Bi(III)-Catalyzed Enantioselective Allylation Reactions of Ketimines

Asymmetric Allylations of ketimines:

Homoallylic amines:

- 3-allyl-3-aminoxantrones
- (R)-psychoxetine
- (-)psilocybin

43 examples, up to 99% yield, up to 99.5% ee

Bi(OAc)₃-chiral phosphoric acid catalyst

Downstream synthetic transformations

DATA AND SOFTWARE AVAILABILITY
www.ccdc.cam.ac.uk/getstructures

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**Bi(III)-Catalyzed Enantioselective Allylation Reactions of Ketimines**

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**SUMMARY**

Chiral homoallylic amines not only are found in pharmaceutically relevant compounds but also serve as versatile building blocks for chemical synthesis. However, catalytic allylation of ketimines with allylboronates, an attractive approach to synthesize chiral homoallylic amine scaffolds remain scarce. Herein, we develop a highly enantioselective allylation of isatin-derived ketimines with boron allylation reagents catalyzed by a Bi(OAc)$_3$-chiral phosphoric acid catalyst system. The reactions are remarkably efficient and mild, most of which were completed in less than an hour at room temperature with only 1/2 mol% (Bi(OAc)$_3$/CPA) catalyst loading. A wide range of chiral 3-allyl 3-aminooxindoles were obtained in excellent yields and enantioselectivities. The synthetic utility was demonstrated by efficient formal synthesis of (+)-AG-041R and (−)-psychotriasine. Preliminary mechanism was studied by control experiments and theoretical calculations.

**INTRODUCTION**

Chiral homoallylic amines not only are widely found in natural products and pharmaceutically relevant compounds (Guan et al., 2003; Ghosh et al., 2006) but also serve as versatile building blocks for chemical synthesis (Scheme 1A) (Sirasani and Andrade, 2011; Lathrop et al., 2016). Therefore, the asymmetric synthesis of chiral homoallylic amine scaffolds is of great interest in the organic chemistry community (Kumar et al., 2016; Wan et al., 2017). In this context, the asymmetric addition reaction of allylboronates to imines has been recognized as one of the most efficient methods for the construction of chiral homoallylic amines (Kennedy and Hall, 2003; Yusu et al., 2011; Huo et al., 2014). Compared with the additions of allylboronates to aldimes (Lou et al., 2007; Lou and Schaus, 2008; Silverio et al., 2013; Wu et al., 2014; Jiang et al., 2017a, 2017b; Jiang and Schaus, 2017), the corresponding asymmetric allylation of ketimines remains scarce, probably owing to the low reactivity of ketimines. Pioneering enantioselective allylation of acyclic ketimines with allylboronates by using DuPHOS-CuF catalyst has been demonstrated in 2006 by Shibasaki group (Scheme 1B) (Wada et al., 2006). In addition, Rh (and Co)-catalyzed enantioselective additions of potassium allyltrifluoroborates to cyclic N-sulfonyl az-ketiminoesters were also reported (Scheme 1C) (Luo et al., 2012; Hepburn et al., 2013; Hepburn and Lam, 2014; Wu et al., 2016). Very recently, Hoveyda reported NHC-CuCl complex-catalyzed highly stereoselective additions of versatile allyl groups to N-H ketimines (Scheme 1D) (Jang et al., 2017). Other methods involve using enantiomerically pure boron allylation reagent (Scheme 1E) (Chen and Aggarwal, 2014) or chiral inducing amine alcohol reagent (Scheme 1F) (Tan et al., 2017). Despite the mentioned achievements, several limitations, including high catalyst loading, long reaction time, harsh reaction conditions, and limited substrates, remain vast challenges to this field. Furthermore, such endeavors have been relying on either the utilization of canonical transition metal catalysis or stoichiometric chiral reagent. In consequence, the discovery of an efficient catalyst system that could enable the allylation of ketimines by allylboration reagents in a more efficient and stereoselective fashion would provide access to chiral homoallylic amines in a sustainable manner.

Over the past few decades, chiral Lewis acid catalysis, a significant approach to obtain optically active compounds, had been well developed (Yamamoto, 2000; Yamamoto and Futatsugi, 2005; Yamamoto and Ishihara, 2008; Liu et al., 2011, 2014; Lv and Luo, 2013; Mlynarski, 2017). Although rare-earth metals, the first-row transition metals, and boron-type compounds are the most popular Lewis acid catalysts, the chiral alkaline-earth metal-based catalysts have also attracted ever-growing interest for meeting the needs of green sustainable chemical synthesis (Hatano et al., 2010; Zhang et al., 2011; Zheng et al., 2011; Li et al., 2013). Bismuth compounds, due to their low toxicity and non-corrosiveness, have always been considered as suitable for designing environmentally benign catalysts (Bothwell et al., 2011; Salvador et al., 2012; Ollevier, 2013; Ondet et al., 2017). However, the asymmetric bismuth catalysis remains a relatively unexplored field (Wada et al., 1997; Kobayashi et al., 2005; Kobayashi and Ogawa, 2006; Koch and...
Thus, the development of efficient catalytic transformations using chiral bismuth system is highly meaningful and desirable.

Chiral 3-amino-2-oxindole is an important structural motif in medicinally relevant compounds (Zhou et al., 2010; Singh and Desta, 2012; Cao et al., 2018). Especially, the homoallylic aminooxindole derivatives not only act directly as an inhibitor of HIV-1 protease (Scheme 1A) but also can be converted into aminooxindole frameworks presented in alkaloids (Scheme 3B and 3C). In 2013, Nakamura demonstrated the enantioselective allylation of isatin-derived ketimines catalyzed by Pd-pincer-complexes and AgF under strict reaction conditions (Nakamura et al., 2013). In 2016, Cai group reported an enantioselective In(OTf)3-catalyzed allylation of ketimines derived from isatins with highly toxic allyltributyltin; however, this method is not suitable for the substrates with electron-withdrawing groups (Chen and Cai, 2016). Herein, we report a Bi(III)-catalyzed asymmetric allylation of isatin-derived ketimines with allylboronates under
| Entry | LA    | CPA   | Solvent | Time | Yield /% | er<sup>[b]</sup> |
|-------|-------|-------|---------|------|----------|-----------------|
| 1<sup>c</sup> | –     | 4     | DCM     | 64 h | n.r.     | –              |
| 2<sup>c</sup> | –     | 5a    | DCM     | 48 h | 17       | 85.9:14.1      |
| 3     | Bi(OAc)<sub>3</sub> | 5a    | CHCl<sub>3</sub> | 20 min | 99       | 87.9:12.1      |
| 4     | Bi(OAc)<sub>3</sub> | 5b    | CHCl<sub>3</sub> | 25 min | 88       | 61.7:38.3      |
| 5     | Bi(OAc)<sub>3</sub> | 5c    | CHCl<sub>3</sub> | 40 min | 98       | 75.3:24.7      |
| 6     | Bi(OAc)<sub>3</sub> | 5d    | CHCl<sub>3</sub> | 25 min | 95       | 55.1:44.9      |
| 7     | Bi(OAc)<sub>3</sub> | 5e    | CHCl<sub>3</sub> | 25 min | 92       | 50.4:49.6      |
| 8     | Bi(OAc)<sub>3</sub> | 6a    | CHCl<sub>3</sub> | 80 min | 99       | 17.0:83.0      |
| 9     | Bi(OAc)<sub>3</sub> | 5a    | DCM     | 20 min | 89       | 86.0:14.0      |
| 10    | Bi(OAc)<sub>3</sub> | 5a    | Toluene | 15 min | 98       | 97.7:2.3       |
| 11    | Bi(OAc)<sub>3</sub> | 5a    | EA      | 15 min | 96       | 98.3:1.7       |
| 12    | Bi(OAc)<sub>3</sub> | 5a    | CH<sub>3</sub>CN | 50 min | 99       | 88.2:11.8      |
| 13    | Bi(OAc)<sub>3</sub> | 5a    | THF     | 75 min | 93       | 97.0:3.0       |
| 14    | Bi(OAc)<sub>3</sub> | 5a    | Dioxane | 45 min | 99       | 96.6:3.4       |
| 15    | Bi(OAc)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 20 min | 99       | 99.2:0.8       |
| 16<sup>d</sup> | Bi(OAc)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 35 min | 96       | 99.1:0.9       |
| 17<sup>d</sup> | Bi(OTf)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 24 h  | 30       | 57.0:43.0      |
| 18<sup>d</sup> | BiCl<sub>3</sub> | 5a    | Et<sub>2</sub>O | 24 h  | 27       | 53.9:46.1      |
| 19<sup>d</sup> | BiBr<sub>3</sub> | 5a    | Et<sub>2</sub>O | 24 h  | 81       | 52.6:47.4      |
| 20<sup>d</sup> | Bi<sub>3</sub> | 5a    | Et<sub>2</sub>O | 24 h  | 92       | 65.5:34.5      |
| 21<sup>d</sup> | Bi(OH)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 24 h  | 20       | 94.8:5.2       |
| 22<sup>d</sup> | Bi(O'Pr)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 60 h  | 94       | 94.9:5.1       |
| 23<sup>d</sup> | Sc(OAc)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 72 h  | <5       | –              |
| 24<sup>d</sup> | In(OAc)<sub>3</sub> | 5a    | Et<sub>2</sub>O | 72 h  | 31       | 55.4:44.6      |
| 25<sup>d</sup> | Cu(OAc)<sub>2</sub> | 5a    | Et<sub>2</sub>O | 52 h  | trace    | –              |

Table 1. Reaction Optimization

(Continued on next page)
RESULTS AND DISCUSSION
Optimization of the Reaction Conditions

Binaphthols have been proved to be efficient catalysts for the reactions of boronate with ketones (Lou et al., 2006; Barnett et al., 2009; Alam et al., 2015) and aldimines (Lou et al., 2007; Lou and Schaus, 2008; Jiang et al., 2017a, 2017b; Jiang and Schaus, 2017); we initially attempted the reaction of the isatin-derived N-Boc-protected ketimine 1a and allylboronic acid pinacol ester 2a with binaphthol 4, yet catalyst 4 could not promote this reaction (Table 1, entry 1). Then we turned our attention to chiral phosphoric acids, which have also been considered as good catalysts to realize the allylboration of aldehydes (Jain and Antilla, 2010). Although chiral phosphoric acid (S)-5a indeed catalyzed the reaction to give product 3a with 85.9:14.1 er, only 17% yield was obtained after 48h (Table 1, entry 2). The reactivity is obviously unsatisfactory.

We suspected that the Brønsted acidity of chiral phosphoric acid is not strong enough to simultaneously activate ketimine 1a and allylboronate 2a. Inspired by Luo’s asymmetric binary acid catalysis (Lv et al., 2011, 2013; Hashimoto et al., 2013; Hatano et al., 2015; Wang et al., 2017; Zhang et al., 2017a) and the bismuth catalyzed allylation of para-quinone with allylboronate 2a developed by our group (Zhang et al., 2017b), we proposed that this transformation was likely to be promoted by the BiX3-chiral phosphoric acid catalyst system and the use of chiral phosphoric acid could ensure the stereochemistry of this process. Gratifyingly, in the presence of (S)-5a and Bi(OAc)3, the model reaction gave product 3a in quantitative yield with 87.9:12.1 er (Table 1, entry 3). We then examined other (S)-BINOL chiral phosphoric acid with Bi(OAc)3, but no better results were achieved (Table 1, entries 4–8). Screening of solvents (Table 1, entries 9–15) revealed that the reaction was favored in Et2O (Table 1, entry 15). When catalyst loading was lowered to 1 mol% Bi(OAc)3 and 2 mol% (S)-5a, the yield (96%) and enantioselectivity (99.1: 0.9 er) essentially remained the same in comparison with those with high catalyst loading (Table 1, entry 16). The counter anions of Bi(III) and different Lewis acids were also investigated in the model reaction. The use of other bismuth salts resulted in either low reactivities or poor stereoselectivities (Table 1, entries 17–22). Exploring other rather mild reaction conditions (Scheme 1G). A wide range of chiral 3-allyl 3-aminooxindoles were smoothly obtained in excellent yields with exceptional stereocontrol to forge the quaternary stereogenic carbon centers (Scheme 1G).

Table 1. Continued

| Entry | LA    | CPA | Solvent | Time | Yield /% | er       |
|-------|-------|-----|---------|------|----------|----------|
| 26    | AgOAc | 5a  | Et2O    | 25 h | 12       | 55.9:44.1|
| 27    | Y(OAc)3 | 5a | Et2O    | 25 h | trace    | –        |
| 28    | La(OAc)3 | 5a | Et2O    | 48 h | 12       | 69.0:31.0|

The reactions were carried out with 1a (0.1 mmol), 2a (0.12 mmol), Bi(OAc)3 (2 mol%), and CPA (3 mol%) in 0.5 mL solvent at room temperature.

Yield of isolated products.

Determined by HPLC analysis.

The reactions were carried out with 1a (0.1 mmol), 2a (0.12 mmol), 10 mol% catalyst in 0.5 mL DCM at room temperature.

The reactions were carried out with 1a (0.2 mmol), 2a (0.24 mmol), Bi(OAc)3 (1 mol%), and (S)-5a (2 mol%) in 1.0 mL Et2O at room temperature.
metal acetates, including Sc(III), In(III), and Y(III), almost all showed poor catalytic activities (Table 1, entries 23–28). Thus, the optimal reaction conditions were finally determined to be 1 mol% Bi(OAc)₃ and 2 mol% (S)-5a in Et₂O (0.2 M) at room temperature (Table 1, entry 16).

Substrate Scope

We then explored the substrate scope of the allylation of isatin-derived ketimines under the optimal reaction conditions. We first investigated the substituents on the phenyl ring of the isatin. As shown in Figure 1, this protocol is amenable to most of N-Boc-protected ketimines derived from N-benzylisatins bearing electron-donating or electron-withdrawing substituents and halogen atoms on the phenyl ring, leading to chiral 3-allyl 3-aminooxindole products (Figures 1, 3a–3p) in high yields (73%–99%) with good to excellent enantioselectivities (91.7: 8.3–99.3: 0.7 er). However, electron-withdrawing substituents on the C5 and C7 of the phenyl ring led to reduced stereoselectivities (Figure 1, 3g and 3p).

Subsequently, the effect of the protecting group at the N1-position were examined (Figure 2). To our delight, the expected product 3q was afforded from ketimine 1q without protecting group on the N1-atoms in 99% yield and 85.1: 14.9 er. An elevated 98.8: 1.2 er was obtained after one single recrystallization from ethyl acetate/n-pentane. In addition, isatin-derived ketimines with phenyl, acetyl, alkyl (R’ = Me, allyl, methoxymethyl or CH₂CH(OEt)₂) at the N1-position, were also efficiently transformed into the
corresponding allylic products (3r-3v) with good to excellent enantioselectivities (92.4: 7.6–99.5: 0.5 er).

When the substituents at the N1-position of ketimines 1 were substituted benzyl groups, we found that the electron effect or the steric hindrance had almost no effect on the reaction results (Figure 2, 3x-3z and 3aa–3af).

Furthermore, other N-alkoxy carbonyl ketimines can also react with 2a and give the products (3ag and 3ah) in good yields and excellent enantioselectivities (Figure 2). And N-phenyl ketimine 1ai could also be transformed into the corresponding allylation product 3ai under the optimal conditions in excellent yield (98%) with good enantioselectivity (94.1:5.9 er).

To expand the scope of this Bi(OAc)3/CPA catalyzed asymmetric allylation method, some other ketimines were also investigated (Scheme 2). To our delight, not only the cyclic N-sulfonyl α-ketiminoester 1aj but also the N-Boc ketimine 1ak derived from pyrazolin-5-one could work smoothly under the optimal conditions and give the desired products 3aj (Wu et al., 2018) and 3ak in excellent yields with good enantioselectivities. In addition, this catalytic system was also proved to be suitable for the asymmetric allylation of isatin (Scheme 2) (Itoh et al., 2009).

