Synthesis S. Hildebrandt et al. Paper

# Formal Total Synthesis of (±)-Rhazinal: Evaluating the Radical Approach

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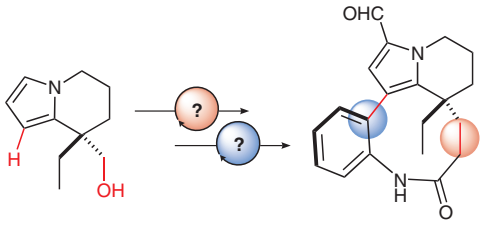


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**Abstract** We describe a formal total synthesis of the racemic natural product rhazinal by a rapid elaboration of a recently reported tetrahydroindolizine intermediate into the cyclization precursor reported by Trauner. The synthesis focuses on the early and convergent introduction of functional groups while the synthetic challenges encountered by this approach are described.

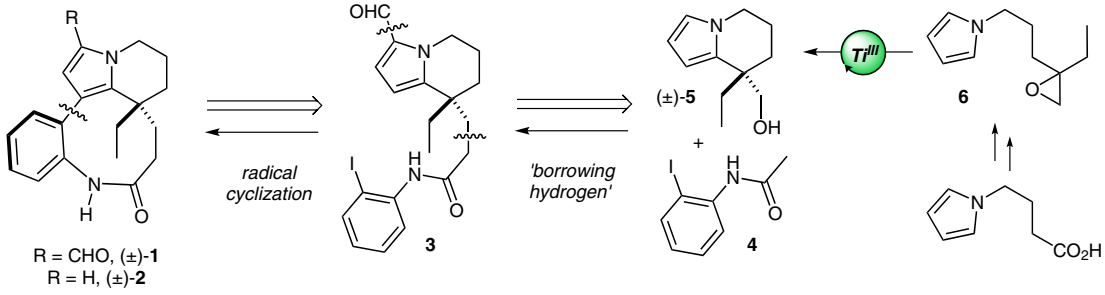
**Key words** rhazinal, natural products, catalysis, radicals, pyrroles

The tetracyclic tetrahydroindolizine alkaloids rhazinal and rhazinilam have attracted considerable attention in the synthetic community as challenging targets for the evaluation of new synthetic methodologies.[1] A recent comprehensive review has summarized the numerous strategies devised for the synthesis of these alkaloids.[2] This article seeks to add a complementary approach to the existing routes that employs modern catalytic methodologies for the efficient synthesis of these natural products.

We recently reported on the catalytic C–H functionalization of pyrroles, proceeding via radical intermediates to construct tetrahydroindolizine scaffolds, as part of our program directed towards the development of efficient catalytic radical reactions.[3,4] By our titanocene(III)-catalyzed transformation we obtained alcohol **5** from epoxide **6** and, ultimately, from the readily available 4-pyrrolylbutanoic acid[5] in a minimum number of operational steps with maximum atom-economy (Scheme 1) and without the formation of undesired side products.

Here, we report an efficient route to the Trauner intermediate **3** starting from **5**.[6] Moreover, we investigated a protecting-group-free radical cyclization of intermediate **3** to form rhazinal (**1**), which would constitute a desirable key step for the construction of the nine-membered lactam.

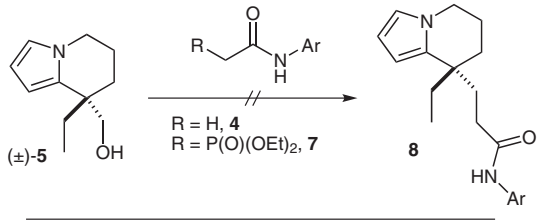
A retrosynthetic analysis of **3** suggests that it can either be accessed via traditional homologation utilizing the Horner–Wadsworth–Emmons (HWE) reaction or through a state-of-the-art 'borrowing hydrogen/hydrogen autotransfer' methodology for the alkylation of **4** with alcohol **5** (Scheme 1).[7] A potential advantage of our approach is the introduction of the unprotected amide functionality that has, as yet, not been realized due to potential reagent or catalyst incompatibilities.




