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# Organocatalyzed Cascade Reactions of Cyclic β-Enamino Esters and α,β-Unsaturated Aldehydes Leading to Indoloquinolizidines and Benzoquinolizidines

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Organocatalyzed cascade reactions between cyclic β-enamino esters and α,β-unsaturated aldehydes have been developed. They provide highly substituted indolo[2,3-*a*]quinolizidines and benzo[*a*]quinolizidines in moderate to good yields and with good to excellent enantioselectivities. Both aromatic and aliphatic α,β-unsaturated aldehydes react readily with enamino esters to furnish the desired products.

## Introduction

Enamine-based organocatalysis has been intensively investigated during the past few years. The mechanism of catalysis of this type involves the in situ formation of an enamine from an amine catalyst and an aldehyde or ketone as a key intermediate, this acting as a nucleophile in a catalytic cycle to provide chiral induction.[1] The employment of stable enamine derivatives (Figure 1), such as enamides and enecarbamates, as nucleophiles in asymmetric catalytic reactions has been reported less frequently.[2–4] Kobayashi and co-workers have recently demonstrated chiral Lewis-acid-catalyzed enantioselective additions of enamides to a series of electron-deficient reactants.[2] Chiral Brønsted acids have also been successfully utilized in place of Lewis acids to promote addition reactions of enamides or enecarbamates to electron-deficient reactants.[3] Wang et al. described cascade cyclization reactions between α,β-unsaturated aldehydes and enamides catalyzed by chiral secondary amines.[4a] Using a similar strategy, Hayashi and co-workers reported a cascade sequence utilizing enecarbamates as nucleophiles.[4b]

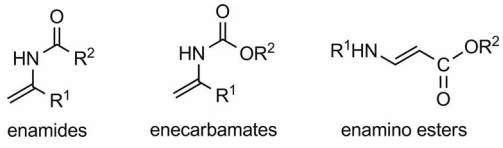


Figure 1. Structures of enamine derivatives.

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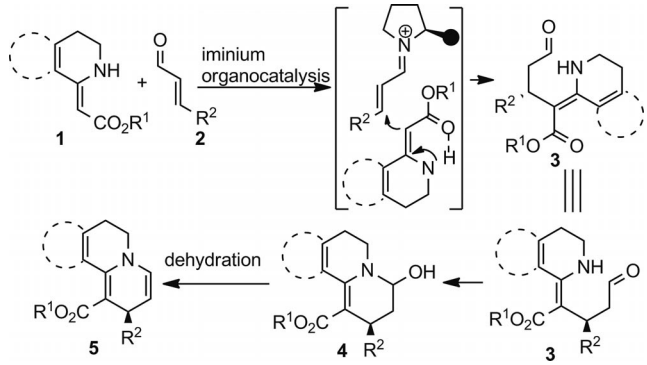
Unlike enamides and enecarbamates, enamino esters, which are also derivatives of enamines, had never been used as nucleophiles in asymmetric catalysis until very recently.[5] In 2010, though, Takemoto et al. described reactions between β-enamino esters and α,β-unsaturated aldehydes promoted by a Brønsted acid/thiourea co-catalyst, affording functionalized 1,4-dihydropyridines with *ee* values of up to 80%.[5a,5b] Kanger and co-workers developed a cascade protocol catalyzed by prolinol TMS ether with enaminones or enamino esters as nucleophiles and α,β-unsaturated aldehydes as electrophiles, yielding 1,4-dihydropyridines with good enantioselectivities.[5c] On the other hand, β-enamino esters are a class of highly versatile building blocks in organic synthesis.[6] In particular, cyclic β-enamino esters have been used in the synthesis of a number of natural products such as indolizidines, quinolizidines, and other alkaloids.[6]

For the past several years we have been engaged in a research program directed towards efficient and enantioselective synthesis of highly substituted quinolizidines by a cascade strategy.[7] Here we report some new results from our work, leading to the multiply substituted quinolizidines **5** (Scheme 1) and **8** (Table 3, below) through asymmetric cascade reactions, catalyzed by a prolinol TMS ether deriv-




Scheme 1. Concept of the cascade reactions between **1** and **2**.

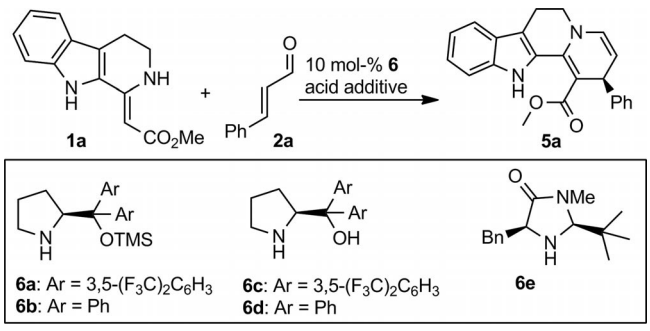
ative,[8] between the cyclic enamino esters **1** or **7** and the α,β-unsaturated aldehydes **2**.[9] Indoloquinolizidines or benzoquinolizidines can be obtained from enamino esters attached to indolyl or phenyl functionalities, respectively.

Our initial proposal for the cascade reactions between the cyclic enamino esters **1** and the α,β-unsaturated aldehydes **2** is shown in Scheme 1.[10] Conjugate addition of the enamino esters **1** to the enals **2** is promoted through the activation of the enals by formation of iminium intermediates to afford the intermediates **3** after release of the catalyst.[1] The aldehydes **3** spontaneously undergo cyclization to afford the hemiaminals **4**.[11] After dehydration of the intermediates **4** in the presence of acid additive, the cyclized products **5** are obtained enantioselectively.

## Results and Discussion

To test the feasibility of this cascade approach, a model reaction between the enamino ester **1a** and cinnamaldehyde (**2a**) was examined under a broad set of conditions (Table 1). We were concerned that there might be regiochemical selectivity issues, arising from competing N- and C-1,4-addition, in the designed cascade sequence. We were delighted to find, however, that no formation of N-adduct was observed in an initial reaction between **1a** and **2a** assisted by catalysis by α,α-diphenylprolinol TMS ether (**6a**, 10 mol-%) and benzoic acid (10 mol-%) at –10 °C in DCM. The indoloquinolizidine **5a** was isolated with moderate yield and enantioselectivity (Table 1, Entry 1). In an attempt to improve the chiral induction, the secondary amine catalysts **6b**–**e** were also screened. Better results could not be obtained by use of the less bulky **6b** or the free α,α-diphenylprolinol derivatives **6c** or **6d**, however, whereas the MacMillan catalyst **6e** was ineffective in this reaction, with no conversion of the starting materials being observed (Table 1, Entries 2–5).

Table 1. Screening studies of the cascade reaction between the enamino ester **1a** and cinnamaldehyde (**2a**).[a]




| Entry | Cat. | Additive | Solvent | $T$ [°C] | $t$ [h] | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|---|---|
| 1 | **6a** | A1 | DCM | –10 | 15 | 53 | 39 |
| 2 | **6b** | A1 | DCM | –10 | 15 | 60 | 17 |
| 3 | **6c** | A1 | DCM | –10 | 22 | 61 | 30 |
| 4 | **6d** | A1 | DCM | –10 | 22 | 51 | 11 |
| 5 | **6e** | A1 | DCM | –10 | 37 | – | – |
| 6 | **6a** | A1 | $CH_3OH$ | –10 | 43 | 25 | 37 |
| 7 | **6a** | A1 | THF | –10 | 43 | – | – |
| 8 | **6a** | A1 | $CH_3CN$ | –10 | 43 | 36 | 17 |
| 9 | **6a** | A1 | $CHCl_3$ | –10 | 23 | 70 | 53 |
| 10 | **6a** | A1 | toluene | –10 | 15 | 69 | 77 |
| 11 | **6a** | A1 | toluene | 0 | 15 | 71 | 51 |
| 12 | **6a** | A1 | toluene | –20 | 40 | 72 | 86 |
| 13 | **6a** | A2 | toluene | –20 | 40 | 48 | 1 |
| 14 | **6a** | A3 | toluene | –20 | 40 | 37 | 11 |
| 15 | **6a** | A4 | toluene | –20 | 40 | 39 | 65 |
| 16 | **6a** | A5 | toluene | –20 | 40 | 62 | 75 |

[a] General conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), **6** (10 mol-%), and additive (10 mol-%) in solvent (0.6 mL). Additives: A1: BzOH; A2: 3,5-$(O_2N)_2C_6H_3CO_2H$; A3: TFA; A4: 4-$O_2NC_6H_4$-$CO_2H$; A5: AcOH. [b] Yields refer to isolated pure products. [c] Enantiomeric excesses were determined by chiral HPLC analysis.

