0, $CHCl_3$); enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{minor} = 2.53 min, t_{major} = 2.94 min; er = 96:4.

(1*S*)-2,3-Dihydro-1,5-dimethyl-3-(methylene)indan-1-ol (10b). The reaction was performed according to the general procedure using 1-(2'-bromo-4'-methylphenyl)ethan-1-one (**3b**) (0.10 g, 0.47 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 8% ethyl acetate in hexane to yield (1*S*)-2,3-dihydro-1,5-dimethyl-3-(methylene)indan-1-ol (**10b**) (0.050 g, 61%) as a colorless oil. IR (neat) 3352, 2969, 1644 cm^{-1}; $[\alpha]_D^{31}$ +24.4 (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 3H), 1.90 (s, 1H), 2.37 (s, 3H), 2.87 (dt, J = 16.4, 2.1 Hz, 1H), 2.93 (dt, J = 16.4, 2.1 Hz, 1H), 5.05 (t, J = 2.1 Hz, 1H), 5.48 (t, J = 2.1 Hz, 1H), 7.13 (br d, J = 7.9 Hz, 1H), 7.28–7.32 (m,

2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.4 (CH_3), 28.1 (CH_3), 49.6 (CH_2), 78.4 (C), 104.1 (CH_2), 121.0 (CH), 122.7 (CH), 130.1 (CH), 138.5 (C), 139.6 (C), 146.0 (C), 147.8 (C); MS (ESI) *m/z* 197 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_{14}NaO$ (MNa^+), 197.0937, found 197.0933. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 99:1, flow rate 1.0 mL/min), t_{minor} = 12.88 min, t_{major} = 13.57 min; er = 96:4.

(1*S*)-2,3-Dihydro-5,6-(methylenedioxy)-1-methyl-3-(methylene)indan-1-ol (10c). The reaction was performed according to the general procedure using 1-(2'-bromo-4',5'-methylenedioxyphenyl)ethan-1-one (**3c**) (0.12 g, 0.50 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 20% diethyl ether in petroleum ether (40–60) to yield (1*S*)-2,3-dihydro-5,6-(methylenedioxy)-1-methyl-3-(methylene)indan-1-ol (**10c**) (0.071 g, 69%) as a colorless oil. IR (neat) 3403, 2970, 1474 cm^{-1}; $[\alpha]_D^{30}$ +35.3 (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 1.45 (s, 3H), 2.86 (t, *J* = 2.0 Hz, 2H), 4.89 (t, *J* = 2.0 Hz, 1H), 5.29 (t, *J* = 2.0 Hz, 1H), 5.94 (d, *J* = 1.2 Hz, 1H), 5.95 (d, *J* = 1.2 Hz, 1H), 6.82 (s, 1H), 6.90 (s, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 27.6 (CH_3), 49.0 (CH_2), 77.4 (C), 99.6 (CH), 100.5 (CH_2), 101.4 (CH_2), 102.5 (CH), 133.4 (C), 145.3 (C), 146.0 (C), 148.7 (C), 149.0 (C); MS (ESI) *m/z* 227 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_{12}NaO_3$ (MNa^+), 227.0679, found 227.0672. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{minor} = 6.04 min, t_{major} = 6.59 min; er = 89.5:10.5.

(1*S*)-2,3-Dihydro-6-methoxy-1-methyl-3-(methylene)indan-1-ol (10d).[10] The reaction was performed according to the general procedure using 1-(2'-bromo-5'-methoxyphenyl)ethan-1-one (**3d**) (0.12 g, 0.50 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 20% diethyl ether in petroleum ether (40–60) to yield (1*S*)-2,3-dihydro-6-methoxy-1-methyl-3-(methylene)indan-1-ol (**10d**) (0.044 g, 47%) as a yellow oil. Spectroscopic data were consistent with the literature.[10] $[\alpha]_D^{30}$ +30.8 (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3OD) δ 1.48 (s, 3H), 2.84 (dt, *J* = 16.4, 1.6 Hz, 1H), 2.89 (dt, *J* = 16.4, 1.6 Hz, 1H), 3.80 (s, 3H), 4.90 (t, *J* = 1.6 Hz, 1H), 5.32 (t, *J* = 1.6 Hz,

