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# Diastereo- and Enantioselective Michael Addition of 3-Substituted Oxindoles to Trifluoromethyl-Substituted Nitro Olefins Catalyzed by a *Cinchona*-Alkaloid-Derived Squaramide

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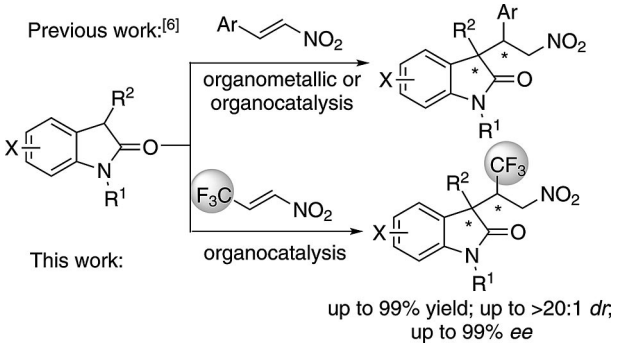
Highly efficient diastereo- and enantioselective Michael addition reactions between 3-substituted oxindoles and trifluoromethylated nitro olefins catalyzed by a quinine-derived squaramide have been investigated. The corresponding adducts, each bearing a chiral tertiary carbon center attached to a trifluoromethyl group and adjacent to a quaternary stereocenter at the C3 position of the oxindole, were obtained in good to excellent yields (up to 99 %) and with high diastereoselectivities (up to >20:1 *dr*) and excellent enantioselectivities (up to 99 % *ee*).

## Introduction

Trifluoromethylated compounds have played a unique and significant role in agricultural and medicinal chemistry due to the fact that the introduction of a trifluoromethyl moiety into an organic structure can greatly modify that system's physicochemical features and consequently its biological properties.[1] Broad research efforts have thus been focused on developing general methods for the synthesis of compounds of this kind, and especially on the enantioselective construction of stereogenic centers bearing $CF_3$ groups.[2] To date, two complementary strategies for the formation of $CF_3$-substituted stereogenic centers involve: (i) direct asymmetric trifluoromethylation with the aid of nucleophilic, electrophilic, or radical reagents, or (ii) asymmetric reactions of prochiral trifluoromethylated substrates.[3]

Recently, oxindoles containing quaternary chiral centers at their 3-positions have emerged as attractive synthetic targets, because this structural motif is widely present in numerous biologically and pharmaceutically active natural products and molecules.[4] Among various excellent approaches for the asymmetric synthesis of 3,3-disubstituted oxindole derivatives,[5] Michael additions of oxindoles to nitro olefins are of particular interest because the Michael adducts can readily be converted into alkaloids or their derivatives.[6] Barbas III[6a] and Shibasaki[6b] independently pioneered highly enantioselective conjugate additions of *N*-Boc-protected 3-alkyl(aryl)oxindoles to nitro olefins (Scheme 1) catalyzed either by chiral thioureas or by chiral homodinuclear $Mn^{III}_2$-Schiff base complexes, and addition of this type has since then been fully investigated by Maruoka,[6c] Cheng,[6d] Yuan,[6e] Zhou,[6f] Enders,[6g] Du,[6h] and their co-workers with use of chiral quaternary ammonium salts, alkyl-substituted bifunctional thioureas, chiral $Ni(OAc)_2$-diamine complexes, cinchonidine-derived phosphoramides, chiral secondary amines, or bifunctional tertiary amine-squaramides as catalysts, respectively. However, to the best of our knowledge, most of these protocols were limited to nitrostyrene derivatives.[7]




Scheme 1. Enantioselective Michael addition of oxindoles to nitro olefins.

As part of our ongoing interest in the asymmetric synthesis of chiral 3,3-disubstituted oxindoles, we have previously developed cinchona-alkaloid-catalyzed enantioselective chlorination of 3-aryl-*N*-Boc-oxindoles with *N*-chlorosuccinimide (NCS)[8a] and Michael additions between 3-aryl-*N*-Boc-oxindoles and phenyl vinyl sulfone[8b] or vinyl

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bisphosphonates.[8c] Considering that the incorporation of tertiary trifluoromethyl stereocenters into heterocycles could provide new drug candidates with unusual biological activities,[9] and that trifluoromethylated nitro olefin have been utilized as valuable and unique acceptors in many asymmetric conjugate additions,[10] we envisioned that cinchona alkaloid catalysts might facilitate Michael additions between 3-aryl-*N*-Boc-oxindoles and trifluoromethylated nitro olefins to afford the desired adducts, each bearing a chiral tertiary carbon center attached to a trifluoromethyl group and adjacent to a quaternary stereocenter at the C3 position of the oxindole, which are of potential biological activity and synthetic potential in organic synthesis (Scheme 1). To the best of our knowledge, there are no examples of organocatalytic asymmetric Michael addition of oxindoles to trifluoromethylated nitro olefins. Here we wish to report our studies on this subject.

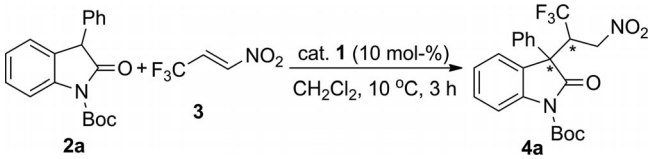
## Results and Discussion

Initial studies were carried out by using the reaction between 3-phenyl-*N*-Boc oxindole **2a** (Table 1) and (*E*)-3,3,3-trifluoro-1-nitroprop-1-ene (**3**) in $CH_2Cl_2$ at 10 °C as model reaction in the presence of a variety of cinchona-alkaloid-derived organocatalysts (Figure 1) to determine the optimal conditions; the results of these experiments are summarized in Table 1. With naturally available quinine (**1a**, Figure 1) as catalyst the reaction took place smoothly and the desired product **4a** was obtained in good yield but with low stereoselectivity (Table 1, Entry 1). The cinchona-alkaloid-derived bifunctional amine-thiourea catalysts **1b** and **1c** showed only moderate catalytic activity in this reaction, affording **4a** in good yields with moderate diastereo- and enantioselectivities (Table 1, Entries 2 and 3).

Chiral squaramides have become increasingly utilized as a new class of hydrogen-bonding donor organocatalysts in many asymmetric Michael addition reactions,[11] so squaramide catalysts **1d**–**f**, based on a chiral cyclohexane-1,2-diamine skeleton, were synthesized and evaluated. To our delight, dimethyl- and pyrrolidine-substituted squaramide catalysts **1d** and **1e** gave much better results, affording the desired product **4a** in good yields and with good stereoselectivites (>20:1 *dr*, 93–94% *ee,* Table 1, Entries 4–6). Further evaluation of cinchona-alkaloid-derived squaramide catalysts **1g**–**m** (Table 1, Entries 7–13) revealed that quinine-derived squaramide **1g** was the best catalyst for this reaction, furnishing **4a** in 89% yield and with >20:1 *dr* and 98.3% *ee* (Table 1, Entry 7). Replacing the bis(trifluoromethyl)phenyl group on the squaramide moiety of **1g** with 4-trifluoromethylphenyl and 4-fluorophenyl groups gave the desired product **4a** with relatively lower enantioselectivities, probably due to the weak acidity of the squaramide ArN–H groups in **1h** and **1i** (Table 1, Entries 7–9).

Quinidine- and cinchonine-derived squaramides **1k**–**m** also promoted this reaction, but gave **4a** with opposite absolute configuration and with much lower *ee* values than those achieved with the corresponding quinine- and cin-

Table 1. Catalyst screening for enantioselective Michael addition of oxindole **2a** to nitro olefin **3**[a].




| Entry | Catalyst **1** | Yield [%][b] | *dr*[c] | *ee* [%][d] |
|---|---|---|---|---|
| 1 | **1a** | 73 | 5.8:1 | 4 |
| 2 | **1b** | 84 | 16:1 | 71 |
| 3 | **1c** | 70 | 8.5:1 | 77 [e] |
| 4 | **1d** | 85 | >20:1 | 93 [e] |
| 5 | **1e** | 85 | >20:1 | 94 [e] |
| 6 | **1f** | 73 | >20:1 | 86 [e] |
| 7 | **1g** | 89 | >20:1 | 98.3 |
| 8 | **1h** | 96 | >20:1 | 97 |
| 9 | **1i** | 87 | >20:1 | 97.7 |
| 10 | **1j** | 85 | >20:1 | 97 |
| 11 | **1k** | 64 | >20:1 | 89 [e] |
| 12 | **1l** | 71 | >20:1 | 89 [e] |
| 13 | **1m** | 89 | >20:1 | 91 [e] |

[a] Unless noted otherwise, all reactions were carried out with oxindole **2a** (0.10 mmol), nitro olefin **3a** (0.15 mmol), and catalyst **1** (10 mol-%) in $CH_2Cl_2$ (1.0 mL) at 10 °C for 3 h. [b] Yield of isolated product. [c] The *dr* of the purified product was determined by $^1$H NMR spectroscopy. [d] The *ee* was determined by HPLC on a chiral stationary phase. [e] The opposite enantiomer was obtained.