The enantioselectivity of the reaction appears to be strongly dependent on the solvent. With methanol as the solvent, the enantioselectivity was comparable to that observed in DCM, but the yield was much lower (Table 1, Entry 6). In THF almost no product was formed (Table 1, Entry 7), whereas use of acetonitrile led both to lower yield and to poorer enantioselectivity than use of DCM (Table 1, Entry 8). Better results were obtained in chloroform and toluene, and the latter proved to be the best solvent (Table 1, Entries 9 and 10).

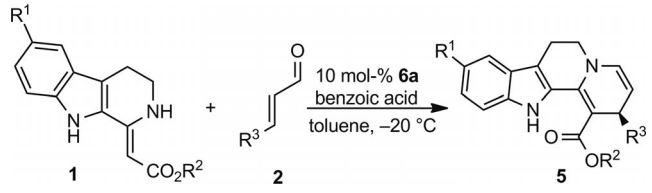
We next examined the influence of temperature (Table 1, Entries 10–12). The reaction gave a higher yield and better enantioselectivity at –20 °C, although with a longer reaction time needed to achieve full conversion of **1a** (Table 1, Entry 12).

Furthermore, acid additives were also screened as sources of counterions for iminium intermediates. A significant dependence of enantioselectivity on the natures of the acids was revealed in the course of our study (Table 1, Entries 12–16). It turned out that benzoic acid (A1) was the most effective in terms of yield and enantioselectivity. Lower enantioselectivities were observed when stronger acids were used: TFA and 3,5-dinitrobenzoic acid, for example, were found to be the least effective.

With the optimized reaction conditions established (Table 1, Entry 12), the scope of this cascade reaction was studied next (Table 2). Initially, we investigated the cascade sequences with the α,β-unsaturated aldehydes **2a**–**i** as electrophiles and the indole-tethered enamino ester **1a** as nucleophile (Table 2, Entries 1–9). As shown in Table 2, the domino reactions proceeded well both for aromatic and for aliphatic α,β-unsaturated aldehydes, providing the cyclized products **5a**–**i** in moderate to good yields. Good enantioselectivities were achieved in all cases except for that of **2e**, which gave only 61% *ee* (Table 2, Entry 5). Next, the enamino esters **1b** and **1c**, with substituents on the indole moiety, and the ethyl enamino ester **1d** were examined (Table 2, Entries 10–17). All the reactions proceeded to give the corresponding cyclized products **5j**–**q** in moderate to good yields and with *ee* values ranging from 72 to 89%. The enamino ester **1d** gave higher enantioselectivities than **1a** (Table 2, Entry 16 vs. Entry 2, and Entry 17 vs. Entry 5). The superior levels of enantioselectivities exhibited by **1d** could be explained in terms of the increased steric encumbrance created by substituents on the ethyl group.

Table 2. Asymmetric cascade reactions of the enamino esters **1a**–**d** and the α,β-unsaturated aldehydes **2a**–**i**.[a]

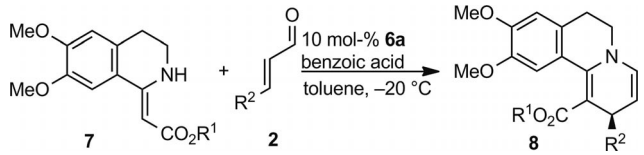



| Entry | $R^1$, $R^2$, **1** | $R^3$, **2** | **5** | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|
| 1 | H, Me, **1a** | $C_6H_5$, **2a** | **5a** | 72 | 86 |
| 2 | H, Me, **1a** | *p*-$BrC_6H_4$, **2b** | **5b** | 77 | 81 |
| 3 | H, Me, **1a** | *p*-$FC_6H_4$, **2c** | **5c** | 51 | 81 |
| 4 | H, Me, **1a** | *o*-$MeOC_6H_4$, **2d** | **5d** | 55 | 71 |
| 5 | H, Me, **1a** | *p*-$MeC_6H_4$, **2e** | **5e** | 54 | 61 |
| 6 | H, Me, **1a** | Me, **2f** | **5f** | 68 | 80 |
| 7 | H, Me, **1a** | Et, **2g** | **5g** | 55 | 83 |
| 8 | H, Me, **1a** | *n*Pr, **2h** | **5h** | 72 | 73 |
| 9 | H, Me, **1a** | $CH_3(CH_2)_6$, **2i** | **5i** | 74 | 82 |
| 10 | MeO, Me, **1b** | *p*-$BrC_6H_4$, **2b** | **5j** | 71 | 82 |
| 11 | Me, Me, **1c** | *p*-$BrC_6H_4$, **2b** | **5k** | 87 | 89 |
| 12 | MeO, Me, **1b** | *p*-$MeC_6H_4$, **2e** | **5l** | 63 | 77 |
| 13 | Me, Me, **1c** | *p*-$MeC_6H_4$, **2e** | **5m** | 63 | 69 |
| 14 | MeO, Me, **1b** | $CH_3(CH_2)_6$, **2i** | **5n** | 74 | 86 |
| 15 | Me, Me, **1c** | $CH_3(CH_2)_6$, **2i** | **5o** | 41 | 81 |
| 16 | H, Et, **1d** | *p*-$BrC_6H_4$, **2b** | **5p** | 51 | 89 |
| 17 | H, Et, **1d** | *p*-$MeC_6H_4$, **2e** | **5q** | 60 | 72 |

[a] See footnote in Table 1 for reaction conditions; reaction time: 20–48 h. [b] Yields refer to isolated pure products. [c] Enantiomeric excesses were determined by chiral HPLC analysis.

To illustrate the power of this catalytic enantioselective cascade reaction further, the cyclic enamino esters **7a** and **7b** (Table 3), containing incorporated dimethoxyphenyl systems, were examined under the same reaction conditions as for **1a**–**d**. In all cases the enamino esters **7** reacted smoothly both with aromatic and with aliphatic α,β-unsaturated aldehydes **2** to afford the cyclized benzoquinolizidines **8** in moderate to good yields with excellent enantioselectivities. It is notable that the cyclic enamino esters **7** containing incorporated substituted phenyl systems generally gave the cyclized products with higher enantioselectivities than the enamino esters **1** containing incorporated indolyl systems.

Table 3. Further expansion of substrate scope.[a]




| Entry | $R^1$, **7** | $R^2$, **2** | **8** | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|
| 1 | Me, **7a** | $C_6H_5$, **2a** | **8a** | 65 | 87 |
| 2 | Me, **7a** | *p*-$BrC_6H_4$, **2b** | **8b** | 71 | 92 |
| 3 | Me, **7a** | *p*-$FC_6H_4$, **2c** | **8c** | 74 | 95 |
| 4 | Me, **7a** | *o*-$MeOC_6H_4$, **2d** | **8d** | 54 | 93 |
| 5 | Me, **7a** | *p*-$MeC_6H_4$, **2e** | **8e** | 56 | 91 |
| 6 | Me, **7a** | Me, **2f** | **8f** | 54 | 91 |
| 7 | Me, **7a** | Et, **2g** | **8g** | 58 | 95 |
| 8 | Me, **7a** | *n*Pr, **2h** | **8h** | 53 | 93 |
| 9 | Me, **7a** | $CH_3(CH_2)_6$, **2i** | **8i** | 63 | 95 |
| 10 | Et, **7b** | $C_6H_5$, **2a** | **8j** | 74 | 93 |
| 11 | Et, **7b** | *p*-$BrC_6H_4$, **2b** | **8k** | 81 | 93 |
| 12 | Et, **7b** | *p*-$MeC_6H_4$, **2e** | **8l** | 57 | 91 |

[a] See footnote in Table 1 for reaction conditions; reaction time: 20–48 h. [b] Yields refer to isolated pure products. [c] Enantiomeric excesses were determined by chiral HPLC analysis.

The collective results shown above (Tables 2 and 3) indicated that this cascade sequence could tolerate a broad spectrum of substrates. This asymmetric catalyzed cascade sequence, leading to multiply substituted indoloquinolizidines and benzoquinolizidines, which are prevalent structural motifs in alkaloids,[12] should be useful in syntheses of alkaloids of these types.

