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Enantioselective Syntheses of Bicyclic Lactams Based on Iridium-Catalyzed Asymmetric Allylic Substitution and Heck Cyclization

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A sequence of reactions that include an iridium-catalyzed regio- and enantioselective allylic amination, the formation of an amide, a ruthenium-catalyzed ring-closing metathesis, and an intramolecular Heck reaction allows for the preparation of [3,3,1]- and [4,3,1]-bicyclic amides. The target compounds have a nitrogen atom at the bridgehead, a nonplanar amide moiety, and a stereogenic center at the one-carbon bridge.

Introduction

Bridged heterocyclic systems that have nitrogen at the bridgehead position are of interest because of their known and potential biological properties.[1,2] For example, the alkaloid quinine (**1**, see Figure 1) has antipyretic, antimalarial, analgesic, and anti-inflammatory effects,[3] and dibenzo[*c*,*f*]azocine **2** is known to be active with regard to the central nervous system (CNS).[4] Methanothieno[2,3-*c*]-azocine **3** and structurally related compounds are inhibitors of protein tyrosine phosphatases,[5] and benzazocine **4** is an inhibitor of biogenic amine transporters.[6]

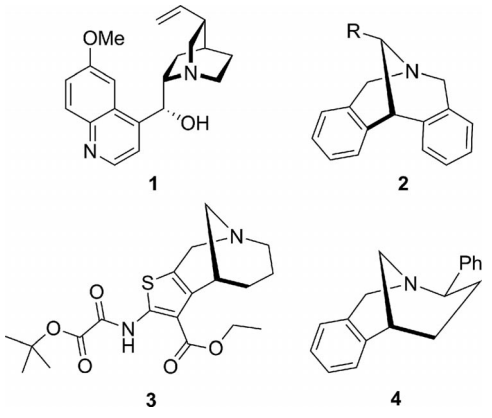
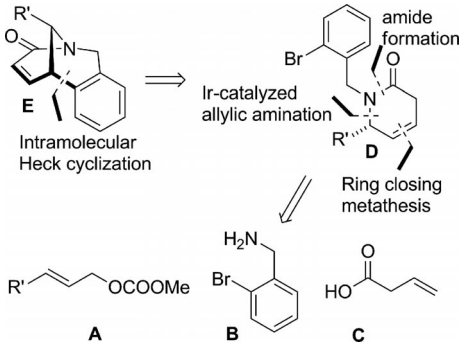


Figure 1. Structures of biologically active bicyclic heterocycles that containing nitrogen in the bridgehead position.

Dibenzoazocine **2** was prepared by using a Friedel–Crafts dual cyclization as the key step,[4b] whereas amine **3** was obtained through the condensation of 1-azabicyclo[3,3,1]-nonan-4-one, sulfur, and *tert*-butylcyanoacetate followed by aromatization.[5] The preparation of the core structure of bridged amine **4** was accomplished by a ceric ammonium nitrate (CAN) mediated radical-initiated ring-opening followed by a ring-closing reaction sequence that started from azabicyclo[3.1.0]hexane-1-ol.[6,7] Bicyclic lactams with the nitrogen atom at the bridgehead position have been elegantly accessed, in particular, through a ring-closing metathesis (RCM) followed by an intramolecular Heck reaction.[8]

The latter strategy was adopted by us in conjunction with an iridium-catalyzed enantioselective allylic amination to provide the starting materials. Thus (see Scheme 1), our route to bicyclic lactam **E** involves an intramolecular Heck reaction of enamide **D**, which in turn can be obtained by an Ir-catalyzed allylic amination between 2-bromobenzylamine (**B**) and carbonate **A** followed by amide formation with vinylacetic acid (**C**) and a ring-closing metathesis reaction.



Scheme 1. Strategy for an enantioselective route to bicyclic lactam **D**.

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Results and Discussion

The Ir-catalyzed allylic substitution reaction, which was introduced in 1997,[9] has emerged as a versatile tool for enantioselective synthesis.[10] High degrees of regio- and enantioselectivity that favor branched substitution products can be obtained. The reactions, of particular interest, are those with N-nucleophiles, that is, aliphatic amines,[11] amides,[12] and anilines[13] to give branched allylic amines, which are often well-suited as starting materials for alkaloid syntheses.[14] In the most often used version of allylic amination, the catalyst is prepared from $[Ir(COD)Cl]_2$ (COD = 1,5-cyclooctadiene) and chiral phosphoramidite **L***, which is activated by base. Commercially available **L1**[15] and often superior **L2**[16] and **L3**[16] were employed as ligands (see Figure 2).

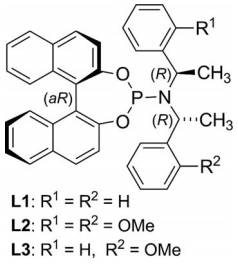


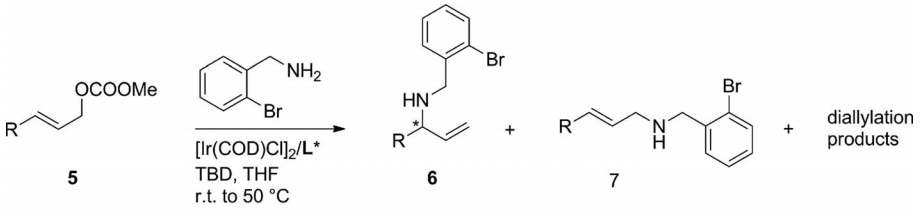
Figure 2. Ligands used for allylic amination.

The reactions between carbonates **5** and (*o*-bromophenyl)methylamine as the nucleophile (see Table 1) were carried out by using the described catalyst system {i.e., $[Ir(COD)]_2$ (2 mol-%)/**L*** (4 mol-%), TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene, 8 mol-%), dry tetrahydrofuran (THF)}, and the reaction temperatures were optimized. Branched amines **6** were obtained in good yields and excellent enantioselectivity (>90% *ee*). The linear allylic amines were not detected, which is likely a result of a diallylation process that occurs faster with the linear than the branched monoallylation products. The absolute configurations of the allylic substitution products **6** were assigned on the basis of a valid rule,[10b,10e] that is thus far without exception.