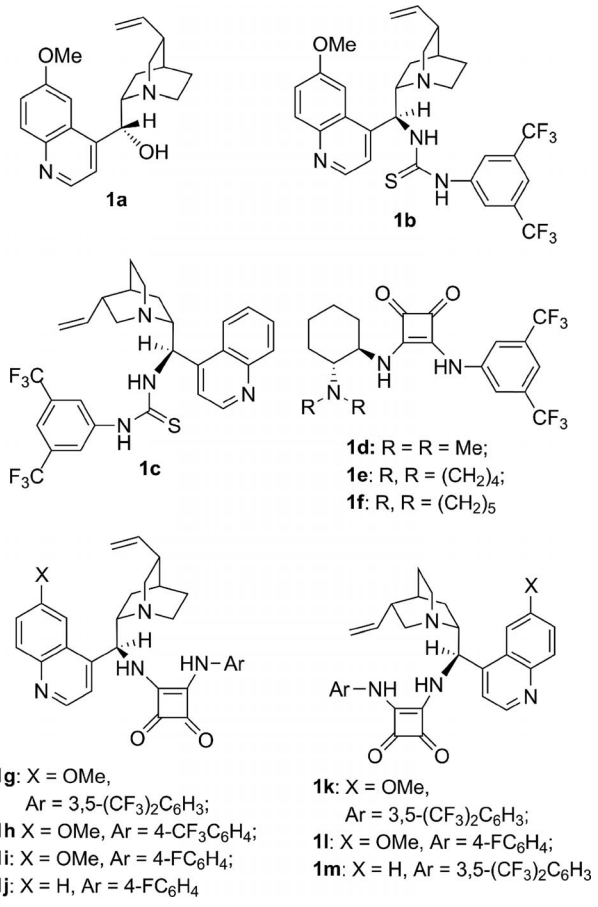



Figure 1. Catalyst screening.

chonidine-derived catalysts **1g–j** (Table 1, Entries 11–13 vs. 7–10).

Solvent effects were then extensively studied. It was found that variations in diastereoselectivity and yield were slight, but significant variations in enantioselectivity were observed. Despite similar yields and *dr* values for these screened solvents, very high *ee* values were obtained in chlorinated solvents (Table 2, Entries 1–3) and in toluene (Table 2, Entry 4), together with good *ee* values in THF (Table 2, Entry 5) and in $CH_3CN$ (Table 2, Entry 6). Dichloromethane was found to be the optimal solvent for this reaction in terms of reactivity and stereoselectivity, affording **4a** in up to 89% yield and with >20:1 *dr* and 98.3% *ee* (Table 2, Entry 1).

Table 2. Optimization of reaction conditions for the enantioselective Michael addition of oxindole **2a** to nitro olefin **3** catalyzed by **1g**[a].

| Entry | Solvent | *T* [°C] | Yield [%][b] | *dr*[c] | *ee* [%][d] |
|---|---|---|---|---|---|
| 1 | $CH_2Cl_2$ | 10 | 89 | >20:1 | 98.3 |
| 2 | $CHCl_3$ | 10 | 88 | >20:1 | 97.8 |
| 3 | DCE | 10 | 90 | >20:1 | 97.0 |
| 4 | toluene | 10 | 89 | >20:1 | 97.6 |
| 5 | THF | 10 | 87 | >20:1 | 87.8 |
| 6 | $CH_3CN$ | 10 | 87 | >20:1 | 88.0 |
| 7[e] | $CH_2Cl_2$ | 10 | 85 | >20:1 | 98.1 |
| 8[f] | $CH_2Cl_2$ | 10 | 73 | >20:1 | 97.1 |
| 9[e] | $CH_2Cl_2$ | 20 | 83 | >20:1 | 97.4 |
| 10[e] | $CH_2Cl_2$ | 0 | 85 | >20:1 | 97.9 |
| 11[e,g] | $CH_2Cl_2$ | 10 | 91 | >20:1 | 97.8 |
| 12[e,g,h] | $CH_2Cl_2$ | 10 | 91 | >20:1 | 97.9 |
| 13[e,g,i] | $CH_2Cl_2$ | 10 | 90 | >20:1 | 98.1 |

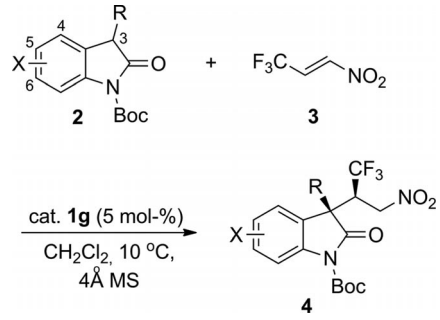
[a] Unless noted otherwise, all reactions were carried out with oxindole **2a** (0.10 mmol), nitro olefin **3** (0.15 mmol), and cat. **1g** (10 mol-%) in solvent (1.0 mL) for 3 h. [b] Yield of isolated product. [c] The *dr* of the purified product was determined by $^1$H NMR spectroscopy. [d] The *ee* was determined by HPLC on a chiral stationary phase. [e] 5 mol-% of cat. **1g**. [f] 3 mol-% of cat. **1g**. [g] 2.0 mL of $CH_2Cl_2$ were used. [h] 30 mg of 3 Å MS were added. [i] 30 mg of 4 Å MS were added.

Further examination of catalyst loading revealed that reducing the equivalent of cat. **1g** from 10 mol-% to 5 mol-% still afforded **4a** with comparable results (Table 2, Entries 7–8). Changes in the reaction temperature were unproductive; similar yields and slightly lower enantioselectivities were obtained with elevated or reduced reaction temperatures (Table 2, Entries 9–10). Changing the concentration of **2a** from 0.1 to 0.05 M was able to improve the yield slightly, but with similar enantioselectivity (Table 2, Entries 11 vs. 7). Furthermore, the reaction produced **4a** with a slight improvement in enantioselectivity and without detriment to the yield when 4 Å molecular sieves were used (Table 1, Entries 12–13).

Optimal reaction conditions have thus been identified as the use of 1.0 equiv. of **2a** and 1.5 equiv. of **3** in dichloromethane (0.05 M for **2a**) at 10 °C in the presence of 5 mol-% catalyst **1g** and 4 Å molecular sieves.

With the optimized reaction conditions to hand, the substrate scope of this reaction was then examined by carrying out a range of reactions in which both X and R in oxindoles **2** were varied (Table 3). For *N*-Boc-3-phenyloxindoles, substituents in either the 5- or the 6-positions were well tolerated and the corresponding adducts were obtained in good yields (80–94%) together with excellent stereoselectivities (>20:1 *dr*, 95–98% *ee*, Table 3, Entries 1–7). Substrates possessing electron-donating groups gave the adducts in higher yields but with slightly lower enantioselectivities than those of the corresponding substrates without substituents or with electron-withdrawing substituents (Table 3, Entries 4 and 5 vs. 1–3).

Table 3. Substrate scope of oxindoles **2** for enantioselective Michael addition to nitro olefin **3**.[a]




| Entry | **2** [X, R] | **4** | Yield [%][b] | *dr*[c] | *ee* [%][d] |
|---|---|---|---|---|---|
| 1 | **2a** [H, Ph] | **4a** | 90 | >20:1 | 98 |
| 2 | **2b** [5-Cl, Ph] | **4b** | 90 | >20:1 | 98 |
| 3 | **2c** [5-Br, Ph] | **4c** | 80 | >20:1 | 95 |
| 4 | **2d** [5-Me, Ph] | **4d** | 94 | >20:1 | 97 |
| 5 | **2e** [5-OMe, Ph] | **4e** | 93 | >20:1 | 97 |
| 6 | **2f** [6-Cl, Ph] | **4f** | 84 | >20:1 | 96 |
| 7 | **2g** [6-Br, Ph] | **4g** | 85 | >20:1 | 95 |
| 8 | **2h** [H, *p*-$FC_6H_4$] | **4h** | 80 | >20:1 | 97 |
| 9 | **2i** [H, *p*Tol] | **4i** | 88 | >20:1 | 96 |
| 10 | **2j** [5-F, *p*Tol] | **4j** | 95 | 20:1 | 92 |
| 11 | **2k** [5-Me, *p*Tol] | **4k** | 96 | >20:1 | 96 |
| 12 | **2l** [5-OMe, *p*Tol] | **4l** | 99 | >20:1 | 97 |
| 13 | **2m** [H, *m*-$FC_6H_4$] | **4m** | 93 | >20:1 | 97 |
| 14 | **2n** [H, *m*Tol] | **4n** | 96 | >20:1 | 98 |
| 15 | **2o** [H, *m*-$MeOC_6H_4$] | **4o** | 84 | >20:1 | 97 |
| 16[e] | **2p** [H, 2-naphthyl] | **4p** | 61 | >20:1 | 99 |
| 17[f] | **2q** [5-F, *o*Tol] | **4q** | trace | n.d | n.d |
| 18[e] | **2r** [H, Me] | **4r** | 93 | 12:1 | 69 |
| 19[e] | **2s** [H, Bn] | **4s** | 80 | >20:1 | 71 |

[a] Unless noted otherwise, all reactions were carried out with oxindoles **2** (0.20 mmol), nitro olefin **3** (0.30 mmol), catalyst **1g** (5 mol-%), and 4 Å MS (30 mg) in $CH_2Cl_2$ (4.0 mL) at 10 °C for 3 h. [b] Yield of isolated product. [c] The *dr* of the purified product was determined by $^1$H NMR spectroscopy. [d] The *ee* was determined by HPLC on a chiral stationary phase. [e] For 24 h. [f] For 48 h.