1H), 6.85 (dd, J = 8.5, 2.3 Hz, 1H), 6.94 (d, J = 2.3 Hz, 1H), 7.39 (d, J = 8.5 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 27.7 (CH_3), 49.1 (CH_2), 54.5 (CH_3), 77.6 (C), 100.4 (CH_2), 106.7 (CH), 115.2 (CH), 121.2 (CH), 132.1 (C), 145.9 (C), 152.5 (C), 160.9 (C); MS (EI) *m/z* 190 (M^+, 84), 175 (100), 160 (10), 132 (11), 115 (14), 88 (12), 61 (17). Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 2.99 min, t_{minor} = 3.67 min; er = 93.5:6.5.

(1*S*)-2,3-Dihydro-6-fluoro-1-methyl-3-(methylene)indan-1-ol (10e). The reaction was performed according to the general procedure using 1-(2'-bromo-5'-fluorophenyl)ethan-1-one (**3e**) (0.054 g, 0.25 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) to yield (1*S*)-2,3-dihydro-6-fluoro-1-methyl-3-(methylene)indan-1-ol (**10e**) (0.020 g, 46%) as a colorless oil. IR (neat) 3356, 2970, 1643, 1605, 1481 cm^{-1}; $[\alpha]_D^{31}$ +18.3 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 1.48 (s, 3H), 2.87 (dt, J = 16.4, 2.1 Hz, 1H), 2.92 (dt, J = 16.4, 2.1 Hz, 1H), 5.02 (t, J = 2.1 Hz, 1H), 5.45 (t, J = 2.1 Hz, 1H), 7.01 (ddd, J = 9.2, 8.6, 2.4 Hz, 1H), 7.10 (dd, J = 8.8, 2.4 Hz, 1H), 7.51 (dd, J = 8.6, 5.2 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 27.5 (CH_3), 48.9 (CH_2), 77.3 (d, $^4J_{C\text{-}F}$ = 2.2 Hz, C), 102.5 (CH_2), 109.3 (d, $^2J_{C\text{-}F}$ = 23.2 Hz, CH), 115.3 (d, $^2J_{C\text{-}F}$ = 24.2 Hz, CH), 121.9 (d, $^3J_{C\text{-}F}$ = 9.1 Hz, CH), 135.3 (d, $^4J_{C\text{-}F}$ = 2.0 Hz, C), 145.3 (C), 153.3 (d, $^3J_{C\text{-}F}$ = 7.1 Hz, C), 163.5 (d, $^1J_{C\text{-}F}$ = 247.5 Hz, C); MS (EI) *m/z* 178 (M^+, 37), 163 (100), 133 (33), 88 (12), 61 (17). HRMS (EI) calcd for $C_{11}H_{11}FO$ (M^+), 178.0794, found 178.0801. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 10.50 min, t_{minor} = 12.92 min; er = 94:6.

(1*S*)-2,3-Dihydro-6-chloro-1-methyl-3-(methylene)indan-1-ol (10f). The reaction was performed according to the general procedure using 1-(2'-bromo-5'-chlorophenyl)ethan-1-one (**3f**) (0.10 g, 0.43 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) to yield (1*S*)-2,3-dihydro-6-chloro-1-methyl-3-(methylene)indan-1-ol (**10f**) (0.044 g, 52% yield) as a colorless oil. IR (neat) 3372, 2924, 1628, 1458 cm^{-1}; $[\alpha]_D^{31}$ +19.5 (*c* 1.2,

$CHCl_3$); ^1H NMR (400 MHz, CD_3OD) δ 1.48 (s, 3H), 2.89 (t, J = 2.0 Hz, 1H), 5.08 (t, J = 2.0 Hz, 1H), 5.52 (t, J = 2.0 Hz, 1H), 7.27 (dd, J = 8.2, 1.9 Hz, 1H), 7.39 (d, J = 1.9 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 27.5 (CH_3), 48.7 (CH_2), 77.4 (C), 103.7 (CH_2), 121.6 (CH), 123.1 (CH), 128.2 (CH), 134.0 (C), 137.9 (C), 145.3 (C), 152.8 (C); MS (EI) *m/z* 194 (M^+, 76), 179 (100), 159 (71), 144 (23), 115 (43), 84 (18); HRMS (EI) calcd for $C_{11}H_{11}{}^{35}ClO$ (M^+), 194.0498, found 194.0491. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 5.33 min, t_{minor} = 5.72 min; er = 95:5.