The coupling reaction between secondary amines **6a**–**6d** and 3-butenoic acid with *N*,*N*′- dicyclohexylcarbodiimide (DCC) and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) gave dienamides **8a**–**8d** (see Scheme 2). The ring-closing metathesis of dienamide **8** by treatment with 5 mol-% of Grubbs I catalyst in refluxing dichloromethane furnished the cyclic products **9** in near quantitative overall yields from **6**.[17]

For the intramolecular Heck reaction[18] of bromides **9**, the reported reaction conditions for similar substrates were initially employed.[10] Thus, upon subjecting a mixture of enamide **9b**, $Pd(PPh_3)_2Cl_2$ (20 mol-%), Et_3N (10 equiv.), and dry *N*,*N*-dimethylformamide (DMF, 0.03 M) to microwave irradiation (300 W) at 110 °C for 1 h, bicyclic lactams **10b** (52%) and **11b** (14%) were obtained (see Scheme 3 and Table 2, Entry 1). These products arise from the insertion of the intermediary aryl-palladium species into the double bond that is *anti* or *syn* to the R (ethyl) group. With catalyst $Pd(OAc)_2/PPh_3$ (10 mol-%), similar results were obtained

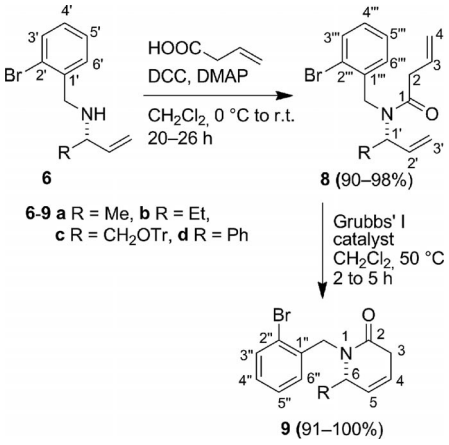
Table 1. Ir-catalyzed asymmetric allylic amination of carbonates **5**.[a]



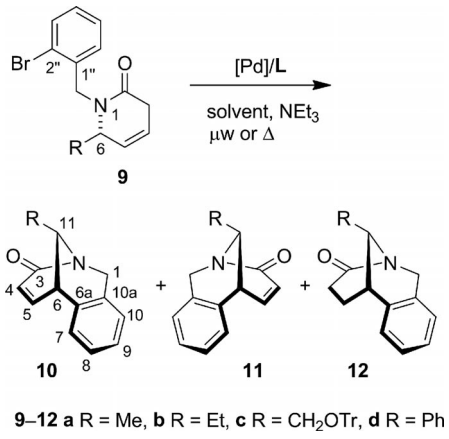
5–7 **a** R = Me, **b** R = Et, **c** R = CH_2OTr, **d** R = Ph

Entry	Carbonate	L*	Time [h]	Temp. [°C]	% Yield[b]	% *ee*[c]
1	**5a**	**L2**	4	50	73	96[d]
2	**5a**	*ent*-**L2**	7	r.t.	78	95[d]
3	**5a**	**L3**	7	50	75	96[d]
4	**5b**	**L2**	20	r.t.	72	93
5	**5b**	*ent*-**L2**	20	r.t.	71	93
6	**5b**	**L3**	15	r.t.	69	95
7	**5b**	**L3**	20	50[e]	74	93
8	**5c**	**L2**	3	50	60	96
9	**5c**	*ent*-**L2**	4	50	54	93
10	**5c**	**L3**	4	50	63	95
11	**5d**	**L2**	6.5	50	83	98
12	**5d**	*ent*-**L2**	5.5	50	86	94
13	**5d**	**L3**	6.5	50	88	97

[a] Reactions were carried out according to GP1 (method A: Ir/**L***/TBD, 2:4:8 mol-%; see Exp. Section). [b] Isolated yields of branched amination products **6**. Regioselectivity was determined by ^1H NMR analysis of the crude product. [c] Enantiomeric excess values were determined by chiral HPLC analysis. [d] In the case of **6a**, it was not possible to measure the *ee* values by chiral HPLC or chiral GC analysis, and, hence, those were measured by using dienamide **8a**. [e] Reactions were conducted at 50 °C for 3 h and then continued at room temp for 15–17 h.



Scheme 2. Synthesis of pyridinones **9** (Tr = triphenylmethyl).



Scheme 3. Pd-catalyzed cyclization of **9** to give bicyclic lactams **10**–**12**.

(see Table 2, Entries 2–4). The catalyst $Pd(OAc)_2$/(±)-BINAP (10 mol-%) was ineffective and led to 80% recovery of the starting material **9b** (see Table 2, Entry 5). With either $Pd(dppf)_2Cl_2$ [10 or 20 mol-%, dppf = 1,1′-bis(diphenylphosphino)ferrocene] or $Pd(PPh_3)_2Cl_2$ (20 mol-%) as catalysts under various concentrations, the yields were poor to moderate (see Table 2, Entries 6–12). Gratifyingly, a low concentration of 0.03 M in conjunction with $Pd(dppf)_2Cl_2$ (10 or 20 mol-%) as the catalyst consistently afforded good results (see Table 2, Entries 13–15).

Cyclization reactions of other enamides **9** were carried out using the optimal conditions for **9b**. In general, the results were similar to those obtained for **9b** (see Table 3). In the case of the amide **9d**, the catalysts $Pd(PPh_3)_2Cl_2$ and $Pd(OAc)_2/PPh_3$ afforded results as good as those obtained with $Pd(dppf)_2Cl_2$ (see Table 3 Entries 5–8). Characterizations of minor isomers **11a**, **11c**, **11d** as well as **12a**, **12c**, and **12d** were carried out with the accumulated material.