**Scheme 1** Retrosynthesis of rhazinal and rhazinilam employing a radical macrocyclization and the borrowing hydrogen methodology for amide alkylation

Attempts of alkylating 2-iodoacetanilide (**4**) with alcohol **5** were initially conducted with the iridium pincer complex **cat-Ir**, which has been introduced as an efficient alcohol oxidation catalyst under high temperature conditions (Table 1).[8] The strong base KO$^t$Bu facilitates enolate formation and subsequent condensation with the formed aldehyde. Unfortunately, no conversion to **8** could be observed under the conditions investigated (entry 1). Changing the pronucleophile to the corresponding diethyl phosphonate **7** to conduct the condensation under HWE conditions did not lead to any conversion either (entry 2). The recently introduced cobalt catalyst **cat-Co**, which is active under similar conditions, also did not show aldehyde or product formation, even at higher catalyst loadings (entry 3).[9] These findings indicate that the bulky transition-metal catalysts are unable to induce the oxidation of the neopentylic alcohol.

**Table 1** Borrowing Hydrogen/Hydrogen Autotransfer Conditions Examined for the Conversion of Alcohol **5** into Amide **8**[a,b]



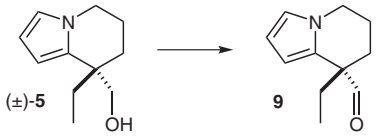

**cat-Ir** **cat-Co**

| Entry | Conditions[b] |
|---|---|
| 1 | **4** (1.5 equiv), KO$^t$Bu (2.5 equiv), **cat-Ir** (2 mol%)[c] |
| 2 | **7** (2 equiv), $K_2CO_3$ (2 equiv), **cat-Ir** (5 mol%)[c] |
| 3 | **4** (3 equiv), KO$^t$Bu (2 equiv), **cat-Co** (15 mol%)[d] |

[a] Ar = 2-iodophenyl; COE = cyclooctene.
[b] No conversion was observed under these conditions.
[c] Toluene, 100 °C, 20 h.
[d] THF, 100 °C, 20 h.

These results foreshadow the problems encountered in the oxidation of **5** to provide **9** when using more common reagents (Table 2). The Dess–Martin periodinane gave unsatisfactory yields under water-accelerated as well as buffered conditions (entries 1 and 2) and the chromium(VI)-based reagents PCC and PDC resulted in an even lower conversion to **9** (entries 3 and 4).[10,11] These reactions were always monitored for complete substrate consumption and, thus, decomposition of the substrate or the product by the reagents employed seems likely. Presumably, this is due to the high nucleophilicity of the pyrrole. In a formal synthesis of rhazinal, Chandrasekhar reported a moderate yield for the Swern oxidation of **5**.[12] In our hands the only viable method for efficient oxidation of **5** proved to be a Ley–Griffith oxidation that produced aldehyde **9** in good yield (entry 5).[13] The sensitive pyrrole moiety remained unchanged by the mild terminal oxidant NMO. The catalyst loading could be lowered to 5 mol% when carefully activated molecular sieves were used.

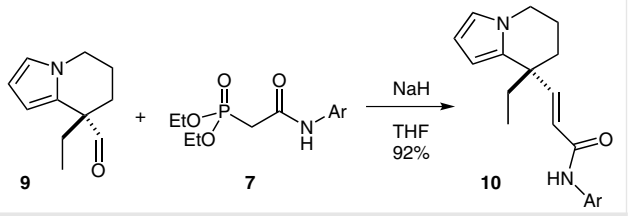
**Table 2** Reaction Conditions Screening for the Efficient Oxidation of Alcohol **5**




| Entry | Conditions | Yield (%) |
|---|---|---|
| 1 | DMP, $H_2O$, $CH_2Cl_2$ | 32 |
| 2 | DMP, $NaHCO_3$, $CH_2Cl_2$ | 26 |
| 3 | PCC, NaOAc, $CH_2Cl_2$ | 6 |
| 4 | PDC, MS, MeCN | 3 |
| 5 | TPAP (5 mol%), NMO, MS, MeCN | 81 |