Further investigation of the substituent at C-3 revealed that the presence of *para*-substituted aryl groups led to smooth reactions, giving the desired adducts in good yields and with high stereoselectivities (Table 3, Entries 8–12). In the cases of oxindoles **2m–o**, substituted at C-3 with *meta*-substituted aryl groups, the corresponding products **4m–o** were obtained in high yields together with excellent stereoselectivities (Table 3, Entries 13–15). Substrate **2p**, bearing a sterically bulky 2-naphthyl group at the oxindole C-3 position, also gave the corresponding product **4p** in moderate

yield and with excellent *dr* and *ee* values on prolongation of the reaction time to 24 h (Table 3, Entry 16). With 3-(*o*-tolyl)-substituted oxindole **2q**, however, the reaction was sluggish and only a trace of desired product **4q** was afforded even after prolongation of the reaction time to 48 h, presumably due to steric hindrance (Table 3, Entry 17). Notably, 3-alkyloxindoles **2r** and **2s** are not suitable substrates for this Michael addition, affording the corresponding adducts **4r** and **4s** in good yields but with only moderate enantioselectivities (Table 3, Entries 18 and 19).

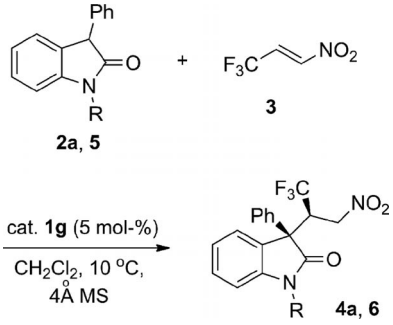
The effect of *N*-protecting group on this Michael addition was also investigated, by subjection of several 3-phenyloxindoles with different *N*-protecting groups to the optimized reaction conditions (Table 4). With *N*-unprotected oxindole **5a**, *N*-methyl-substituted oxindole **5b**, and *N*-benzyl-substituted oxindole **5c** as the corresponding substrates the reactions were more sluggish than in the case of *N*-Boc-substituted oxindole **2a**, affording the corresponding adducts **6a**–**c** in moderate yields (27–66%) but with moderate to good diastereoselectivies (6:1–16:1 *dr*) and good to excellent enantioselectivities (83–98% *ee*) on prolongation of the reaction time to up to 6 days (Table 4, Entries 2–4 vs. 1). *N*-Acetyl-protected oxindole **5d** gave the corresponding product **6d** in good yield along with high *dr* and *ee* values with a reaction time prolonged to 3 days (Table 4, Entry 5). *N*-Methoxycarbonyl- and *N*-Cbz-protected oxindoles **5e** and **5f**, however, gave high yields along with high stereoselectivities (>20:1 *dr*, 96–98% *ee*), thus indicating that the presence of a *N*-carbonate protecting group is crucial for satisfactory reactivity and good stereochemical outcome (Table 4, Entries 6 and 7).

The absolute and relative configurations of the major diastereomers of adducts **4** were unambiguously assigned by X-ray crystallographic analysis of the optically pure compound **4f**,[12] which was obtained by recrystallization from chloroform (Table 3, Entry 8). The configuration of the stereogenic center of the major diastereomer of product **4f** at the C3 position was determined to be *R* and that at the remaining stereocenter also as *R* (Figure 2). The configurations of other adducts **4** and **6** were then assigned by analogy.

On the basis of the above results and commonly accepted mechanism, a plausible transition-state model as shown in Scheme 2 is proposed. The nitro group of olefin **3** is H-bonded to the squaramide motif, whereas oxindole is deprotonated by the quinuclidine nitrogen of catalyst **1g**, resulting in a single H-bonding interaction between the OH group of the enolized oxindole and the tertiary amine. Additionally, a weak H-bonding interaction might concurrently be produced between the carbonyl group of Boc and the enolized oxindole, which enables the enolized oxindole to attack much more easily the nitroolfin from the *Re*-face, leading to formation of the two newly generated stereocenters with (3*R*,2′*R*) configuration.

To illustrate the synthetic utility of the Michael addition products **4**, we next explored their transformations into some trifluoromethylated natural product analogues, which might possess important biological activity and are hence

Table 4. Substrate scope of oxindoles **5** for the enantioselective Michael addition to nitro olefin **3**.[a]




| Entry | **2**, **5** [R] | **4**, **6** | *t* [h] | Yield [%][b] | *dr*[c] | *ee* [%][d] |
|---|---|---|---|---|---|---|
| 1 | **2a** [Boc] | **4a** | 3 | 90 | >20:1 | 98 |
| 2 | **5a** [H] | **6a** | 120 | 66 | 8:1 | 83 |
| 3 | **5b** [Me] | **6b** | 144 | 27 | 6:1 | 90 |
| 4 | **5c** [Bn] | **6c** | 24 | 37 | 16:1 | 98 |
| 5 | **5d** [Ac] | **6d** | 72 | 86 | >20:1 | 97 |
| 6 | **5e** [$CO_2Me$] | **6e** | 3 | 98 | >20:1 | 98 |
| 7 | **5f** [Cbz] | **6f** | 3 | 99 | >20:1 | 96 |

[a] Unless noted otherwise, all reactions were carried out with oxindoles **2** or **5** (0.20 mmol), isocyanoacetate **3a** (0.30 mmol), catalyst **1g** (5 mol-%), and 4 Å MS (30 mg) in $CH_2Cl_2$ (4.0 mL) at 10 °C. [b] Yield of isolated product. [c] The *dr* of the purified product was determined by $^1$H NMR spectroscopy. [d] The *ee* was determined by HPLC on a chiral stationary phase.

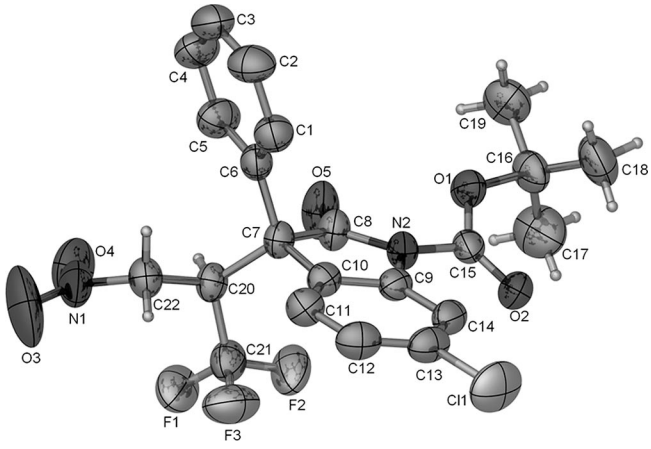
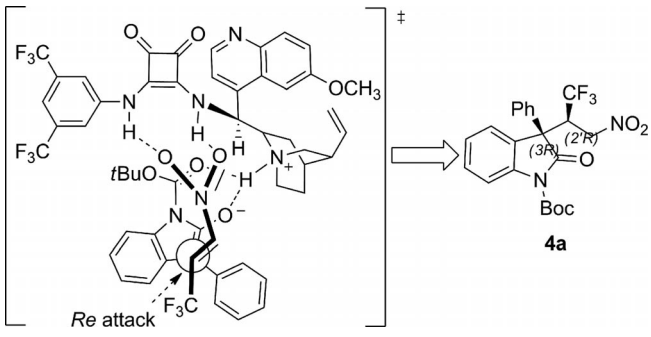


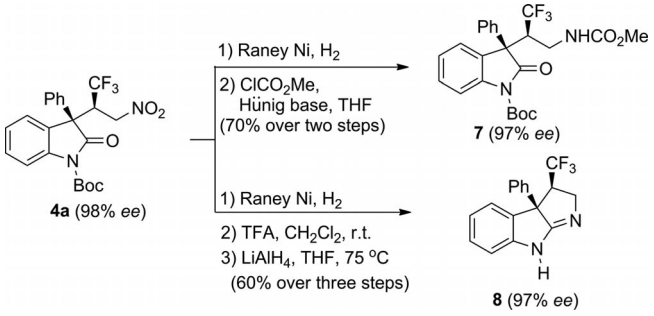

Figure 2. ORTEP drawing of **4f**.




Scheme 2. Proposed transition state model.

valuable for drug discovery. Raney nickel reduction of adduct **4a** followed by methyl carbamate formation, for example, provided compound **7**.[6a] Moreover, trifluoromethyl-substituted 2,3,3a,8-tetrahydropyrrolo[2,3-*b*]indole derivative **8**, with a core structure similar to those of many important natural products,[13] can easily be obtained by Raney nickel reduction of adduct **4a** followed by removal of the Boc protecting group with trifluoroacetic acid in $CH_2Cl_2$ and reductive cyclization in good yield and without any effect on the enantioselectivity (Scheme 3).[6c]




Scheme 3. Synthetic transformations of adduct **4a**.