The stereochemical outcome of this cascade sequence was determined unambiguously by single-crystal X-ray diffraction analysis of **5p** (Figure 2).[13] The absolute configurations of other cyclized products could be assigned by analogy. The stereochemistry at C-2 of **5p** is that resulting

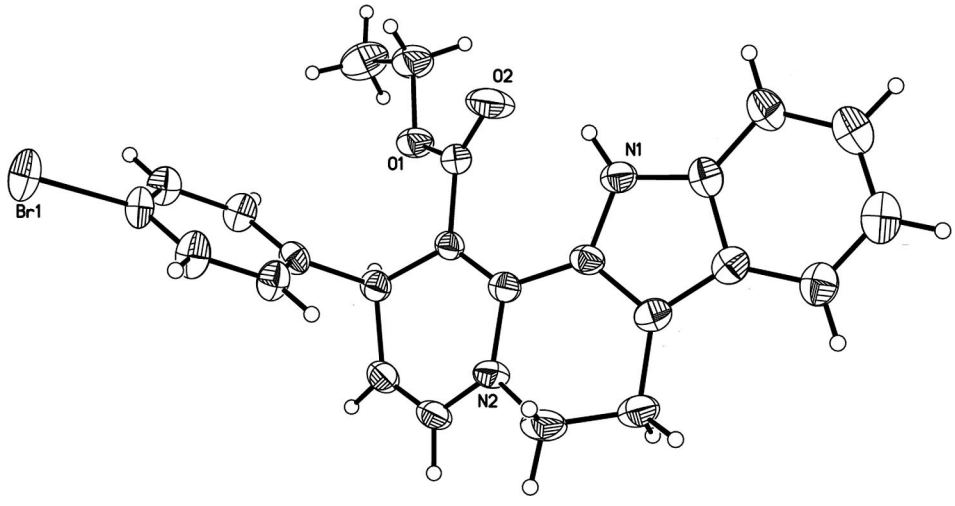



Figure 2. X-ray structure of **5p**.

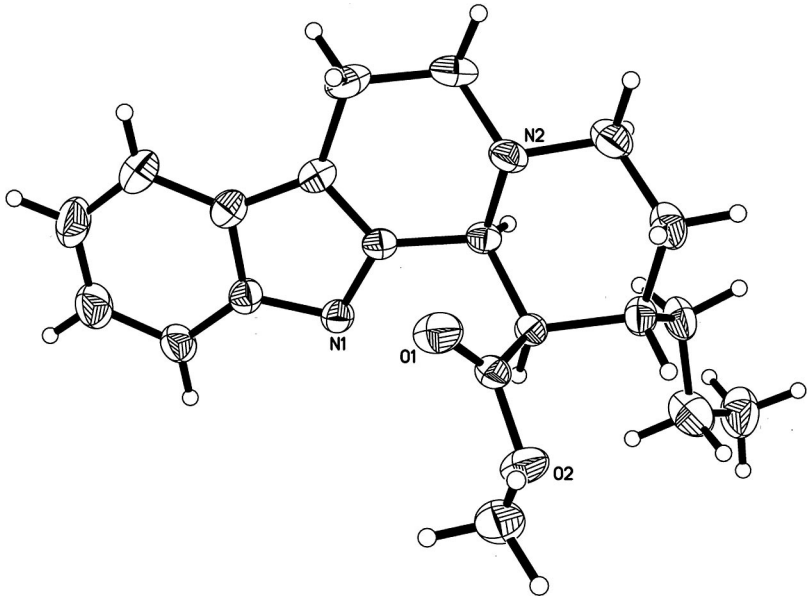
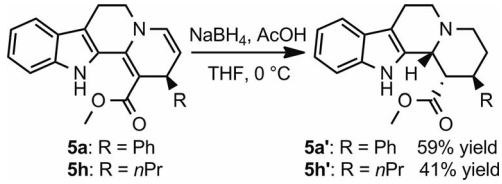



Figure 3. Relative stereochemistry of **5h′**.

from conjugate addition of the enamino ester **1d** to the α,β-unsaturated iminium intermediate (Scheme 1) from the less hindered *re*-face.

To explore the synthetic potential of our current method, the polycyclic compounds **5a** and **5h** were chosen for further manipulation (Scheme 2). Reduction of the dihydropyridine moieties in **5a** and **5h** to piperidines, with the creation of two new stereochemical centers, was explored. The reduction reactions were carried out with $NaBH_4$ as reductant at 0 °C in THF as solvent in the presence of AcOH.[14] Interestingly, in each case only one out of the four possible diastereomers was predominantly obtained in moderate yield after column chromatography separation. The relative stereochemistry of the reduced products was assigned by single-crystal X-ray diffraction analysis of **5h′** (Figure 3).[13]




Scheme 2. Further transformation of **5a** and **5h**.

## Conclusions

We have demonstrated that cyclic enamino esters can be also employed as nucleophiles in asymmetric iminium organocatalysis. Conjugate additions of cyclic enamino esters to α,β-unsaturated aldehydes were catalyzed by chiral secondary amines in the presence of acid additives. After release of the catalyst from the intermediate and subsequent cyclization, a series of highly substituted indoloquinolizidines and benzoquinolizidines were easily obtained in moderate to good yields and with good to excellent enantioselectivities.

## Experimental Section

**General Information:** Thin-layer chromatography (TLC) was carried out on 0.25 mm silica gel plates with visualization with UV light and/or by staining with ethanolic phosphomolybdic acid (PMA) or iodine. Flash column chromatography was performed on silica gel H (10–40 μm). NMR spectra were recorded with a Bruker AM 500 instrument (500 MHz). Chemical shifts ($\delta$) are given in ppm relative to TMS, coupling constants ($J$) in Hz. Optical rotations were recorded with a JASCO P1030 instrument. High-resolution mass spectra were recorded with a Bruker ApeXIII 7.0 TESLA FTMS instrument. Enantiomeric excesses were determined by chiral HPLC with Waters or Shimadzu instruments.

**Syntheses of the Cyclic Enaminoesters 1a–d and 7a–b:** These substrates were prepared according to a literature procedure[9] and purified by silica gel column chromatography with elution with hexane/ethyl acetate.

**Methyl 2-(3,4-Dihydro-2*H*-pyrido[3,4-*b*]indol-1(9*H*)-ylidene)acetate (1a):**[15a] $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 8.30 (s, 1 H), 8.14 (s, 1 H), 7.57 (d, $J$ = 8.0 Hz, 1 H), 7.38 (d, $J$ = 8.2 Hz, 1 H), 7.31–7.26 (m, 1 H), 7.18–7.11 (m, 1 H), 4.90 (s, 1 H), 3.71 (s, 3 H), 3.57 (td, $J$ = 6.8, 2.6 Hz, 2 H), 3.00 (t, $J$ = 6.8 Hz, 2 H) ppm.

**Methyl 2-{6-Methoxy-3,4-dihydro-2*H*-pyrido[3,4-*b*]indol-1(9*H*)-ylidene}acetate (1b):** $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 8.30 (s, 1 H), 8.02 (s, 1 H), 7.30–7.26 (m, 1 H), 6.95 (dt, $J$ = 8.7, 2.4 Hz, 2 H), 4.87 (s, 1 H), 3.89–3.84 (m, 3 H), 3.70 (s, 3 H), 3.57 (td, $J$ = 6.8 and 2.6 Hz, 2 H), 2.96 (t, $J$ = 6.8 Hz, 2 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 171.1, 154.5, 150.9, 132.5, 128.5, 126.4, 115.7, 115.5, 112.6, 100.6, 55.8, 50.5, 40.6, 20.7 ppm. HRMS (ESI): calcd. for $C_{15}H_{17}N_2O_3$ 273.1233; found 273.1242.

**Methyl 2-{6-Methyl-3,4-dihydro-2*H*-pyrido[3,4-*b*]indol-1(9*H*)-ylidene}acetate (1c):** $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 8.29 (s, 1 H), 8.02 (s, 1 H), 7.35 (d, $J$ = 0.7 Hz, 1 H), 7.28 (s, 1 H), 7.11 (dd, $J$ =

8.4, 1.3 Hz, 1 H), 4.87 (s, 1 H), 3.70 (s, 3 H), 3.56 (td, $J$ = 6.8, 2.5 Hz, 2 H), 2.96 (t, $J$ = 6.8 Hz, 2 H), 2.45 (s, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 171.1, 150.9, 135.6, 129.7, 127.8, 126.5, 119.1, 115.7, 111. 3, 50.5, 40.6, 21.5, 20.7 ppm. HRMS (ESI): calcd. for $C_{19}H_{22}NO_4$ 257.1285; found 257.1287.

**Ethyl 2-{3,4-Dihydro-2*H*-pyrido[3,4-*b*]indol-1(9*H*)-ylidene}acetate (1d):**[15b] $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 8.30 (s, 1 H), 8.13 (s, 1 H), 7.57 (d, $J$ = 7.9 Hz, 1 H), 7.37 (d, $J$ = 8.2 Hz, 1 H), 7.29 (dd, $J$ = 11.7, 4.6 Hz, 1 H), 4.89 (s, 1 H), 4.17 (q, $J$ = 7.1 Hz, 2 H), 3.57 (td, $J$ = 6.8, 2.5 Hz, 2 H), 2.99 (t, $J$ = 6.8 Hz, 2 H), 1.30 (t, $J$ = 7.1 Hz, 3 H) ppm.

**Methyl 2-[6,7-Dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-ylidene]acetate (7a):** $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 9.00 (s, 1 H), 7.11 (s, 1 H), 6.66 (s, 1 H), 5.05 (s, 1 H), 3.90 (d, $J$ = 9.9 Hz, 6 H), 3.70 (s, 3 H), 3.42 (td, $J$ = 6.4, 3.2 Hz, 2 H), 2.83 (t, $J$ = 6.4 Hz, 2 H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ = 171.47, 156.49, 151.07, 147.83, 130.00, 121.52, 110.61, 108.01, 56.05, 55.97, 50.24, 38.93, 28.53 ppm.