Further exploration of the substrate scope was focused on the allyl boron reagent (Scheme 2). When potassium allyltrifluoroborate and allyl boric acid were used, the corresponding product 3a was obtained with 92.4:7.6 er and 93.1:6.9 er, respectively. It should be noted that this Bi(OAc)3/CPA catalytic system is applicable to a variety of boron allylation reagent, whereas previous reports are often limited to the
particular one. The α-addition product 3am (91% yield, 5.8:1 d.r., and 96.6:3.4 er) resulted in the reaction of 1a and 2d. When β-methyl branch allylboronic acid pinacol ester reacted with 1a under the optimal conditions, the desired product 3an was obtained in good yield (84%) with depressed enantioselectivity (79.4:20.6 er). Moreover, the reaction of pinacolyl isoprenylboronate and ketimine 1a could also give the desired product 3ao in good yield (69%) and moderate enantioselectivity (84.4:15.6 er).

**Large-Scale Reaction and Synthetic Applications**

To probe the efficiency of current asymmetric allylation strategy in preparative synthesis, a gram-scale reaction of 1a and 2a was investigated under optimal reaction conditions. To our delight, the corresponding product 3a was obtained without any loss of the enantioselectivity (Scheme 3A). To illustrate the applicability of our method in organic synthesis, the product was applied to synthesize some pharmaceuticals and N-containing heterocyclic oxindole compounds. Firstly, as shown in Scheme 3B, the allylation product 3a underwent complete oxidation and reduction to give the compound 7. Compound 7 can be oxidized to an aldehyde intermediate and provided key compound 8 by reductive amination, which can be converted to (−)-psychotriazaine (Dai et al., 2017). Compound 3a underwent hydroboration-oxidation followed by an intramolecular Mitsunobu reaction to afford spirocyclic amine 10 (98.7:1.3 er). The N-allylation of 3a can also offer product 11 in high yield, and its ring-closing metathesis gave spirocyclic amine 12 in high yield with maintained er value by using Grubbs second catalyst. In addition, the β-amino ester 13 was afforded by oxidation of 3a followed by esterification. Boc removal followed by cyclization led to spiro-β-lactam 15 in 67% yield and 98.8:1.2 er. Thereafter, oxidation of 3v followed by an esterification afforded compound 16 without any loss of enantioselectivity (99.6:0.4 er). And the compound 16 could be transformed into (+)-AG-041R, which is a potent gastrin/CCK-B receptor antagonist (Scheme 3C) (Sato et al., 2009).

**Mechanistic Considerations**

We performed control experiments to investigate whether bismuth acetate and chiral phosphoric acid work in a synergic manner on the activity and enantioselectivity of the asymmetric allylation (Table 2). The reaction proceeded smoothly in the presence of Bi(OAc)₃ and gave a racemic product (Table 2, entry 1). When only chiral phosphoric acid (S)-5a existed, 14% yield and 62.4: 37.6 er could be achieved in 48 h (Table 2, entry 2). Considering that the hydrolysis of Bi(OAc)₃ produces acetic acid, we performed the reaction under the condition of only 2 mol% AcOH, and 12% racemic product could be given (Table 2, entry 3). If adding 3 mol% (S)-5a on the basis of condition C, we could afford the product in 17% yield with 71.6:28.4 er in 48 h (Table 2, entry 4). Therefore, the effect of Lewis acid’s hydrolysis on the reaction results could be excluded. These experimental results demonstrated that the reactivity and stereoselectivity should be controlled by Bi(OAc)₃ and chiral phosphoric acid together.
Preliminary experiments were conducted to illustrate the mechanism of the Bi(OAc)₃/CPA catalytic system. ESI-MS experiment (cationic mode) gave two peaks m/z 1027.27 and 1728.45 corresponding to 5a, Bi(OAc)₂ and (5a)₂, Bi(OAc)₂ (for details, see Supplemental Information). A positive nonlinear effect between the catalyst’s ee value and product’s ee value was observed under optimal reaction conditions (Figure 3) (Liu et al., 2011; Wang et al., 2017), which indicates that more than one molecule of the chiral acid (S)-5a is likely to be involved in the transition state of the enantio-differentiating step. The α-selectivity was observed with 1-methylallylboronic acid pinacol ester (Scheme 2, substrate scope part); thus, we speculated that the reaction should occur through a B-to-Bi transmetalation process (Chakrabarti et al., 2010).

Scheme 3. Large-Scale Reaction and Transformations of the Products
(A) The gram-scale reaction.
(B) The versatile transforms of 3a.
(C) The formal synthesis of (+)-AG-041R.

Reagents and conditions: (a) KMnO₄, NaO₄, H₂O, room temperature, 2 d; (b) Et₃N, CICO₂Et, THF, −10°C, 1 h; (c) NaBH₄, H₂O, 0°C to room temperature, 4 h; (d) DMP, NaHCO₃, DCM, room temperature, 1 h; (e) CH₃NH₂·HCl, Et₃N, MgSO₄, MeOH, room temperature, overnight, then NaBH₄, 0°C; (f) 9-BBN, THF, 0°C to room temperature, 24 h; (g) AcONa, H₂O₂ (30% aq.), 0°C to room temperature, 5 h; (h) Ph₃P, DEAD, DCM, 0°C to room temperature, overnight; (i) NaH, DMF, Allyl bromide, room temperature, 30 min; (j) Grubbs second, toluene, 60°C, 20 min; (k) Mel, C₆H₅CO₂H, CH₃CN, room temperature, 8 h; (l) TFA, DCM, room temperature, 3 h; (m) 2 M NaOH (aq.), MeOH, 2 h; (n) MsCl, NaHCO₃, CH₃CN, 80°C, 18 h.

Preliminary experiments were conducted to illustrate the mechanism of the Bi(OAc)₃/CPA catalytic system. ESI-MS experiment (cationic mode) gave two peaks m/z 1027.27 and 1728.45 corresponding to 5a·Bi(OAc)₂ and (5a)₂·Bi(OAc)₂ (for details, see Supplemental Information). A positive nonlinear effect between the catalyst’s ee value and product’s ee value was observed under optimal reaction conditions (Figure 3) (Liu et al., 2011; Wang et al., 2017), which indicates that more than one molecule of the chiral acid (S)-5a is likely to be involved in the transition state of the enantio-differentiating step. The α-selectivity was observed with 1-methylallylboronic acid pinacol ester (Scheme 2, substrate scope part); thus, we speculated that the reaction should occur through a B-to-Bi transmetalation process (Chakrabarti et al., 2010).
The mechanism of the catalytic system has been further investigated by theoretical calculations (for computational details, see Supplemental Information). Two mechanistic possibilities that differ by the coordination number were considered. A single CPA ligand is present in M1, whereas two chiral ligands are present in M2 (Figure 4). Mechanism M1 can be discarded based on the large energy barrier (at least 6.1 kcal/mol unfavorable) in which the single CPA served as a typical anionic ligand. Two CPA ligands perform different roles in M2, in which one serves as a typical anionic ligand and the other performs as a neutral ligand and acid catalyst simultaneously. We have examined different relative orientations of substrate 1q and Bi-allyl species (details in the Supplemental Information), and the most stable TS corresponding to the structure was shown (M2 in Figure 4). On examination of TS-2p-(R), we found that the C=O group of the ketimine is coordinated with the Bi and the C=N group is activated by the proton of phosphoric acid simultaneously. In the most stable TS-2P-(R), substrate 1q is oriented with the bulky Boc group into an open quadrant of the catalyst and TS-2P-(S) with the bulky Boc group toward the catalyst lying 1.1 kcal/mol above the most

| Entry | Conditions                          | Results                   |
|-------|-------------------------------------|---------------------------|
| 1     | Only 2 mol% Bi(OAc)₃                 | 1.5 h, 99% yield, rac     |
| 2     | Only 3 mol% (S)-5a                   | 48 h, 14% yield, 62.4:37.6 er |
| 3     | Only 2 mol% AcOH                     | 48 h, 12% yield, rac      |
| 4     | 2 mol% AcOH + 3 mol% (S)-5a          | 48 h, 17% yield, 71.6:28.4 er |

Table 2. Control Experiments

The mechanism of the catalytic system has been further investigated by theoretical calculations (for computational details, see Supplemental Information). Two mechanistic possibilities that differ by the coordination number were considered. A single CPA ligand is present in M1, whereas two chiral ligands are present in M2 (Figure 4). Mechanism M1 can be discarded based on the large energy barrier (at least 6.1 kcal/mol unfavorable) in which the single CPA served as a typical anionic ligand. Two CPA ligands perform different roles in M2, in which one serves as a typical anionic ligand and the other performs as a neutral ligand and acid catalyst simultaneously. We have examined different relative orientations of substrate 1q and Bi-allyl species (details in the Supplemental Information), and the most stable TS corresponding to the structure was shown (M2 in Figure 4). On examination of TS-2p-(R), we found that the C=O group of the ketimine is coordinated with the Bi and the C=N group is activated by the proton of phosphoric acid simultaneously. In the most stable TS-2P-(R), substrate 1q is oriented with the bulky Boc group into an open quadrant of the catalyst and TS-2P-(S) with the bulky Boc group toward the catalyst lying 1.1 kcal/mol above the most.

Figure 3. Nonlinear Effect Experiment
For the major diastereomer, determined by HPLC analysis on a chiral stationary phase, averaged over two runs (see also Table S3).
Figure 4. Transition State Structures and Relative Free Energies (in kcal/mol)
See also Figures S167–S170; and Tables S3 and S4–S10.
stable TS. Calculations predict 86.5: 13.5 er for the (R)-product, which is consistent well with experimental 85.1: 14.9 er.

Limitations of Study
The reaction only gave poor yield (30%) and poor enantioselectivity (57.0:43.0 er) with the widely used Bi(OTf)3 instead of Bi(OAc)3 (Table 1, entry 17).

Conclusion
In summary, we have developed a highly efficient and enantioselective asymmetric allylation of isatin-derived ketimines with allylboronates promoted by a binary acid system containing bismuth acetate and chiral phosphoric acid. As far as we know, this is the first successful application of the catalyst system of Bi(III) Lewis acid and chiral phosphoric acid in asymmetric catalysis. This is an unreported catalytic system in asymmetric allylation of ketimines. As a result, a series of chiral 3-allyl 3-aminooxindoles were obtained in excellent yields (up to 99%) and enantioselectivities (up to 99.5: 0.5 er). The synthetic utility was demonstrated not only by formal synthesis of (+)-AG-041R and (–)-psychotriasine but also by the transformation of the allylation products into valuable chiral 3-spirocyclic oxindoles. Preliminary mechanism study by control experiments and theoretical calculations shows that two chiral phosphoric acids, in which one serves as an anionic ligand and the other performs as a neutral ligand and acid catalyst simultaneously, have participated in this allylation strategy. We anticipate that this work will provide a broad prospect for the future application of bismuth in asymmetric catalysis.

METHODS
All methods can be found in the accompanying Transparent Methods supplemental file.

DATA AND SOFTWARE AVAILABILITY
The crystallography data have been deposited at the Cambridge Crystallographic Data Center (CCDC) under accession number CCDC: 1849656 (10) and can be obtained free of charge from www.ccdc.cam.ac.uk/getstructures.

SUPPLEMENTAL INFORMATION
Supplemental Information can be found online at https://doi.org/10.1016/j.isci.2019.06.006.

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AUTHOR CONTRIBUTIONS
J.W. developed the asymmetric catalytic reaction. J.W. and Q.Z. expanded the substrate scope, performed the synthetic applications, and characterized all the products. B.Z. and C.Y. performed the theoretical calculations. X.L. directed the investigations. J.W., X.L., and J.-P.C. wrote the manuscript.

DECLARATION OF INTERESTS
The authors declare no competing interests.

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Supplemental Information

Bi(III)-Catalyzed Enantioselective Allylation Reactions of Ketimines

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Supplementary Figures

Figure S1. $^1$H NMR spectrum of $1h$, related to Figure 1.

Figure S2. $^{13}$C NMR spectrum of $1h$, related to Figure 1.
Figure S3. $^1$H NMR spectrum of 1i, related to Figure 1.

Figure S4. $^{13}$C NMR spectrum of 1i, related to Figure 1.
Figure S5. $^1$H NMR spectrum of 3a, related to Figure 1.

Figure S6. $^{13}$C NMR spectrum of 3a, related to Figure 1.
Figure S7. HPLC spectrum of 3a, related to Figure 1.
Figure S8. HPLC spectrum of 3a, related to Scheme 2.

Figure S9. HPLC spectrum of 3a, related to Scheme 2.
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Figure S11. $^{13}$C NMR spectrum of 3b, related to Figure 1.
Figure S12. HPLC spectrum of 3b, related to Figure 1.
Figure S13. $^1$H NMR spectrum of 3c, related to Figure 1.

Figure S14. $^{13}$C NMR spectrum of 3c, related to Figure 1.
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Figure S16. $^1$H NMR spectrum of 3d, related to Figure 1.

Figure S17. $^{13}$C NMR spectrum of 3d, related to Figure 1.
Figure S18. $^{19}$F NMR spectrum of 3d, related to Figure 1.
Figure S19. HPLC spectrum of 3d, related to Figure 1.
Figure S20. $^1$H NMR spectrum of 3e, related to Figure 1.

Figure S21. $^{13}$C NMR spectrum of 3e, related to Figure 1.
Figure S22. HPLC spectrum of 3e, related to Figure 1.
Figure S23. $^1$H NMR spectrum of 3f, related to Figure 1.

Figure S24. $^{13}$C NMR spectrum of 3f, related to Figure 1.
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Figure S26. $^1$H NMR spectrum of 3g, related to Figure 1.

Figure S27. $^{13}$C NMR spectrum of 3g, related to Figure 1.
**Figure S28.** HPLC spectrum of 3g, related to Figure 1.
Figure S29. $^1$H NMR spectrum of 3h, related to Figure 1.

Figure S30. $^{13}$C NMR spectrum of 3h, related to Figure 1.
Figure S31. HPLC spectrum of 3h, related to Figure 1.
Figure S32. $^1$H NMR spectrum of 3i, related to Figure 1.

Figure S33. $^{13}$C NMR spectrum of 3i, related to Figure 1.
Figure S34. $^{19}$F NMR spectrum of 3i, related to Figure 1.
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Figure S36. $^1$H NMR spectrum of 3j, related to Figure 1.

Figure S37. $^{13}$C NMR spectrum of 3j, related to Figure 1.
Figure S38. HPLC spectrum of 3j, related to Figure 1.
Figure S39. $^1$H NMR spectrum of 3k, related to Figure 1.

Figure S40. $^{13}$C NMR spectrum of 3k, related to Figure 1.
Figure S41. HPLC spectrum of 3k, related to Figure 1.
Figure S42. $^1$H NMR spectrum of 3l, related to Figure 1.

Figure S43. $^{13}$C NMR spectrum of 3l, related to Figure 1.
Figure S44. $^{19}$F NMR spectrum of 3l, related to Figure 1.
Figure S45. HPLC spectrum of 3l, related to Figure 1.
Figure S46. $^1$H NMR spectrum of 3m, related to Figure 1.

Figure S47. $^{13}$C NMR spectrum of 3m, related to Figure 1.
Figure S48. HPLC spectrum of 3m, related to Figure 1.
Figure S49. $^1$H NMR spectrum of 3n, related to Figure 1.

Figure S50. $^{13}$C NMR spectrum of 3n, related to Figure 1.
Figure S51. HPLC spectrum of 3n, related to Figure 1.
Figure S52. $^1$H NMR spectrum of 3o, related to Figure 1.

Figure S53. $^{13}$C NMR spectrum of 3o, related to Figure 1.
Figure S54. HPLC spectrum of 3o, related to Figure 1.
Figure S55. $^1$H NMR spectrum of 3p, related to Figure 1.

Figure S56. $^{13}$C NMR spectrum of 3p, related to Figure 1.
**Figure S57.** $^{19}$F NMR spectrum of 3p, related to Figure 1.
Figure S58. HPLC spectrum of 3p, related to Figure 1.
Figure S59. $^1$H NMR spectrum of 3q, related to Figure 2.

Figure S60. $^{13}$C NMR spectrum of 3q, related to Figure 2.
Figure S61. HPLC spectrum of 3q, related to Figure 2.
Figure S62. $^1$H NMR spectrum of 3r, related to Figure 2.