## Conclusions

We have developed efficient diastereo- and enantioselective Michael additions of 3-substituted oxindoles to a trifluoromethyl-substituted nitro olefin catalyzed by a quinine-derived bifunctional squaramide catalyst. A wide variety of substituted oxindoles, with different electronic and steric properties, were tolerated in these catalytic enantioselective Michael additions, which afforded the corresponding adducts in high yields (up to 99%) along with good to excellent diastereo- and enantioselectivities (up to >20:1 *dr*, up to 99% *ee*). Furthermore, the adducts can readily be transformed into trifluoromethylated natural product analogues for medicinal research. Investigations directed towards fully understanding the reaction mechanism and developing more effective addition reactions between oxindoles and other electrophiles are continuing.

## Experimental Section

**General:** NMR spectra were recorded with a Bruker AVANCE 400 MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard; *J* values are given in Hz. IR spectra were recorded with a Bruker tensor 27 infrared spectrometer. Chiral HPLC was performed with a Shimadzu SPD-10A series instrument and chiral columns. MS (EI) and HRMS (ESI or EI) were recorded with a Waters LCT Premier XE spectrometer or a Finnigan MA$^+$ spectrometer. Optical rotations were determined with a PolAAr 3005 high-accuracy polarimeter; $[a]_D$ values are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. Flash column chromatography was performed with silica gel (300–400 mesh). Melting points were measured with a digital apparatus. Unless otherwise noted, all commercially obtained reagents were used without further purification. All reactions were carried out under air in closed systems. Oxindoles **2**[14]or **5**,[15] nitro olefin **3**,[16] and catalysts **1**[17] were prepared by literature methods. Racemic Michael addition products for chiral HPLC analysis were prepared from the corresponding oxindoles **2** or **5** (0.20 mmol) and olefin **3** (0.30 mmol) in the presence of DABCO (0.2 mmol) in $CH_2Cl_2$ (2.0 mL) at room temperature.

**General Procedure for Enantioselective Michael Addition of Oxindoles 2 or 5 to Nitro Olefin 3 with Catalysis by 1g:** A solution of nitro olefin **3** (0.3 mmol), cat. **1g** (0.01 mmol), and 4 Å molecular sieves (30 mg) in $CH_2Cl_2$ (4.0 mL) was stirred at 10 °C for 15 min, followed by addition of the oxindole **2** or **5** (0.2 mmol). The resulting mixture was stirred at 10 °C for 3–144 h until the reaction was complete (monitoring by TLC). After concentration, the residue was directly subjected to flash column chromatography on silica gel (petroleum ether/ethyl acetate 25:1 as eluent) to furnish the corresponding adduct **4** or **6**.

***tert*-Butyl (*R*)-2-Oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4a):** Yield 81.0 mg (90%). White solid, m.p. 125.7–127.5 °C. $[a]_D^{25}$ = +166.3 (*c* = 3.40, $CH_2Cl_2$); 98% *ee* (Chiralpak AS-H; hexane/propan-2-ol 98:2; 0.8 mL min$^{-1}$; 254 nm; $t_{minor}$ = 12.99 min, $t_{major}$ = 15.85 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.03 (d, *J* = 8.4 Hz, 1 H, ArH), 7.50 (td, *J* = 8.0, 1.2 Hz, 1 H, ArH), 7.36 (s, 5 H, ArH), 7.32 (td, *J* = 7.6, 0.8 Hz, 1 H, ArH), 7.14 (d, *J* = 7.6 Hz, 1 H, ArH), 4.87–4.79 (m, 2 H, $CH_2$), 4.52–4.47 (m, 1 H, CH), 1.60 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.4, 148.7, 139.9, 135.0, 130.1, 129.6, 129.3, 127.4, 125.7, 125.1 (d, *J* = 280.9 Hz), 124.5, 124.4, 116.2, 85.1, 71.2, 55.1, 48.6 (q, *J* = 25.8 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 6.8 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1794, 1768, 1737, 1566, 1373, 1343, 1296, 1249, 1148 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{21}F_3N_2NaO_5$ [M + Na]$^+$ 473.1300; found 473.1305.

***tert*-Butyl (*R*)-5-Chloro-2-oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4b):** Yield 87.0 mg (90%). White solid, m.p. 143.2–145.0 °C. $[a]_D^{25}$ = +241.6 (*c* = 3.40, $CH_2Cl_2$); 98% *ee* (Chiralcel OD-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 12.00 min, $t_{minor}$ = 25.94 min); >20:1 *dr*. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 8.01 (d, *J* = 9.2 Hz, 1 H, ArH), 7.48 (dd, *J* = 9.2, 2.4 Hz, 1 H, ArH), 7.41–7.33 (m, 5 H, ArH), 7.12 (d, *J* = 2.4 Hz, 1 H, ArH), 4.86–4.79 (m, 2 H, $CH_2$), 4.46 (dd, *J* = 12.0, 6.8 Hz, 1 H, CH), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ = 172.7, 148.5, 138.6, 134.3, 130.2, 130.1, 129.8, 129.6, 127.2, 126.2, 125.7, 125.0 (d, *J* = 280.8 Hz), 117.5, 85.5, 70.9, 55.2, 48.4 (d, *J* = 26.0 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 6.8 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1796, 1771, 1738, 1568, 1475, 1373, 1331, 1296, 1249, 1149, 761 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}ClF_3N_2NaO_5$ [M + Na]$^+$ 507.0911; found 507.0912.

***tert*-Butyl (*R*)-5-Bromo-2-oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4c):** Yield 85.5 mg (80%). White solid, m.p. 134.0–135.1 °C. $[a]_D^{25}$ = +260.7 (*c* = 4.20, $CH_2Cl_2$); 95% *ee* (Chiralcel OD-H; hexane/propan-2-ol 90:10; 0.7 mL min$^{-1}$; 230 nm; $t_{major}$ = 6.86 min, $t_{minor}$ = 12.90 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.96 (d, *J* = 8.8 Hz, 1 H, ArH), 7.63 (dd, *J* = 8.8, 2.0 Hz, 1 H, ArH), 7.40–7.38 (m, 3 H, ArH), 7.35–7.33 (m, 2 H, ArH), 7.25 (d, *J* = 1.6 Hz, 1 H, ArH), 4.86–4.79 (m, 2 H, $CH_2$), 4.46 (dd, *J* = 12.4, 6.8 Hz, 1 H, CH), 1.58 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 172.6, 148.5, 139.1, 134.4, 133.2, 129.8, 129.6, 128.5, 127.2, 126.6, 125.0 (d, *J* = 280.7 Hz), 117.9, 117.4, 85.5, 71.0, 55.1, 48.4 (d, *J* = 26.0 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1796, 1771, 1738, 1567, 1474,

1373, 1331, 1296, 1249, 1149, 823 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}BrF_3N_2NaO_5$ [M + Na]$^+$ 551.0405; found 551.0411.

***tert*-Butyl (*R*)-5-Methyl-2-oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4d):** Yield 87.1 mg (94%). White solid, m.p. 154.8–156.3 °C. $[\alpha]_D^{25}$ = +162.8 (*c* = 4.30, $CH_2Cl_2$); 97% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 13.50 min, $t_{minor}$ = 15.95 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.90 (d, *J* = 8.4 Hz, 1 H, ArH), 7.36 (s, 5 H, ArH), 7.30 (d, *J* = 8.4 Hz, 1 H, ArH), 6.93 (s, 1 H, ArH), 4.89–4.79 (m, 2 H, $CH_2$), 4.49 (d, *J* = 13.6 Hz, 1 H, CH), 2.44 (s, 3 H, $CH_3$), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.5, 148.7, 137.6, 135.2, 134.2, 130.6, 129.5, 129.2, 127.4, 126.5 (d, *J* = 280.8 Hz), 126.1, 124.4, 115.9, 84.9, 71.2, 55.2, 48.4 (q, *J* = 26.1 Hz), 27.9, 21.1 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.5 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1792, 1765, 1737, 1566, 1491, 1373, 1334, 1310, 1246, 1151, 821 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{23}F_3N_2NaO_5$ [M + Na]$^+$ 487.1457; found 487.1457.

***tert*-Butyl (*R*)-5-Methoxy-2-oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4e):** Yield 88.7 mg (93%). White solid, m.p. 136.5–137.1 °C. $[\alpha]_D^{25}$ = +295.9 (*c* = 4.00, $CH_2Cl_2$); 97% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 16.45 min, $t_{minor}$ = 35.87 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.97 (d, *J* = 9.2 Hz, 1 H, ArH), 7.37 (br. s, 5 H, ArH), 7.01 (dd, *J* = 9.2, 2.4 Hz, 1 H, ArH), 6.67 (d, *J* = 1.2 Hz, 1 H, ArH), 4.86–4.79 (m, 2 H, $CH_2$), 4.51–4.46 (m, 1 H, CH), 3.86 (s, 3 H, $OCH_3$), 1.58 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.3, 156.6, 148.8, 135.0, 133.3, 129.6, 129.2, 127.4, 125.7, 125.1 (d, *J* = 281.1 Hz), 117.0, 113.9, 112.7, 84.8, 71.1, 55.7, 55.4, 48.4 (q, *J* = 25.9 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1794, 1765, 1736, 1568, 1490, 1373, 1296, 1279, 1248, 1151, 846, 818, 735 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{23}F_3N_2NaO_6$ [M + Na]$^+$ 503.1406; found 503.1407.