(1*S*)-2,3-Dihydro-6-nitro-1-methyl-3-(methylene)indan-1-ol (10g). The reaction was performed according to the general procedure using 1-(2'-bromo-5'-nitrophenyl)ethan-1-one (**3g**) (0.029 g, 0.10 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 30% diethyl ether in petroleum ether (40–60) to yield (1*S*)-2,3-dihydro-6-nitro-1-methyl-3-(methylene)indan-1-ol (**10g**) (0.0090 g, 19%) as a yellow oil. IR (neat) 3372, 2970, 1520, 1342 cm^{-1}; $[\alpha]_D{}^{30}$ +45.0 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, CD_3OD) δ 1.55 (s, 3H), 2.92–3.04 (m, 2H), 5.32 (t, J = 2.2 Hz, 1H), 5.78 (t, J = 2.2 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 8.18 (dd, J = 8.5, 2.2 Hz, 1H), 8.26 (d, J = 2.2 Hz, 1H); ^{13}C NMR (126 MHz, CD_3OD) δ 27.5 (CH_3), 48.5 (CH_2), 77.2 (C), 108.0 (CH_2), 118.5 (CH), 121.2 (CH), 123.5 (CH), 144.8 (C), 145.3 (C), 148.4 (C), 152.3 (C); MS (ESI) *m/z* 228 (MNa^+, 100); HRMS (ESI) calcd for $C_{11}H_{11}NNaO_3$ (MNa^+), 228.0631, found 228.0625. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 93:7, flow rate 2.0 mL/min), t_{major} = 3.84 min, t_{minor} = 4.18 min; er = 93.5:6.5.

(5*S*)-5,7-Dimethylcyclopenta[b]pyridin-5-ol (11h). The reaction was performed according to the general procedure using 1-(2'-bromo-3'-pyridyl)ethan-1-one (**3h**) (0.080 g, 0.40 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 10% ethyl acetate in petroleum ether (40–60) to yield (5*S*)-5,7-dimethylcyclopenta[b]pyridin-5-ol (**11h**) (0.040 g, 63%) as a yellow oil. IR (neat) 3322, 2972, 1603, 1572, 1474 cm^{-1}; $[\alpha]_D{}^{31}$ +24.2 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, CD_3OD) δ 1.53 (s, 3H), 2.10 (d, J = 1.6 Hz, 3H), 6.36 (q, J = 1.6 Hz, 1H), 7.19 (dd, J = 7.4, 5.3 Hz,

1H), 7.74 (dd, J = 7.4, 1.4 Hz, 1H), 8.30 (dd, J = 5.3, 1.4 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 10.4 (CH_3), 22.8 (CH_3), 77.7 (C), 120.7 (CH), 128.8 (CH), 138.8 (C), 143.1 (CH), 144.5 (C), 147.4 (CH), 161.9 (C); MS (EI) *m/z* 161 (M^+, 75), 146 (100), 132 (12), 117 (14); HRMS (EI) calcd for $C_{10}H_{11}NO$ (M^+), 161.0841, found 161.0835. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 11.95 min, t_{minor} = 18.05 min; er = 92.5:7.5.