Figure S63. $^{13}$C NMR spectrum of 3r, related to Figure 2.
Figure S64. HPLC spectrum of 3r, related to Figure 2.
Figure S65. $^1$H NMR spectrum of 3s, related to Figure 2.

Figure S66. $^{13}$C NMR spectrum of 3s, related to Figure 2.
Figure S67. HPLC spectrum of 3s, related to Figure 2.
Figure S68. $^1$H NMR spectrum of 3t, related to Figure 2.

Figure S69. $^{13}$C NMR spectrum of 3t, related to Figure 2.
Figure S70. HPLC spectrum of 3t, related to Figure 2.
Figure S71. $^1$H NMR spectrum of 3u, related to Figure 2.

Figure S72. $^{13}$C NMR spectrum of 3u, related to Figure 2.
Figure S73. HPLC spectrum of 3u, related to Figure 2.
Figure S74. $^1$H NMR spectrum of $3v$, related to Figure 2.

Figure S75. $^{13}$C NMR spectrum of $3v$, related to Figure 2.
Figure S76. HPLC spectrum of 3v, related to Figure 2.
Figure S77. $^1$H NMR spectrum of 3w, related to Figure 2.

Figure S78. $^{13}$C NMR spectrum of 3w, related to Figure 2.
Figure S79. HPLC spectrum of 3w, related to Figure 2.
Figure S80. $^1$H NMR spectrum of 3x, related to Figure 2.

Figure S81. $^{13}$C NMR spectrum of 3x, related to Figure 2.
Figure S82. HPLC spectrum of 3x, related to Figure 2.
Figure S83. $^1$H NMR spectrum of 3y, related to Figure 2.

Figure S84. $^{13}$C NMR spectrum of 3y, related to Figure 2.
Figure S85. $^{19}$F NMR spectrum of 3y, related to Figure 2.
Figure S86. HPLC spectrum of 3y, related to Figure 2.
Figure S87. $^1$H NMR spectrum of 3z, related to Figure 2.

Figure S88. $^{13}$C NMR spectrum of 3z, related to Figure 2.
Figure S89. HPLC spectrum of 3z, related to Figure 2.
Figure S90. $^1$H NMR spectrum of 3aa, related to Figure 2.

Figure S91. $^{13}$C NMR spectrum of 3aa, related to Figure 2.
Figure S92. $^{19}$F NMR spectrum of 3aa, related to Figure 2.
Figure S93. HPLC spectrum of 3aa, related to Figure 2.
Figure S94. $^1$H NMR spectrum of 3ab, related to Figure 2.

Figure S95. $^{13}$C NMR spectrum of 3ab, related to Figure 2.
Figure S96. HPLC spectrum of 3ab, related to Figure 2.
Figure S97. $^1$H NMR spectrum of $3\text{ac}$, related to Figure 2.

Figure S98. $^{13}$C NMR spectrum of $3\text{ac}$, related to Figure 2.
Figure S99. HPLC spectrum of 3ac, related to Figure 2.
Figure S100. $^1$H NMR spectrum of 3ad, related to Figure 2.

Figure S101. $^{13}$C NMR spectrum of 3ad, related to Figure 2.
Figure S102. HPLC spectrum of 3ad, related to Figure 2.
Figure S103. $^1$H NMR spectrum of 3ae, related to Figure 2.

Figure S104. $^{13}$C NMR spectrum of 3ae, related to Figure 2.
**Figure S105.** HPLC spectrum of 3ae, related to **Figure 2.**
Figure S106. $^1$H NMR spectrum of 3af, related to Figure 2.

Figure S107. $^{13}$C NMR spectrum of 3af, related to Figure 2.
Figure S108. $^{19}$F NMR spectrum of 3af, related to Figure 2.
Figure S109. HPLC spectrum of 3af, related to Figure 2.
Figure S110. $^1$H NMR spectrum of 3ag, related to Figure 2.

Figure S111. $^{13}$C NMR spectrum of 3ag, related to Figure 2.
Figure S112. HPLC spectrum of 3ag, related to Figure 2.
Figure S113. $^1$H NMR spectrum of 3ah, related to Figure 2.

Figure S114. $^{13}$C NMR spectrum of 3ah, related to Figure 2.
Figure S115. HPLC spectrum of 3ah, related to Figure 2.
Figure S116. $^1$H NMR spectrum of 3ai, related to Figure 2.

Figure S117. $^{13}$C NMR spectrum of 3ai, related to Figure 2.
Figure S118. HPLC spectrum of 3ai, related to Figure 2.
Figure S119. $^1$H NMR spectrum of 3aj, related to Scheme 2.

Figure S120. $^{13}$C NMR spectrum of 3aj, related to Scheme 2.
Figure S121. HPLC spectrum of 3aj, related to Scheme 2.
Figure S122. $^1$H NMR spectrum of 3ak, related to Scheme 2.

Figure S123. $^{13}$C NMR spectrum of 3ak, related to Scheme 2.
Figure S124. HPLC spectrum of 3ak, related to Scheme 2.
Figure S125. $^1$H NMR spectrum of 3aI, related to Scheme 2.

Figure S126. $^{13}$C NMR spectrum of 3aI, related to Scheme 2.
Figure S127. HPLC spectrum of 3al, related to Scheme 2.
Figure S128. $^1$H NMR spectrum of 3am, related to Scheme 2.

Figure S129. $^{13}$C NMR spectrum of 3am, related to Scheme 2.
Figure S130. HPLC spectrum of 3am, related to Scheme 2.
Figure S131. $^1$H NMR spectrum of 3an, related to Scheme 2.

Figure S132. $^{13}$C NMR spectrum of 3an, related to Scheme 2.
Figure S133. HPLC spectrum of 3an, related to Scheme 2.
Figure S134. $^1$H NMR spectrum of 3ao, related to Scheme 2.

Figure S135. $^{13}$C NMR spectrum of 3ao, related to Scheme 2.
Figure S136. HPLC spectrum of 3ao, related to Scheme 2.
Figure S137. $^1$H NMR spectrum of 7, related to Scheme 3.

Figure S138. $^{13}$C NMR spectrum of 7, related to Scheme 3.
Figure S139. HPLC spectrum of 7, related to Scheme 3.
Figure S140. $^1$H NMR spectrum of 8, related to Scheme 3.

Figure S141. $^{13}$C NMR spectrum of 8, related to Scheme 3.
Figure S142. HPLC spectrum of 8, related to Scheme 3.
Figure S143. $^1$H NMR spectrum of 9, related to Scheme 3.

Figure S144. $^{13}$C NMR spectrum of 9, related to Scheme 3.
Figure S145. HPLC spectrum of 9, related to Scheme 3.
Figure S146. $^1$H NMR spectrum of 10, related to Scheme 3.

Figure S147. $^{13}$C NMR spectrum of 10, related to Scheme 3.
Figure S148. HPLC spectrum of 10, related to Scheme 3.
Figure S149. $^1$H NMR spectrum of 11, related to Scheme 3.

Figure S150. $^{13}$C NMR spectrum of 11, related to Scheme 3.
Figure S151. HPLC spectrum of 11, related to Scheme 3.
Figure S152. $^1$H NMR spectrum of 12, related to Scheme 3.

Figure S153. $^{13}$C NMR spectrum of 12, related to Scheme 3.
Figure S154. HPLC spectrum of 12, related to Scheme 3.
Figure S155. $^1$H NMR spectrum of 13, related to Scheme 3.

Figure S156. $^{13}$C NMR spectrum of 13, related to Scheme 3.
Figure S157. HPLC spectrum of 13, related to Scheme 3.
Figure S158. $^1$H NMR spectrum of 14, related to Scheme 3.

Figure S159. $^{13}$C NMR spectrum of 14, related to Scheme 3.
Figure S160. HPLC spectrum of 14, related to Scheme 3.
Figure S161. $^1$H NMR spectrum of 15, related to Scheme 3.

Figure S162. $^{13}$C NMR spectrum of 15, related to Scheme 3.
Figure S163. HPLC spectrum of 15, related to Scheme 3.
Figure S164. $^1$H NMR spectrum of 16, related to Scheme 3.

Figure S165. $^{13}$C NMR spectrum of 16, related to Scheme 3.
Figure S166. HPLC spectrum of 16, related to Scheme 3.
Data S1. ESI-MS experiment. To a sample bottle was added (S)-5a (0.01 mmol), Bi(OAc)$_3$ (0.01 mmol), and CH$_3$CN (0.5 mL). After 30 min stirring at rt, the supernate was diluted with CH$_3$CN and subjected to analysis by ESI-MS, related to Figure 3 and Figure 4.

Data S2. Single X-ray structure of 10, related to Scheme 3.
Table S1: Crystal data and structure refinement, related to Scheme 3.

| Identification code | Empirical formula | C_{23}H_{26}N_{2}O_{3} |
|---------------------|------------------|------------------------|
| Formula weight      |                  |                         |
| Temperature / K     |                  |                         |
| Crystal system      | Orthorhombic     |                         |
| Space group         | P2_12_1_2_1      |                         |
| a / Å, b / Å, c / Å |                  | 9.50943(4), 13.71174(5), 15.80478(8) |
| α/°, β/°, γ/°       | 90, 90, 90       |                         |
| Volume / Å^3        |                  | 2060.799(15)           |
| Z                   | 4                |                         |
| ρ_{calc} / mg mm^{-3} | 1.220        |
| μ / mm^{-1}         | 0.649            |                         |
| F(000)              | 808              |                         |
| Crystal size / mm^3 |                  | 0.34 × 0.3 × 0.22       |
| Theta range for data collection | 4.269 to 79.328° |
| Index ranges        |                  | -12 ≤ h ≤ 12, -17 ≤ k ≤ 17, -15 ≤ l ≤ 18 |
| Reflections collected |              | 24804                  |
| Independent reflections |            | 4340[R(int) = 0.0242] |
| Data/restraints/parameters |          | 4340/10/273            |
| Goodness-of-fit on F^2 |               | 1.079                  |
| Final R indexes [I>2σ (I)] |          | R_1 = 0.0268, wR_2 = 0.0734 |
| Final R indexes [all data] |          | R_1 = 0.0270, wR_2 = 0.0736 |
| Largest diff. peak/hole / e Å^3 |          | 0.128/-0.123          |

Table S2. Detailed reaction optimization, related to Table 1.
The reactions (entries 1-22) were carried out with 1a (0.1 mmol), 2a (0.12 mmol) in 0.5 mL solvent, while other entries were carried out with 1a (0.2 mmol), 2a (0.24 mmol) in 1.0 mL solvent. b Yield of isolated product. c Determined by HPLC analysis. d The reaction was performed at 0 °C.
Table S3. Detailed nonlinear effect experiment, related to Figure 3.

![Chemical structure](image)

| Entry | er-5a | er-1 | er-2 |
|-------|-------|------|------|
| A     | 50:50 | 49.0:51.0 | 51.9:48.1 |
| B     | 60:40 | 66.7:33.3 | 68.9:31.1 |
| C     | 70:30 | 82.2:17.8 | 82.2:17.8 |
| D     | 80:20 | 89.0:11.0 | 91.9:8.1 |
| E     | 90:10 | 96.0:4.0  | 96.8:3.2 |
| F     | 99.5:0.5 | 98.7:1.3 | 98.8:1.2 |

*The reactions were carried out with 1a (0.2 mmol), 2a (0.24 mmol) in 1.0 mL Et₂O at room temperature, and the er determined by HPLC analysis.*
Computational Details

All density functional theory (DFT) calculations were performed with Gaussian 09 (Frisch et al., 2009). The system size, particularly for the catalyst, and conformational degrees of freedom make full QM geometry optimization unreasonable. So geometry optimization of all the minima and transition states involved was carried out at the hybrid ONIOM(QM:MM) (Morokuma et al., 1996; Morokuma and Vreven, 2000; Morokuma et al., 2015) methods which have provided reasonable agreement with experimental results for the study of similar systems (Simón and Goodman, 2008; Simón and Goodman, 2010; Simón and Goodman, 2011; Simón and Goodman, 2012; Simón and Paton, 2015; Simón and Paton, 2016; Simón and Paton, 2017; Simón and Paton, 2018). Atoms that participate in bond forming/breaking events or in establishing H-bond interactions were included in the high level layer and were treated by a QM method and the rest of the atoms of the catalysts were included in the low level layer and were studied by a MM method. Atoms in different ONIOM layers are illustrated in 3D structures with the high level (HL) layer as “ball & stick” type and the low level (LL) layer as “wireframe” type. Additionally, atoms in the low level layer are hid in schemes. Figures were prepared with Pymol software. During optimization and TSs searches, the M06-2X (Zhao and Truhlar, et al., 2008) hybrid meta-GGA functional with the 6-31G(d) basis set for C, H, O, N and P atoms and LANL2DZ (Hay and Wadt, 1985) effective core potential (ECP) and split-valence basis set for Bi atoms was used for the QM layer. The low level layer was treated with a UFF (Rappe et al., 1992) force field. Single point energies used the M06-2X (Zhao and Truhlar, et al., 2008) hybrid meta-GGA functional with 6-311+G(d,p) basis set for C, H, O, N and P and the SDD (Andrae et al., 1990) ECP for Bi atoms in conjunction with the SMD implicit solvation model to account for the solvation effects of diethylether.

Figure S167. Optimized eclipsed conformation of TS-1P-(R), related to Figure 4.
Figure S168. Optimized eclipsed conformation of TS-1P-(S), related to Figure 4.

Figure S169. Optimized eclipsed conformation of TS-2P-(R), related to Figure 4.

Figure S170. Optimized eclipsed conformation of TS-2P-(S), related to Figure 4.
Transparent Methods

General information

Commercial reagents were used as received, unless otherwise indicated. \(^1\)H and \(^{13}\)C NMR were recorded on a Bruker - DPX 400 spectrometer. \(^{19}\)F NMR were recorded on a Varian NMR 400 spectrometer. Tetramethylsilane (TMS) served as the internal standard for \(^1\)H NMR, and CDCl\(_3\) served as the internal standard for \(^{13}\)C NMR. The following abbreviations were used to designate the multiplicities: \(s = \text{singlet}\); \(d = \text{doublet}\); \(t = \text{triplet}\); \(q = \text{quartet}\); \(m = \text{multiplet}\); \(br = \text{broad}\). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). HPLC analysis was performed using Chiralcel columns purchased. Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. ESI-MS studies on catalytic complex were conducted on Thermo LTQ XL. Isatin-derived ketimines \(1\) (Bittner et al., 1985; Wang et al., 2012; Shi et al., 2013; Mao et al., 2014; Zhou and Yua, 2015; Nakamura and Takahashi, 2015; Babu et al., 2015) and allylboronic acid pinacol ester \(2\) \(d, 2e\) (Maulide et al., 2013) were prepared according to the reported literature procedure.

General procedure for Asymmetric Allylation of Isatin-Derived Ketimines with Allylboronates.

\[
\begin{array}{c}
\text{1} \quad \text{Bi(OAc)}_3 (1 \text{ mol\%}) \\
+ \text{B(pin)} (2 \text{ mol\%}) \\
\rightarrow \text{3}
\end{array}
\]

To a stirred solution of isatin-derived ketimines \(1\) (0.2 mmol), Bi(OAc)_3 (1 mol%) and chiral phosphoric acid catalyst 5a (2 mol%) in Et\(_2\)O (1.0 mL) was added allyl pinacol boronic ester \(2\) (0.24 mmol). The reaction was stirred at room temperature until completed. Then, the crude mixture was direct purified by flash chromatography (petroleum ether/EtOAc = 5/1) to afford the product 3.

Characterization data of ketimines \(1h, 1i\), and products 3.