The structure of **10d** was confirmed by single-crystal X-ray diffraction analysis. As expected, the relative orientation of the phenyl group that is present at the bridging carbon is *anti* to the other aromatic ring, and the nitrogen attains a twisted nonplanar amide bond[19] (see Figure 3).

Finally, the synthesis of a one-carbon homologated bicyclic lactam was carried out. The coupling reaction between amine **6b** and 4-pentenoic acid by treatment with DCC gave dienamide **8bb** in high yield. The ring-closing metathesis reaction with Grubbs I catalyst under the previously optimized conditions failed to furnish amide **9bb**. However, employing Grubbs II catalyst resulted in a nearly quantitative yield (see Scheme 4). The key intramolecular Heck reaction furnished bicyclic lactams **10bb** and **11bb** as major and minor isomers, respectively. Neither a reduction of the double bond nor a double-bond shift into the α,β-position were observed.

Table 2. Screening of conditions for the Pd-catalyzed cyclization of **9b** to give **10b**–**12b** according to Scheme 3.[a,b]

Entry	Catalyst [mol-%]	Conc. [M]	Temp. [°C]	Time [h]	% Recovered	% Yield[c]		
					9b	**10b**	**11b**	**12b**
1[d]	$Pd(PPh_3)_2Cl_2$ (20)	0.03	110	1	–	52	14	–
2[e]	$Pd(OAc)_2/PPh_3$ (10)[f]	0.06	80	1.5	38	45	8	–
3[e]	$Pd(OAc)_2/PPh_3$ (10)[f]	0.1	120	1	–	52	–	–
4[g]	$Pd(OAc)_2/PPh_3$ (10)[f]	0.03	100	2	–	53	18	–
5[g]	$Pd(OAc)_2$/(±) BINAP (10)[h]	0.03	100	2	80	–	–	–
6[e]	$Pd(dppf)_2Cl_2$ (20)	0.1	120	1.5	–	37	–	–
7[d]	$Pd(dppf)_2Cl_2$ (20)	0.03	120	1.16	100	–	–	–
8[d]	$Pd(dppf)_2Cl_2$ (20)	0.1	120	0.5	–	42	–	–
9[d]	$Pd(PPh_3)_2Cl_2$ (20)	0.1	120	0.66	–	11	–	–
10[d]	$Pd(PPh_3)_2Cl_2$ (20)	0.1	100	0.66	–	34	11	–
11[d]	$Pd(dppf)_2Cl_2$ (10)	0.06	100	1.5	–	49	6	5
12[d]	$Pd(dppf)_2Cl_2$ (10)	0.06	100	24	–	47	–	14
13[d]	$Pd(dppf)_2Cl_2$ (10)	0.03	100	2	–	62	8	8
14[d]	$Pd(dppf)_2Cl_2$ (20)	0.03	120	0.5	–	60	6	3
15[d]	$Pd(dppf)_2Cl_2$ (20)	0.03	120	0.66	–	59	11	4

[a] DMF was used as the solvent, except that toluene was used for Entry 7. [b] Reactions were conducted under microwave irradiation, except that conventional heating was used for Entry 12. [c] Isolated yields of pure products. [d] NEt_3 (10 equiv.) was used as base. [e] Cs_2CO_3 (3–4 equiv.) was used as base. [f] PPh_3 (20 mol-%) was used. [g] NEt_3 (5 equiv.) was used as base. [h] (±)-BINAP [2,2′-bis(diphenylphospino)-1,1′-binapthyl, 20 mol-%] was used.

Table 3. Pd-catalyzed Heck cyclization according to Scheme 3.[a]

Entry	Reaction conditions	Products [% yield][b,c]		
1[d]	$Pd(dppf)_2Cl_2$ (20 mol-%), 120 °C, 0.5 h	**10a** (53)	**11a** (5)	**12a** (3)
2[d]	$Pd(dppf)_2Cl_2$ (20 mol-%), 120 °C, 0.41 h	**10a** (58)	**11a** (7)	**12a** (2)
3[d]	$Pd(dppf)_2Cl_2$ (10 mol-%), 100 °C, 2 h	**10b** (62)	**11b** (8)	**12b** (8)
4[d]	$Pd(dppf)_2Cl_2$ (20 mol-%), 120 °C, 1 h	**10c** (58)	**11c** (14)	**12c** (3)
5[d]	$Pd(PPh_3)_2Cl_2$ (10 mol-%), 110 °C, 1.5 h	**10d** (70)	–	**12d** (5)
6[d]	$Pd(dppf)_2Cl_2$ (20 mol-%), 120 °C, 0.66 h	**10d** (60)	–	**12d** (5)
7[d]	$Pd(dppf)_2Cl_2$ (20 mol-%), 120 °C, 1 h	**10d** (70)	–	**12d** (4)
8[e]	$Pd(OAc)_2/PPh_3$ (10 mol-%), 120 °C, 1.5 h	**10d** (63)	–	**12d** (3)

[a] Solvent: DMF, c(**9**) = 0.03 M, microwave irridiation. [b] Isolated yields of chromatographically pure products. [c] We were unable to collect data for isomer **11d**. [d] NEt_3 (10 equiv.) was used as base. [e] NEt_3 (5 equiv.) was used as base.