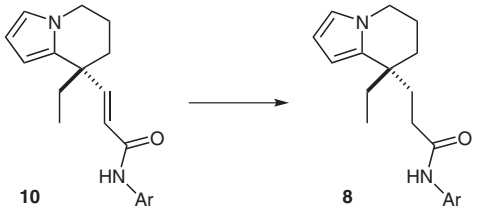
HWE reaction of aldehyde **9** with diethyl phosphonate **7**, which can be prepared easily from 2-bromo-*N*-(2-iodophenyl)acetamide (see experimental section) via an Arbuzov reaction, furnished the unsaturated amide **10** in excellent yield at room temperature (Scheme 2).[14] From this point, reduction of the conjugated double bond in **10** leads to a direct cyclization precursor. The reduction of the unsaturated amide posed multiple problems. First, the pyrrole moiety can still react under Lewis acid catalysis, leading to inhibition or decomposition of reagents and the substrate. Second, the approach to the α,β-unsaturated amide is sterically hindered due to the adjacent quaternary carbon. This may lead either to prolonged reaction times or, in the worst case, the prevention of catalyst binding. Additionally, the iodoarene functionality is prone to undergoing defunctionalization under reductive conditions. With these potential restrictions in mind, only a few reduction methods seemed to be viable options (Table 3). Reduction of the conjugated double bond with Stryker's reagent (entry 1) or borane-catalyzed hydrosilylation (entry 2) led to no conversion to **8**.[15,16] Also, the cobalt-mediated conjugate reduction with stoichiometric $NaBH_4$ (entry 3) did not lead to the desired product, but to the dehalogenated arene arising from reaction with in situ formed Co(I).[17] $NaBH_4$ itself (entry 4) led to slight conversion to the product, because $NaBH_4$ decomposed in methanol before completion of the reduction or was only poorly soluble in aprotic solvents. Eventually, hydrogenation with catalysts inert to carbon–halogen bonds led to success. Wilkinson's catalyst [$RhCl(PPh_3)_3$] gave poor conversion in the presence of $H_2$ (4 bar).[18] Crabtree's catalyst [$Ir(COD)(PCy_3)py]PF_6$] led to about 50% conversion to **8**

with $H_2$ (4 bar) and, gratifyingly, full conversion occurred at higher $H_2$ pressure (40 bar) with a catalyst loading of 2 mol% (entry 7). The high pressure might be necessary to overcome product inhibition and to ensure regeneration of the active catalyst from inactive catalyst dimers.[19]




**Scheme 2** HWE reaction to form the unsaturated amide **10** (Ar = 2-iodophenyl)

**Table 3** Reaction Conditions Screening for the Selective Reduction of Unsaturated Amide **10**[a]



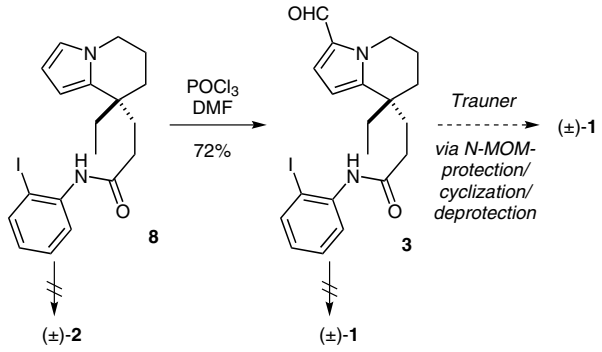

| Entry | Conditions | Conversion (%) |
|---|---|---|
| 1 | $[CuH(PPh_3)]_6$, toluene | – |
| 2 | $B(C_6F_5)_3$ (0.5 mol%), PHMS, $CH_2Cl_2$[b] | – |
| 3 | $CoCl_2$, $NaBH_4$, MeOH–DMF | 100[c] |
| 4 | $NaBH_4$, MeOH–THF | 35 |
| 5 | $RhCl(PPh_3)_3$ (5 mol%), $H_2$ (4 bar), toluene | 20 |
| 6 | $[Ir(COD)(PCy_3)py]PF_6$ (5 mol%), $H_2$ (4 bar), $CH_2Cl_2$ | 55 |
| 7 | $[Ir(COD)(PCy_3)py]PF_6$ (2 mol%), $H_2$ (40 bar) | 92[d] |

[a] Ar = 2-iodophenyl.
[b] PHMS = poly(hydromethylsiloxane).
[c] Defunctionalization of the iodoarene.
[d] Yield of product **8**.