\(\text{tert-butyl (1-benzyl-6-methoxy-2-oxoindolin-3-ylidene)carbamate (1h)}\)

Yellow solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.59 (d, \(J = 8.5\) Hz, 1H), 7.38 - 7.27 (m, 5H), 6.52 (dd, \(J = 8.6, 2.0\) Hz, 1H), 6.24 (dd, \(J = 7.2, 2.1\) Hz, 1H), 4.89 (s, 1H), 4.86 (s, 1H), 3.82 (s, 1H), 3.78 (s, 2H), 1.63 (s, 6H), 1.45 (s, 6H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\))
CDCl₃ δ 180.56, 168.13, 165.83, 159.68, 153.19, 149.43, 134.76, 129.03, 128.96, 128.12, 128.00, 127.37, 107.92, 107.55, 98.28, 98.06, 56.03, 55.78, 43.97, 28.23, 28.06; HRMS (ESI): m/z calcd for C₂₁H₂₃N₂O₄ [M+H]^+: 367.1658; found: 367.1655.

tert-butyl (1-benzyl-6-fluoro-2-oxindolin-3-ylidene)carbamate (1i)

Yellow solid; ¹H NMR (400 MHz, CDCl₃) δ 7.70 - 7.60 (m, 1H), 7.40 - 7.26 (m, 5H), 6.74 (t, J = 8.9 Hz, 1H), 6.44 (d, J = 8.0 Hz, 1H), 4.87 (s, 2H), 1.64 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 167.20 (d, J = 256.7 Hz), 160.28, 157.47, 151.61, 149.44 (d, J = 11.7 Hz), 134.16, 129.10, 128.26, 127.41, 126.51 (d, J = 11.1 Hz), 115.39, 110.42 (d, J = 23.4 Hz), 99.36 (d, J = 27.9 Hz), 83.71, 44.16, 28.05; HRMS (ESI): m/z calcd for C₂₀H₂₀FN₂O₃ [M+H]^+: 355.1458; found: 355.1451.

(R)-tert-butyl (3-allyl-1-benzyl-2-oxindolin-3-yl)carbamate (3a)

White solid, 72.6mg, 96% yield, 99.2:0.8 er; [α]D²⁷ = +12.0 (c = 0.3, CHCl₃); MP 63 - 64 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, J = 7.2 Hz, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.26 - 7.23 (m, 2H), 7.17 (t, J = 7.7 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.71 (ddt, J = 17.4, 10.1, 7.4 Hz, 1H), 5.36 - 5.04 (m, 4H), 4.79 (br, 1H), 2.63 (dd, J = 13.4, 7.4 Hz, 1H), 2.50 (dd, J = 13.4, 7.4 Hz, 1H), 1.26 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 176.75, 153.69, 142.31, 135.90, 130.07, 128.68, 128.61, 127.51, 127.40, 122.72, 122.52, 121.43, 109.16, 80.40, 60.83, 44.06, 42.31, 28.06; HRMS (ESI): m/z calcd for C₂₉H₂₇N₂O₃ [M+H]^+: 379.2016; found: 379.2017; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 9.8 min (minor) and tᵣ = 11.9 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-5-methyl-2-oxindolin-3-yl)carbamate (3b)

White solid, 76.9mg, 98% yield, 99.2:0.8 er; [α]D²⁷ = +32.6 (c = 1.0, CHCl₃); MP 95 - 96 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.37 - 7.27 (m, 4H), 7.25 (t, J = 7.1 Hz, 1H), 7.07 (s, 1H), 6.96 (d, J = 7.8 Hz, 2H), 6.57 (d, J = 7.9 Hz, 2H), 5.82 - 5.64 (m, 1H), 5.30 - 5.15 (m, 4H), 4.78 (s, 1H), 2.61 (dd, J = 13.4, 7.4 Hz, 1H), 2.48 (dd, J = 13.5,
7.4 Hz, 1H), 2.30 (s, 3H), 1.27 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 176.68, 153.76, 139.89, 136.00, 132.02, 130.24, 128.88, 128.65, 127.45, 127.37, 123.53, 121.29, 108.92, 80.33, 60.90, 44.06, 42.38, 28.10, 21.15; HRMS (ESI): \(m/z\) calcd for C\(_{24}\)H\(_{29}\)N\(_2\)O\(_3\) [M+H]\(^{+}\): 393.2173; found: 393.2170; HPLC: Daicel Chiralpak IC, \(n\)-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda\) = 210 nm, \(t_R\) = 11.6 min (minor) and \(t_R\) = 15.2 min (major).

\((R)\)-\textit{tert}-butyl (3-allyl-1-benzyl-5-methoxy-2-oxoindolin-3-yl)carbamate (3c)

White solid, 77.5mg, 95% yield, 99.3:0.7 \(ee\); \([\alpha]_D^{27}\) = +34.2 (c = 1.0, CHCl\(_3\)); MP 89 - 90 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.26 - 7.13 (m, 5H), 6.78 (d, \(J = 2.5\) Hz, 1H), 6.58 (dd, \(J = 8.6, 2.5\) Hz, 1H), 6.48 (d, \(J = 8.5\) Hz, 1H), 5.23 - 5.06 (m, 3H), 4.99 (s, 1H), 4.68 (s, 1H), 3.65 (s, 3H), 2.52 (dd, \(J = 13.5, 7.3\) Hz, 1H), 2.39 (dd, \(J = 13.4, 7.5\) Hz, 1H), 1.19 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 176.44, 155.95, 153.74, 135.96, 135.75, 131.95, 130.05, 128.66, 127.47, 127.39, 121.38, 112.69, 110.37, 109.52, 80.40, 61.20, 55.76, 44.14, 42.34, 28.11; HRMS (ESI): \(m/z\) calcd for C\(_{24}\)H\(_{29}\)N\(_2\)O\(_3\) [M+H]\(^{+}\): 409.2122; found: 409.2124; HPLC: Daicel Chiralpak IC, \(n\)-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda\) = 210 nm, \(t_R\) = 13.3 min (minor) and \(t_R\) = 15.3 min (major).

\((R)\)-\textit{tert}-butyl (3-allyl-1-benzyl-5-fluoro-2-oxoindolin-3-yl)carbamate (3d)

White solid, 76.9mg, 97% yield, 96.4:3.6 \(ee\); \([\alpha]_D^{27}\) = +6.7 (c = 0.3, CHCl\(_3\)); MP 68 - 69 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.35 - 7.24 (m, 5H), 7.01 (dd, \(J = 7.8, 2.6\) Hz, 1H), 6.86 (td, \(J = 8.9, 2.6\) Hz, 1H), 6.59 (dd, \(J = 8.6, 4.1\) Hz, 1H), 5.69 (ddt, \(J = 17.3, 10.1, 7.4\) Hz, 1H), 5.35 - 5.10 (m, 3H), 5.05 (s, 1H), 4.84 (s, 1H), 2.63 (dd, \(J = 13.5, 7.4\) Hz, 1H), 2.49 (dd, \(J = 13.4, 7.5\) Hz, 1H), 1.32 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 176.44, 159.24 (d, \(J = 241.5\) Hz), 153.70, 138.21, 135.58, 132.25, 129.60, 128.74, 127.63, 127.36, 121.72, 111.78 (d, \(J = 23.3\) Hz), 110.92 (d, \(J = 24.8\) Hz), 109.74, 80.63, 61.15, 44.21, 42.11, 28.10; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -125.73; HRMS (ESI): \(m/z\) calcd for C\(_{23}\)H\(_{26}\)FN\(_2\)O\(_3\) [M+H]\(^{+}\): 397.1922; found: 397.1919; HPLC: Daicel Chiralpak IC, \(n\)-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda\) = 210 nm, \(t_R\) = 7.3 min (minor) and \(t_R\) = 8.3 min (major).
White solid, 81.6mg, 99% yield, 96.6:3.4 er; \([\alpha]D^{27} = +36.8\ (c = 1.0, \text{CHCl}_3); \) MP 105 - 106 °C; \(^1H\) NMR (400 MHz, CDCl3) \(\delta\) 7.36 - 7.29 (m, 4H), 7.29 - 7.27 (m, 1H), 7.23 (d, J = 2.1 Hz, 1H), 7.13 (dd, J = 8.3, 2.1 Hz, 1H), 6.60 (d, J = 8.3 Hz, 1H), 5.69 (ddt, J = 17.3, 10.1, 7.4 Hz, 1H), 5.30 - 5.15 (m, 3H), 5.07 (s, 1H), 4.83 (s, 1H), 2.61 (dd, J = 13.4, 7.3 Hz, 1H), 2.48 (dd, J = 13.4, 7.5 Hz, 1H), 1.31 (s, 9H); \(^{13}C\) NMR (101 MHz, CDCl3) \(\delta\) 176.35, 153.77, 140.89, 135.43, 132.27, 129.54, 128.85, 128.00, 127.68, 127.35, 123.18, 121.83, 110.20, 80.70, 60.94, 44.18, 42.08, 28.13; HRMS (ESI): m/z calcd for C\(_{23}\)H\(_{25}\)ClN\(_2\)O\(_3\) [M+Na\(^+\)]\(^+\): 435.1451, 437.1422; found: 435.1450, 437.1401; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda = 210\) nm, \(t_R = 6.8\) min (minor) and \(t_R = 7.6\) min (major).

\((R)-\text{tert-butyl (3-allyl-1-benzyl-5-bromo-2-oxoindolin-3-yl)carbamate (3f)}\)

Yellow solid, 61.8mg, 73% yield, 93.8:6.2 er; \([\alpha]D^{28} = +67.4\ (c = 1.0, \text{CHCl}_3); \) MP 151 - 152 °C; \(^1H\) NMR (400 MHz, CDCl3) \(\delta\) 8.14 (dd, J = 8.1, 2.0 Hz, 1H), 8.12 (s, 1H), 7.39 - 7.26 (m, 5H), 6.76 (d, J = 7.6 Hz, 1H), 5.66 (ddt, J = 17.3, 10.1, 7.4 Hz, 1H), 5.34 (s, 1H), 5.26 (d, J = 5.9 Hz, 1H), 5.22 (s, 1H), 5.03 (br, 1H), 4.99 (br, 1H), 2.65 (dd, J = 13.5, 7.3 Hz, 1H), 2.53 (dd, J = 13.5, 7.6 Hz, 1H), 1.35 (s, 9H); \(^{13}C\) NMR (101 MHz, CDCl3) \(\delta\) 177.00, 153.68, 148.06, 143.44, 134.69, 131.45, 128.93, 128.82, 127.99, 127.34, 125.90, 122.46, 118.42, 108.89, 99.99, 81.13, 60.63, 44.46,
41.76, 28.13; HRMS (ESI): m/z calcd for C_{23}H_{24}N_{3}O_{5} [M-H]: 422.1716; found: 422.1717; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 9:1, Flow rate = 1.0 mL/min, λ = 210 nm, t_R = 16.1 min (major) and t_R = 19.1 min (minor).

(R)-tert-butyl (3-allyl-1-benzyl-6-methoxy-2-oxoindolin-3-yl)carbamate (3h)

White solid, 76.7mg, 94% yield, 99.0:1.0 er; [α]_{D}^{27} = +29.6 (c = 1.0, CHCl_3); MP 105 - 106 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.40 - 7.21 (m, 5H), 7.15 (dd, J = 8.2 Hz, 1H), 6.51 (dd, J = 8.2, 2.3 Hz, 1H), 6.29 (d, J = 2.3 Hz, 1H), 5.70 (ddt, J = 17.3, 10.1, 7.4 Hz, 1H), 5.31 - 5.14 (m, 4H), 4.73 (s, 1H), 3.71 (s, 3H), 2.62 (dd, J = 17.3, 10.1, 7.4 Hz, 1H), 5.31 - 5.14 (m, 4H), 4.73 (s, 1H), 3.71 (s, 3H), 2.62 (dd, J = 13.4, 7.4 Hz, 1H), 2.47 (dd, J = 13.4, 7.4 Hz, 1H), 1.28 (s, 9H); ^13C NMR (101 MHz, CDCl_3) δ 177.19, 160.33, 153.76, 143.63, 135.85, 130.26, 128.69, 127.52, 127.41, 123.46, 121.21, 106.08, 97.37, 80.26, 60.53, 55.33, 44.08, 42.43, 28.13; HRMS (ESI): m/z calcd for C_{24}H_{29}N_{2}O_{4} [M+H]^+: 409.2122; found: 409.2126; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, t_R = 12.2 min (minor) and t_R = 14.2 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-6-fluoro-2-oxoindolin-3-yl)carbamate (3i)

White solid, 77.6mg, 98% yield, 98.7:1.3 er; [α]_{D}^{27} = +10.8 (c = 1.0, CHCl_3); MP 97 - 98 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.39 - 7.24 (m, 5H), 7.19 (ddd, J = 7.9, 5.2, 2.2 Hz, 1H), 6.70 (t, J = 8.8 Hz, 1H), 6.43 (d, J = 8.9 Hz, 1H), 5.78 - 5.54 (m, 1H), 5.31 - 5.16 (m, 3H), 5.10 (s, 1H), 4.76 (s, 1H), 2.62 (dd, J = 13.6, 7.4 Hz, 1H), 2.48 (dd, J = 13.5, 7.5 Hz, 1H), 1.29 (s, 9H); ^13C NMR (101 MHz, CDCl_3) δ 177.19, 160.33, 153.76, 143.63, 135.85, 130.26, 128.69, 127.52, 127.41, 123.46, 121.21, 106.08, 97.37, 80.26, 60.53, 55.33, 44.08, 42.43, 28.13; HRMS (ESI): m/z calcd for C_{22}H_{28}FN_{2}O_{4} [M+H]^+: 397.1922; found: 397.1918; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, t_R = 7.1 min (minor) and t_R = 8.4 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-6-chloro-2-oxoindolin-3-yl)carbamate (3j)
White solid, 79.1mg, 96% yield, 97.5:2.5 er; [α]D27 = +19.8 (c = 1.0, CHCl3); MP 127 - 128 °C; 1H NMR (400 MHz, CDCl3) δ 7.38 - 7.26 (m, 5H), 7.16 (d, J = 7.9 Hz, 1H), 7.00 (dd, J = 7.9, 1.9 Hz, 1H), 6.69 (s, 1H), 5.66 (ddt, J = 17.4, 10.0, 7.4 Hz, 1H), 5.28 - 5.16 (m, 3H), 5.08 (s, 1H), 4.76 (s, 1H), 2.61 (dd, J = 13.4, 7.3 Hz, 1H), 2.47 (dd, J = 13.4, 7.5 Hz, 1H), 1.29 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 176.71, 153.70, 143.58, 135.32, 134.31, 129.63, 128.82, 127.74, 127.35, 123.63, 122.45, 121.72, 109.82, 80.65, 60.61, 44.19, 42.09, 28.12; HRMS (ESI): m/z calcd for C23H25ClN2O3 [M+Na]+: 435.1451, 437.1422; found: 435.1450, 437.1370; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 6.6 min (minor) and tR = 7.7 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-6-bromo-2-oxoindolin-3-yl)carbamate (3k)

White solid, 84.8mg, 93% yield, 98.6:1.4 er; [α]D27 = +26.4 (c = 1.0, CHCl3); MP 139 - 140 °C; 1H NMR (400 MHz, CDCl3) δ 7.39 - 7.27 (m, 5H), 7.16 (dd, J = 7.9, 1.6 Hz, 1H), 7.11 (d, J = 7.9 Hz, 1H), 6.83 (s, 1H), 5.66 (ddt, J = 17.3, 10.0, 7.4 Hz, 1H), 5.27 - 5.15 (m, 3H), 5.06 (s, 1H), 4.76 (s, 1H), 2.61 (dd, J = 13.5, 7.3 Hz, 1H), 2.47 (dd, J = 13.4, 7.5 Hz, 1H), 1.30 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 176.61, 153.69, 143.71, 135.32, 129.06, 128.83, 127.74, 127.35, 125.40, 124.00, 122.18, 121.77, 112.52, 80.67, 60.66, 44.17, 42.02, 28.13; HRMS (ESI): m/z calcd for C23H26BrN2O3 [M+H]+: 457.1121, 459.1106; found: 457.1121, 459.1104; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 6.6 min (minor) and tR = 7.7 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-2-oxo-6-(trifluoromethyl)indolin-3-yl)carbamate (3l)