**Ethyl 2-[6,7-Dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-ylidene]acetate (7b):**[15c] $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 9.03 (s, 1 H), 7.12 (s, 1 H), 6.65 (s, 1 H), 5.05 (s, 1 H), 4.16 (q, $J$ = 7.1 Hz, 2 H), 3.89 (d, $J$ = 8.4 Hz, 6 H), 3.42 (td, $J$ = 6.4, 3.2 Hz, 2 H), 2.82 (t, $J$ = 6.4 Hz, 2 H), 1.30 (t, $J$ = 7.1 Hz, 3 H) ppm.

**Typical Asymmetric Organocatalyzed Cascade Reaction Procedure:** The α,β-unsaturated aldehyde **2a** (0.12 mmol, 1.2 equiv.) was added under Ar with stirring to a solution of the cyclic enamino ester **1a** (0.1 mmol, 1.0 equiv.) in toluene (0.6 mL). After the mixture had been cooled to –20 °C, the catalyst **6a** (0.1 mmol, 0.1 equiv.) and benzoic acid (0.1 mmol, 0.1 equiv.) were added. The reaction was monitored by TLC. After complete consumption of **1a**, the reaction mixture was loaded directly onto a silica gel column and eluted with hexane/ethyl acetate to afford **5a** as a white solid in 72% yield with 86% *ee*.

**Methyl (*S*)-2-Phenyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5a):** $[\alpha]_D^{25}$ = –79.29 ($c$ = 1.13, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.24 (s, 1 H), 7.54 (d, $J$ = 8 Hz, 1 H), 7.41 (d, $J$ = 8 Hz, 1 H), 7.21–7.25 (m, 5 H), 7.13–7.17 (m, 1 H), 7.10 (t, $J$ = 8 Hz, 1 H), 6.13 (d, $J$ = 7 Hz, 1 H), 5.13 (t, $J$ = 7 Hz, 1 H), 4.73 (d, $J$ = 7 Hz, 1 H), 3.78–3.73 (m, 1 H), 3.69 (s, 3 H), 3.64–3.67 (m, 1 H), 3.00–3.09 (m, 2 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 148.0, 143.0, 136.3, 130.3, 128.5, 127.2, 127.0, 126.3, 125.0, 124.3, 119.7, 118.9, 115.7, 112.3, 107.3, 96.2, 51.8, 51.3, 39.9, 20.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{19}N_2O_2$ 355.1441; found 355.1457. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 8.64 min (minor enantiomer), $t_R$ = 12.19 min (major enantiomer).

**Methyl (*S*)-2-(4-Bromophenyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5b):** $[\alpha]_D^{25}$ = –75.79 ($c$ = 1.03, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.24 (s, 1 H), 7.56 (d, $J$ = 8 Hz, 1 H), 7.44 (d, $J$ = 8 Hz, 1 H), 7.38 (d, $J$ = 9 Hz, 2 H), 7.27 (t, $J$ = 8 Hz, 1 H), 7.15 (d, $J$ = 9 Hz, 2 H), 7.12 (t, $J$ = 8 Hz, 1 H), 6.15 (d, $J$ = 7 Hz, 1 H), 5.11 (t, $J$ = 7 Hz, 1 H), 4.71 (d, $J$ = 7 Hz, 1 H), 3.78–3.73 (m, 1 H), 3.71 (s, 3 H), 3.68–3.65 (m, 1 H), 3.05–2.95 (m, 2 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 147.0, 143.1, 136.3, 131.5, 130.5, 128.8, 127.0, 125.0, 124.4, 120.0, 119.8, 119.0, 115.9, 112.3, 106.8, 95.7, 51.8, 51.3, 39.5, 21.7 ppm. HRMS (ESI): calcd. for $C_{23}H_{18}BrN_2O_2$ 433.0546; found 433.0566. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 9.63 min (minor enantiomer), $t_R$ = 12.82 min (major enantiomer).

**Methyl (*S*)-2-(4-Fluorophenyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5c):** $[\alpha]_D^{25}$ = –229.35 ($c$ = 0.58, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.23 (s, 1 H), 7.56 (d, $J$ = 8 Hz, 1 H), 7.43 (d, $J$ = 8 Hz, 1 H), 7.25–7.20 (m, 3 H), 7.11 (t, $J$ = 8 Hz, 1 H), 6.94 (t, $J$ = 9 Hz, 2 H), 6.16 (d, $J$ = 7 Hz, 1 H), 5.12 (t, $J$ = 7 Hz, 1 H), 4.72 (d, $J$ = 7 Hz, 1 H), 3.73–3.81 (m, 1 H), 3.71 (s, 3 H), 3.66–3.71 (m, 1 H), 2.95–3.13 (m, 2 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 143.0, 142.9, 136.3, 130.4, 128.5, 128.4, 127.0, 125.0, 124.4, 119.7, 119.0, 115.8, 115.2, 115.1, 112.3, 107.1, 96.2, 51.8, 51.3, 39.2, 20.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{18}FN_2O_2$ 373.1347; found 373.1359. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 8.10 min (minor enantiomer), $t_R$ = 11.46 min (major enantiomer).

**Methyl (*S*)-2-(2-Methoxyphenyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]-quinolizine-1-carboxylate (5d):** $[\alpha]_D^{25}$ = –274.64 ($c$ = 0.63, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.37 (s, 1 H), 7.57 (d, $J$ = 8 Hz, 1 H), 7.47 (d, $J$ = 8 Hz, 1 H), 7.24–7.29 (m, 1 H), 7.09–7.18 (m, 3 H), 6.81–6.85 (m, 2 H), 6.04 (d, $J$ = 7 Hz, 1 H), 5.28 (t, $J$ = 7 Hz, 1 H), 5.11 (d, $J$ = 7 Hz, 1 H), 3.88 (s, 3 H), 3.68–3.73 (m, 1 H), 3.64 (s, 3 H), 3.60–3.63 (m, 1 H), 2.99–3.10 (m, 2 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.8, 155.7, 143.9, 136.3, 135.5, 130.2, 127.5, 127.3, 127.1, 125.1, 124.2, 120.9, 119.7, 118.9, 115.5, 112.4, 110.5, 106.9, 94.0, 55.5, 51.9, 51.1, 33.9, 20.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{21}N_2O_3$ 385.1547; found 385.1557. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 9.30 min (minor enantiomer), $t_R$ = 12.44 min (major enantiomer).

**Methyl (*S*)-2-(*p*-Tolyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5e):** $[\alpha]_D^{25}$ = –89.42 ($c$ = 0.57, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.26 (s, 1 H), 7.56 (d, $J$ = 8 Hz, 1 H), 7.44 (d, $J$ = 8 Hz, 1 H), 7.27–7.25 (m, 1 H), 7.17 (d, $J$ = 8 Hz, 2 H), 7.10–7.14 (m, 1 H), 7.08 (d, $J$ = 8 Hz, 2 H), 6.14 (d, $J$ = 7 Hz, 1 H), 5.14 (t, $J$ = 7 Hz, 1 H), 4.71 (d, $J$ = 7 Hz, 1 H), 3.74–3.80 (m, 1 H), 3.71 (s, 3 H), 3.65–3.70 (m, 1 H), 2.98–3.12 (m, 2 H), 2.30 (s, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 145.1, 142.8, 136.3, 135.8, 130.2, 129.2, 127.3, 126.9, 125.1, 124.2, 119.7, 118.9, 115.7, 112.3, 107.5, 96.3, 51.8, 51.3, 39.4, 21.1, 20.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{21}N_2O_2$: 369.1598; found 369.1610. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 7.48 min (minor enantiomer), $t_R$ = 9.50 min (major enantiomer).

**Methyl (*R*)-2-Methyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5f):** $[\alpha]_D^{25}$ = –43.33 ($c$ = 0.33, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.27 (s, 1 H), 7.54 (d, $J$ = 8 Hz, 1 H), 7.44 (d, $J$ = 8 Hz, 1 H), 7.25 (t, $J$ = 8 Hz, 1 H), 7.11 (t, $J$ = 8 Hz, 1 H), 6.08 (d, $J$ = 7 Hz, 1 H), 5.03 (t, $J$ = 7 Hz, 1 H), 3.80 (s, 3 H), 3.73–3.76 (m, 1 H), 3.61–3.68 (m, 1 H), 3.48–3.56 (m, 1 H), 2.89–3.10 (m, 2 H), 1.02 (d, $J$ = 6.6 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 143.1, 136.2, 130.6, 127.6, 125.1, 124.1, 119.6, 118.9, 115.1, 112.3, 108.5, 97.7, 51.8, 50.9, 28.5, 23.6, 20.9 ppm. HRMS (ESI): calcd. for $C_{18}H_{17}N_2O_2$ 293.1285; found 293.1294. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 6.10 min (minor enantiomer), $t_R$ = 8.63 min (major enantiomer).