(1*S*)-2,3-Dihydro-1-ethyl-3-(methylene)indan-1-ol (10i). The reaction was performed according to the general procedure using 2'-bromopropiophenone (**3i**) (0.10 g, 0.47 mmol). The crude mixture was purified by silica gel flash chromatography, eluting with 10% diethyl ether in petroleum ether (40–60) to yield (1*S*)-2,3-dihydro-1-ethyl-3-(methylene)indan-1-ol (**10i**) (0.048 g, 59%) as a yellow oil. IR (neat) 3348, 2932, 1628, 1458 cm^{-1}; $[\alpha]_D^{31}$ +8.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, CD_3OD) δ 0.81 (t, J = 7.5 Hz, 3H), 1.76 (dq, J = 13.3, 7.5 Hz, 1H), 1.88 (dq, J = 13.3, 7.5 Hz, 1H), 2.77 (dt, J = 16.4, 2.1 Hz, 1H), 2.96 (dt, J = 16.4, 2.1 Hz, 1H), 5.04 (t, J = 2.1 Hz, 1H), 5.49 (t, J = 2.1 Hz, 1H), 7.25–7.32 (m, 2H), 7.35–7.40 (m, 1H), 7.48–7.53 (m, 1H); ^{13}C NMR (126 MHz, CD_3OD) δ 7.5 (CH_3), 33.9 (CH_2), 45.7 (CH_2), 80.7 (C), 102.3 (CH_2), 120.0 (CH), 123.3 (CH), 128.0 (CH), 128.3 (CH), 140.0 (C), 146.8 (C), 149.6 (C); MS (ESI) *m/z* 197 (MNa^+, 100); HRMS (ESI) calcd for $C_{12}H_{14}NaO$ (MNa^+), 197.0937, found 197.0932. Enantiomeric excess was determined by HPLC analysis with a chiralcel OD-H column (hexane:^{i}PrOH 95:5, flow rate 1.0 mL/min), t_{major} = 2.38 min, t_{minor} = 2.80 min; er = 94:6.

(3*S*)-2,3-Dihydro-3-hydroxy-3-methyl-1-indanone (14). (3*S*)-2,3-Dihydro-1-methyl-3-(methylene)indan-1-ol [**(*S*)-10a**] (0.300 g, 1.87 mmol) was dissolved in a mixture of dichloromethane (60 mL) and methanol (60 mL) and cooled to −78 °C. The reaction mixture was purged with oxygen and then ozone was bubbled through until the clear solution turned to blue. The excess ozone was purged with oxygen and then with argon. Triphenylphosphine (1.47 g, 5.61 mmol) was added portionwise to the mixture with vigorous stirring. The reaction mixture was allowed to return to room temperature over 2 h. The reaction mixture was concentrated *in vacuo*. The resulting residue was

purified by silica gel flash column chromatography, eluting with 20% diethyl ether in petroleum ether (40–60) to give (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (0.250 g, 81%) as a yellow oil. IR (neat) 3393, 2972, 1701, 1603 cm^{-1}; $[\alpha]_D^{31}$ +96.9 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.73 (s, 3H), 2.15 (s, 1H), 2.91 (s, 2H), 7.44–7.53 (m, 1H), 7.68–7.75 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 29.3 (CH_3), 53.8 (CH_2), 74.5 (C), 123.2 (CH), 123.6 (CH), 129.4 (CH), 135.4 (C), 135.6 (CH), 158.6 (C), 203.2 (C); MS (EI) *m/z* 162 (M^+, 88), 147 (100), 129 (53), 115 (43), 91 (22), 84 (38), 77 (19); HRMS (EI) calcd for $C_{10}H_{10}O_2$ (M^+), 162.0681, found 162.0680.

(1*S*,3*S*)-2,3-Dihydro-1-(methyl)indan-1,3-diol (15). To a stirred solution of (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (0.020 g, 0.12 mmol) in 1,2-dichloroethane (2 mL) was added sodium triacetoxyborohydride (0.038 g, 0.18 mmol) and acetic acid (0.0070 mL, 0.12 mmol) at room temperature under an argon atmosphere. Sodium triacetoxyborohydride (0.038 g, 0.18 mmol) and acetic acid (0.0070 mL, 0.12 mmol) were then added after two days. The reaction mixture was stirred at room temperature for a total of 6 days and then quenched with 1 M sodium hydroxide solution (2 mL). After phase separation, the aqueous layer was extracted with dichloromethane (2 × 5 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification of the crude material using silica gel flash column chromatography, eluting with 5% methanol in dichloromethane gave (1*S*,3*S*)-2,3-dihydro-1-(methyl)indan-1,3-diol (**15**) (0.015 g, 75% yield) as a white solid. Mp 97–99 °C; IR (neat) 3331, 2967, 1092 cm^{-1}; $[\alpha]_D^{31}$ +48.5 (*c* 0.6, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.70 (s, 3H), 1.76 (s, 1H), 1.90 (s, 1H), 2.10 (dd, *J* = 13.5, 5.0 Hz, 1H), 2.63 (dd, *J* = 13.5, 6.5 Hz, 1H), 5.41 (br t, *J* = 6.0 Hz, 1H), 7.33–7.45 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.7 (CH_3), 52.6 (CH_2), 73.6 (CH), 79.4 (C), 122.3 (CH), 124.5 (CH), 129.1 (CH), 129.1 (CH), 144.3 (C), 147.4 (C); MS (ESI) *m/z* 187 (MNa^+, 98); HRMS (ESI) calcd for $C_{10}H_{12}NaO_2$ (MNa^+), 187.0730, found 187.0730.