With an efficient synthesis of **8** in hand, we prepared Trauner's intermediate **3** via Vilsmeier formylation (Table 4). This reaction completes the formal total synthesis of rhazinal. Trauner's successful synthesis of **1** proceeds via Pd-catalyzed macrolactamization that requires MOM-protection of the amide nitrogen and, as a consequence, an additional deprotection step.[6,20] We were attracted by the idea of radical macrocyclizations of the unprotected amides **3** and **8** for a protecting-group-free conclusion of the total syntheses of **1** and **2**.

To this end, we focused on the visible-light-mediated generation of aryl radicals from the corresponding iodides through photoredox catalysts. The defunctionalization of

**Table 4** Attempts to Initiate a Free-Radical Cyclization of **3** and **8** onto the Pyrrole Aromatic System




| Entry | Substrate | Conditions[a] |
|---|---|---|
| 1 | **3** | $[Ir(dtbbpy)(ppy)_2]PF_6$ (2 mol%), $Et_3N$, 15 W lamp[b] |
| 2 | **3** | $[Ir(ppy)_3]$ (5 mol%), $Et_3N$, 15 W lamp[b] |
| 3 | **3** | $Et_3B$, $(Me_3Si)_3SiH$, air[c] |
| 4 | **8** | $[Ir(dtbbpy)(ppy)_2]PF_6$ (2 mol%), $Et_3N$, 15 W lamp[d] |

[a] dtbbpy = 4,4′-bis(*tert*-butyl)-2,2′-bipyridine; ppy = 2-(2-pyridyl)phenyl.
[b] No conversion.
[c] Full conversion to an unidentified mixture of products.
[d] Decomposition of starting material.

aryl iodides by Ir photoredox catalysts has been described by Stephenson.[21] Therefore, $[Ir(ppy)_3]$, which also shows oxidative quenching from Ir(III)* to Ir(IV), as well as $[Ir(dtbbpy)(ppy)_2]PF_6$ were tested for the conversion of **3** to **1** (entries 1 and 2) under visible-light irradiation. Unfortunately, neither **1** nor the defunctionalized arene could be detected in the crude reaction mixture. To evaluate the radical cyclization strategy itself, stoichiometric radical generation was performed with $Et_3B$ and $(Me_3Si)_3SiH$ (TTMSS, entry 3).[22] While full consumption of the starting material was observed, we were unable to detect **1** in the crude reaction mixture. Treatment of **8** under the same conditions as **3** led to decomposition of the starting material (entry 4).

In conclusion, we have devised a simple and efficient route to Trauner's intermediate **3** in the total synthesis of rhazinal from the readily available alcohol **5**. The synthesis features an early incorporation of the necessary iodoacetanilide moiety that posed several synthetic challenges, all of which could be solved. A direct radical macrocyclization of **3** and **8** that would have provided a more direct access to **1** and **2** via photoredox catalysis or classical radical chain reaction methodology failed.