White solid, 88.3mg, 99% yield, 98.5:1.5 er; [α]D28 = +17.4 (c = 1.0, CHCl3); MP 170 - 171 °C; 1H NMR (400 MHz, CDCl3) δ 7.47 - 7.27 (m, 7H), 6.90 (s, 1H), 5.67 (ddt, J = 17.3, 10.0, 7.4 Hz, 1H), 5.26 - 5.20 (m, 3H), 5.11 (br, 1H), 4.86 (br, 1H), 2.63 (dd, J = 13.5, 7.3 Hz, 1H), 2.49 (dd, J = 13.5, 7.5 Hz, 1H), 1.33 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 176.57, 153.74, 142.99, 135.18, 130.98 (q, J = 32.4 Hz), 129.35, 128.85,
127.82, 127.41, 125.20, 122.86, 122.49, 121.90, 119.65 (q, J = 4.3 Hz), 105.77, 80.80, 60.81, 44.26, 41.94, 28.06; 19F NMR (376 MHz, CDCl3) δ -62.44; HRMS (ESI): m/z calcd for C24H25F3N2NaO3 [M+Na]+: 469.1715; found: 469.1714; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 5.3 min (minor) and tR = 5.7 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-7-methyl-2-oxoindolin-3-yl)carbamate (3m)

![Image of compound 3m]

White solid, 77.6mg, 99% yield, 97.8:2.2 er; [α]D27 = -0.8 (c = 1.0, CHCl3); MP 116 - 117 °C; 1H NMR (400 MHz, CDCl3) δ 7.36 - 7.19 (m, 5H), 7.12 (t, J = 4.4 Hz, 1H), 6.95 (d, J = 4.5 Hz, 2H), 5.78 (ddt, J = 17.5, 10.4, 7.5 Hz, 1H), 5.29 - 5.20 (m, 5H), 2.62 (dd, J = 13.5, 7.4 Hz, 1H), 2.50 (dd, J = 13.5, 7.5 Hz, 1H), 2.25 (s, 3H), 1.30 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 177.77, 153.71, 140.40, 137.93, 132.67, 131.42, 130.27, 128.74, 127.04, 125.98, 122.59, 121.35, 120.64, 119.71, 80.33, 60.20, 45.36, 42.82, 28.13, 18.85; HRMS (ESI): m/z calcd for C24H29N2O3 [M+H]+: 393.2173; found: 393.2171; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 10.6 min (minor) and tR = 15.5 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-7-chloro-2-oxoindolin-3-yl)carbamate (3n)

![Image of compound 3n]

White solid, 79.1mg, 96% yield, 97.1:2.9 er; [α]D27 = -7.0 (c = 1.0, CHCl3); MP 116 - 117 °C; 1H NMR (400 MHz, CDCl3) δ 7.38 - 7.18 (m, 5H), 7.16 (d, J = 7.6 Hz, 2H), 6.97 (t, J = 7.7 Hz, 1H), 5.78 - 5.63 (m, 1H), 5.36 (s, 2H), 5.27 - 5.14 (m, 1H), 2.59 (dd, J = 13.5, 7.3 Hz, 1H), 2.48 (dd, J = 13.4, 7.5 Hz, 1H), 1.30 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 177.34, 153.63, 138.46, 137.73, 131.24, 129.56, 128.42, 127.01, 126.74, 123.42, 121.83, 121.19, 115.51, 80.74, 60.43, 45.11, 42.52, 28.09; HRMS (ESI): m/z calcd for C23H20ClN2O3 [M+Na]+: 435.1451, 437.1422; found: 435.1451, 437.1365; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 6.8 min (minor) and tR = 9.3 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-7-bromo-2-oxoindolin-3-yl)carbamate (3o)
White solid, 89.4mg, 98% yield, 96.2:3.8 er; $[\alpha]_D^{27} = -8.8$ (c = 1.0, CHCl$_3$); MP 117 - 118 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.38 - 7.27 (m, 5H), 7.26 - 7.22 (m, 1H), 7.20 (d, $J = 7.3$ Hz, 1H), 6.91 (t, $J = 7.7$ Hz, 1H), 5.77 - 5.61 (m, 1H), 5.40 (q, $J = 16.5$ Hz, 2H), 5.27 - 5.10 (m, 3H), 2.59 (dd, $J = 13.5$, 7.3 Hz, 1H), 2.48 (dd, $J = 13.5$, 7.5 Hz, 1H), 1.31 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 177.53, 153.66, 139.95, 137.67, 134.60, 134.05, 129.56, 128.41, 126.94, 126.64, 123.81, 121.80, 121.75, 102.56, 80.74, 60.40, 44.77, 42.55, 28.11; HRMS (ESI): $m/z$ calcd for C$_{23}$H$_{26}$BrN$_2$O$_3$ [M+H]$^+$: 457.1121, 459.1106; found: 457.1123, 459.1105; HPLC: Daicel Chiralpak IC, $n$-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda$ = 210 nm, $t_R$ = 6.9 min (minor) and $t_R$ = 10.2 min (major).

(R)-tert-butyl (3-allyl-1-benzyl-2-oxo-7-(trifluoromethyl)indolin-3-yl)carbamate (3p)

White solid, 87.4mg, 98% yield, 91.7:8.3 er; $[\alpha]_D^{27} = +27.2$ (c = 1.0, CHCl$_3$); MP 129 - 130 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.56 (d, $J = 8.1$ Hz, 1H), 7.46 (d, $J = 7.3$ Hz, 1H), 7.35 - 7.18 (m, 5H), 7.15 (t, $J = 7.8$ Hz, 1H), 5.69 (ddt, $J = 17.4$, 10.2, 7.4 Hz, 1H), 5.34 (s, 1H), 5.30 - 4.95 (m, 4H), 2.60 (dd, $J = 13.5$, 7.3 Hz, 1H), 2.49 (dd, $J = 13.5$, 7.6 Hz, 1H), 1.29 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 178.13, 153.63, 136.64, 136.47, 129.31, 128.20, 126.81 (q, $J = 6.0$ Hz), 126.23, 126.05, 124.78, 122.01, 112.75 (q, $J = 32.7$ Hz), 80.9, 59.26, 46.04 (q, $J = 4.0$ Hz), 42.55, 28.01; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -54.44; HRMS (ESI): $m/z$ calcd for C$_{24}$H$_{24}$F$_3$N$_2$O$_3$ [M-H]$^-$: 445.1739; found: 445.1740; HPLC: Daicel Chiralpak IC, $n$-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda$ = 210 nm, $t_R$ = 4.9 min (minor) and $t_R$ = 6.9 min (major).

(R)-tert-butyl (3-allyl-2-oxoindolin-3-yl)carbamate (3q)

White solid, 40.3mg, 70% yield, 98.8:1.2 er; $[\alpha]_D^{27} = +12.8$ (c = 0.5, CHCl$_3$); MP 124 - 125 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.14 (s, 1H), 7.24 - 7.21 (m, 2H), 7.03 (t, $J = 7.5$ Hz, 1H), 6.86 (d, $J = 7.8$ Hz, 1H), 5.76 (dq, $J = 17.0$, 9.0, 8.4 Hz, 1H), 5.29 -
5.15 (m, 3H), 2.58 (dd, J = 13.6, 7.6 Hz, 1H), 2.48 (dd, J = 13.6, 7.3 Hz, 1H), 1.26 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 179.21, 153.98, 140.55, 130.92, 129.95, 128.69, 122.90, 122.41, 121.40, 110.33, 80.71, 61.36, 41.90, 28.01; HRMS (ESI): m/z calcd for C\(_{16}\)H\(_{21}\)N\(_2\)O\(_3\) [M+H]\(^+\): 289.1547; found: 289.1547; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda\) = 210 nm, t\(_R\) = 5.6 min (minor) and t\(_R\) = 10.7 min (major).

\((R)\)-tert-butyl (3-allyl-2-oxo-1-phenylindolin-3-yl)carbamate (3r)

![Structure](image)

White solid, 69.9mg, 96% yield, 92.4:7.6 \(\text{er}\); \([\alpha]_D^{27}\) = +22.6 (c = 1.0, CHCl\(_3\)); MP 79 - 80 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.56 - 7.42 (m, 4H), 7.39 (t, J = 7.3 Hz, 1H), 7.32 (d, J = 7.3 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 7.9 Hz, 1H), 5.73 (ddt, J = 17.4, 10.2, 7.4 Hz, 1H), 5.33 - 5.09 (m, 3H), 2.68 (dd, J = 13.3, 7.3 Hz, 1H), 2.58 (dd, J = 13.3, 7.5 Hz, 1H), 1.27 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 176.05, 153.81, 143.17, 134.62, 130.28, 129.88, 129.53, 128.56, 127.93, 126.52, 122.99, 122.93, 121.44, 109.37, 80.52, 61.09, 42.40, 28.14; HRMS (ESI): m/z calcd for C\(_{25}\)H\(_{25}\)N\(_2\)O\(_3\) [M+H]\(^+\): 365.1860; found: 365.1859; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda\) = 210 nm, t\(_R\) = 6.7 min (minor) and t\(_R\) = 24.9 min (major).

\((R)\)-tert-butyl (3-allyl-1-methyl-2-oxoindolin-3-yl)carbamate (3s)

![Structure](image)

White solid, 51.3mg, 85% yield, 98.9:1.1 \(\text{er}\); \([\alpha]_D^{27}\) = +47.2 (c = 0.5, CHCl\(_3\)); MP 129 - 130 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.30 (t, J = 7.7 Hz, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.06 (t, J = 7.5 Hz, 1H), 6.84 (d, J = 7.7 Hz, 1H), 5.72 (ddt, J = 17.4, 10.2, 7.4 Hz, 1H), 5.23 (d, J = 9.1 Hz, 1H), 5.19 (s, 1H), 5.15 (s, 1H), 3.23 (s, 3H), 2.56 (dd, J = 13.5, 7.7 Hz, 1H), 2.42 (dd, J = 13.5, 7.2 Hz, 1H), 1.22 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 176.62, 153.68, 143.14, 130.03, 128.69, 122.62, 122.47, 121.24, 108.06, 80.29, 60.83, 42.04, 27.98, 26.36; HRMS (ESI): m/z calcd for C\(_{16}\)H\(_{21}\)N\(_2\)O\(_3\) [M+H]\(^+\): 303.1703; found: 303.1698; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda\) = 210 nm, t\(_R\) = 14.0 min (minor) and t\(_R\) = 18.9 min (major).

\((R)\)-tert-butyl (1,3-diallyl-2-oxoindolin-3-yl)carbamate (3t)
White solid, 64.9 mg, 99% yield, 98.4:1.6 er; [α]D²⁷ = +40.2 (c = 1.0, CHCl₃); MP 130 - 131 ºC; ¹H NMR (400 MHz, CDCl₃) δ 7.30 - 7.22 (m, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.82 (d, J = 7.5 Hz, 1H), 5.84 (ddt, J = 17.2, 10.3, 5.2 Hz, 1H), 5.70 (ddt, J = 17.4, 10.1, 7.4 Hz, 1H), 5.36 - 5.26 (m, 1H), 5.26 - 5.15 (m, 3H), 5.15 (br, 1H), 4.55 (br, 1H), 4.18 (br, 1H), 2.59 (dd, J = 13.4, 7.5 Hz, 1H), 2.46 (dd, J = 13.4, 7.4 Hz, 1H), 1.24 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 176.36, 153.66, 142.36, 131.51, 130.51, 130.02, 128.58, 122.67, 122.44, 121.33, 117.53, 109.02, 80.31, 60.82, 42.57, 42.22, 28.05; HRMS (ESI): m/z calcld for C₁₉H₂₅N₂O₃ [M+H]+: 329.1860; found: 329.1864; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 10.8 min (minor) and tR = 12.7 min (major).

(R)-tert-butyl (3-allyl-1-(methoxymethyl)-2-oxoindolin-3-yl)carbamate (3u)

White solid, 65.1 mg, 98% yield, 99.3:0.7 er; [α]D²⁷ = +23.4 (c = 1.0, CHCl₃); MP 105 - 106 ºC; ¹H NMR (400 MHz, CDCl₃) δ 7.34 - 7.22 (m, 2H), 7.09 (t, J = 8.0 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 5.70 (ddt, J = 17.4, 10.1, 7.4 Hz, 1H), 5.28 - 5.16 (m, 4H), 5.09 (br, 1H), 3.38 (s, 3H), 2.59 (dd, J = 13.4, 7.3 Hz, 1H), 2.47 (dd, J = 13.4, 7.6 Hz, 1H), 1.25 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 177.20, 153.63, 141.49, 129.89, 128.84, 123.00, 122.68, 121.40, 109.54, 80.43, 71.69, 61.16, 56.49, 42.30, 28.03; HRMS (ESI): m/z calcld for C₁₈H₂₄N₂O₄ [M+Na]+: 355.1634; found: 355.1633; HPLC: Daicel Chiralpak AD-H, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 7.2 min (major) and tR = 22.7 min (minor).

(R)-tert-butyl (3-allyl-1-(2,2-diethoxyethyl)-2-oxoindolin-3-yl)carbamate (3v)

White solid, 80.0 mg, 99% yield, 99.5:0.5 er; [α]D²⁷ = +52.0 (c = 0.5, CHCl₃); MP 47 - 48 ºC; ¹H NMR (400 MHz, CDCl₃) δ 7.29 - 7.18 (m, 2H), 7.04 - 7.00 (m, 2H), 5.70 (ddt, J = 17.3, 10.1, 7.4 Hz, 1H), 5.25 - 5.13 (m, 2H), 5.11 (br, 1H), 4.70 (t, J = 5.4 Hz, 1H), 4.07 (d, J = 14.3 Hz, 1H), 3.73 (ddq, J = 9.3, 7.0, 4.7 Hz, 2H), 3.61 - 3.45 (m, 3H), 2.55 (dd, J = 13.4, 7.6 Hz, 1H), 2.43 (dd, J = 13.4, 7.2 Hz, 1H), 1.32 - 1.06 (m, 15H); ¹³C NMR (101 MHz, CDCl₃) δ 176.87, 153.64, 142.88, 130.13, 128.38, 122.37, 122.25, 121.05, 109.57, 100.59, 80.25, 63.62, 62.91, 60.62, 43.65, 42.18, 27.98, 15.27;
HRMS (ESI): m/z calcd for C_{22}H_{32}N_{2}NaO_{5} [M+Na]^+: 427.2209; found: 427.2207; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, t_R = 7.1 min (minor) and t_R = 8.3 min (major).

(R)-tert-butyl (1-acetyl-3-allyl-2-oxoindolin-3-yl)carbamate (3w)

White solid, 61.4 mg, 93% yield, 96.7:3.3 er; [α]_D^{27} = +8.4 (c = 1.0, CHCl₃); MP 129 - 130 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.23 (d, J = 8.2 Hz, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.29 - 7.16 (m, 2H), 5.58 (ddt, J = 17.3, 10.5, 7.5 Hz, 1H), 5.30 (s, 1H), 5.21 (d, J = 7.3 Hz, 1H), 5.18 (s, 1H), 2.67 (s, 3H), 2.56 (dd, J = 13.3, 7.0 Hz, 1H), 2.49 (dd, J = 13.4, 7.7 Hz, 1H), 1.20 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 177.36, 170.73, 153.65, 139.49, 129.12, 125.20, 122.14, 121.89, 116.54, 81.10, 61.42, 42.71, 27.91, 26.64; HRMS (ESI): m/z calcd for C_{18}H_{22}N_{2}NaO₄ [M+Na]^+: 353.1477; found: 353.1477; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, t_R = 4.6 min (minor) and t_R = 5.4 min (major).

(R)-tert-butyl (3-allyl-1-(2-methylbenzyl)-2-oxoindolin-3-yl)carbamate (3x)

White solid, 77.6 mg, 99% yield, 98.5:1.5 er; [α]_D^{27} = -1.8 (c = 1.0, CHCl₃); MP 84 - 85 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, J = 7.4 Hz, 1H), 7.24 - 7.14 (m, 4H), 7.15 - 7.07 (m, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.62 (d, J = 7.7 Hz, 1H), 5.80 (ddt, J = 17.5, 10.2, 7.4 Hz, 1H), 5.35 - 5.21 (m, 3H), 5.16 (br, 1H), 4.75 (br, 1H), 2.67 (dd, J = 13.5, 7.5 Hz, 1H), 2.54 (dd, J = 13.5, 7.4 Hz, 1H), 2.41 (s, 3H), 1.30 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 176.90, 153.71, 142.61, 135.44, 133.36, 130.41, 130.17, 128.70, 127.30, 126.42, 126.19, 122.70, 122.57, 121.55, 109.37, 80.37, 60.88, 42.35, 42.17, 28.14, 19.31; HRMS (ESI): m/z calcd for C_{24}H_{29}N_{2}O_{3} [M+H]^+: 393.2178; found: 393.2178; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, t_R = 7.4 min (minor) and t_R = 11.6 min (major).