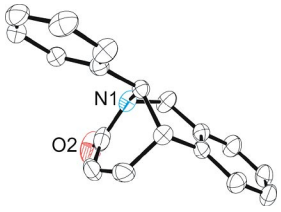
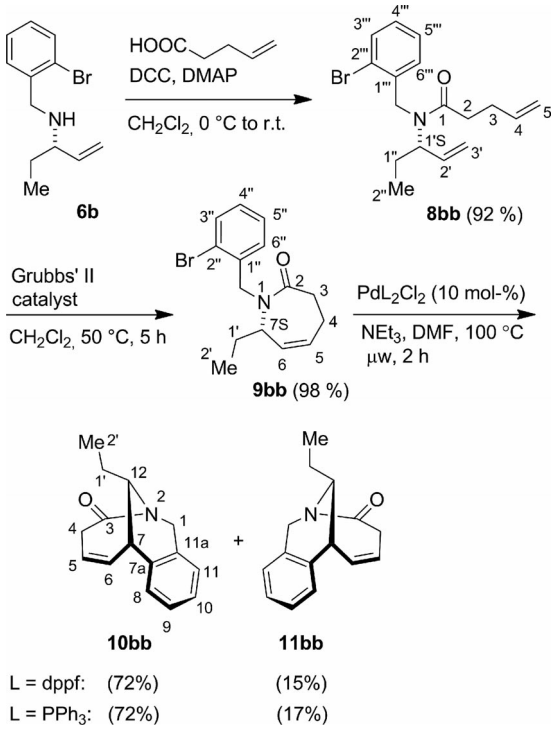


Figure 3. X-ray crystal structure of **10d**.[20]



Scheme 4. Synthesis of bicyclic lactams **10bb** and **11bb** starting from amine **6b**.

Conclusions

In summary, we have developed an efficient enantioselective synthesis of bicyclic lactams with nitrogen at the bridgehead position and, as a consequence, a twisted nonplanar amide group. The highly regio- and enantioselective Ir-catalyzed allylic amination and Pd-catalyzed intramolecular Heck reactions were employed as the key steps.

Experimental Section

General Methods: The ^1H NMR spectroscopic data were recorded with a Bruker AC 300 (300 MHz) or Bruker Avance 500 (500 MHz) spectrometer at room temp. with the samples dissolved in $CDCl_3$. Chemical shifts are reported in δ units relative to $CHCl_3$ (δ_H = 7.26 ppm), TMS (δ_H = 0.00 ppm), or toluene [δ_H = 2.11 ppm (central line of the quintet)]. The ^{13}C NMR spectroscopic data were recorded with a Bruker AC 300 (75 MHz) or Bruker Avance 500 (125 MHz) spectrometer at room temp. with the sample dissolved in $CDCl_3$. Chemical shifts are reported in δ units relative to $CDCl_3$ [δ_C = 77.16 ppm (central line of the triplet)]. The abbreviations used throughout are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), and br. s (broad singlet). The assignment of the signals was confirmed by $^1H,^1H$-COSY, $^1H,^{13}C$-COSY, and DEPT spectroscopic analyses. Numbers of atoms were derived by using ACD/ChemSketch, and the numbers are provided in the Supporting Information with the spectra. Optical rotations were measured in a thermostatted cuvette (1 dm) by using a mercury lamp with a Perkin–Elmer 341 Polarimeter. Concentration (c) is given in g per 100 mL. HRMS were recorded with a JEOL JMS-700 instrument (EI and FAB) or a Bruker ApexQe instrument (ESI). Elemental analyses were carried out at the Organisch-Chemisches Institut, Universität Heidelberg. Enantiomeric excess values were determined by chiral GC analysis with the HP 5890 instrument or by chiral HPLC analysis with the HP 1090 or HP 1100 instrument. For HPLC, the columns from Daicel that were used are Chiralpak AD-H (250 × 4.6 mm, 5 µm) with the guard cartridge AD-H (10 × 4 mm, 5 µm) and Chiralpak AS-H (250 × 4.6 mm, 5 µm) with the guard cartridge AS-H (10 × 4 mm, 5 µm). For GC, a permethyl β-cyclodextrin column by Chrompack (WCOT fused silica, Cp-Cyclodextrin-B-236-M-19, 25 m × 0.25 mm) was used. For preparative HPLC, a Gilson-305 pump coupled with a Knauser UV detector 2600 and a silica gel column (Latek, silica, 5µ, 21 × 250 mm) were used. All microwave experiments were carried out using CEM Discover Labmate™ instrument [method: Chem. Driver™ software, with microwave vials (10 mL), closed vessel, power: 300 W, temperature: 100–120 °C (25 to 120 min)]. All reactions were carried out in glassware that was dried with a heat gun under argon. Success with any of the following procedures for the iridium-catalyzed allylic substitutions required dry THF (content of H_2O <30 mg/L, Karl Fischer titration). Anhydrous TBD is hygroscopic and, hence, was stored in a desiccator over KOH (alternatevely small amounts were stored under argon in a Schlenk tube), and measuring its mass was carried out rapidly.

General Procedure (GP1) for Iridium-Catalyzed Allylic Substitutions: Under argon, a Schlenk tube was dried with a heat gun and then charged with a solution of $[Ir(COD)Cl]_2$ (13.4 mg, 20 µmol) and the chiral ligand **L*** (40 µmol) in dry THF (1.0 mL, content of

H_2O <30 mg/L, Karl-Fischer titration). Anhydrous TBD (11.1 mg, 80 μmol) was added, and the mixture was stirred for 5 min (for **L2**) or 30 min (for **L3**). Carbonate **5** (1 mmol) and 2-bromobenzylamine (1.1–1.2 mmol) were then added, and the mixture was stirred at the stated temperature (r.t.–50 °C) and time, at which either complete conversion or no further conversion was detected by TLC or GC–MS analysis. For the workup procedure, the mixture was concentrated in vacuo. The regioselectivity of the reaction was determined by ^{1}H NMR analysis of the crude product or by isolating the regioisomers. Purification by flash chromatography on silica gel afforded pure amination product **6**.