***tert*-Butyl (*R*)-6-Chloro-2-oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4f):** Yield 80.3 mg (84%). White solid, m.p. 129.0–130.0 °C. $[\alpha]_D^{25}$ = +134.7 (*c* = 3.00, $CH_2Cl_2$); 96% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 11.90 min, $t_{minor}$ = 14.01 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.12 (d, *J* = 1.6 Hz, 1 H, ArH), 7.38–7.33 (m, 5 H, ArH), 7.32 (dd, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.07 (d, *J* = 8.0 Hz, 1 H, ArH), 4.81–4.78 (m, 2 H, $CH_2$), 4.48–4.42 (m, 1 H, CH), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.0, 148.5, 140.9, 136.1, 134.5, 129.7, 129.5, 127.3, 126.5, 125.1 (d, *J* = 281.0 Hz), 124.6, 122.8, 117.0, 85.7, 71.0, 54.9, 48.5 (q, *J* = 26.0 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 6.4 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1797, 1773, 1738, 1568, 1373, 1338, 1295, 1243, 1147, 841, 770 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}ClF_3N_2NaO_5$ [M + Na]$^+$ 507.0911; found 507.0901.

***tert*-Butyl (*R*)-6-Bromo-2-oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4g):** Yield 89.3 mg (85%). White solid, m.p. 123.7–125.1 °C. $[\alpha]_D^{25}$ = +154.8 (*c* = 1.00, $CH_2Cl_2$); 95% *ee* (Chiralpak AD-H; hexane/propan-2-ol 98:2; 0.8 mL min$^{-1}$; 254 nm; $t_{minor}$ = 8.01 min, $t_{major}$ = 9.01 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.28 (d, *J* = 1.6 Hz, 1 H, ArH), 7.47 (dd, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.38–7.33 (m, 5 H, ArH), 7.01 (d, *J* = 8.4 Hz, 1 H, ArH), 4.82–4.78 (m, 2 H, $CH_2$), 4.47–4.43 (m, 1 H, CH), 1.60 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 172.8, 148.5, 141.0, 134.4, 129.8, 129.5, 127.6, 127.3, 126.8, 125.0 (d, *J* = 281.2 Hz), 124.0, 123.3, 119.8, 85.7, 71.0, 55.0, 48.4 (q, *J* = 26.0 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 6.8 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1797, 1774, 1738, 1567, 1477, 1373, 1337, 1294, 1281, 1244, 1148, 841, 759 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}BrF_3N_2NaO_5$ [M + Na]$^+$ 551.0405; found 551.0400.

***tert*-Butyl (*R*)-3-(4-Fluorophenyl)-2-oxo-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4h):** Yield 75.0 mg (80%). White solid, m.p. 117.9–119.7 °C. $[\alpha]_D^{25}$ = +170.2 (*c* = 3.70, $CH_2Cl_2$); 97% *ee* (Chiralpak AS-H; hexane/propan-2-ol 98:2; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 13.39 min, $t_{major}$ = 16.03, min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.03 (d, *J* = 8.0 Hz, 1 H, ArH), 7.50 (td, *J* = 8.4, 0.8 Hz, 1 H, ArH), 7.36 (dd, *J* = 8.4, 5.2 Hz, 2 H, ArH), 7.31 (dd, *J* = 7.6, 0.8 Hz, 1 H, ArH), 7.14 (d, *J* = 7.2 Hz, 1 H, ArH), 7.05 (t, *J* = 8.4 Hz, 2 H, ArH), 4.84 (dd, *J* = 14.4, 8.8 Hz, 1 H, CH), 4.75 (quint-d, *J* = 8.8, 1.6 Hz, 1 H, CH), 4.74 (d, *J* = 14.4 Hz, 1 H, CH), 1.60 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.3, 163.0 (d, *J* = 249.4 Hz), 148.6, 139.9, 130.7 (d, *J* = 3.0 Hz), 130.3, 129.5 (d, *J* = 8.2 Hz), 125.6, 125.0 (d, *J* = 280.8 Hz), 124.6, 124.2, 116.6 (d, *J* = 21.5 Hz), 116.3, 85.3, 71.1, 54.6, 48.6 (q, *J* = 25.9 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.9 (d, *J* = 7.5 Hz, 3 F), –111.6 ppm. IR (film): $\tilde{\nu}$ = 1793, 1767, 1738, 1566, 1509, 1372, 1341, 1296, 1239, 1148, 835, 761 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}F_4N_2NaO_5$ [M + Na]$^+$ 491.1206; found 491.1205.

***tert*-Butyl (*R*)-2-Oxo-3-(*p*-tolyl)-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4i):** Yield 81.5 mg (88%). White solid, m.p. 109.5–110.6 °C. $[\alpha]_D^{25}$ = +144.3 (*c* = 4.00, $CH_2Cl_2$); 96% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 13.02 min, $t_{minor}$ = 14.88 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.03 (d, *J* = 8.4 Hz, 1 H, ArH), 7.49 (td, *J* = 8.4, 1.2 Hz, 1 H, ArH), 7.31 (dd, *J* = 7.2, 0.4 Hz, 1 H, ArH), 7.24 (d, *J* = 8.4 Hz, 2 H, ArH), 7.16 (d, *J* = 8.0 Hz, 2 H, ArH), 7.14 (d, *J* = 8.0 Hz, 1 H, ArH), 4.87–4.77 (m, 2 H, $CH_2$), 4.52 (d, *J* = 13.2 Hz, 1 H, CH), 2.31 (s, 3 H, $CH_3$), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.5, 148.7, 139.9, 139.4, 132.0, 130.3, 130.0, 127.2, 125.7, 125.1 (d, *J* = 280.9 Hz), 124.5, 124.4, 116.1, 85.0, 71.2, 54.8, 48.5 (q, *J* = 25.8 Hz), 27.9, 20.8 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1794, 1767, 1737, 1566, 1466, 1372, 1342, 1296, 1248, 1149, 760 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{23}F_3N_2NaO_5$ [M + Na]$^+$ 487.1457; found 487.1444.

***tert*-Butyl (*R*)-5-Fluoro-2-oxo-3-(*p*-tolyl)-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4j):** Yield 79.6 mg (95%). White solid, m.p. 157.9–158.5 °C. $[\alpha]_D^{25}$ = +78.6 (*c* = 4.50, $CH_2Cl_2$); 92% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 11.60 min, $t_{minor}$ = 17.32 min); 20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.05 (dd, *J* = 8.8, 4.8 Hz, 1 H, ArH), 7.23–7.17 (m, 5 H, ArH), 6.85 (dd, *J* = 7.6, 2.4 Hz, 1 H, ArH), 4.84–4.77 (m, 2 H, $CH_2$), 4.51–4.46 (m, 1 H, CH), 2.32 (s, 3 H, $CH_3$), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ = 173.1, 159.5 (d, *J* = 243.9 Hz), 148.7, 139.7, 136.0, 131.4, 130.5, 127.1, 126.3 (d, *J* = 7.6 Hz), 125.1 (d, *J* = 281.2 Hz), 117.6 (d, *J* = 8.0 Hz), 116.8 (d, *J* = 22.4 Hz), 113.1 (d, *J* = 24.3 Hz), 85.3, 71.0, 55.1, 48.4 (q, *J* = 26.2 Hz), 27.9, 20.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.8 (d, *J* = 6.4 Hz, 3 F), –116.7 (m) ppm. IR (film): $\tilde{\nu}$ = 1792, 1772, 1734, 1566, 1458, 1376, 1245, 1148, 1126, 821, 720 $cm^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{22}F_4N_2NaO_5$ [M + Na]$^+$ 505.1363; found 505.1365.

***tert*-Butyl (*R*)-5-Methyl-2-oxo-3-(*p*-tolyl)-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4k):** Yield 91.0 mg (96%). White solid, m.p. 130.2–131.3 °C. $[\alpha]_D^{25}$ = +118.3 (*c* = 4.00, $CH_2Cl_2$); 96% *ee* (Chiralpak IC-H; hexane/propan-2-ol 99:1;

0.7 mL min$^{-1}$; 254 nm; $t_{major}$ = 12.85 min, $t_{minor}$ = 15.00 min); >20:1 *dr*. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 7.90 (d, *J* = 8.4 Hz, 1 H, ArH), 7.28 (dd, *J* = 8.0, 0.8 Hz, 1 H, ArH), 7.23 (d, *J* = 8.0 Hz, 2 H, ArH), 7.16 (d, *J* = 8.4 Hz, 2 H, ArH), 6.91 (s, 1 H, ArH), 4.85 (dd, *J* = 14.0, 9.2 Hz, 1 H, CH), 4.78 (quint., *J* = 8.0 Hz, 1 H, CH), 4.51 (d, *J* = 14.4 Hz, 1 H, CH), 2.44 (s, 3 H, $CH_3$), 2.31 (s, 3 H, $CH_3$), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ = 173.6, 148.8, 139.3, 137.6, 134.2, 132.2, 130.6, 130.3, 127.3, 126.1, 125.2 (d, *J* = 279.7 Hz), 124.6, 115.9, 84.8, 71.3, 55.0, 48.4 (q, *J* = 25.9 Hz), 27.9, 21.2, 20.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1791, 1765, 1737, 1566, 1491, 1373, 1335, 1311, 1246, 1151, 1123, 821, 739 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{24}H_{25}F_3KN_2O_5$ [M + K]$^+$ 517.1353; found 517.1302.