(R)-tert-butyl (3-allyl-1-(2-fluorobenzyl)-2-oxoindolin-3-yl)carbamate (3y)
White solid, 77.6 mg, 98% yield, 99.3:0.7 er; [α]_D^{27} = +18.0 (c = 1.0, CHCl₃); MP 86 - 87 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.40 (t, J = 7.7 Hz, 1H), 7.29 - 7.16 (m, 3H), 7.11 - 6.99 (m, 3H), 6.77 (d, J = 7.8 Hz, 1H), 5.71 (ddt, J = 17.4, 10.1, 7.4 Hz, 1H), 5.31 - 5.05 (m, 4H), 4.90 (br, 1H), 2.61 (dd, J = 13.5, 7.5 Hz, 1H), 2.48 (dd, J = 13.4, 7.4 Hz, 1H), 1.27 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 176.90, 160.56 (d, J = 246.1 Hz), 153.73, 142.01, 129.99, 129.82, 129.27 (d, J = 6.9 Hz), 128.75, 124.47 (d, J = 3.7 Hz), 122.85 (d, J = 14.0 Hz), 122.69 (d, J = 3.4 Hz), 121.45 , 115.27 (d, J = 21.3 Hz), 108.85, 80.45, 60.87, 42.24 , 37.29 (d, J = 5.3 Hz), 28.05; ¹⁹F NMR (376 MHz, CDCl₃) δ -124.04; HRMS (ESI): m/z calcd for C₂₃H₂₆FN₂O₃ [M+H]⁺: 397.1927; found: 397.1922; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 2:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 6.1 min (minor) and tᵣ = 7.1 min (major).

(R)-tert-butyl (3-allyl-1-(3-methylbenzyl)-2-oxoindolin-3-yl)carbamate (3z)

White solid, 77.6 mg, 99% yield, 98.9:1.1 er; [α]_D^{27} = +7.2 (c = 1.0, CHCl₃); MP 85 - 86 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.25 (d, J = 6.1 Hz, 1H), 7.22 - 7.13 (m, 4H), 7.06 (d, J = 7.5 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.82 - 5.61 (m, 1H), 5.30 - 5.15 (m, 3H), 5.07 (br, 1H), 4.77 (br, 1H), 2.63 (dd, J = 13.4, 7.4 Hz, 1H), 2.50 (dd, J = 13.4, 7.4 Hz, 1H), 2.31 (s, 3H), 1.26 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 176.76, 153.74, 142.43, 138.38, 135.81, 130.51, 130.13, 128.62, 128.51, 128.28, 128.14, 124.45, 122.66, 122.49, 121.36, 109.21, 80.34, 60.90, 44.05, 42.28, 28.09, 21.42. HRMS (ESI): m/z calcd for C₂₄H₂₈FN₂O₃ [M+H]⁺: 393.2178; found: 393.2174; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 10.2 min (minor) and tᵣ = 14.1 min (major).

(R)-tert-butyl (3-allyl-1-(3-fluorobenzyl)-2-oxoindolin-3-yl)carbamate (3aa)
White solid, 78.4 mg, 99% yield, 98:1:19 \textit{er}; [\alpha]_D^27 = +15.4 (c = 1.0, CHCl$_3$); MP 62 - 63 °C; \textsuperscript{1}H NMR (400 MHz, CDCl$_3$) \( \delta \) 7.33 - 7.23 (m, 2H), 7.20 - 7.14 (m, 2H), 7.10 (d, \( J = 9.7 \) Hz, 1H), 7.04 (t, \( J = 7.5 \) Hz, 1H), 6.94 (td, \( J = 8.5, 2.5 \) Hz, 1H), 6.66 (d, \( J = 7.8 \) Hz, 1H), 5.69 (ddt, \( J = 17.3, 10.0, 7.4 \) Hz, 1H), 5.33 - 5.14 (m, 3H), 5.02 (s, 2H), 2.63 (dd, \( J = 13.4, 7.3 \) Hz, 1H), 2.50 (dd, \( J = 13.4, 7.5 \) Hz, 1H), 1.28 (s, 9H); \textsuperscript{13}C NMR (101 MHz, CDCl$_3$) \( \delta \) 176.77, 163.10 (d, \( J = 246.3 \) Hz), 153.71, 142.08, 138.47 (d, \( J = 6.6 \) Hz), 130.45, 130.20 (d, \( J = 8.0 \) Hz), 129.96, 128.68, 122.93, 122.74 (d, \( J = 3.5 \) Hz), 121.51, 114.60, 114.39 (d, \( J = 21.3 \) Hz), 114.53, 114.30 (d, \( J = 22.6 \) Hz), 108.99, 80.46, 60.90, 43.56, 42.23, 28.08; \textsuperscript{19}F NMR (376 MHz, CDCl$_3$) \( \delta \) -112.57; HRMS (ESI): \( m/z \) calcd for C$_{23}$H$_{26}$FN$_2$O$_3$ [M+H]$^+$: 397.1927; found: 397.1926; HPLC: Daicel Chiralpak IC, \textit{n}-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \( \lambda = 210 \) nm, \( t_R = 8.1 \) min (minor) and \( t_R = 10.0 \) min (major).

\textit{(R)-tert-butyl (3-allyl-1-(4-methylbenzyl)-2-oxoindolin-3-yl)carbamate (3ab)}

White solid, 77.6 mg, 99% yield, 98:6:1.4 \textit{er}; [\alpha]_D^27 = +7.8 (c = 1.0, CHCl$_3$); MP 121 - 122 °C; \textsuperscript{1}H NMR (400 MHz, CDCl$_3$) \( \delta \) 7.25 (d, \( J = 7.8 \) Hz, 3H), 7.16 (t, \( J = 7.8 \) Hz, 1H), 7.11 (d, \( J = 7.8 \) Hz, 2H), 7.01 (t, \( J = 7.5 \) Hz, 1H), 6.71 (d, \( J = 7.8 \) Hz,1H), 5.72 (ddt, \( J = 17.2, 9.8, 7.3 \) Hz, 1H), 5.33 - 5.00 (m, 4H), 4.71 (br, 1H), 2.62 (dd, \( J = 13.4, 7.5 \) Hz, 1H), 2.48 (dd, \( J = 13.4, 7.3 \) Hz, 1H), 2.31 (s, 3H), 1.26 (s, 9H); \textsuperscript{13}C NMR (101 MHz, CDCl$_3$) \( \delta \) 176.71, 153.74, 142.41, 137.14, 132.89, 130.58, 130.13, 129.34, 128.58, 127.43, 122.68, 120.20 (d, \( J = 8.0 \) Hz, 1H), 129.96, 128.68, 122.93, 122.74 (d, \( J = 3.5 \) Hz), 121.51, 114.60, 114.39 (d, \( J = 21.3 \) Hz), 114.53, 114.30 (d, \( J = 22.6 \) Hz), 108.99, 80.46, 60.90, 43.56, 42.23, 28.08; HRMS (ESI): \( m/z \) calcd for C$_{24}$H$_{29}$N$_2$O$_3$ [M+H]$^+$: 393.2178; found: 393.2172; HPLC: Daicel Chiralpak IC, \textit{n}-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \( \lambda = 210 \) nm, \( t_R = 11.2 \) min (minor) and \( t_R = 14.6 \) min (major).

\textit{(R)-tert-butyl (3-allyl-1-(4-(tert-butyl)benzyl)-2-oxoindolin-3-yl)carbamate (3ac)}
White solid, 75.5mg, 87% yield; \([\alpha]_D^{27} = +10.0\) (c = 1.0, CHCl₃); MP 100 - 101 °C; \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.34 - 7.29 (m, 3H), 7.30 - 7.22 (m, 2H), 7.18 (t, \(J = 7.7\) Hz, 1H), 7.02 (t, \(J = 7.5\) Hz, 1H), 6.74 (d, \(J = 7.8\) Hz, 1H), 5.73 (ddt, \(J = 17.3, 10.0, 7.4\) Hz, 1H), 5.28 - 4.99 (m, 4H), 4.71 (br, 1H), 2.63 (dd, \(J = 13.5, 7.5\) Hz, 1H), 2.49 (dd, \(J = 13.5, 7.4\) Hz, 1H), 1.29 (s, 18H); \(^13\)C NMR (101 MHz, CDCl₃) \(\delta\) 176.73, 153.74, 142.41, 132.89, 130.12, 128.59, 127.17, 125.61, 122.69, 122.46, 121.41, 109.22, 80.39, 60.84, 43.72, 42.31, 34.50, 31.34, 28.04; HRMS (ESI): \(m/z\) calcld for C\(_{27}\)H\(_{35}\)N\(_2\)O\(_3\) [M+H]\(^+\): 435.2648; found: 435.2649; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda = 210\) nm, \(t_R = 10.5\) min (minor) and \(t_R = 12.5\) min (major).

(R)-tert-butyl (3-allyl-1-(4-chlorobenzyl)-2-oxoindolin-3-yl)carbamate (3ad)

White solid, 81.6mg, 99% yield; \([\alpha]_D^{27} = +21.6\) (c = 1.0, CHCl₃); MP 131 - 132 °C; \(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 7.33 - 7.24 (m, 1H), 7.17 (t, \(J = 7.7\) Hz, 1H), 7.03 (t, \(J = 7.5\) Hz, 1H), 6.65 (d, \(J = 7.8\) Hz, 1H), 5.68 (ddt, \(J = 17.3, 10.2, 7.4\) Hz, 1H), 5.32 - 5.14 (m, 3H), 4.97 (br, 2H), 2.62 (dd, \(J = 13.4, 7.4\) Hz, 1H), 2.48 (dd, \(J = 13.4, 7.5\) Hz, 1H), 1.29 (s, 9H); \(^13\)C NMR (101 MHz, CDCl₃) \(\delta\) 176.74, 153.68, 142.02, 134.38, 133.33, 129.96, 128.84, 128.65, 122.74 (d, \(J = 6.6\) Hz, 1H), 121.47, 109.01, 80.45, 60.83, 43.40, 42.24, 28.09; HRMS (ESI): \(m/z\) calcld for C\(_{23}\)H\(_{25}\)ClN\(_2\)O\(_3\) [M+Na]\(^+\): 435.1451, 437.1422; found: 435.1451, 437.1406; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, \(\lambda = 210\) nm, \(t_R = 9.0\) min (minor) and \(t_R = 11.0\) min (major).

(R)-tert-butyl (3-allyl-1-(4-bromobenzyl)-2-oxoindolin-3-yl)carbamate (3ae)
White solid, 90.3mg, 99% yield, 98.7:1.3 er; [α]D27 = +15.3 (c = 0.3, CHCl3); MP 138 - 139 °C; 1H NMR (400 MHz, CDCl3) δ 7.45 - 7.42 (m, 2H), 7.31 - 7.23 (m, 3H), 7.18 (t, J = 7.8 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 5.74 - 5.63 (m, 1H), 5.34 - 5.16 (m, 3H), 4.94 (br, 2H), 2.62 (dd, J = 13.5, 7.4 Hz, 1H), 2.48 (dd, J = 13.5, 7.4 Hz, 1H), 1.29 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 176.72, 153.69, 142.03, 134.92, 131.78, 130.46, 129.96, 129.19, 128.65, 122.78, 122.70, 121.43, 108.99, 80.43, 60.84, 43.45, 42.24, 28.10; HRMS (ESI): m/z calcd for C23H26BrN2O3 [M+H]+: 457.1212, 459.1106; found: 457.1124, 459.1102; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 9.2 min (minor) and tR = 11.4 min (major).

(R)-tert-butyl (3-allyl-2-oxo-1-(4-(trifluoromethyl)benzyl)indolin-3-yl)carbamate (3af)

White solid, 86.5mg, 97% yield, 97.1:2.9 er; [α]D27 = +21.8 (c = 1.0, CHCl3); MP 127 - 128 °C; 1H NMR (400 MHz, CDCl3) δ 7.61 - 7.48 (m, 4H), 7.27 (d, J = 7.5 Hz, 1H), 7.18 (t, J = 7.7 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 5.70 (ddt, J = 17.3, 10.1, 7.4 Hz, 1H), 5.32 - 5.16 (m, 3H), 5.02 (br, 2H), 2.63 (dd, J = 13.4, 7.3 Hz, 1H), 2.50 (dd, J = 13.4, 7.5 Hz, 1H), 1.30 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 176.81, 153.70, 141.90, 139.95, 129.91, 128.71, 127.65, 125.67 (q, J = 3.8 Hz), 122.83, 121.53, 108.92, 80.50, 60.85, 43.58, 42.23, 28.10; 19F NMR (376 MHz, CDCl3) δ -62.47; HRMS (ESI): m/z calcd for C24H25FN2NaO3 [M+Na]+: 469.1715; found: 469.1710; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 6.7 min (minor) and tR = 7.7 min (major).

(R)-benzyl (3-allyl-1-benzyl-2-oxoindolin-3-yl)carbamate (3ag)
White solid, 65.9mg, 80% yield, 97.7:2.3 er; $\left[\alpha\right]_{D}^{27} = -2.4$ (c = 1.0, CHCl$_3$); MP 92 - 93°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.50 - 7.20 (m, 10H), 7.17 (t, $J = 7.7$ Hz, 1H), 7.03 (t, $J = 7.5$ Hz, 1H), 6.66 (s, 1H), 5.72 (ddt, $J = 17.3, 10.1, 7.4$ Hz, 1H), 5.51 (s, 1H), 5.31 - 5.16 (m, 2H), 5.00 (s, 4H), 2.67 (dd, $J = 13.4, 7.6$ Hz, 1H), 2.53 (dd, $J = 13.4, 7.3$ Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 176.33, 154.35, 142.45, 135.77, 129.90, 128.91, 128.73, 128.51, 128.23, 127.52, 127.26, 127.26, 122.89, 122.68, 121.66, 109.48, 67.26, 60.92, 44.09, 42.13; HRMS (ESI): $m/z$ calcd for C$_{26}$H$_{24}$N$_2$O$_3$ [M+Na$^+$]: 435.1685; found: 435.1678; HPLC: Daicel Chiralpak IC, $n$-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda = 210$ nm, $t_R = 20.3$ min (major) and $t_R = 30.8$ min (minor).

(R)-ethyl (3-allyl-1-benzyl-2-oxoindolin-3-yl)carbamate (3ah)

White solid, 60.2mg, 86% yield, 95.9:4.1 er; $\left[\alpha\right]_{D}^{27} = +19.6$ (c = 0.5, CHCl$_3$); MP 110 - 111°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37 - 7.30 (m, 4H), 7.28 - 7.23 (m, 2H), 7.16 (t, $J = 7.7$ Hz, 1H), 7.02 (t, $J = 7.5$ Hz, 1H), 6.68 (d, $J = 7.8$ Hz, 1H), 5.74 (ddt, $J = 17.4, 10.1, 7.4$ Hz, 1H), 5.41 (s, 1H), 5.30 - 5.18 (m, 2H), 5.06 (d, $J = 15.8$ Hz, 1H), 4.86 (d, $J = 15.9$ Hz, 1H), 4.01 (s, 2H), 2.67 (dd, $J = 13.4, 7.5$ Hz, 1H), 2.53 (dd, $J = 13.4, 7.3$ Hz, 1H), 1.16 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 176.46, 154.55, 142.42, 135.79, 130.01, 128.85, 128.72, 127.50, 127.27, 122.79, 122.62, 121.54, 109.36, 61.29, 60.80, 44.13, 42.13, 14.33; HRMS (ESI): $m/z$ calcd for C$_{21}$H$_{23}$N$_2$O$_3$ [M+H$^+$]: 351.1709; found: 351.1709; HPLC: Daicel Chiralpak IC, $n$-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda = 210$ nm, $t_R = 14.3$ min (major) and $t_R = 18.0$ min (minor).