(+)-(*S*)-*N*-(2-Bromobenzyl)but-3-en-2-amine [(+)-(*S*)-6a]: GP1 was carried out with $[Ir(COD)Cl]_2$ (53.7 mg, 80 μmol), (*R*,*R*,*aR*)-**L3** (91.1 mg, 160 μmol), anhydrous TBD (44.5 mg, 320 μmol), carbonate **5a** (520 mg, 4 mmol), and 2-bromobenzylamine (818.6 mg, 4.4 mmol) in dry THF (4 mL) at 50 °C for 7 h. For TLC, R_f (**6a**) = 0.20–0.40, R_f (**5a**) = 0.80 (petroleum ether/ethyl acetate, 4:1; $KMnO_4$). Purification of the crude product by flash chromatography on silica (50 g; petroleum ether/ethyl acetate, from 95:5 to 4:1) gave (+)-(*S*)-**6a** (720 mg, 75%) as a yellow oil. $[a]_D^{20}$ = +1.1 (*c* = 1.01, $CHCl_3$); 96%*ee*. In this particular case, it was not possible to measure the *ee* value directly, and it was measured after the DCC coupling reaction to give **8a**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (dd, *J* = 8.0, 1.1 Hz, 1 H, 3′-H), 7.38 (dd, *J* = 7.6, 1.6 Hz, 1 H, 6′-H), 7.27 (ddd, *J* = 7.4, 7.4, 1.1 Hz, 1 H, 5′-H), 7.11 (ddd, *J* = 7.6, 7.6, 1.7 Hz, 1 H, 4′-H), 5.74 (ddd, *J* = 17.3, 10.0, 7.5 Hz, 1 H, 3-H), 5.15 (dd, *J* = 17.2, 1.6 Hz, 1 H, 4-H_Z), 5.09 (dd, *J* = 10.1, 1.7 Hz, 1 H, 4-H_E), 3.87 (d, *J* = 13.7 Hz, 1 H, N-CH_{2a}-Ar), 3.76 (d, *J* = 13.7 Hz, 1 H, N-CH_{2b}-Ar), 3.21 (dq, *J* = 7.0, 6.7 Hz, 1 H, 2-H), 1.19 (d, *J* = 6.4 Hz, 3 H, 1-H), 1.55 (s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.6 (d, C-3), 139.6 (s, C-1′), 132.9 (d, C-3′), 130.6 (d, C-6′), 128.6 (d, C-4′), 127.5 (d, C-5′), 124.1 (s, C-2′), 115.0 (t, C-4), 56.1 (d, C-2), 51.5 (t, N-*C*H_2-Ar), 22.0 (q, C-1) ppm. HRMS (ESI+): calcd. for $C_{11}H_{15}{}^{79}BrN^+$ [M + H]$^+$ 240.0382; found 240.0383; calcd. for $C_{11}H_{15}{}^{81}BrN^+$ [M + H]$^+$ 242.0362; found 242.0362. $C_{11}H_{14}BrN$ (240.14): calcd. C 55.02, H 5.88, Br 33.27, N 5.83; found C 54.78, H 5.83, Br 32.98, N 5.73.

(–)-(*S*)-*N*-(2-Bromobenzyl)pent-1-en-3-amine [(–)-(*S*)-6b]: GP1 was carried out with $[Ir(COD)Cl]_2$ (53.7 mg, 80 μmol), (*R*,*R*,*aR*)-**L3** (91.1 mg, 160 μmol), anhydrous TBD (44.5 mg, 320 μmol), carbonate **5b** (576 mg, 4 mmol), and 2-bromobenzylamine (818.6 mg, 4.4 mmol) in dry THF (4 mL) at 50 °C for 3 h and then at room temperature for 17 h. For TLC, R_f (**6b**) = 0.20–0.40, R_f (**5b**) = 0.80 (petroleum ether/ethyl acetate, 7:3; $KMnO_4$). Purification of the crude product by flash chromatography on silica (50 g; petroleum ether/ethyl acetate, from 95:5 to 4:1) gave (–)-(*S*)-**6b** (755 mg, 74%) as a yellow oil. $[a]_D^{20}$ = –8.3 (*c* = 1.02, $CHCl_3$); 93%*ee* by HPLC. HPLC [Chiralpak AD-H (250 × 4.6 mm, 5 μm) with guard cartridge AD-H (10 × 4 mm, 5 μm), *n*-hexane/2-propanol (99:1) and 0.1% diethylamine, 0.5 mL/min]: t_R = 9.93 min [(+)-(*R*)-**6b**] and t_R = 10.47 min [(–)-(*S*)-**6b**]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (dd, *J* = 7.9, 1.1 Hz, 1 H, 3′-H), 7.38 (dd, *J* = 7.5, 1.7 Hz, 1 H, 6′-H), 7.27 (ddd, *J* = 7.4, 7.4, 1.3 Hz, 1 H, 5′-H), 7.11 (ddd, *J* = 7.6, 7.6, 1.7 Hz, 1 H, 4′-H), 5.64 (ddd, *J* = 16.9, 10.4, 8.2 Hz, 1 H, 2-H), 5.17 (dd, *J* = 10.5, 1.8 Hz, 1 H, 3-H_E), 5.14 (ddd, *J* = 16.9, 1.8, 0.7 Hz, 1 H, 3-H_Z), 3.89 (d, *J* = 13.7 Hz, 1 H, N-CH_{2a}-Ar), 3.73 (d, *J* = 13.7 Hz, 1 H, N-CH_{2b}-Ar), 2.92 (ddd, *J* = 8.0, 7.9, 5.7 Hz, 1 H, 1-H), 1.68–1.32 (m, 2 H, 4-H), 1.63 (s, 1 H, NH), 0.88 (t, *J* = 7.4 Hz, 3 H, 5-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2 (d, C-2), 139.7 (s, C-1′), 132.9 (d, C-3′), 130.7 (d, C-6′), 128.6 (d, C-4′), 127.5 (d, C-5′), 124.2 (s, C-2′), 116.5 (t, C-3), 62.9 (d, C-1), 51.4 (t, N-*C*H_2-Ar), 28.6 (t, C-4), 10.5 (q, C-5) ppm. HRMS (ESI+): calcd. for $C_{12}H_{17}{}^{79}BrN^+$ [M + H]$^+$ 254.0539; found 254.0539. $C_{12}H_{16}BrN$ (254.17): calcd. C 56.71, H 6.35, Br 31.44, N 5.51; found C 56.61, H 6.32, Br 31.23, N 5.43.