***tert*-Butyl (*R*)-5-Methoxy-2-oxo-3-(*p*-tolyl)-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4l):** Yield 98.0 mg (99%). White solid, m.p. 148.3–150.1 °C. $[\alpha]_D^{25}$ = +171.0 (*c* = 4.80, $CH_2Cl_2$); 97% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 16.55 min, $t_{minor}$ = 34.53 min); >20:1 *dr*. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 7.96 (d, *J* = 9.2 Hz, 1 H, ArH), 7.25 (d, *J* = 8.8 Hz, 2 H, ArH), 7.17 (d, *J* = 8.0 Hz, 2 H, ArH), 7.01 (dd, *J* = 9.2, 2.4 Hz, 1 H, ArH), 6.67 (d, *J* = 2.4 Hz, 1 H, ArH), 4.84 (dd, *J* = 13.6, 8.8 Hz, 1 H, CH), 4.79 (quint., *J* = 8.8 Hz, 1 H, CH), 4.50 (d, *J* = 13.2 Hz, 1 H, CH), 3.86 (s, 3 H, $OCH_3$), 2.31 (s, 3 H, $CH_3$), 1.59 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR ($CDCl_3$, 100 MHz): $\delta$ = 173.5, 156.5, 148.8, 139.4, 133.2, 131.9, 130.2, 127.2, 125.9, 125.1 (d, *J* = 280.9 Hz), 117.0, 113.8, 112.7, 84.7, 71.2, 55.7, 55.1, 48.3 (q, *J* = 26.0 Hz), 27.9, 20.8 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.5 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1791, 1765, 1735, 1567, 1509, 1350, 1298, 1248, 1152, 816, 739 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{24}H_{25}F_3N_2NaO_6$ [M + Na]$^+$ 517.1562; found 517.1535.

***tert*-Butyl (*R*)-3-(3-Fluorophenyl)-2-oxo-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4m):** Yield 86.4 mg (93%). White solid, m.p. 135.7–137.5 °C. $[\alpha]_D^{25}$ = +174.4 (*c* = 4.20, $CH_2Cl_2$); 97% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 13.11 min, $t_{minor}$ = 16.40 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.03 (d, *J* = 8.4 Hz, 1 H, ArH), 7.51 (td, *J* = 8.8, 1.2 Hz, 1 H, ArH), 7.40–7.31 (m, 2 H, ArH), 7.26 (d, *J* = 8.0 Hz, 1 H, ArH), 7.14 (d, *J* = 7.2 Hz, 1 H, ArH), 7.06 (tdd, *J* = 8.0, 2.4, 0.8 Hz, 1 H, ArH), 7.03–6.98 (m, 1 H, ArH), 4.85 (dd, *J* = 14.4, 8.8 Hz, 1 H, CH), 4.75 (qd, *J* = 7.6, 1.6 Hz, 1 H, CH), 4.47 (d, *J* = 14.8 Hz, 1 H, CH), 1.60 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 172.9, 163.1 (d, *J* = 247.5 Hz), 148.6, 139.9, 137.5 (d, *J* = 6.9 Hz), 131.3 (d, *J* = 8.4 Hz), 130.4, 125.6, 125.0 (d, *J* = 281.1 Hz), 124.7, 123.9, 123.2 (d, *J* = 2.7 Hz), 116.6, 116.4, 115.0 (d, *J* = 24.3 Hz), 85.3, 71.1, 54.9, 48.6 (q, *J* = 26.1 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.8 (d, *J* = 7.1 Hz, 3 F), –109.6 (m) ppm. IR (film): $\tilde{\nu}$ = 1793, 1768, 1738, 1484, 1467, 1373, 1340, 1294, 1247, 1146, 841, 760 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}F_4KN_2O_5$ [M + K]$^+$ 507.0945; found 507.0930.

***tert*-Butyl (*R*)-2-Oxo-3-(*m*-tolyl)-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4n):** Yield 89.1 mg (96%). White solid, m.p. 132.5–134.1 °C. $[\alpha]_D^{25}$ = +121.6 (*c* = 4.40, $CH_2Cl_2$); 98% *ee* (Chiralcel OD-H; hexane/propan-2-ol 99:1; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 15.28 min, $t_{minor}$ = 29.03 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.03 (d, *J* = 8.0 Hz, 1 H, ArH), 7.49 (t, *J* = 8.0 Hz, 1 H, ArH), 7.31 (t, *J* = 7.6 Hz, 1 H, ArH), 7.22 (d, *J* = 7.6 Hz, 1 H, ArH), 7.20 (s, 1 H, ArH), 7.14 (t, *J* = 8.0 Hz, 2 H, ArH), 7.10 (d, *J* = 7.6 Hz, 1 H, ArH), 4.87–4.79 (m, 2 H, $CH_2$), 4.50 (d, *J* = 12.8 Hz, 1 H, CH), 2.31 (s, 3 H, $CH_3$), 1.60 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.4, 148.8, 139.9, 139.5, 135.0, 130.07, 130.02, 129.4, 128.0, 125.7, 125.1 (d, *J* = 280.8 Hz), 124.53, 124.48, 124.4, 116.2, 85.1, 71.3, 55.1, 48.5 (q, *J* = 25.9 Hz), 27.9, 21.5 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 6.8 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1794, 1767, 1737, 1566, 1482, 1466, 1372, 1342, 1295, 1174, 1148, 1128, 742 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{23}F_3N_2NaO_5$ [M + Na]$^+$ 487.1457; found 487.1458.

***tert*-Butyl (*R*)-3-(3-Methoxyphenyl)-2-oxo-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4o):** Yield 80.2 mg (84%). White solid, m.p. 146.0–147.7 °C. $[\alpha]_D^{25}$ = +150.7 (*c* = 4.00, $CH_2Cl_2$); 97% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 15.30 min, $t_{minor}$ = 17.87 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.04 (d, *J* = 8.4 Hz, 1 H, ArH), 7.51 (t, *J* = 7.6 Hz, 1 H, ArH), 7.33 (t, *J* = 7.6 Hz, 1 H, ArH), 7.28 (t, *J* = 8.0 Hz, 1 H, ArH), 7.15 (d, *J* = 7.6 Hz, 1 H, ArH), 6.95 (s, 1 H, ArH), 6.90 (d, *J* = 8.4 Hz, 2 H, ArH), 4.90–4.79 (m, 2 H, $CH_2$), 4.54 (d, *J* = 12.8 Hz, 1 H, CH), 3.79 (s, 3 H, $OCH_3$), 1.62 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.3, 160.3, 148.7, 139.9, 136.5, 130.5, 130.1, 125.7, 125.1 (d, *J* = 280.8 Hz), 124.5, 120.9, 119.6, 116.2, 114.8, 113.2, 85.1, 71.2, 55.2, 55.1, 48.5 (q, *J* = 25.9 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.8 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1794, 1767, 1737, 1566, 1466, 1372, 1341, 1294, 1249, 1147, 840, 773, 759 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{23}F_3KN_2O_6$ [M + K]$^+$ 519.1145; found 519.1133.

***tert*-Butyl (*R*)-3-(Naphthalen-2-yl)-2-oxo-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4p):** Yield 70.0 mg (61%). White solid, m.p. 150.7–152.0 °C. $[\alpha]_D^{25}$ = +117.7 (*c* = 3.50, $CH_2Cl_2$); 99% *ee* (Chiralpak AS-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{minor}$ = 20.39 min, $t_{major}$ = 24.15 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.10 (d, *J* = 8.4 Hz, 1 H, ArH), 7.92 (d, *J* = 9.2 Hz, 1 H, ArH), 7.83 (d, *J* = 8.0 Hz, 1 H, ArH), 7.76 (d, *J* = 8.8 Hz, 1 H, ArH), 7.70 (d, *J* = 8.0 Hz, 1 H, ArH), 7.49–7.46 (m, 4 H, ArH), 7.39 (t, *J* = 7.6 Hz, 1 H, ArH), 7.23 (d, *J* = 7.6 Hz, 1 H, ArH), 4.98 (quint., *J* = 8.0 Hz, 1 H, CH), 4.88 (dd, *J* = 14.8, 9.2 Hz, 1 H, CH), 4.51 (d, *J* = 14.8 Hz, 1 H, CH), 1.60 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.3, 148.7, 140.0, 133.1, 132.8, 132.3, 130.2, 130.0, 128.3, 127.7, 127.5, 127.4, 126.9, 125.8, 125.2 (d, *J* = 280.8 Hz), 124.6, 124.4, 123.7, 116.3, 85.1, 71.2, 55.3, 48.4 (q, *J* = 25.9 Hz), 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.6 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1793, 1766, 1737, 1565, 1482, 1466, 1372, 1339, 1293, 1246, 1148, 759 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{26}H_{23}F_3N_2NaO_5$ [M + Na]$^+$ 523.1457; found 523.1428.