(R)-3-allyl-1-benzyl-3-(phenylamino)indolin-2-one (3ai)

White solid, 69.4mg, 98% yield, 94.1:5.9 er; $\left[\alpha\right]_{D}^{27} = -80.4$ (c = 1.0, CHCl$_3$); MP 83 - 84°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34 - 7.16 (m, 7H), 7.02 (t, $J = 7.6$ Hz, 1H), 6.93 (t, $J = 6.9$ Hz, 2H), 6.79 (d, $J = 7.9$ Hz, 1H), 6.67 (t, $J = 7.3$ Hz, 1H), 6.21 (d, $J = 7.1$ Hz, 2H), 5.85 - 5.66 (m, 1H), 5.22 (dd, $J = 19.4, 13.8$ Hz, 2H), 5.05 (d, $J = 15.5$ Hz, 1H), 4.80 (d, $J = 15.4$ Hz, 1H), 3.77 (s, 1H), 2.76 (dd, $J = 13.4, 6.9$ Hz, 1H), 2.63 (dd, $J = 13.3, 7.8$ Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 177.67, 145.19, 141.90,
(R)-ethyl 3-allyl-2,3-dihydrobenzo[d]isothiazole-3-carboxylate 1,1-dioxide (3aj)

Colorless Oil, 51.1mg, 91% yield, 94.0:6.0 er; [α]D²⁸ = +61.6 (c = 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, J = 4.7 Hz, 2H), 7.74 (d, J = 5.4 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 5.84 - 5.69 (m, 2H), 5.24 - 5.13 (m, 2H), 4.31 (ddq, J = 10.5, 7.1, 3.5 Hz, 2H), 2.96 (dd, J = 13.9, 7.8 Hz, 1H), 2.73 (dd, J = 13.9, 6.5 Hz, 1H), 1.33 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 169.51, 137.65, 135.45, 133.53, 130.93, 130.53, 125.01, 121.49, 120.89, 68.78, 63.60, 44.62, 14.15; HRMS (ESI): m/z calcd for C₁₃H₁₆N₂O₄ [M+H]⁺: 282.0800; found: 282.0798; HPLC: Daicel Chiralpak OD-H, n-hexane/i-PrOH = 9:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 24.2 min (minor) and tᵣ = 44.5 min (major).

 tert-butyl (4-allyl-3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl) carbamate (3ak)

White solid, 64.5mg, 98% yield, 85.3:14.7 er; [α]D²⁸ = -7.2 (c = 1.0, CHCl₃); MP 143 - 144 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, J = 8.1 Hz, 2H), 7.38 (t, J = 7.8 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 5.69 (td, J = 17.0, 15.9, 7.9 Hz, 1H), 5.33 - 5.09 (m, 3H), 2.53 (dd, J = 13.5, 7.8 Hz, 1H), 2.45 (dd, J = 13.4, 7.0 Hz, 1H), 2.10 (s, 3H), 1.36 (s, 9H); ¹³C NMR (101 MHz, CDCl₃) δ 172.37, 160.28, 153.86, 138.11, 128.76, 128.25, 124.88, 121.76, 118.72, 81.61 (d, J = 82.5 Hz), 65.88, 38.72, 28.06, 13.25; HRMS (ESI): m/z calcd for C₁₈H₂₃N₃NaO₃ [M+Na]⁺: 352.1637; found: 352.1635; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 9:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 8.1 min (minor) and tᵣ = 10.3 min (major).

(S)-3-allyl-1-benzyl-3-hydroxyindolin-2-one (3al)
White solid, 54.1mg, 97% yield, 91:8:8.2 er; $\left[\alpha\right]_D^{28} = -39.2$ (c = 1.0, CHCl$_3$); 1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37 (d, J = 7.3 Hz, 1H), 7.32 - 7.21 (m, 5H), 7.17 (t, J = 7.8 Hz, 1H), 7.03 (t, J = 7.5 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 5.68 - 5.50 (m, 1H), 5.16 - 5.03 (m, 2H), 4.99 (d, J = 15.7 Hz, 1H), 4.70 (d, J = 15.7 Hz, 1H), 3.26 (br, 1H), 2.79 (dd, J = 13.4, 6.3 Hz, 1H), 2.67 (dd, J = 13.3, 8.4 Hz, 1H); 13C NMR (101 MHz, CDCl$_3$) $\delta$ 178.17, 142.43, 135.43, 130.60, 129.80, 129.54, 128.75, 127.67, 127.31, 124.19, 123.13, 120.47, 109.48, 76.11, 43.85, 43.01; HRMS (ESI): m/z calcd for C$_{18}$H$_{17}$NNaO$_2$ [M+Na]$^+$: 302.1157; found: 302.1155; HPLC: Daicel Chiralpak OJ-H, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda$ = 210 nm, t$_R$ = 7.6 min (minor) and t$_R$ = 10.8 min (major).

(R)-tert-butyl (1-benzyl-3-(but-3-en-2-yl)-2-oxoindolin-3-yl)carbamate (3am)

White solid, 71.3mg, 91% yield, 5.8:1 dr; $\left[\alpha\right]_D^{27} = +53.2$ (c = 0.5, CHCl$_3$); MP 109 -110 °C; 1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.46 - 7.36 (m, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.18 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 7.4 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.90 (dt, J = 17.0, 9.8 Hz, 1H), 5.40 - 5.13 (m, 3H), 5.08 (d, J = 15.4 Hz, 1H), 4.76 (s, 1H), 2.63 (dt, J = 13.8, 7.1 Hz, 1H), 1.26 (s, 9H), 0.87 (d, J = 6.9 Hz, 3H); 13C NMR (101 MHz, CDCl$_3$) $\delta$ 176.20, 153.87, 143.44, 137.08, 136.02, 128.62, 127.66, 127.48, 122.55, 118.60, 108.79, 80.23, 63.52, 46.46, 44.23, 28.05, 14.52; HRMS (ESI): m/z calcd for C$_{24}$H$_{29}$N$_2$O$_3$ [M+H]$^+$: 393.2178; found: 393.2176; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda$ = 210 nm, t$_R$ = 8.7 min (major) and t$_R$ = 46.5 min (minor).

(R)-tert-butyl (1-benzyl-3-(2-methylallyl)-2-oxoindolin-3-yl)carbamate (3an)

White solid, 65.9mg, 84% yield, 79.4:20.6 er; $\left[\alpha\right]_D^{28} = -6.2$ (c = 1.0, CHCl$_3$); MP 116 - 118 °C; 1H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36 (d, J = 7.1 Hz, 2H), 7.31 (t, J = 7.2 Hz, 3H), 7.27 - 7.24 (m, 1H), 7.16 (t, J = 7.4 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 5.29 (s, 1H), 5.10 (d, J = 12.0 Hz, 1H), 4.75 (d, J = 37.3 Hz, 3H), 2.62 (s,
2H), 1.41 (s, 3H), 1.26 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 176.74, 153.71, 142.91, 138.38, 135.85, 128.66, 128.58, 127.43, 123.09, 122.39, 117.53, 109.06, 80.33, 61.71, 45.53, 44.14, 28.08, 23.96; HRMS (ESI): m/z calcd for C$_{25}$H$_{28}$N$_2$NaO$_3$ [M+Na$^+$]: 415.1998; found: 415.1995; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda$ = 210 nm, t$_R$ = 10.7 min (major) and t$_R$ = 13.3 min (minor).

(R)-tert-butyl (1-benzyl-3-(2-methylenebut-3-en-1-yl)-2-oxoindolin-3-yl) carbamate (3ao)

![Chemical structure](image)

Colorless oil, 55.0 mg, 69% yield, 84.4:15.6 er; [α]$_D^{23}$ = 14.6 (c = 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.35 (d, J = 6.7 Hz, 2H), 7.31 (t, J = 7.2 Hz, 2H), 7.25 (dd, J = 9.6, 6.9 Hz, 2H), 7.14 (t, J = 7.7 Hz, 1H), 6.96 (t, J = 7.5 Hz, 1H), 6.66 (d, J = 7.8 Hz, 1H), 6.22 (dd, J = 17.6, 10.9 Hz, 1H), 5.38 (br, 1H), 5.20 (d, J = 17.6 Hz, 1H), 5.13 (s, 1H), 5.08 (br, 1H), 4.99 (d, J = 10.9 Hz, 1H), 4.84 (s, 1H), 4.75 (br, 1H), 2.92 (d, J = 13.2 Hz, 1H), 2.63 (d, J = 13.2 Hz, 1H), 1.25 (s, 9H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 176.87, 153.71, 142.63, 138.55, 135.93, 128.63, 128.59, 127.47, 123.78, 122.05, 121.37, 114.82, 108.98, 80.33, 61.74, 44.14, 38.56, 28.06; HRMS (ESI): m/z calcd for C$_{26}$H$_{28}$N$_2$NaO$_3$ [M+Na$^+$]: 427.1998; found: 427.1997; HPLC: Daicel Chiralpak IC, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, $\lambda$ = 210 nm, t$_R$ = 9.2 min (major) and t$_R$ = 11.7 min (minor).

**Product Derivatizations.**

![Chemical structure](image)

(R)-tert-butyl (1-benzyl-3-(2-hydroxyethyl)-2-oxoindolin-3-yl)carbamate (7)

(Laschat and Kunz, 1991; Kung et al., 2011)

To a stirred solution of KMnO$_4$ (28.44 mg, 0.18 mmol) and NaIO$_4$ (1.80 g, 8.40 mmol) in water (30 mL) was added compound 3a (1.20 mmol) at room temperature, and the suspension was stirred until 3a was completely consumed. The reaction
mixture was extracted five times with ether (300 mL). The combined organic layers were dried with MgSO\textsubscript{4}, filtered and evaporated in vacuo. The residue was directly used for the next step without further purification.

The above residue acid was dissolved in THF (5 mL) and the solution was cooled to -10 °C. Et\textsubscript{3}N (183 µL, 1.32 mmol) and ethyl chloroformate (126 µL, 1.32 mmol) were added dropwise to this solution. After stirring for 60 min, the reaction mixture was filtered off. NaBH\textsubscript{4} (95.76 mg, 2.52 mmol) was dissolved in 5 mL H\textsubscript{2}O and cooled with an ice bath, then the above filtrate was added slowly to this solution. Returned to room temperature and stirred for 4 h, acidified with 1 M HCl until the pH = 2 - 3. The organic phase was separated and water phase was extracted with EtOAc (20 mL× 3). The organic phases were washed with Sat. NaHCO\textsubscript{3} and brine, then dried with MgSO\textsubscript{4}. Filtered and concentrated in vacuo, and the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/5) to afford colorless liquid 7 (279.6 mg, 61% yield, 98.8:1.2 er), [α]\textsubscript{D}\textsuperscript{27} = +11.6 (c = 0.5, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.37 - 7.30 (m, 5H), 7.26 (t, J = 3.5 Hz, 1H), 7.17 (t, J = 7.7 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.72 (d, J = 7.8 Hz, 2H), 5.15 (s, 2H), 4.83 (s, 2H), 3.92 (dddd, J = 46.8, 11.4, 7.1, 3.7 Hz, 2H), 2.97 (s, 1H), 2.05 (dddd, J = 46.8, 11.4, 7.1, 3.7 Hz, 2H), 1.30 (s, 9H); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) δ 177.90, 154.24, 141.88, 135.89, 128.79, 128.54, 127.59, 127.33, 122.79, 122.71, 109.27, 80.23, 61.69, 58.04, 44.06, 39.15, 28.11; HRMS (ESI): m/z calcd for C\textsubscript{22}H\textsubscript{27}N\textsubscript{2}O\textsubscript{4} [M+H]\textsuperscript{+}: 383.1971; found: 383.1969; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, t\textsubscript{R} = 6.5 min (major) and t\textsubscript{R} = 10.8 min (minor).

\((R)\text{-}\text{tert-butyl } \ (1\text{-}\text{benzyl}-3\text{-}(2\text{-}(\text{methylamino})\text{ethyl})\text{-}2\text{-}\text{oxoindolin-3-yl})\text{carbamate (8)}\) (Kung et al., 2011; Shao et al., 2017)

A mixture of amino alcohol 7 (199.00 mg, 0.52 mmol), NaHCO\textsubscript{3} (436.8 mg, 5.20mmol) and Dess-Martin periodinane reagent (331.00 mg, 0.78 mmol) in DCM (5 mL) was stirred at room temperature for 1 h. 2.5 mL Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} (1.0 M) was added and the resulting mixture was vigorously stirred for 15 min. Saturated NaHCO\textsubscript{3} (5 mL) was then added and extracted with DCM (10 mL × 3). The combined organic layers was dried with MgSO\textsubscript{4} and concentrated in vacuo to afford crude product. In a 50 mL round bottom flask under argon atmosphere, the above crude product, methylamine hydrochloride (351.00 mg, 5.20 mmol) and MgSO\textsubscript{4} (249.60 mg, 2.08 mmol) were placed. Methanol (10 mL) and Et\textsubscript{3}N (721 µL, 5.20 mmol) were added in order at room temperature. After overnight stirring, NaBH\textsubscript{4} (59.28 mg, 1.56 mmol) was added at 0°C. After stirring at room temperature for 0.5 h, the reaction mixture was quenched with water, and extracted with EtOAc (10 mL × 3). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4} and filtered. Concentrated in vacuo, and the residue was purified by silica gel column chromatography (ethyl acetate to DCM/MeOH = 15/1) to afford compound 8 as yellow liquid (174.6 mg, 85% yield, 99.5:0.5 er); [α]\textsubscript{D}\textsuperscript{27} = +18.4 (c = 0.5, CHCl\textsubscript{3}); \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.39 - 7.37 (m, 2H), 7.33 (t, J = 7.5 Hz, 2H), 7.30 - 7.23 (m, 3H), 7.18 (t, J = 14.8 Hz, 1H), 7.02 (t, J = 7.5 Hz, 1H), 6.73 (d, J = 7.8 Hz, 1H), 5.10 (br, 1H), 4.79 (br, 1H), 3.02 (s,
2H), 2.61 (s, 4H), 2.38 (ddt, J = 14.2, 10.0, 6.2 Hz, 1H), 1.23 (s, 9H); \[^{13}\text{C}\ NMR\ (101\ MHz, \text{CDCl}_3)\ \delta\ 176.60,\ 154.35,\ 141.87,\ 135.72,\ 130.28,\ 128.94,\ 128.89,\ 127.52,\ 123.27,\ 122.73,\ 109.26,\ 80.31,\ 60.35,\ 53.48,\ 44.55,\ 44.17,\ 33.46,\ 33.37,\ 28.07;\ HRMS\ (ESI):\ m/z\ \text{calcd\ for\ C}_{23}\text{H}_{30}\text{N}_3\text{O}_3\ \text{[M+H]}^+:\ 396.2287;\ \text{found}:\ 396.2286;\ \text{HPLC:}\ \text{Daicel\ Chiralpak\ IF,}\ m-\text{hexane/i-PrOH = 3:2, Flow\ rate\ =\ 1.0\ mL/min,}\ \lambda = 210\ nm,\ t_R = 15.4\ min\ (major)\ and\ t_R = 30.4\ min\ (minor).\)

**\((R)\text{-tert-butyl}\ 1\text{-benzyl-3-(3-hydroxypropyl)-2-oxoindolin-3-yl}\text{carbamate (9)}** (Shibasaki et al., 2003)