**Methyl (*R*)-2-Ethyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5g):** $[\alpha]_D^{25}$ = –166.85 ($c$ = 0.28, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.27 (s, 1 H), 7.53 (d, $J$ = 8 Hz, 1 H), 7.44 (d, $J$ = 8 Hz, 1 H), 7.24 (t, $J$ = 8 Hz, 1 H), 7.12 (t, $J$ = 8 Hz, 1 H), 6.13 (d, $J$ = 7 Hz, 1 H), 5.02 (t, $J$ = 7 Hz, 1 H), 3.79 (s, 3 H), 3.77–3.74 (m, 1 H), 3.68–3.61 (m, 1 H), 3.47 (m, 1 H), 3.01–3.07 (m, 1 H), 2.93–2.98 (m, 1 H), 1.28–1.22 (m, 2 H), 0.86 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.8, 143.3, 136.1, 131.1, 127.5, 125.1, 124.0, 119.6, 118.8, 115.1, 112.3, 106.6, 96.1, 51.7,

50.8, 34.7, 30.4, 20.8, 9.4 ppm. HRMS (ESI): calcd. for $C_{19}H_{19}N_2O_2$ 307.1441; found 307.1451. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 5.90 min (minor enantiomer), $t_R$ = 8.32 min (major enantiomer).

**Methyl (*R*)-2-Propyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5h):** $[a]_D^{25}$ = –162.50 ($c$ = 0.28, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.27 (s, 1 H), 7.53 (d, $J$ = 8 Hz, 1 H), 7.44 (d, $J$ = 8 Hz, 1 H), 7.24 (t, $J$ = 8 Hz, 1 H), 7.10 (t, $J$ = 8 Hz, 1 H), 6.11 (d, $J$ = 7 Hz, 1 H), 5.04 (t, $J$ = 7 Hz, 1 H), 3.79 (s, 3 H), 3.78–3.72 (m, 1 H), 3.63 (m, 1 H), 3.52 (m, 1 H), 2.85–3.10 (m, 2 H), 1.32–1.39 (m, 2 H), 1.25–1.32 (m, 4 H), 0.88 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.7, 143.2, 136.1, 130.9, 127.5, 125.1, 124.0, 119.6, 118.8, 115.0, 112.3, 107.1, 96.5, 51.7, 50.8, 40.3, 33.1, 20.9, 18.1, 14.2 ppm. HRMS (ESI): calcd. for $C_{20}H_{21}N_2O_2$ 321.1598; found 321.1601. HPLC (Phenomenex Chiralpak amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 5.63 min (minor enantiomer), $t_R$ = 8.32 min (major enantiomer).

**Methyl (*R*)-2-Heptyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5i):** $[a]_D^{25}$ = –125.67 ($c$ = 0.93, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.29 (s, 1 H), 7.54 (d, $J$ = 8 Hz, 1 H), 7.45 (d, $J$ = 8 Hz, 1 H), 7.25 (t, $J$ = 8 Hz, 1 H), 7.10 (t, $J$ = 8 Hz, 1 H), 6.11 (d, $J$ = 7.5 Hz, 1 H), 5.05 (t, $J$ = 7.5 Hz, 1 H), 3.79 (s, 3 H), 3.72–3.78 (m, 1 H), 3.61–3.65 (m, 1 H), 3.47–3.53 (m, 1 H), 3.02–3.05 (m, 1 H), 2.92–2.99 (m, 1 H), 1.42–1.15 (m, 12 H), 0.85 (t, $J$ = 7.4 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.8, 143.2, 136.2, 130.9, 127.5, 125.1, 124.0, 119.6, 118.8, 115.0, 112.3, 107.2, 96.6, 51.7, 50.8, 38.0, 33.3, 32.0, 29.7, 29.4, 25.0, 22.7, 20.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{24}H_{29}N_2O_2$ 377.2224; found 377.2234. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 4.97 min (minor enantiomer), $t_R$ = 7.87 min (major enantiomer).

**Methyl (*S*)-2-(4-Bromophenyl)-9-methoxy-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5j):** $[a]_D^{25}$ = –192.18 ($c$ = 1.1, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.21 (s, 1 H), 7.37 (d, $J$ = 8.5 Hz, 2 H), 7.33 (d, $J$ = 8 Hz, 1 H), 7.14 (d, $J$ = 8.5 Hz, 2 H), 6.91–6.96 (m, 2 H), 6.14 (d, $J$ = 7 Hz, 1 H), 5.10 (t, $J$ = 7 Hz, 1 H), 4.70 (d, $J$ = 7 Hz, 1 H), 3.87 (s, 3 H), 3.71–3.76 (m, 1 H), 3.69 (s, 3 H), 3.63–3.67 (m, 1 H), 2.98–3.01 (m, 2 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 154.2, 147.0, 143.2, 132.4, 131.5, 130.5, 129.8, 129.0, 128.8, 127.5, 125.1, 120.0, 115.4, 113.3, 106.8, 99.5, 55.8, 51.8,51.3, 39.4, 20.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{20}BrN_2O_3$ 463.0652; found 463.0671. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 17.47 min (minor enantiomer), $t_R$ = 22.07 min (major enantiomer).

**Methyl (*S*)-2-(4-Bromophenyl)-9-methyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5k):** $[a]_D^{25}$ = –220.46 ($c$ = 0.73, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.14 (s, 1 H), 7.38 (d, $J$ = 8.5 Hz, 2 H), 7.31–7.35 (m, 2 H), 7.15 (d, $J$ = 8.5 Hz, 2 H), 7.08–7.12 (m, 1 H), 6.14 (d, $J$ = 7 Hz, 1 H), 5.10 (t, $J$ = 7 Hz, 1 H), 4.70 (d, $J$ = 7 Hz, 1 H), 3.73–3.77 (m, 1 H), 3.70 (s, 3 H), 3.65–3.68 (m, 1 H), 2.97–3.02 (m, 2 H), 2.46 (s, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 147.1, 143.2, 134.8, 131.5, 130.6, 129.1, 128.8, 127.0, 126.4, 125.2, 120.0, 118.3, 115.5, 112.0, 106.7, 100.0, 95.4, 51.8, 51.4, 39.5, 21.6, 20.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{20}B_rN_2O_2$ 447.0703; found 447.0720. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 8.79 min (minor enantiomer), $t_R$ = 12.28 min (major enantiomer).

**Methyl (*S*)-9-Methoxy-2-(*p*-tolyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]-quinolizine-1-carboxylate (5l):** $[a]_D^{25}$ = –83.43 ($c$ = 0.83, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.26 (s, 1 H), 7.35 (d, $J$ = 10 Hz, 1 H), 7.19 (d, $J$ = 8.5 Hz, 2 H), 7.10 (d, $J$ = 8.5 Hz, 2 H), 6.93–6.98 (m, 2 H), 6.16 (d, $J$ = 7 Hz, 1 H), 5.16 (t, $J$ = 7 Hz, 1 H), 4.72 (d, $J$ = 7 Hz, 1 H), 3.89 (s, 3 H), 3.76–3.79 (m, 1 H), 3.72 (s, 3 H), 3.66–3.72 (m, 1 H), 2.97–3.11 (m, 2 H), 2.32 (s, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 145.1, 143.0, 135.8, 131.6, 130.2, 129.9, 129.2, 128.6, 127.8, 126.9, 125.1, 115.4, 115.1, 113.3, 107.5, 99.5, 55.8, 51.8, 51.3, 39.4, 21.1, 20.9 ppm. HRMS (ESI): calcd. for $C_{25}H_{23}N_2O_3$ 399.1703; found 399.1695. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 14.37 min (minor enantiomer), $t_R$ = 17.82 min (major enantiomer).

**Methyl (*S*)-9-Methyl-2-(*p*-tolyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]-quinolizine-1-carboxylate (5m):** $[a]_D^{25}$ = –116.42 ($c$ = 0.67, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.14 (s, 1 H), 7.30–7.35 (m, 2 H), 7.16 (d, $J$ = 8 Hz, 2 H), 7.05–7.10 (m, 3 H), 6.13 (d, $J$ = 7 Hz, 1 H), 5.13 (t, $J$ = 7 Hz, 1 H), 4.70 (d, $J$ = 7 Hz, 1 H), 3.79–3.72 (m, 1 H), 3.70 (s, 3 H), 3.69–3.61 (m, 1 H), 3.09–2.89 (m, 2 H), 2.45 (s, 3 H), 2.29 (s, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 145.2, 143.0, 135.8, 134.7, 130.2, 129.2, 128.9, 127.3, 126.9, 126.1, 125.2, 118.3, 115.2, 112.0, 107.4, 96.0, 64.3, 51.7, 51.3, 39.4, 21.6, 21.1 ppm. HRMS (ESI): calcd. for $C_{25}H_{23}N_2O_2$ 383.1754; found 383.1766. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 7.81 min (minor enantiomer), $t_R$ = 10.92 min (major enantiomer).