General procedure for the reductive amination reactions. To a solution of (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (1 equiv.) in 1,2-dichloroethane (2 mL/mmol) was added the amine (1.1–1.5 equiv.) and sodium triacetoxyborohydride (1.4–1.5 equiv) at room temperature under an argon

atmosphere. The same amounts of amine and hydride source were added after 2 days. The reaction mixture was stirred at room temperature up to 6 days and then quenched with 1 M sodium hydroxide solution (2 mL/mmol). After phase separation, the aqueous layer was extracted with dichloromethane (2 × 5 mL/mmol), dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification using silica gel flash column chromatography, eluting with methanol in dichloromethane gave the 3-amino-substituted 2,3-dihydro-1-(methyl)indan-1-ols.

(1*S*,3*S*)-3-Benzylamino-2,3-dihydro-1-(methyl)indan-1-ol (16a). The reaction was performed according to the general procedure using (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (0.032 g, 0.20 mmol) and benzylamine (0.024 mL, 0.22 mmol). The reaction mixture was stirred at room temperature for 3 days. Purification of the crude material using silica gel flash column chromatography, eluting with 5% methanol in dichloromethane gave (1*S*,3*S*)-3-benzylamino-2,3-dihydro-1-(methyl)indan-1-ol (**16a**) (0.042 g, 84%) as a yellow oil. IR (neat) 3312, 2965, 1452 cm^{-1}; $[\alpha]_D^{31}$ +22.9 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 1.60–1.77 (m, 5H), 1.98 (dd, *J* = 13.2, 6.5 Hz, 1H), 2.59 (dd, *J* = 13.2, 6.5 Hz, 1H), 3.88 (d, *J* = 13.0 Hz, 1H), 3.93 (d, *J* = 13.0 Hz, 1H), 4.48 (t, *J* = 6.5 Hz, 1H), 7.22–7.44 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.1 (CH_3), 50.4 (CH_2), 51.7 (CH_2), 59.8 (CH), 79.4 (C), 122.3 (CH), 124.5 (CH), 127.0 (CH), 128.2 (2 × CH), 128.2 (CH), 128.5 (2 × CH), 128.7 (CH), 140.5 (C), 145.0 (C), 147.4 (C); MS (ESI) *m/z* 254 (MH^+, 100); HRMS (ESI) calcd for $C_{17}H_{20}NO$ (MH^+), 254.1539, found 254.1534.

(1*S*,3*S*)-2,3-Dihydro-3-(4'-methoxybenzyl)amino-1-(methyl)indan-1-ol (16b). The reaction was performed according to the general procedure using (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (0.020 g, 0.12 mmol) and 4-methoxybenzylamine (0.018 mL, 0.014 mmol). The reaction mixture was stirred at room temperature for 6 days. Purification of the crude material using silica gel flash column chromatography, eluting with 5% methanol in dichloromethane gave (1*S*,3*S*)-2,3-dihydro-3-(4'-methoxybenzyl)amino-1-(methyl)indan-1-ol (**16b**) (0.029 g, 84%) as a yellow oil. IR (neat) 3360, 2961, 1611, 1512 cm^{-1}; $[\alpha]_D^{31}$ +19.1 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.50–1.77 (m, 5H), 1.99

(dd, J = 13.3, 6.5 Hz, 1H), 2.60 (dd, J = 13.3, 6.5 Hz, 1H), 3.80 (s, 3H), 3.83 (d, J = 12.8 Hz, 1H), 3.88 (d, J = 12.8 Hz, 1H), 4.49 (t, J = 6.5 Hz, 1H), 6.83–6.91 (m, 2H), 7.27–7.43 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.1 (CH_3), 50.4 (CH_2), 51.2 (CH_2), 55.3 (CH_3), 59.7 (CH), 79.4 (C), 113.8 (2 × CH), 122.2 (CH), 124.4 (CH), 128.2 (CH), 128.7 (CH), 129.3 (2 × CH), 132.6 (C), 145.1 (C), 147.3 (C), 158.7 (C); MS (ESI) *m/z* 284 (MH^+, 100); HRMS (ESI) calcd for $C_{18}H_{22}NO_2$ (MH^+), 284.1645, found 284.1640.