All reactions involving air- or moisture-sensitive compounds were carried out in oven-dried glassware under argon using standard Schlenk and vacuum-line techniques. All solvents were either dried and deoxygenated by distillation (THF over Na/K alloy) before use or purified inside an M-Braun MB-SPS-800 solvent purification system

and used after degasification. Commercially available chemicals were used without further purification. $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker spectrometers. $^1$H NMR chemical shifts were calibrated by using the residual undeuterated solvent as internal reference ($CHCl_3$, δ = 7.26; $C_6HD_5$, δ = 7.16). $^{13}$C NMR chemical shifts were calibrated by using the solvent peak as internal reference ($CDCl_3$, δ = 77.16; $C_6D_6$, δ = 128.06). IR spectra of samples prepared as neat films were recorded on a Nicolet 380 ATR IR spectrometer. High-resolution mass spectra were obtained on a Thermoquest MAT 95 CL instrument. Column chromatography was carried out on silica gel (230–400 mesh) supplied by Merck and Macherey-Nagel. TLC was performed on silica gel on aluminum plates and the compounds were detected with the Seebach staining mixture. Solvent mixtures consisting of EtOAc and cyclohexane were used as eluents for silica gel chromatography.

### 2-Bromo-*N*-(2-iodophenyl)acetamide

To a solution of commercially available 2-iodoaniline (5.356 g, 24.5 mmol, 1.00 equiv) in $CH_2Cl_2$ (60 mL) cooled to 0 °C was added $Et_3N$ (4.2 mL, 29.4 mmol, 1.20 equiv) followed by bromoacetyl bromide (2.5 mL, 29.4 mmol, 1.20 equiv). The mixture was stirred at 0 °C for 1 h and warmed to r.t. The organic phase was washed with 1 N aq HCl (60 mL), sat. aq $NaHCO_3$ (60 mL), and brine (60 mL) and dried over anhyd $MgSO_4$. The solvent was removed under reduced pressure to yield the product as a colorless powder, which was used without further purification.

Yield: 7.330 g (21.6 mmol, 88%); colorless powder; mp 113–115 °C.

IR (neat): 3240, 1660, 1530, 1175 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.59 (br s, 1 H), 8.21 (dd, *J* = 8.3, 1.6 Hz, 1 H), 7.81 (dd, *J* = 8.0, 1.5 Hz, 1 H), 7.45–7.32 (m, 1 H), 6.90 (ddd, *J* = 8.0, 7.4, 1.6 Hz, 1 H), 4.08 (s, 2 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 163.8, 139.2, 137.7, 129.4, 126.8, 121.8, 90.0, 29.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_8H_7BrINONa$: 361.8653; found: 361.8648.

### Diethyl [(2-Iodophenyl)carbamoyl]methylphosphonate (7)

$P(OEt)_3$ (4.8 mL, 28.1 mmol, 1.30 equiv) was added to a solution of 2-bromo-*N*-(2-iodophenyl)acetamide (7.330 g, 21.6 mmol, 1.00 equiv) in DCE (20 mL) at r.t. and then the mixture was heated to 90 °C for 4 h under stirring. The solvent was removed under reduced pressure and the remaining oil was purified by column chromatography.

Yield: 7.200 g (18.1 mmol, 84%); beige solid; $R_f$ = 0.1 (cyclohexane–EtOAc, 50:50); mp 75–77 °C.

IR (neat): 1675, 1530, 1225 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.50 (s, 1 H), 8.14–8.07 (m, 1 H), 7.79 (dd, *J* = 8.0, 1.3 Hz, 1 H), 7.32 (ddd, *J* = 8.4, 7.2, 1.4 Hz, 1 H), 6.89–6.81 (m, 1 H), 4.21 (p, *J* = 7.3 Hz, 4 H), 3.06 (d, *J* = 20.8 Hz, 2 H), 1.42–1.27 (m, 6 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 162.6, 139.3, 138.6, 129.1, 126.5, 122.9, 90.1, 63.2, 63.1, 37.7, 36.0, 16.6, 16.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{17}INO_4PNa$: 419.9838; found: 419.9832.

### *rac*-8-Ethyl-5,6,7,8-tetrahydroindolizine-8-carbaldehyde (9)

A Schlenk tube was charged with activated 4 Å MS (1.5 g) and anhyd 4-methylmorpholine *N*-oxide (0.768 g, 6.3 mmol, 2.00 equiv) under argon. A solution of *rac*-**5**[3] (0.565 g, 3.2 mmol, 1.00 equiv) in anhyd MeCN (15 mL) was added and the mixture was stirred at r.t. TPAP (0.056 g, 0.16 mmol, 0.05 equiv) was added in one portion and the mixture was stirred at r.t. for 1 h. The solids were removed by filtration and the solvent was removed under reduced pressure. The crude was purified by column chromatography.