To a stirred solution of compound 3a (869.40 mg, 2.3 mmol) in dry THF (5.0 mL) was added 9-BBN (0.5 M in THF, 11.50 mL, 5.7 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 24 h. H\textsubscript{2}O\textsubscript{2} (30%, 12.70 mL) and NaOAc (20%, 16.10 mL) were added in order at 0 °C, and the resulting mixture was stirred for 5 h at room temperature. The aqueous layer was extracted with EtOAc (20 mL x 3), and the combined organic layers were dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}. After filtration and evaporation, the crude mixture was purified by silica gel column chromatography (ethyl acetate/petrolatum ether = 1/1) to give compound 9 as white solid (867.4 mg, 95% yield, \(98.3:1.7\text{ e.r.}\)); \([\alpha]_\text{D}^27 = +22.0\ (c = 1.0, \text{CHCl}_3);\ \text{MP} 72-73\ o\text{C};\ \text{1H NMR (400 MHz, CDCl}_3)\ \delta\ 7.37\ (d, J = 7.2 Hz, 2H),\ 7.31\ (t, J = 7.3 Hz, 2H),\ 7.28-7.23\ (m, 2H),\ 7.18\ (t, J = 7.8 Hz, 1H),\ 6.72\ (d, J = 7.8 Hz, 1H),\ 5.48\ (s, 1H),\ 5.08\ (br, 1H),\ 4.80\ (br, 1H),\ 3.56\ (t, J = 6.2 Hz, 2H),\ 2.09-1.90\ (m, 2H),\ 1.56-1.48\ (m, 2H),\ 1.26\ (s, 9H);\ \[^{13}\text{C}\ \text{NMR (101 MHz, CDCl}_3)\ \delta\ 177.76,\ 154.23,\ 142.39,\ 135.96,\ 128.72,\ 127.52,\ 122.67,\ 109.26,\ 80.30,\ 61.76,\ 61.58,\ 44.12,\ 34.64,\ 28.08,\ 25.70;\ \text{HRMS (ESI):}\ m/z\ \text{calcd\ for\ C}_{23}\text{H}_{29}\text{N}_2\text{O}_4\ \text{[M+H]}^+:\ 397.2127;\ \text{found}:\ 397.2122;\ \text{HPLC:}\ \text{Daicel\ Chiralpak\ AD - H,}\ m-\text{hexane/i-PrOH = 4:1, Flow\ rate\ =\ 1.0\ mL/min,}\ \lambda = 210\ nm,\ t_R = 8.4\ min\ (major)\ and\ t_R = 13.6\ min\ (minor).\)**

\[\text{(R)-tert-butyl 1-benzyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate (10)}\] (Lam et al., 2013)

To a stirred solution of compound 9 (79.20 mg, 0.20 mmol) and Ph\textsubscript{3}P (68.10 mg, 0.26 mmol) in DCM (2 mL) at 0 °C was added a solution of DEAD (38.00 μL, 0.24 mmol) in DCM (2 mL). The resulting mixture was warmed to room temperature slowly, and then stirred overnight. The reaction was quenched with EtOH (1 mL) and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (ethyl acetate/petroleum ether = 1/2) to afford compound 10 as white solid (54.1 mg, 72% yield, 98.7:1.3 er); \([\alpha]_\text{D}^27 = -11.1\ (c = 0.2, \text{CHCl}_3);\ \text{MP} 106-107\ o\text{C};\ \text{1H NMR (400 MHz, CDCl}_3)\ \delta\ 7.39 - 7.27\ (m, 5H),\ 7.20 - 7.15\ (m, 2H),\ 7.01\ (t, J = 7.0 Hz, 1H),\ 5.72\ (d, J = 8.5 Hz, 1H),\ 5.28\ (d, J = 15.5 Hz, 1H),\ 4.45\ (d, J = 10.0 Hz, 2H),\ 4.17\ (d, J = 8.5 Hz, 1H),\ 3.56\ (t, J = 6.2 Hz, 2H),\ 2.09-1.90\ (m, 2H),\ 1.56-1.48\ (m, 2H),\ 1.26\ (s, 9H);\ \[^{13}\text{C}\ \text{NMR (101 MHz, CDCl}_3)\ \delta\ 177.76,\ 154.23,\ 142.39,\ 135.96,\ 128.76,\ 128.45,\ 127.57,\ 127.48,\ 122.69,\ 122.63,\ 109.08,\ 80.20,\ 61.76,\ 61.58,\ 44.12,\ 34.64,\ 28.08,\ 25.70;\ \text{HRMS (ESI):}\ m/z\ \text{calcd\ for\ C}_{23}\text{H}_{29}\text{N}_2\text{O}_4\ \text{[M+H]}^+:\ 397.2127;\ \text{found}:\ 397.2122;\ \text{HPLC:}\ \text{Daicel\ Chiralpak\ AD - H,}\ m-\text{hexane/i-PrOH = 4:1, Flow\ rate\ =\ 1.0\ mL/min,}\ \lambda = 210\ nm,\ t_R = 8.4\ min\ (major)\ and\ t_R = 13.6\ min\ (minor).\)**
= 15.5 Hz, 1H), 3.92 - 3.76 (m, 2H), 2.49 - 2.38 (m, 1H), 2.36 - 2.25 (m, 1H), 2.20 - 2.08 (m, 2H), 0.99 (s, 9H); 13C NMR (101 MHz, CDCl₃) δ 177.73, 152.96, 142.22, 136.03, 132.86, 128.80, 128.38, 127.69, 127.53, 122.68, 121.86, 108.70, 80.02, 66.84, 48.10, 43.96, 39.94, 27.78, 23.04; HRMS (ESI): m/z calcd for C₂₃H₂₇N₂O₃ [M+H]⁺: 379.2022; found: 379.2018; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 19:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 23.8 min (major) and tᵣ = 27.6 min (minor).

(R)- tert-buty l allyl(3-allyl-1-benzyl-2-oxoindolin-3-yl)carbamate (11) (Nakamura et al., 2013)

To a stirred solution of compound 3a (124.70 mg, 0.33 mmol) in DMF (2.0 mL) was added NaH (60% in oil, 15.80 mg, 0.39 mmol) at 0°C. The resulting mixture was warmed to room temperature, after stirring for 30 min, allylbromide (31.50 μL, 0.36 mmol) was added. The resulting mixture continued to stir for 30 min until disappearance of 3a monitored by TLC. The crude mixture was directly purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/5) to give compound 11 as white solid (130.7 mg, 98% yield, 98.5:1.5 er); [α]D²⁷ = -56.8 (c = 1.0, CHCl₃); MP 51 - 52 oC; ¹H NMR (400 MHz, CDCl₃) δ 7.40 (d, J = 7.4 Hz, 2H), 7.31 - 7.23 (m, 3H), 7.20 - 7.12 (m, 2H), 6.99 (t, J = 7.5 Hz, 1H), 6.69 (d, J = 7.7 Hz, 1H), 6.12 - 6.02 (m, 1H), 5.41 (d, J = 17.3 Hz, 1H), 5.26 (d, J = 10.3 Hz, 1H), 5.20 - 5.05 (m, 2H), 4.94 (d, J = 16.9 Hz, 1H), 4.78 (d, J = 10.0 Hz, 1H), 4.54 (d, J = 15.6 Hz, 1H), 4.36 (d, J = 18.8 Hz, 1H), 4.18 (dd, J = 17.1, 6.7 Hz, 1H), 2.88 - 2.77 (m, 2H), 1.16 (s, 9H); ¹C NMR (101 MHz, CDCl₃) δ 176.81, 154.30, 142.82, 136.74, 136.12, 131.75, 130.30, 128.48, 128.16, 128.07, 127.48, 122.36, 122.21, 120.27, 116.28, 108.53, 80.83, 66.06, 46.64, 44.34, 40.93, 28.04; HRMS (ESI): m/z calcd for C₂₆H₃₁N₂O₃ [M+H]⁺: 419.2335; found: 419.2329; HPLC: Daicel Chiralpak IA, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tᵣ = 5.4 min (major) and tᵣ = 7.9 min (minor).

(R)- tert-buty l 1-benzyl-2-oxo-3',6'-dihydro-1'H-spiro[indoline-3,2'-pyridine]-1'-carboxylate (12) (Nakamura et al., 2013)

A mixture of compound 11 (121.20 mg, 0.30 mmol) and Grubbs 2nd (25.47 mg, 0.03 mmol) in toluene (2.0 mL) was stirred for 20 min at 60 °C. After cooling to room temperature, the crude mixture was directly purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/6) to give compound 12 as white solid (92.5 mg, 79% yield, 98.5:1.5 er); [α]D²⁷ = +70.2 (c = 1.0, CHCl₃); MP 89 - 90
°C; 1H NMR (400 MHz, CDCl3) δ 7.35 - 7.31 (m, 4H), 7.27 - 7.23 (m, 1H), 7.18 - 7.11 (m, 2H), 6.92 (t, J = 7.5 Hz, 1H), 6.68 (d, J = 7.7 Hz, 1H), 6.22 - 6.18 (m, 1H), 6.02 - 5.95 (m, 1H), 5.34 (d, J = 15.6 Hz, 1H), 4.52 (s, 1H), 4.28 (d, J = 15.7 Hz, 1H), 4.15 (d, J = 17.6 Hz, 1H), 2.81 (dp, J = 17.6, 2.8 Hz, 1H), 2.15 (dd, J = 15.8, 6.6 Hz, 1H), 1.21 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 177.21, 154.17, 141.61, 136.14, 133.46, 128.74, 128.21, 127.53, 127.28, 123.12, 122.26, 108.80, 80.86, 61.18, 43.92, 43.29, 34.99, 28.06; HRMS (ESI): m/z calcd for C24H27N2O3 [M+H]+: 391.2022; found: 391.2016; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 19:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 20.7 min (major) and tR = 30.5 min (minor).

(R)-methyl 2-(1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxindolin-3-yl)acetate (13) (Laschat and Kunz, 1991; Shao et al., 2017)

To a stirred solution of KMnO4 (28.444 mg, 0.18 mmol) and NaIO4 (1.80 g, 8.40 mmol) in water (30 mL) was added compound 3a (1.2 mmol) at room temperature, and the suspension was stirred until 3a was completely consumed. The reaction mixture was extracted five times with ether (100 mL). The combined organic layers were dried with MgSO4, filtered and evaporated in vacuo. The residue was directly used for the next step without further purification.

To a stirred solution of the above residue in CH3CN (30 mL) were added Cs2CO3 (782.4 mg, 2.4 mmol) and MeI (150 µL, 2.4 mmol) at room temperature for 8 h, and water was added. The reaction mixture was extracted with EtOAc (30 mL× 3). The combined organic layers were washed with brine, dried with Na2SO4, filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/5, v/v) to afford white solid 13 (340.6mg, 68% yield, 98.7:1.3 er); [α]D27 = +46.6 (c = 1.0, CHCl3); MP 53-54 °C; 1H NMR (400 MHz, CDCl3) δ 7.37 (d, J = 7.1 Hz, 2H), 7.32 (t, J = 7.3 Hz, 2H), 7.30 - 7.23 (m, 2H), 7.18 (t, J = 7.7 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.71 (d, J = 7.8 Hz, 1H), 6.35 (s, 1H), 5.08 (br, 1H), 4.82 (br, 1H), 3.69 (s, 3H), 2.96 (d, J = 15.0 Hz, 1H), 2.59 (d, J = 15.0 Hz, 1H), 1.29 (s, 9H); 13C NMR (101 MHz, CDCl3) δ 175.55, 170.19, 153.79, 142.29, 135.75, 129.56, 129.14, 128.76, 127.59, 127.37, 122.96, 122.80, 109.41, 80.40, 59.25, 52.20, 44.21, 40.90, 28.12; HRMS (ESI): m/z calcd for C23H27N2O3 [M+H]+: 411.1920; found: 411.1912; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 3:2, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 8.0 min (major) and tR = 23.6 min (minor).
(R)-methyl 2-(3-amino-1-benzyl-2-oxoindolin-3-yl)acetate (14) (Melchiorre et al., 2008)

To a stirred solution of compound 13 (271.50 mg, 0.66 mmol) in DCM (5 mL) was added TFA (983.00 μL, 13.20 mmol) at 0°C. After stirring for 2 h at room temperature, the mixture was cooled to 0°C and sat. NaHCO₃ (20 mL) was added. The aqueous layer was extracted with DCM (10 mL × 3) and the combined organic layers were dried over MgSO₄. Filtered and concentrated in vacuo, the residue was purified by silica gel column chromatography (ethyl acetate/petroleum ether = 1/1) to give compound 14 as white solid (191.9 mg, 94% yield, 99.0:1.0 er); [α]D₂₇ = +57.4 (c = 1.0, CHCl₃); MP 52-53°C; ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, J = 7.4 Hz, 1H), 7.38 - 7.30 (m, 4H), 7.29 - 7.26 (m, 1H), 7.20 (td, J = 7.7, 1.3 Hz, 1H), 7.04 (t, J = 7.6 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 5.05 - 4.81 (dd, J = 42.3, 15.6 Hz, 2H), 3.52 (s, 3H), 3.00 (s, 2H), 1.92 (s, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 179.18, 169.95, 142.72, 135.74, 130.81, 129.36, 128.80, 127.67, 127.41, 123.71, 122.93, 109.47, 58.47, 51.73, 44.01, 42.45; HRMS (ESI): m/z calcld for C₁₈H₁₉N₂O₃ [M+H]+: 311.1396 found: 311.1393; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 9:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 28.0 min (major) and tR = 30.2 min (minor).

(R)-1'-benzylspiro[azetidine-2,3'-indoline]-2',4-dione (15) (Shibasaki et al., 2010)

A mixture of compound 14 (91.50 mg, 0.295 mmol), 2 M aq. NaOH (0.45 mL) and MeOH (0.90 mL) was stirred for 2 h at room temperature. Acidified the reaction mixture by 1 M aq. HCl, and then the reaction mixture was evaporated at 50°C to give a crude carboxylic acid. To a round bottom flask with the crude carboxylic acid were added NaHCO₃ (123.98 mg, 1.48 mmol), the MsCl (68.50 μL, 0.89 mmol) and CH₃CN (3 mL) were added in order under argon atmosphere. The reaction mixture was stirred for 18 h at 80°C. After cooling to room temperature, the mixture was filtered and washed with 2.5% MeOH in EtOAc. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel flash column chromatography (ethyl acetate/petroleum ether = 1/1) to afford compound 15 as white solid (54.9 mg, 67% yield, 98.8:1.2 er); [α]D₀²⁷ = +82.4 (c = 0.5, CHCl₃); MP 116-117°C; ¹H NMR (400 MHz, CDCl₃) δ 7.46 (d, J = 7.3 Hz, 1H), 7.37 - 7.23 (m, 4H), 7.11 (t, J = 7.5 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 6.22 (s, 1H), 4.92 (dd, J = 33.4, 15.5 Hz, 2H), 3.41 (dd, J = 105.7, 14.5 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 175.38, 166.49, 142.70, 135.22, 130.32, 128.93, 127.94, 127.44, 126.76, 123.49, 109.76, 55.99, 51.11, 44.30; HRMS (ESI): m/z calcld for C₁₇H₁₉N₂O₂ [M+H]+: 279.1134; found: 279.1131; HPLC: Daicel Chiralpak AD - H, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 11.1 min (major) and tR = 13.1 min (minor).
(R)-methyl 2-(3-((tert-butoxycarbonyl)amino)-1-(2,2-diethoxyethyl)-2-oxoindolin-3-yl) acetate (16) (Laschat and Kunz, 1991; Shao et al., 2017)

According to the approach to compound 13, compound 16 could be afforded as colorless liquid (54.1 mg, 62% yield, 99.6:0.4 er); [α]D27 = +51.3 (c = 0.3, CHCl3); 1H NMR (400 MHz, CDCl3) δ 7.28 - 7.22 (m, 2H), 7.05 (d, J = 7.9 Hz, 1H), 7.00 (t, J = 7.5 Hz, 1H), 6.31 (s, 1H), 4.74 (t, J = 5.4 Hz, 1H), 4.01 (s, 1H), 3.77 - 3.72 (m, 2H), 3.69 (s, 3H), 3.60 - 3.50 (m, 2H), 2.70 (dd, J = 14.7, 15.1 Hz, 2H), 1.25 (s, 9H), 1.20 - 1.04 (m, 6H); 13C NMR (101 MHz, CDCl3) δ 175.66, 170.32, 153.70, 142.85, 129.33, 128.90, 122.62, 122.52, 109.92, 100.46, 80.23, 63.53, 63.23, 58.98, 52.15, 43.73, 40.71, 28.06, 15.28, 15.23; HRMS (ESI): m/z calcd for C22H32N2NaO7 [M+Na]+: 459.2107; found: 459.2099; HPLC: Daicel Chiralpak AD-H, n-hexane/i-PrOH = 4:1, Flow rate = 1.0 mL/min, λ = 210 nm, tR = 8.1 min (major) and tR = 17.4 min (minor).

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