(1*S*,3*S*)-3-Allylamino-2,3-dihydro-1-(methyl)indan-1-ol (16c). The reaction was performed according to the general procedure using (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (0.020 g, 0.12 mmol) and allylamine (0.013 mL, 0.18 mmol). The reaction mixture was stirred at room temperature for 6 days. Purification of the crude material using silica gel flash column chromatography, eluting with 5% methanol in dichloromethane gave (1*S*,3*S*)-3-allylamino-2,3-dihydro-1-(methyl)indan-1-ol (**16c**) (0.019 g, 78%) as a yellow oil. IR (neat) 3329, 2967, 1452 cm^{-1}; $[\alpha]_D^{31}$ +30.3 (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.55–1.85 (m, 5H), 1.93 (dd, J = 13.3, 6.7 Hz, 1H), 2.60 (dd, J = 13.3, 6.7 Hz, 1H), 3.37 (dd, J = 14.0, 6.0 Hz, 1H), 3.42 (dd, J = 14.0, 6.0 Hz, 1H), 4.49 (t, J = 6.7 Hz, 1H), 5.13 (dd, J = 10.5, 1.5 Hz, 1H), 5.25 (dd, J = 17.0, 1.5 Hz, 1H), 5.98 (ddt, J = 17.0, 10.5, 6.0 Hz, 1H), 7.28–7.44 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.0 (CH_3), 50.2 (CH_2), 50.4 (CH_2), 59.7 (CH), 79.3 (C), 116.2 (CH_2), 122.3 (CH), 124.4 (CH), 128.3 (CH), 128.8 (CH), 136.7 (CH), 144.8 (C), 147.3 (C); MS (ESI) *m/z* 204 (MH^+, 100); HRMS (ESI) calcd for $C_{13}H_{18}NO$ (MH^+), 204.1383, found 204.1382.

(1*S*,3*S*)-2,3-Dihydro-1-methy-3-(morpholino)indan-1-ol (16d). The reaction was performed according to the general procedure using (3*S*)-2,3-dihydro-3-hydroxy-3-methyl-1-indanone (**14**) (0.020 g, 0.12 mmol) and morpholine (0.016 mL, 0.18 mmol). The reaction mixture was stirred at rt for 6 days. Purification of the crude material using silica gel flash column chromatography, eluting with 8% methanol in dichloromethane gave (1*S*,3*S*)-2,3-dihydro-1-methy-3-(morpholino)indan-1-ol (**16d**) (0.022 g, 79%) as a light brown solid. Mp 84–86 °C; IR (neat) 3410, 2961, 1452 cm^{-1}; $[\alpha]_D^{31}$ +74.8 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65–1.77 (m, 4H), 2.20 (d, J = 7.2 Hz, 2H), 2.48 (dt, J = 11.2,

4.4 Hz, 2H), 2.53 (dt, J = 11.2, 4.4 Hz, 2H), 3.71 (t, J = 4.4 Hz, 4H), 4.54 (t, J = 7.2 Hz, 1H), 7.27–7.42 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 27.5 (CH_3), 40.5 (CH_2), 49.2 (2 × CH_2), 67.2 (CH), 67.4 (2 × CH_2), 79.1 (C), 122.2 (CH), 125.5 (CH), 128.3 (CH), 128.5 (CH), 142.5 (C), 147.6 (C); MS (ESI) *m/z* 234 (MH^+, 100); HRMS (ESI) calcd for $C_{14}H_{20}NO_2$ (MH^+), 234.1489, found 234.1490.

SUPPORTING INFORMATION AVAILABLE. X-Ray data for compounds **15** and **16d**, HPLC traces for all indanols and, ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

ACKNOWLEDGEMENT. Financial support from the University of Glasgow (studentship to R.J.F.) and EPSRC (studentship to E.D.D.C., EP/P505534/1) is gratefully acknowledged.

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