***tert*-Butyl (*S*)-3-Methyl-2-oxo-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4r):** Yield 71.6 mg (93%). White solid, m.p. 121.3–123.1 °C. $[\alpha]_D^{25}$ = +3.2 (*c* = 3.50, $CH_2Cl_2$); 69% *ee* (Chiralpak AD-H; hexane/propan-2-ol 98:2; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 12.36 min, $t_{major}$ = 14.34 min); 12:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.91 (d, *J* = 8.4 Hz, 1 H, ArH), 7.40–7.35 (m, 1 H, ArH), 7.23–7.17 (m, 2 H, ArH), 4.92 (dd, *J* = 14.8, 4.0 Hz, 1 H, CH), 4.80 (dd, *J* = 14.8, 2.8 Hz, 1 H, CH), 4.03–3.99 (m, 1 H, CH), 1.64 (s, 9 H, 3 × $CH_3$), 1.50 (s, 3 H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 175.6, 148.7, 138.7, 129.5, 127.9, 125.0 (d, *J* = 280.8 Hz), 124.8, 123.1, 115.7, 85.1, 70.5, 47.9 (q, *J* = 26.3 Hz), 47.0, 27.9, 23.2 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 8.3 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1759, 1720, 1567, 1466, 1373, 1274, 1240, 1185, 1130, 763 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{17}H_{19}F_3KN_2O_5$ [M + K]$^+$ 427.0883; found 427.0883.

***(S)-tert*-Butyl 3-Benzyl-2-oxo-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (4s):** Yield 74.2 mg (80%). White solid,

m.p. 118.3–119.7 °C. $[\alpha]_D^{25}$ = –1.9 (*c* = 3.40, $CH_2Cl_2$); 71% *ee* (Chiralpak AD-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{minor}$ = 26.62 min, $t_{major}$ = 29.50 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.55 (d, *J* = 8.0 Hz, 1 H, ArH), 7.35 (d, *J* = 7.6 Hz, 1 H, ArH), 7.29 (td, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.24 (t, *J* = 7.2 Hz, 1 H, ArH), 7.07 (t, *J* = 7.6 Hz, 1 H, ArH), 6.98 (t, *J* = 7.6 Hz, 2 H, ArH), 6.63 (d, *J* = 7.6 Hz, 2 H, ArH), 5.05 (dd, *J* = 14.8, 4.4 Hz, 1 H, CH), 4.92 (dd, *J* = 14.8, 6.4 Hz, 1 H, CH), 4.31–4.26 (m, 1 H, CH), 3.21 (d, *J* = 12.0 Hz, 1 H, CH), 3.08 (d, *J* = 12.0 Hz, 1 H, CH), 1.50 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 174.3, 147.9, 139.8, 131.8, 129.8, 129.6, 127.7, 127.4, 125.3, 125.0 (d, *J* = 280.8 Hz), 124.5, 123.4, 115.4, 84.4, 70.7, 53.2, 47.8 (q, *J* = 26.2 Hz), 42.7, 27.8 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.1 (d, *J* = 9.0 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1789, 1768, 1738, 1566, 1468, 1372, 1339, 1291, 1248, 1149, 1094, 772 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{23}H_{23}F_3KN_2O_5$ [M + K]$^+$ 503.1196; found 503.1209.

**(*R*)-3-Phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indolin-2-one (6a):** Yield 46.3 mg (66%). White solid, m.p. 210.3–212.2 °C. $[\alpha]_D^{25}$ = +130.2 (*c* = 2.30, $CH_2Cl_2$); 83% *ee* (Chiralpak AD-H; hexane/propan-2-ol 95:5; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 29.73 min, $t_{major}$ = 39.02 min); 8:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.82 (s, 1 H, NH), 7.43–7.39 (m, 3 H, ArH), 7.38–7.35 (m, 3 H, ArH), 7.22–7.14 (m, 2 H, ArH), 7.07 (d, *J* = 7.6 Hz, 1 H, ArH), 4.85 (dd, *J* = 14.4, 9.2 Hz, 1 H, CH), 4.74 (qd, *J* = 8.0, 2.0 Hz, 1 H, CH), 4.50 (d, *J* = 14.0 Hz, 1 H, CH) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 177.5, 141.0, 135.2, 129.9, 129.5, 129.1, 127.3, 126.2, 126.0, 125.2 (d, *J* = 280.9 Hz), 122.8, 111.4, 71.4, 55.2 (d, *J* = 1.3 Hz), 48.1 (q, *J* = 26.2 Hz) ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –66.0 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1794, 1767, 1737, 1566, 1466, 1372, 1341, 1294, 1249, 1147, 840, 773, 759 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{17}H_{12}F_3N_2O_3$ [M – H]$^+$ 349.0800; found 349.0796.

**(*R*)-1-Methyl-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]-indolin-2-one (6b):** Yield 20.0 mg (27%). White solid, m.p. 112.3–114.1 °C. $[\alpha]_D^{25}$ = +209.0 (*c* = 1.0, $CH_2Cl_2$); 90% *ee* (Chiralpak AS-H; hexane/propan-2-ol 95:5; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 22.80 min, $t_{major}$ = 33.39 min); 6:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.49–7.43 (m, 3 H, ArH), 7.40–7.34 (m, 3 H, ArH), 7.24–7.17 (m, 2 H, ArH), 6.98 (d, *J* = 7.6 Hz, 1 H, ArH), 4.84 (dd, *J* = 14.4, 8.8 Hz, 1 H, CH), 4.75 (qd, *J* = 7.6, 1.6 Hz, 1 H, CH), 4.50 (d, *J* = 14.0 Hz, 1 H, CH), 3.19 (s, 3 H, $NCH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 175.1, 143.9, 135.3, 129.9, 129.5, 129.1, 127.3, 126.1, 125.6, 125.2 (d, *J* = 280.8 Hz), 122.7, 109.5, 71.5, 54.6, 48.3 (q, *J* = 26.0 Hz), 26.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –66.1 ppm. IR (film): $\tilde{\nu}$ = 1719, 1613, 1564, 1495, 1472, 1374, 1351, 1281, 1246, 1173, 1126, 802, 762 cm$^{-1}$. MS (EI): *m*/*z* (%) = 364 [M]$^+$ (48), 223 (14), 222 (100), 148 (93), 207 (8), 194 (6). HRMS (EI): calcd. for $C_{18}H_{15}F_3N_2O_3$ [M]$^+$ 364.1035; found 364.1036.

**(*R*)-1-Benzyl-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]-indolin-2-one (6c):** Yield 32.2 mg (37%). White solid, m.p. 135.1–137.2 °C. $[\alpha]_D^{25}$ = +332.6 (*c* = 1.50, $CH_2Cl_2$); 98% *ee* (Chiralpak AS-H; hexane/propan-2-ol 98:2; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 33.10 min, $t_{major}$ = 37.97 min); 16:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.39–7.36 (m, 2 H, ArH), 7.32–7.23 (m, 4 H, ArH), 7.20–7.15 (m, 3 H, ArH), 7.11–7.07 (m, 4 H, ArH), 6.79 (d, *J* = 8.0 Hz, 1 H, ArH), 4.84–4.75 (m, 4 H, 2 $CH_2$), 4.46 (d, *J* = 13.2 Hz, 1 H, CH) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 175.2, 143.0, 135.6, 135.0, 129.8, 129.5, 129.1, 128.7, 127.7, 127.2, 127.1, 126.0, 125.7, 125.2 (d, *J* = 280.9 Hz), 122.7, 110.6, 71.5, 54.7, 48.0 (q, *J* = 26.0 Hz), 44.4 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.8 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1714, 1611, 1563, 1467, 1377, 1189, 1173, 1119, 806 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{24}H_{19}F_3N_2NaO_3$ [M + Na]$^+$ 463.1245; found 463.1248.

**(*R*)-1-Acetyl-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]-indolin-2-one (6d):** Yield 70.0 mg (86%). White solid, m.p. 120.1–121.3 °C. $[\alpha]_D^{25}$ = +166.4 (*c* = 3.50, $CH_2Cl_2$); 97% *ee* (Chiralpak AD-H; hexane/propan-2-ol 98:2; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 15.61 min, $t_{major}$ = 29.25 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.40 (d, *J* = 8.0 Hz, 1 H, ArH), 7.52 (td, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.39–7.34 (m, 6 H, ArH), 7.16 (d, *J* = 7.2 Hz, 1 H, ArH), 4.90–4.81 (m, 2 H, $CH_2$), 4.52 (d, *J* = 12.4 Hz, 1 H, CH), 2.60 (s, 3 H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 176.0, 170.6, 140.2, 134.9, 130.3, 129.7, 129.5, 127.3, 125.5, 125.3, 125.1 (d, *J* = 280.9 Hz), 124.6, 117.6, 71.1, 55.3, 48.4 (q, *J* = 26.0 Hz), 26.5 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.8 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1760, 1721, 1570, 1374, 1293, 1187, 1132, 783 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{19}H_{15}F_3N_2NaO_4$ [M + Na]$^+$ 415.0882; found 415.0886.