Yield: 0.453 g (2.6 mmol, 81%); colorless oil; $R_f$ = 0.6 (cyclohexane–EtOAc, 80:20).

IR (neat): 2960, 1720, 1450 cm$^{-1}$.

$^1$H NMR (400 MHz, $C_6D_6$): δ = 9.26 (d, *J* = 1.5 Hz, 1 H), 6.36–6.31 (m, 2 H), 6.05 (dd, *J* = 3.6, 1.7 Hz, 1 H), 3.22–3.06 (m, 2 H), 2.10 (dddd, *J* = 13.4, 5.7, 3.1, 1.0 Hz, 1 H), 1.67–1.39 (m, 3 H), 1.36–1.26 (m, 1 H), 1.06 (dddd, *J* = 13.4, 11.9, 3.3, 1.5 Hz, 1 H), 0.65 (t, *J* = 7.5 Hz, 3 H).

$^{13}$C NMR (100 MHz, $C_6D_6$): δ = 198.9, 127.4, 120.8, 108.7, 106.4, 51.4, 44.8, 29.2, 24.6, 21.2, 8.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{15}NONa$: 200.1051; found: 200.1046.

### *rac*-3-(8-Ethyl-5,6,7,8-tetrahydroindolizin-8-yl)-*N*-(2-iodophenyl)prop-2-enamide (10)

NaH (60 wt% in mineral oil, 0.493 g, 12.3 mmol, 2.00 equiv) was added portionwise to a solution of **7** (2.693 g, 6.8 mmol, 1.10 equiv) in anhyd THF (36 mL) under argon over 15 min at r.t., and the mixture was stirred until gas evolution ceased. A solution of **9** (1.092 g, 6.2 mmol, 1.00 equiv) in anhyd THF (36 mL) was added and the mixture was stirred for 2 d at r.t. $H_2O$ (70 mL) was added and the mixture was extracted with EtOAc (3 × 70 mL). The combined organic phase was dried over anhyd $MgSO_4$ and the volatiles were removed under reduced pressure. The crude was purified by column chromatography.

Yield: 2.382 g (5.7 mmol, 92%); white solid; $R_f$ = 0.4 (cyclohexane–EtOAc, 80:20); mp 119–121 °C.

IR (neat): 3270, 2925, 1670, 1635, 1510, 1430 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.35–8.24 (m, 1 H), 7.76 (dd, *J* = 7.9, 1.4 Hz, 1 H), 7.40–7.30 (m, 2 H), 7.06 (d, *J* = 15.2 Hz, 1 H), 6.83 (ddd, *J* = 7.9, 7.3, 1.6 Hz, 1 H), 6.19 (d, *J* = 3.5 Hz, 1 H), 5.99 (d, *J* = 3.5 Hz, 1 H), 5.65 (d, *J* = 15.2 Hz, 1 H), 4.04–3.95 (m, 1 H), 3.91–3.79 (m, 1 H), 2.03–1.73 (m, 6 H), 0.95 (t, *J* = 7.4 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 164.3, 154.4, 138.9, 138.5, 132.1, 129.4, 126.0, 123.2, 122.2, 119.4, 107.8, 105.5, 90.2, 45.5, 42.6, 33.9, 30.9, 20.3, 8.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}IN_2ONa$: 443.0596; found: 443.0591.

### *rac*-3-(8-Ethyl-5,6,7,8-tetrahydroindolizin-8-yl)-*N*-(2-iodophenyl)propanamide (8)

Crabtree's catalyst [Ir(COD)($PCy_3$)py]$PF_6$ (0.097 g, 0.12 mmol, 0.02 equiv) was added to a solution of **10** (2.545 g, 6.1 mmol, 1.00 equiv) in $CH_2Cl_2$ (40 mL) inside a Parr 5500 microreactor hydrogenation apparatus. The apparatus was flushed with argon and finally placed under $H_2$ (40 atm) pressure; the solution was stirred for 7 h at r.t. Upon completion of the reaction, the solvent was removed under reduced pressure. The crude was purified by column chromatography.