(–)-(*R*)-*N*-(2-Bromobenzyl)-1-(trityloxy)but-3-en-2-amine [(–)-(*R*)-6c]: GP1 was carried out with $[Ir(COD)Cl]_2$ (26.8 mg, 40 μmol), (*R*,*R*,*aR*)-**L3** (45.6 mg, 80 μmol), anhydrous TBD (22.3 mg, 160 μmol), carbonate **5c** (776.9 mg, 2 mmol), and 2-bromobenzylamine (409.3 mg, 2.2 mmol) in dry THF (2 mL) at 50 °C for 4 h. For TLC, R_f (**6c**) = 0.50, R_f (**5c**) = 0.60 (petroleum ether/ethyl acetate, 6:1; $KMnO_4$). Purification of the crude product by flash chromatography on silica (40 g; petroleum ether/ethyl acetate, from 96:4 to 9:1) gave (–)-(*R*)-**6c** (627 mg, 63%) as a yellow oil. $[a]_D^{20}$ = –21.9 (*c* = 1.17, $CHCl_3$); 95%*ee* by HPLC. HPLC [Chiralpak AD-H (250 × 4.6 mm, 5 μm) with guard cartridge AD-H (10 × 4 mm, 5 μm), *n*-hexane/2-propanol (98:2), 0.5 mL/min]: t_R = 10.45 min [(+)-(*S*)-**6c**] and t_R = 11.48 min [(–)-(*R*)-**6c**]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 7.7, 1.1 Hz, 1 H, 3′′-H), 7.50–7.32 (m, 6 H, trityl-H), 7.36 (dd, *J* = 7.5, 1.6 Hz, 1 H, 6′′-H), 7.33–7.13 (m, 10 H, 5′′-H, trityl-H), 7.11 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1 H, 4′′-H), 5.62 (ddd, *J* = 17.3, 10.1, 7.2 Hz, 1 H, 3-H), 5.19 (dd, *J* = 17.4, 1.3 Hz, 1 H, 4-H_Z), 5.14 (ddd, *J* = 10.1, 7.2, 1.6 Hz, 1 H, 4-H_E), 3.88 (d, *J* = 13.9 Hz, 1 H, N-CH_{2a}-Ar), 3.73 (d, *J* = 13.9 Hz, 1 H, N-CH_{2b}-Ar), 3.30–3.03 (m, 2 H, 1-H), 3.23 (ddd, *J* = 7.9, 7.9, 3.7 Hz, 1 H, 2-H), 2.31 (s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.1 (s, 3 C, C-1′), 139.6 (s, C-1′′), 138.0 (d, C-3), 133.0 (d, C-3′′), 130.6 (d, C-6′′), 128.8 (d, 6 C, trityl-C), 128.6 (d, C-4′′), 127.9 (d, 6 C, trityl-Ph-C), 127.4 (d, C-5′′), 127.1 (d, 3 C, C-4′), 124.3 (s, C-2′′), 117.9 (t, C-4), 86.8 [s, O-*C*-(Ph)$_3$], 66.7 (t, C-1), 60.8 (d, C-2), 51.2 (t, N-*C*H_2-Ar) ppm. HRMS (ESI+): calcd. for $C_{30}H_{29}{}^{79}BrNO^+$ [M + H]$^+$ 498.1427; found 498.1428; calcd. for $C_{30}H_{28}{}^{81}BrNONa^+$ [M + Na]$^+$ 520.1246; found 520.1248. $C_{30}H_{28}BrNO$ (498.45): calcd. C 72.29, H 5.66, Br 16.03, N 2.81; found C 72.01, H 5.76, Br 16.05, N 2.74.

(–)-(*R*)-*N*-(2-Bromobenzyl)-1-phenylprop-2-en-1-amine [(–)-(*R*)-6d]: GP1 was carried out with $[Ir(COD)Cl]_2$ (53.7 mg, 80 μmol), (*R*,*R*,*aR*)-**L3** (91.1 mg, 160 μmol), anhydrous TBD (44.5 mg, 320 μmol), carbonate **5d** (768 mg, 4 mmol), and 2-bromobenzylamine (818.6 mg, 4.4 mmol) in dry THF (4 mL) at 50 °C for 6.5 h. For TLC, R_f (**6d**) = 0.50, R_f (**5d**) = 0.50 (petroleum ether/ethyl acetate, 9:1; $KMnO_4$). Purification of the crude product by flash chromatography on silica (50 g; petroleum ether to petroleum ether/ethyl acetate, 95:5) gave (–)-(*R*)-**6d** (1.06 g, 88%) as a yellow oil. $[a]_D^{20}$ = –2.7 (*c* = 0.99, $CHCl_3$); 97%*ee* by HPLC. HPLC [Chiralpak AS-H (250 × 4.6 mm, 5 μm) with guard cartridge AS-H (10 × 4 mm, 5 μm), *n*-hexane/2-propanol (99.9:0.1) and 1% diethylamine, 0.5 mL/min]: t_R = 12.09 min [(+)-(*S*)-**6d**] and t_R = 13.20 min [(–)-(*R*)-**6d**]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 8.0, 1.1 Hz, 1 H, 3′′-H), 7.44–7.15 (m, 7 H, 6′′-H, 5′′-H, Ar-H), 7.09 (ddd, *J* = 7.7, 7.6, 1.8 Hz, 1 H, 4′′-H), 5.95 (ddd, *J* = 17.2, 10.1, 7.1 Hz, 1 H, 2-H), 5.23 (ddd, *J* = 17.1, 1.3, 1.2 Hz, 1 H, 3-H_Z), 5.12 (ddd, *J* = 10.1, 1.4, 0.8 Hz, 1 H, 3-H_E), 4.19 (d, *J* = 7.2 Hz, 1 H, 1-H), 3.83 (d, *J* = 14.0 Hz, 1 H, N-CH_{2a}-Ar), 3.77 (d, *J* = 14.0 Hz, 1 H, N-CH_{2b}-Ar), 1.86 (s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.7 (s, C-1′), 141.0 (d, C-2), 139.4 (s, C-1′′), 132.9 (d, C-3′′), 130.6 (d, C-6′′), 128.7 (d, 3 C, C-4′′, Ar-C), 127.5 (d, 2 C, Ar-C), 127.4 (d, C-5′′), 127.4 (d, C-4′), 124.1 (s, C-2′′), 115.4 (t, C-3), 65.2 (d, C-1), 51.5 (t, N-*C*H_2-Ar) ppm. HRMS (ESI+): calcd. for $C_{16}H_{17}{}^{79}BrN^+$ [M + H]$^+$ 302.0539; found 302.0540. $C_{16}H_{16}BrN$ (302.21): calcd. C 63.59, H 5.34, Br 26.44, N 4.63; found C 63.42, H 5.34, Br 26.71, N 4.58.