**Methyl (*R*)-2-Heptyl-9-methoxy-2,6,7,12-tetrahydroindolo[2,3-*a*]-quinolizine-1-carboxylate (5n):** $[a]_D^{25}$ = –256.61 ($c$ = 0.61, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.25 (s, 1 H), 7.34 (d, $J$ = 10 Hz, 1 H), 6.90–6.95 (m, 2 H), 6.10 (d, $J$ = 7 Hz, 1 H), 5.04 (t, $J$ = 7 Hz, 1 H), 3.86 (s, 3 H), 3.78 (s, 1 H), 3.71–3.77 (m, 1 H), 3.59–3.66 (m, 1 H), 3.48–3.53 (m, 1 H), 2.94–3.01 (m, 1 H), 2.89–2.92 (m, 1 H), 1.36–1.19 (m, 12 H), 0.87 (t, $J$ = 7.0 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.7, 154.1, 143.2, 131.5, 130.9, 128.0, 125.2, 115.1, 114.5, 113.2, 107.2, 99.5, 96.3, 55.8, 51.7, 50.9, 38.0, 33.2, 32.0, 29.7, 29.4, 25.0, 22.7, 20.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{25}H_{31}N_2O_3$ 407.2329; found 407.2344. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 8.52 min (minor enantiomer), $t_R$ = 13.06 min (major enantiomer).

**Methyl (*R*)-2-Heptyl-9-methyl-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5o):** $[a]_D^{25}$ = –325.27 ($c$ = 0.61, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.17 (s, 1 H), 7.35 (d, $J$ = 8.5 Hz, 1 H), 7.30 (s, 1 H), 7.07 (d, $J$ = 8.5 Hz, 1 H), 6.10 (d, $J$ = 7.5 Hz, 1 H), 5.04 (t, $J$ = 7.5 Hz, 1 H), 3.78 (s, 3 H), 3.71–3.77 (m, 1 H), 3.62–3.66 (m, 1 H), 3.48–3.53 (m, 1 H), 2.45 (s, 3 H), 1.34–1.21 (m, 12 H), 0.87 (t, $J$ = 7.0 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.7, 143.3, 134.6, 130.9, 128.8, 127.6, 125.9, 125.3, 118.2, 114.6, 111.9, 107.1, 96.3, 51.6, 50.9, 38.0, 33.3, 32.0, 29.7, 29.4, 25.0, 22.7, 21.6, 20.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{25}H_{31}N_2O_2$ 391.2380; found 391.2392. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 5.08 min (minor enantiomer), $t_R$ = 8.50 min (major enantiomer).

**Ethyl (*S*)-2-(4-Bromophenyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5p):** $[a]_D^{25}$ = –89.46 ($c$ = 0.52, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.29 (s, 1 H), 7.56 (d, $J$ = 8 Hz, 1 H), 7.43 (d, $J$ = 8 Hz, 1 H), 7.38 (d, $J$ = 8.5 Hz, 2 H), 7.27 (t, $J$ = 8 Hz, 1 H), 7.16 (d, $J$ = 8.5 Hz, 2 H), 7.12 (t, $J$ = 8 Hz, 1 H), 6.15 (d, $J$ = 7 Hz, 1 H), 5.07 (t, $J$ = 7 Hz, 1 H), 4.73 (d, $J$ = 7 Hz, 1 H), 4.08–4.22 (m, 2 H), 3.73–3.80 (m, 1 H), 3.65–3.71 (m, 1 H), 2.97–3.19 (m,

2 H), 1.23 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 169.9, 147.3, 142.8, 136.3, 131.4, 130.5, 129.0, 127.1, 125.0, 124.4, 120.0, 119.8, 118.9, 115.8, 112.3, 106.7, 96.3, 60.6, 51.4, 39.8, 20.9, 14.2 ppm. HRMS (ESI): calcd. for $C_{24}H_{20}B_rN_2O_2$ 447.0703; found 447.0720. HPLC (Phenomenex amylose-2, hexane/2-propanol 10:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 8.24 min (minor enantiomer), $t_R$ = 8.75 min (major enantiomer).

**Ethyl (*S*)-2-(*p*-Tolyl)-2,6,7,12-tetrahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5q):** $[\alpha]_D^{25}$ = –128.17 ($c$ = 0.61, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 12.31 (s, 1 H), 7.56 (d, $J$ = 8 Hz, 1 H), 7.43 (d, $J$ = 8 Hz, 1 H), 7.24 (t, $J$ = 8 Hz, 1 H), 7.19 (d, $J$ = 7.5 Hz, 2 H), 7.11 (t, $J$ = 8 Hz, 1 H), 7.07 (d, $J$ = 7.5 Hz, 2 H), 6.14 (d, $J$ = 7 Hz, 1 H), 5.11 (t, $J$ = 7 Hz, 1 H), 4.73 (d, $J$ = 7 Hz, 1 H), 4.07–4.25 (m, 2 H), 3.73–3.82 (m, 1 H), 3.64–3.72 (m, 1 H), 2.97–3.14 (m, 2 H), 2.30 (s, 3 H), 1.25 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.2, 145.4, 142.4, 136.2, 135.8, 130.1, 129.1, 127.3, 127.1, 125.1, 124.1, 119.6, 118.9, 115.5, 112.3, 107.4, 97.0, 60.5, 51.3, 39.7, 21.1, 21.0, 14.2 ppm. HRMS (ESI): calcd. for $C_{25}H_{23}N_2O_2$ 383.1754; found 383.1766. HPLC (Daicel Chiralpak ADH, hexane/2-propanol 4:1, flow rate 0.7 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 6.89 min (minor enantiomer), $t_R$ = 7.66 min (major enantiomer).

**Methyl (*S*)-9,10-Dimethoxy-2-phenyl-6,7-dihydro-2*H*-pyrido[2,1-*a*]-isoquinoline-1-carboxylate (8a):** $[\alpha]_D^{25}$ = –257.76 ($c$ = 0.97, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.35 (d, $J$ = 7.5 Hz, 2 H), 7.30 (t, $J$ = 7.5 Hz, 2 H), 7.19 (t, $J$ = 7.5 Hz, 1 H), 6.92 (s, 1 H), 6.65 (s, 1 H), 6.11 (d, $J$ = 7 Hz, 1 H), 5.02 (t, $J$ = 7 Hz, 1 H), 4.52 (d, $J$ = 7 Hz, 1 H), 3.91 (s, 3 H), 3.77 (s, 3 H), 3.50–3.55 (m, 1 H), 3.49 (s, 3 H), 3.48–3.41 (m, 1 H), 2.95–3.05 (m, 1 H), 2.69 (dt, $J$ = 14.8, 3.5 Hz, 1 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 150.4, 148.4, 146.7, 145.2, 130.4, 129.5, 128.5, 127.2, 126.3, 122.3, 114.3, 109.7, 105.8, 94.5, 56.2, 56.0, 50.9, 49.0, 41.0, 29.5 ppm. HRMS (ESI): calcd. for $C_{23}H_{23}NNaO_4$ 400.1519; found 400.1531. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 17.22 min (minor enantiomer), $t_R$ = 13.19 min (major enantiomer).

**Methyl (*S*)-2-(4-Bromophenyl)-9,10-dimethoxy-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8b):** $[\alpha]_D^{25}$ = –210.45 ($c$ = 0.92, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.40 (d, $J$ = 8 Hz, 2 H), 7.23 (d, $J$ = 8 Hz, 2 H), 6.86 (s, 1 H), 6.64 (s, 1 H), 6.13 (d, $J$ = 7.5 Hz, 1 H), 4.97 (t, $J$ = 7.5 Hz, 1 H), 4.47 (d, $J$ = 7.5 Hz, 1 H), 3.91 (s, 3 H), 3.77 (s, 3 H), 3.52 (dd, $J$ = 12.5, 3 Hz, 1 H), 3.49 (s, 3 H), 3.42–3.48 (m, 1 H), 3.03–2.95 (m, 1 H), 2.68 (dt, $J$ = 12.5, 3 Hz, 1 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.2, 150.5, 147.4, 146.7, 145.3, 131.5, 130.4, 129.8, 129.1, 122.1, 120.0, 114.2, 109.8, 105.2, 94.1, 56.2, 56.0, 50.9, 49.0, 40.5, 29.4 ppm. HRMS (ESI): calcd. for $C_{23}H_{21}B_rNO_4$ 454.0649; found 454.0665. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 20.64 min (minor enantiomer), $t_R$ = 12.18 min (major enantiomer).