Yield: 2.354 g (5.6 mmol, 92%); yellow oil; $R_f$ = 0.4 (cyclohexane–EtOAc, 80:20).

IR (neat): 3270, 2935, 1665, 1510, 1285 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 8.30–8.09 (m, 1 H), 7.76 (dd, *J* = 8.0, 1.4 Hz, 1 H), 7.43–7.28 (m, 2 H), 6.91–6.75 (m, 1 H), 6.14 (s, 1 H), 5.92 (br s, 1 H), 3.90 (t, *J* = 6.1 Hz, 2 H), 2.37 (dd, *J* = 9.6, 7.3 Hz, 2 H), 2.02 (dtd, *J* = 14.6, 7.0, 6.4, 4.8 Hz, 4 H), 1.84–1.56 (m, 4 H), 0.88 (t, *J* = 7.4 Hz, 3 H).

$^{13}$C NMR (75 MHz, $CDCl_3$): δ = 171.8, 138.9, 138.4, 134.8, 129.3, 125.9, 125.1, 122.2, 118.9, 107.5, 104.3, 90.1, 45.5, 37.8, 35.3, 33.7, 30.8, 20.3, 8.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{23}IN_2OH$: 423.0933; found: 423.0935.

### *rac*-3-(8-Ethyl-3-formyl-5,6,7,8-tetrahydroindolizin-8-yl)-*N*-(2-iodophenyl)propanamide (3)

DMF (2.1 mL, 26.8 mmol, 5.00 equiv) was dissolved in $CH_2Cl_2$ (25 mL), and $POCl_3$ (0.55 mL, 5.9 mmol, 1.10 equiv) was added at r.t. The solution was stirred for 15 min and then cooled to 0 °C. A solution of **8** (2.264 g, 5.4 mmol, 1.00 equiv) in $CH_2Cl_2$ (25 mL) was added over 5 min and the mixture was stirred for 3 h while allowed to warm to r.t. Half-saturated $K_2CO_3$ solution (50 mL) was added and the mixture was stirred for 30 min. The mixture was extracted with $CH_2Cl_2$ (3 × 50 mL), washed with $H_2O$ (100 mL), and dried over anhyd $MgSO_4$. The solvent was removed under reduced pressure and the crude was purified by column chromatography.

Yield: 1.739 g (3.9 mmol, 72%); foamy semi-solid; $R_f$ = 0.6 (cyclohexane–EtOAc, 50:50).

IR (neat): 3270, 2935, 1735, 1645 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 9.41 (s, 1 H), 8.15 (d, *J* = 8.9 Hz, 1 H), 7.76 (dd, *J* = 8.0, 1.4 Hz, 1 H), 7.35 (br s, 1 H), 7.32 (ddd, *J* = 8.5, 7.4, 1.5 Hz, 1 H), 6.90 (d, *J* = 4.1 Hz, 1 H), 6.86–6.80 (m, 1 H), 6.09 (d, *J* = 4.2 Hz, 1 H), 4.40 (dt, *J* = 14.1, 5.9 Hz, 1 H), 4.31 (dt, *J* = 13.6, 6.4 Hz, 1 H), 2.44–2.32 (m, 1 H), 2.27 (dq, *J* = 15.1, 7.9, 7.1 Hz, 1 H), 2.13–2.06 (m, 2 H), 2.04–1.97 (m, 2 H), 1.82–1.64 (m, 4 H), 0.87 (t, *J* = 7.4 Hz, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 178.7, 171.0, 146.2, 138.9, 138.2, 131.0, 129.4, 126.1, 124.8, 122.2, 107.6, 90.2, 45.6, 38.4, 35.4, 33.7, 33.4, 29.0, 19.7, 8.7.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{23}IN_2O_2Na$: 473.0702; found: 473.0701.

The data are in agreement with the literature.[6]

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## Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588956.

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