General Procedure (GP2) for DCC Coupling Reaction: A cold (0 °C) solution of amine **6** (1 mmol) in dry dichloromethane (4–6 mL) under argon was treated with DCC (1.1–1.2 mmol), DMAP (5–

10 mol-%), and then vinylacetic acid or 4-pentenoic acid (1.1–1.2 mmol). The mixture was slowly warmed to room temperature and was then stirred for 15–72 h. The reaction mixture was filtered through Celite in a short column (12 × 3 cm), which was rinsed with diethyl ether. The filtrate was concentrated in vacuo, and the residue of crude **8** was purified by flash chromatography on silica.

(–)-*N*-(2-Bromobenzyl)-*N*-[(*S*)-1-methylprop-2-en-1-yl]but-3-enamide [(–)-(*S*)-8a]: GP2 was carried out with amine (*S*)-**6a** (590 mg, 2.46 mmol), dry dichloromethane (9 mL), DCC (608.6 mg, 2.95 mmol), DMAP (30.0 mg, 10 mol-%), and vinylacetic acid (254 mg, 2.95 mmol) at r.t. for 26 h. For TLC, R_f (**8a**) = 0.45, R_f (**6a**) = 0.20–0.40 (petroleum ether/ethyl acetate, 4:1; $KMnO_4$). The reaction mixture was filtered through Celite (12 × 3 cm) with diethyl ether (50 mL), and the filtrate was concentrated in vacuo. Purification of the crude product by flash chromatography on silica (50 g; petroleum ether/ethyl acetate, from 95:5 to 4:1) gave (–)-(*S*)-**8a** (680 mg, 90%) as a yellow oil. $[a]_D^{20}$ = –45.9 (*c* = 0.99, $CHCl_3$); 96%*ee* by HPLC. HPLC [Chiralpak AS-H (250 × 4.6 mm, 5 μm) with guard cartridge AS-H (10 × 4 mm, 5 μm), *n*-hexane/2-propanol (95:5), 0.5 mL/min]: t_R = 28.45 min [(–)-(*S*)-**8a**] and t_R = 33.64 min [(+)-(*R*)-**8a**]. ^{1}H NMR (500 MHz, $CDCl_3$, signals from rotamers): δ = 7.56 (d, *J* = 8.0 Hz) and 7.48 (d, *J* = 8.0 Hz) [1 H, 3′′′-H], 7.31 (dd, *J* = 7.4, 7.4 Hz) and 7.22 (dd, *J* = 7.4, 7.4 Hz) [1 H, 5′′′-H], 7.22 (d, *J* = 7.4 Hz) and 7.12 (d, *J* = 7.7 Hz) [1 H, 6′′′-H], 7.15 (dd, *J* = 7.7, 7.7 Hz) and 7.06 (dd, *J* = 7.5, 7.5 Hz) [1 H, 4′′′-H], 6.16–5.88 (m, 1 H, C*H*=CH_2), 5.88–5.70 (m, 1 H, C*H*=CH_2), 5.46–5.31 (m) and 4.68–4.54 (m) [1 H, 1′-H], 5.33–5.06 (m) and 5.01 (d, *J* = 17.3 Hz) [4 H, 2 CH=CH_2], 4.73 (d, *J* = 16.7 Hz), 4.42 (d, *J* = 18.7 Hz), 4.37 (d, *J* = 18.7 Hz) and 4.33 (d, *J* = 16.7 Hz) [2 H, N-CH_2-Ar], 3.43–3.23 (m) and 3.05–2.86 (m) [2 H, 2-H], 1.20 (d, *J* = 7.1 Hz) and 1.19 (d, *J* = 7.1 Hz) [3 H, 1′′-H] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0 (s) and 171.7 (s) [C-1], 137.7 (d) and 137.7 (d) [*C*H=CH_2], 137.1 (s) [C-1′′′], 133.0 (d) and 132.5 (d) [C-3′′′], 131.8 (d) and 131.7 (d) [*C*H=CH_2], 128.9 (d) and 128.1 (d) [C-4′′′], 128.1 (d) and 127.7 (d) [C-5′′′], 127.5 (d) and 127.4 (d) [C-6′′′], 122.3 (s) and 122.2 (s) [C-2′′′], 118.2 (t) and 118.0 (t) [CH=*C*H_2], 116.6 (t) and 116.3 (t) [CH=*C*H_2], 55.0 (d) and 51.4 (d) [C-1′], 47.7 (t) and 45.7 (t) [N-*C*H_2-Ar], 39.3 (t, C-2), 18.2 (q) and 16.5 (q) [C-1′′] ppm. HRMS (ESI+): calcd. for $C_{15}H_{18}{}^{79}BrNO^+$ [M + H]$^+$ 308.0644; found 308.0649; calcd. for $C_{15}H_{18}{}^{81}BrNO^+$ [M + H]$^+$ 310.0624; found 310.0629. $C_{15}H_{18}BrNO$ (308.21): calcd. C 58.45, H 5.89, Br 25.92, N 4.54; found C 58.31, H 5.85, Br 25.65, N 4.82.