**Methyl (*S*)-2-(4-Fluorophenyl)-9,10-dimethoxy-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8c):** $[\alpha]_D^{25}$ = –329.13 ($c$ = 0.79, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.30 (dd, $J$ = 8.5, 4.5 Hz, 2 H), 6.96 (t, $J$ = 8.5 Hz, 2 H), 6.87 (s, 1 H), 6.64 (s, 1 H), 6.12 (d, $J$ = 7.5 Hz, 1 H), 4.99 (t, $J$ = 7.5 Hz, 1 H), 4.49 (d, $J$ = 6.2 Hz, 1 H), 3.91 (s, 3 H), 3.77 (s, 3 H), 3.52 (td, $J$ = 12.5, 3 Hz, 1 H), 3.49 (s, 3 H), 3.42–3.48 (m, 1 H), 2.95–3.04 (m, 1 H), 2.68 (dt, $J$ = 12.5, 3.5 Hz, 1 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 150.5, 146.7, 145.1, 144.2, 130.4, 129.6, 128.7, 128.6, 122.2, 115.2, 114.2, 109.8, 105.6, 94.6, 56.2, 56.0, 50.9, 48.9, 40.3, 29.5 ppm. HRMS (ESI): calcd. for $C_{23}H_{21}FNO_4$ 394.1449; found 394.1463. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 11.24 min (minor enantiomer), $t_R$ = 9.10 min (major enantiomer).

**Methyl (*S*)-9,10-Dimethoxy-2-(2-methoxyphenyl)-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8d):** $[\alpha]_D^{25}$ = –201.21 ($c$ = 0.71, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.22 (dd, $J$ = 7.5, 1.5 Hz, 1 H), 7.16 (td, $J$ = 7.5, 1.5 Hz, 1 H), 7.08 (s, 1 H), 6.89 (t, $J$ = 7.5 Hz, 1 H), 6.87 (d, $J$ = 7.5 Hz, 1 H), 6.67 (s, 1 H), 5.96 (d, $J$ = 7.5 Hz, 1 H), 5.13 (d, $J$ = 7.5 Hz, 1 H), 4.93 (d, $J$ = 7.5 Hz, 1 H), 3.93 (s, 3 H), 3.87 (s, 3 H), 3.82 (s, 3 H), 3.49 (s, 3 H), 3.43–3.48 (m, 1 H), 3.33–3.43 (m, 1 H), 2.95–3.04 (m, 1 H), 2.68 (dt, $J$ = 15, 4 Hz, 1 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 155.6, 150.4, 146.7, 146.2, 136.1, 130.4, 129.2, 127.9, 127.1, 122.3, 121.0, 114.2, 110.6, 109.8, 105.8, 92.3, 56.2, 56.0, 55.6, 50.9, 48.9, 34.8, 29.5 ppm. HRMS (ESI): calcd. for $C_{24}H_{24}NO_5$ 406.1649; found 406.1661. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 11.57 min (minor enantiomer), $t_R$ = 9.67 min (major enantiomer).

**Methyl (*S*)-9,10-Dimethoxy-2-(*p*-tolyl)-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8e):** $[\alpha]_D^{25}$ = –285.45 ($c$ = 0.57, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.24 (d, $J$ = 8 Hz, 2 H), 7.11 (t, $J$ = 8 Hz, 2 H), 6.94 (s, 1 H), 6.64 (s, 1 H), 6.09 (d, $J$ = 7.5 Hz, 1 H), 5.00 (dd, $J$ = 7.5, 6.5 Hz, 1 H), 4.47 (d, $J$ = 6.5 Hz, 1 H), 3.91 (s, 3 H), 3.77 (s, 3 H), 3.50–3.55 (m, 1 H), 3.49 (s, 3 H), 3.41–3.48 (m, 1 H), 2.95–3.03 (m, 1 H), 2.68 (dt, $J$ = 15, 3.5 Hz, 1 H), 2.37 (s, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.3, 150.3, 146.6, 145.6, 145.1, 135.8, 130.3, 129.3, 129.2, 127.0, 122.3, 114.3, 109.7, 106.0, 94.7, 56.2, 56.0, 50.9, 49.0, 40.7, 29.5, 21.1 ppm. HRMS (ESI): calcd. for $C_{24}H_{24}NO_4$ 390.1700; found 390.1701. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 15.01 min (minor enantiomer), $t_R$ = 9.28 min (major enantiomer).

**Methyl (*R*)-9,10-Dimethoxy-2-methyl-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8f):** $[\alpha]_D^{25}$ = –14.38 ($c$ = 0.51, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 6.91 (s, 1 H), 6.61 (s, 1 H), 5.98 (d, $J$ = 7.4 Hz, 1 H), 4.86 (dd, $J$ = 7.4, 6.2 Hz, 1 H), 3.90 (s, 3 H), 3.83 (s, 3 H), 3.54 (s, 3 H), 3.48 (td, $J$ = 12.5, 3 Hz, 1 H), 3.43–3.36 (m, 1 H), 3.37–3.42 (m, 1 H), 3.27–3.34 (m, 1 H), 2.88–2.97 (m, 1 H), 2.62 (dt, $J$ = 15, 3.5 Hz, 1 H), 1.10 (d, $J$ = 6 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 150.1, 146.6, 130.2, 129.6, 122.5, 114.0, 109.7, 106.7, 93.9, 56.1, 55.9, 50.8, 48.9, 30.0, 29.5, 24.4 ppm. HRMS (ESI): calcd. for $C_{18}H_{20}NO_4$ 314.1387; found 314.1387. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 8.29 min (minor enantiomer), $t_R$ = 7.00 min (major enantiomer).

**Methyl (*R*)-2-Ethyl-9,10-dimethoxy-6,7-dihydro-2*H*-pyrido[2,1-*a*]-isoquinoline-1-carboxylate (8g):** $[\alpha]_D^{25}$ = –189.40 ($c$ = 0.28, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 6.95 (s, 1 H), 6.64 (s, 1 H), 6.07 (d, $J$ = 7.5 Hz, 1 H), 4.88 (dd, $J$ = 7.5, 6 Hz, 1 H), 3.93 (s, 3 H), 3.85 (s, 3 H), 3.56 (s, 3 H), 3.37–3.53 (m, 2 H), 3.24–3.29 (m, 1 H), 2.91–3.01 (m, 1 H), 2.64 (dt, $J$ = 15, 3.5 Hz, 1 H), 1.40–1.55 (m, 2 H), 0.92 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 150.1, 146.6, 145.5, 130.2, 130.1, 122.5, 114.1, 109.7, 104.9, 93.9, 56.1, 55.9, 50.8, 48.8, 36.0, 30.8, 29.5, 9.1 ppm. HRMS (ESI): calcd. for $C_{19}H_{22}NO_4$ 328.1543; found 328.1553. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 7.74 min (minor enantiomer), $t_R$ = 6.69 min (major enantiomer).

**Methyl (*R*)-9,10-Dimethoxy-2-propyl-6,7-dihydro-2*H*-pyrido[2,1-*a*]-isoquinoline-1-carboxylate (8h):** $[\alpha]_D^{25}$ = –177.35 ($c$ = 0.46, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 6.91 (s, 1 H), 6.61 (s, 1 H), 6.02 (d, $J$ = 7 Hz, 1 H), 4.88 (dd, $J$ = 7, 6.5 Hz, 1 H), 3.90 (s, 3 H), 3.83 (s, 3 H), 3.37–3.52 (m, 2 H), 3.24–3.29 (m, 1 H), 2.90–2.99 (m, 1

H), 2.61 (dt, $J$ = 15, 3.5 Hz, 1 H), 1.32–1.47 (m, 4 H), 0.91 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 150.1, 146.6, 145.5,130.1, 130.0, 122.5, 114.1, 109.7, 105.5, 94.1, 56.1, 55.9, 50.8, 48.8, 40.7, 34.5, 29.5, 18.0, 14.4 ppm. HRMS (ESI): calcd. for $C_{20}H_{24}NO_4$ 342.1700; found 342.1715. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 7.49 min (minor enantiomer), $t_R$ = 6.22 min (major enantiomer).

**Methyl (*R*)-2-Heptyl-9,10-dimethoxy-6,7-dihydro-2*H*-pyrido[2,1-*a*]-isoquinoline-1-carboxylate (8i):** $[a]_D^{25}$ = –22.21 ($c$ = 0.37, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 6.91 (s, 1 H), 6.61 (s, 1 H), 6.02 (d, $J$ = 7 Hz, 1 H), 4.88 (dd, $J$ = 7, 6.5 Hz, 1 H), 3.90 (s, 3 H), 3.82 (s, 3 H), 3.53 (s, 3 H), 3.48 (td, $J$ = 12, 3 Hz, 1 H), 3.40 (dt, $J$ = 12, 4 Hz, 1 H), 3.25 (q, $J$ = 6 Hz, 1 H), 2.90–2.97 (m, 1 H), 2.61 (dt, $J$ = 15, 3 Hz, 1 H), 1.46–1.37 (m, 3 H), 1.32–1.20 (m, 9 H), 0.85 (t, $J$ = 7.0 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.5, 150.1, 146.6, 145.4, 130.1, 130.0, 122.5, 114.1, 109.7, 105.4, 94.3, 56.1, 55.9, 50.8, 48.8, 38.4, 34.7, 32.0, 29.8, 29.5, 29.4, 24.8, 22.7, 14.2 ppm. HRMS (ESI): calcd. for $C_{24}H_{32}NO_4$ 398.2326; found 398.2338. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 6.83 min (minor enantiomer), $t_R$ = 5.90 min (major enantiomer).