**Methyl (*R*)-2-Oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (6e):** Yield 80.5 mg (98%). White solid, m.p. 117.4–119.0 °C. $[\alpha]_D^{25}$ = +163.8 (*c* = 4.00, $CH_2Cl_2$); 98% *ee* (Chiralpak AS-H; hexane/propan-2-ol 95:5; 0.7 mL min$^{-1}$; 254 nm; $t_{minor}$ = 28.18 min, $t_{major}$ = 55.76 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.11 (d, *J* = 8.4 Hz, 1 H, ArH), 7.53 (td, *J* = 8.4, 1.2 Hz, 1 H, ArH), 7.38–7.34 (m, 6 H, ArH), 7.17 (d, *J* = 7.2 Hz, 1 H, ArH), 4.89–4.80 (m, 2 H, $CH_2$), 4.50 (d, *J* = 12.8 Hz, 1 H, CH), 3.96 (s, 3 H, $OCH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.4, 151.0, 139.4, 134.7, 130.3, 129.7, 129.5, 127.3, 125.8, 125.1 (d, *J* = 280.8 Hz), 124.9, 124.4, 116.3, 71.1, 55.2, 54.2, 48.4 (q, *J* = 26.0 Hz) ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.7 (d, *J* = 7.1 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1799, 1769, 1744, 1566, 1483, 1467, 1439, 1378, 1346, 1297, 1242, 1178, 1129, 762 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{19}H_{15}F_3N_2NaO_5$ [M + Na]$^+$ 431.0831; found 431.0836.

**Benzyl (*R*)-2-Oxo-3-phenyl-3-[(2′*R*)-1,1,1-trifluoro-3-nitropropan-2-yl]indoline-1-carboxylate (6f):** Yield 96.0 mg (99%). White solid, m.p. 100.9–102.3 °C. $[\alpha]_D^{25}$ = +107.7 (*c* = 4.90, $CH_2Cl_2$); 96% *ee* (Chiralpak IC-H; hexane/propan-2-ol 98:2; 0.5 mL min$^{-1}$; 254 nm; $t_{major}$ = 24.19 min, $t_{minor}$ = 28.24 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.11 (d, *J* = 8.4 Hz, 1 H, ArH), 7.53 (d, *J* = 7.6 Hz, 1 H), 7.50–7.47 (m, 2 H, ArH), 7.41–7.34 (m, 9 H, ArH), 7.17 (d, *J* = 7.6 Hz, 1 H, CH), 5.41 (dd, *J* = 28.4, 12.4 Hz, 2 H, $OCH_2$), 4.89–4.83 (m, 2 H, CH), 4.55–4.50 (m, 1 H, CH) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.2, 150.3, 139.4, 134.7, 134.5, 130.2, 129.6, 129.4, 128.6, 128.5, 128.0, 127.4, 125.8, 125.1 (d, *J* = 280.9 Hz), 124.8, 124.4, 116.3, 71.1, 69.0, 55.2, 48.5 (q, *J* = 25.9 Hz) ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –65.6 (d, *J* = 6.8 Hz, 3 F) ppm. IR (film): $\tilde{\nu}$ = 1798, 1772, 1742, 1568, 1449, 1436, 1380, 1296, 1228, 1181, 736 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{25}H_{19}F_3N_2NaO_5$ [M + Na]$^+$ 507.1144; found 507.1137.

**Synthetic Transformation of Adducts 4a:** Adduct **4a** (40.0 mg, 0.08 mmol) was added to a suspension of Raney Ni (15 mg) in MeOH (1.0 mL). The flask was evacuated and refilled with $H_2$ three times. The reaction mixture was stirred at room temperature under $H_2$ (balloon) for 2 h and was then filtered through celite and washed with methanol several times. The filtrate was concentrated and dissolved in THF (1.5 mL). Hünig base (20 uL, 0.12 mmol) and chloromethyl formate (0.1 mL, 1.3 mmol) were added slowly to this solution. The reaction mixture was then allowed to warm to room temperature and stirred overnight. After dilution with $CH_2Cl_2$, then reaction was quenched with saturated aqueous $Na_2CO_3$ solution. The aqueous layer was separated and extracted with $CH_2Cl_2$ (3× 5 mL). The combined organic layers were dried

with $Na_2SO_4$, filtered, and concentrated. The residue was then purified by silica gel flash column chromatography with petroleum ether/ethyl acetate (6:1 v/v) as eluent to afford **7** as a white solid (27 mg, 70% over two steps), m.p. 153.0–153.7 °C. $[a]_D^{25}$ = +283.8 ($c$ = 0.8, $CH_2Cl_2$); 97% *ee* (Chiralpak IC-H; hexane/propan-2-ol 90:10; 0.7 mL min$^{-1}$; 254 nm; $t_{major}$ = 33.25 min, $t_{minor}$ = 42.07 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.98 (d, $J$ = 8.0 Hz, 1 H, ArH), 7.45 (td, $J$ = 8.4, 1.2 Hz, 1 H, ArH), 7.37–7.27 (m, 7 H, ArH), 4.85–4.84 (m, 1 H, NH), 3.94–3.92 (m, 1 H, CH), 3.63 (s, 3 H, $OCH_3$), 3.62–3.57 (m, 2 H, $CH_2$), 1.58 (s, 9 H, 3 × $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 174.6, 156.4, 148.9, 140.0, 135.5, 129.5, 128.9, 128.6, 127.6, 126.6, 126.4 (d, $J$ = 281.2 Hz), 125.5, 124.1, 115.8, 84.7, 55.3, 52.3, 50.3 (q, $J$ = 23.4 Hz), 37.7, 27.9 ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –62.9 ppm. IR (film): $\tilde{\nu}$ = 1792, 1730, 1289, 1160, 1120, 1024, 775 cm$^{-1}$. MS (EI): *m*/*z* (%)=478 $[M]^+$ (1), 346 (29), 208 (100), 180 (20), 165 (7). HRMS (EI): calcd. for $C_{24}H_{25}F_3N_2O_5$ $[M]^+$ 478.1716; found 478.1720.

**(3*R*,3a*R*)-3a-Phenyl-3-(trifluoromethyl)-2,3,3a,8-tetrahydropyrrolo-[2,3-*b*]indole (8):** Adduct **4a** (90.0 mg, 0.2 mmol) was added to a suspension of Raney Ni (30 mg) in MeOH (2.0 mL). The flask was evacuated and refilled with $H_2$ three times. The reaction mixture was stirred at room temperature under $H_2$ (balloon) for 2 h and was then filtered through celite and washed with methanol several times. The filtrate was concentrated and dissolved in $CH_2Cl_2$ (1 mL). TFA (228 mg, 2.0 mmol, 10 equiv.) was added to this solution, and the mixture was stirred at room temperature for 0.5 h. Concentrated and dried under vacuum for 1 h, the resulted residue was added to a suspension of $LiAlH_4$ (72 mg, 2.0 mmol, 10 equiv.) in THF (1.5 mL). The mixture was then heated at 75 °C for 2 h. After having cooled to room temperature, the reaction mixture was quenched with ethyl acetate (4.0 mL) and $H_2O$ (0.5 mL) and concentrated and the residue was purified by silica gel flash column chromatography with petroleum ether/ethyl acetate (2:1 v/v) as eluent to afford **8** as a white solid (36.0 mg, 60% overall yield for three steps), m.p. 173.7–174.9 °C. $[a]_D^{25}$ = –105.2 ($c$ = 1.40, $CH_2Cl_2$); 97% *ee* (Chiralpak AS-H; hexane/propan-2-ol 90:10; 0.7 mL min$^{-1}$; 254 nm; $t_{major}$ = 15.37 min, $t_{minor}$ = 12.67 min); >20:1 *dr*. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.67 (d, $J$ = 7.6 Hz, 1 H, ArH), 7.40 (d, $J$ = 7.6 Hz, 2 H, ArH), 7.31 (t, $J$ = 7.6 Hz, 3 H, ArH), 7.25 (s, 1 H, NH), 7.19 (t, $J$ = 7.6 Hz, 1 H, ArH), 7.00 (t, $J$ = 7.6 Hz, 1 H, ArH), 6.79 (d, $J$ = 7.6 Hz, 1 H, ArH), 4.15–4.11 (m, 1 H, CH), 4.05–3.99 (m, 1 H, CH), 3.36–3.30 (m, 1 H, CH) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 180.4, 148.7, 132.6, 132.0, 129.0, 128.5, 127.82, 127.80, 125.3 (d, $J$ = 276.4 Hz), 125.2, 121.4, 111.7, 63.0, 57.3, 53.8 (q, $J$ = 27.8 Hz) ppm. $^{19}$F NMR (376 MHz, $CDCl_3$): $\delta$ = –63.4 ppm. IR (film): $\tilde{\nu}$ = 1685, 1462, 1391, 1284, 1122, 646 cm$^{-1}$. HRMS (ESI-TOF): calcd. for $C_{17}H_{14}F_3N_2$ $[M + H]^+$ 303.1109; found 303.1100.

**Supporting Information** (see footnote on the first page of this article): NMR spectra of new compounds, HPLC traces for the determination of the enantiomeric excesses of compounds **4** and **6**–**8**, and X-ray crystal data for product **4f**.

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