**Ethyl (*S*)-9,10-Dimethoxy-2-phenyl-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8j):** $[a]_D^{25}$ = –457.30 ($c$ = 0.93, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.33–7.38 (m, 2 H), 7.29 (t, $J$ = 8 Hz, 2 H), 7.17 (t, $J$ = 8 Hz, 1 H), 6.95 (s, 1 H), 6.64 (s, 1 H), 6.11 (d, $J$ = 7 Hz, 1 H), 5.00 (dd, $J$ = 7, 6 Hz, 1 H), 4.53 (d, $J$ = 6 Hz, 1 H), 3.93–4.02 (m, 2 H), 3.90 (d, $J$ = 5.0 Hz, 3 H), 3.77 (s, 3 H), 3.41–3.54 (m, 1 H), 2.94–3.03 (m, 1 H), 2.70 (dt, $J$ = 15, 4 Hz, 1 H), 1.01 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 169.9, 150.3, 148.5, 146.6, 144.9, 130.3, 129.5, 128.4, 127.3, 126.2, 122.4, 114.5, 109.7, 105.6, 95.1, 59.6, 56.1, 56.0, 49.0, 41.2, 29.5, 14.1 ppm. HRMS (ESI): calcd. for $C_{24}H_{24}NO_4$ 390.1700; found 390.1702. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 13.55 min (minor enantiomer), $t_R$ = 10.46 min (major enantiomer).

**Ethyl (*S*)-2-(4-Bromophenyl)-9,10-dimethoxy-6,7-dihydro-2*H*-pyrido[2,1-*a*]isoquinoline-1-carboxylate (8k):** $[a]_D^{25}$ = –235.23 ($c$ = 0.37, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.40 (d, $J$ = 7.5 Hz, 2 H), 7.23 (d, $J$ = 7.5 Hz, 2 H), 6.90 (s, 1 H), 6.64 (s, 1 H), 6.12 (d, $J$ = 7.5 Hz, 1 H), 4.96 (dd, $J$ = 7.5, 6.5 Hz, 1 H), 4.48 (d, $J$ = 6.5 Hz, 1 H), 3.91–4.02 (m, 2 H), 3.90 (s, 3 H), 3.76 (s, 3 H), 3.42–3.53 (m, 2 H), 2.96–3.02 (m, 1 H), 2.68 (td, $J$ = 15, 4 Hz, 1 H), 1.01 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 169.8, 150.4, 147.6, 146.6, 145.1, 131.4, 130.3, 129.8, 129.1, 122.2, 112.0, 114.5, 109.8, 105.0, 94.7, 59.7, 56.1, 56.0, 49.0, 40.6, 29.5, 14.1 ppm. HRMS (ESI): calcd. for $C_{24}H_{23}BrNO_4$ 468.0805; found 468.0823. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 20.44 min (minor enantiomer), $t_R$ = 10.60 min (major enantiomer).

**Ethyl (*S*)-9,10-Dimethoxy-2-(*p*-tolyl)-6,7-dihydro-2*H*-pyrido[2,1-*a*]-isoquinoline-1-carboxylate (8l):** $[a]_D^{25}$ = –235.45 ($c$ = 0.65, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.24 (d, $J$ = 8 Hz, 2 H), 7.10 (d, $J$ = 8 Hz, 2 H), 6.95 (s, 1 H), 6.64 (s, 1 H), 6.09 (d, $J$ = 7 Hz, 1 H), 4.99 (dd, $J$ = 7, 6 Hz, 1 H), 4.48 (d, $J$ = 6 Hz, 1 H), 3.92–4.02 (m, 2 H), 3.91 (s, 3 H), 3.77 (s, 3 H), 3.41–3.55 (m, 2 H), 2.95–3.03 (m, 1 H), 2.68 (dt, $J$ = 15, 3.5 Hz, 1 H), 2.31 (s, 3 H), 1.02 (t, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.0, 150.3, 146.5, 145.8, 144.8, 135.7, 130.3, 129.4, 129.2, 127.1, 122.4, 114.5, 109.7, 105.9, 95.2, 59.6, 56.1, 56.0, 49.0, 40.7, 29.6, 21.1, 14.1 ppm. HRMS (ESI): calcd. for $C_{25}H_{26}NO_4$ 404.1856; found 404.1868. HPLC (Phenomenex amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 16.75 min (minor enantiomer), $t_R$ = 8.33 min (major enantiomer).

**Procedure for Reduction of 5a and 5h:** Sodium borohydride (34 mg, 0.855 mmol) and AcOH (0.6 mL) were added at 0 °C to a suspension of **5a** (63 mg, 0.177 mmol) in THF (2 mL). The reaction mixture was stirred at 0 °C for 2 h. The reaction was quenched with aqueous saturated $NH_4Cl$ solution (5 mL) and the mixture extracted with EtOAc (3 × 10 mL). The organic layers were combined and dried with anhydrous $Na_2SO_4$. After concentration under reduced pressure, the residue was purified by flash silica gel chromatography with elution with hexane/ethyl acetate to afford **5a′** as a white solid in 59% yield.

**Methyl (1*S*,2*R*,12b*R*)-2-Phenyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5a′):** $[a]_D^{25}$ = –96.15 ($c$ = 0.13, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 7.88 (s, 1 H), 7.48 (d, $J$ = 7.5 Hz, 1 H), 7.28–7.36 (m, 5 H), 7.21–7.26 (m, 1 H), 7.07–7.16 (m, 2 H), 3.67–3.71 (m, 1 H), 3.43 (t, $J$ = 4 Hz, 1 H), 3.33–3.39 (m, 1 H), 3.25 (dd, $J$ = 11, 5.0 Hz, 1 H), 3.16 (s, 3 H), 2.97–3.12 (m, 3 H), 2.67–2.75 (m, 1 H), 2.50–2.63 (m, 2 H), 1.81–1.87 (m, 1 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 170.6, 142.2, 136.5, 132.0, 128.5, 127.4, 127.3, 126.9, 121.6, 119.5, 118.3, 111.0, 110.2, 62.7, 56.1, 53.9, 51.3, 49.8, 44.2, 25.9, 21.4 ppm. HRMS (ESI): calcd. for $C_{23}H_{25}N_2O_2$ 361.1911; found 361.1921. HPLC (Phenomenex Chiralpak amylose-2, hexane/2-propanol 2:1, flow rate 1.00 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 9.96 min (minor enantiomer), $t_R$ = 11.54 min (major enantiomer).

**Methyl (1*S*,2*R*,12b*R*)-2-Propyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine-1-carboxylate (5h′):** $[a]_D^{25}$ = –588.2 ($c$ = 0.17, $CHCl_3$). $^1$H NMR ($CDCl_3$, 500 MHz): $\delta$ = 9.68 (br., 1 H), 7.48 (d, $J$ = 8 Hz, 1 H), 7.39 (d, $J$ = 8 Hz, 1 H), 7.17 (t, $J$ = 8 Hz, 1 H), 7.10 (t, $J$ = 8 Hz, 1 H), 4.49–4.69 (br., 1 H), 3.80 (s, 3 H), 3.15–3.35 (m, 2 H), 2.98–3.07 (m, 1 H), 2.95 (dd, $J$ = 11, 3.5 Hz, 1 H), 2.85 (td, $J$ = 12, 3.5 Hz, 1 H), 2.61–2.72 (m, 2 H), 1.69–1.91 (m, 2 H), 1.31–1.44 (m, 3 H), 1.08–1.23 (m, 2 H), 0.87 (t, $J$ = 6.5 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$, 125 MHz): $\delta$ = 175.6, 135.6, 130.1, 126.6, 121.8, 119.3, 118.0, 111.5, 107.9, 56.0, 52.5, 51.8, 51.0, 35.4, 32.6, 29.7, 22.0, 19.4, 17.1, 14.2 ppm. HRMS (ESI): calcd. for $C_{20}H_{27}N_2O_2$ 327.2067; found 327.2074. HPLC (AS-H column, hexane/2-propanol 19:1, flow rate 0.5 mL min$^{-1}$, $\lambda$ = 220 nm): $t_R$ = 11.49 min (minor enantiomer), $t_R$ = 16.62 min (major enantiomer).

**Supporting Information** (see footnote on the first page of this article): NMR spectra of **1a**–**d** and **7a**–**b**; NMR spectra and HPLC analysis of the products.

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