(–)-*N*-(2-Bromobenzyl)-*N*-[(*S*)-1-ethylprop-2-en-1-yl]but-3-enamide [(–)-(*S*)-8b]: GP2 was carried out with amine (*S*)-**6b** (660 mg, 2.60 mmol), dry dichloromethane (10 mL), DCC (643.3 mg, 3.12 mmol), DMAP (31.7 mg, 10 mol-%), and vinylacetic acid (268.4 mg, 3.12 mmol) at r.t. for 20 h. For TLC, R_f (**8b**) = 0.65, R_f (**6b**) = 0.20–0.40 (petroleum ether/ethyl acetate, 7:3; $KMnO_4$). The reaction mixture was filtered through Celite (12 × 3 cm) with diethyl ether (50 mL), and the filtrate was concentrated in vacuo. Purification of the crude product by flash chromatography on silica (50 g; petroleum ether/ethyl acetate, from 9:1 to 4:1) gave (–)-(*S*)-**8b** (820 mg, 98%) as a yellow oil. $[a]_D^{20}$ = –32.5 (*c* = 1.00, $CHCl_3$); 95%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$, signals from rotamers): δ = 7.55 (d, *J* = 7.7 Hz) and 7.47 (d, *J* = 7.7 Hz) [1 H, 3′′′-H], 7.40–6.94 (m, 3 H, 4′′′-H, 5′′′-H, 6′′′-H), 6.20–5.82 (m, 1 H, C*H*=CH_2), 5.82–5.60 (m, 1 H, C*H*=CH_2), 5.33–4.86 (m, 4 H, 2 CH=CH_2), 5.08–4.84 (m) and 4.32–4.18 (m) [1 H, 1′-H], 4.70–4.38 (m, 2 H, N-CH_2-Ar), 3.32 (d, *J* = 6.4 Hz) and 3.70–2.80 (m) [2 H, 2-H], 1.72–1.48 (m, 2 H, 1′′-H), 0.88 (t, *J* = 7.4 Hz) and 0.85 (t, *J* = 7.5 Hz) [3 H, 2′′-H] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.0 (s) and 172.0 (s) [C-1], 137.5 (s) and 136.9 (s) [C-1′′′], 136.1 (d) and 135.9 (d) [*C*H=CH_2], 132.9 (d) and 132.5 (d) [C-3′′′], 131.9 (d) and 131.8 (d) [*C*H=CH_2], 128.9 (d) and 128.7 (d) [C-4′′′], 128.2 (d) and 127.9 (d) [C-6′′′], 127.6 (d) and 127.4 (d) [C-5′′′], 122.4 (s) and 122.2 (s) [C-2′′′], 118.3 (t) and 118.2 (t) [CH=*C*H_2], 118.0 (t) and 117.3 (t) [CH=*C*H_2], 62.0 (d) and 58.7 (d) [C-1′], 48.3 (t) and 45.7 (t) [N-*C*H_2-Ar], 39.4 (t, C-2), 25.6 (t) and 24.8 (t) [C-1′′], 11.2 (q) and 11.0 (q) [C-2′′] ppm. HRMS (ESI+): calcd. for $C_{16}H_{21}{}^{79}BrNO^+$ [M + H]$^+$ 322.0801; found 322.0803; calcd. for $C_{16}H_{20}{}^{79}BrNONa^+$ [M + Na]$^+$ 344.0620; found 344.0623. $C_{16}H_{20}BrNO$ (322.24): calcd. C 59.64, H 6.26, Br 24.80, N 4.35; found C 59.69, H 6.26, Br 24.74, N 4.38.

(–)-*N*-(2-Bromobenzyl)-*N*-{(*R*)-1-[(trityloxy)methyl]prop-2-en-1-yl}but-3-enamide [(–)-(*R*)-8c]: GP2 was carried out with amine (*R*)-**6c** (1.02 g, 2.05 mmol), dry dichloromethane (6.83 mL), DCC (507.1 mg, 2.46 mmol), DMAP (12.5 mg, 10 mol-%), and vinylacetic acid (211.6 mg, 2.46 mmol) at r.t. for 23 h. For TLC, R_f (**8c**) = 0.50, R_f (**6c**) = 0.52 (petroleum ether/ethyl acetate, 4:1; $KMnO_4$). The reaction mixture was filtered through Celite (12 × 3 cm) with diethyl ether (50 mL), and the filtrate was concentrated in vacuo. Purification of the crude product by flash chromatography on silica (50 g; petroleum ether/ethyl acetate, from 95:5 to 6:1) gave (–)-(*R*)-**8c** (1.10 g, 95%) as a yellow oil. $[a]_D^{20}$ = –14.5 (*c* = 0.66, $CHCl_3$); 95%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$, signals from rotamers): δ = 7.52 (d, *J* = 8.0 Hz) and 7.45 (d, *J* = 8.0 Hz) [1 H, 3′′′′-H], 7.70–6.80 (m, 18 H, 4′′′′-H, 5′′′′-H, 6′′′′-H, trityl-ArH), 6.24–5.80 (m, 1 H, C*H*=CH_2), 5.83 (ddd, *J* = 17.2, 10.4, 6.8 Hz) and 5.62 (ddd, *J* = 16.9, 10.9, 5.8 Hz) [1 H, C*H*=CH_2], 5.40–4.90 (m, 4 H, 2 CH=CH_2), 5.35–5.10 (m) and 4.80–4.54 (m) [1 H, 1′-H], 4.70–4.30 (m, 2 H, N-CH_2-Ar), 3.63–2.80 (m, 4 H, 1′′-H, 2-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.2 (s, C-1), 143.7 (s) and 143.5 (s) [3 C, C-1′′′], 137.0 (s) and 136.8 (s) [C-1′′′′], 133.7 (d) and 133.6 (d) [*C*H=CH_2], 132.7 (d) and 132.3 (d) [C-3′′′′], 131.9 (d) and 131.7 (d) [*C*H=CH_2], 128.7 (d) and 128.6 (d) [6 C, trityl-Ph-C], 128.0 (d) and 127.9 (d) [6 C, trityl-Ph-C], 127.8 (d) and 127.6 (d) [C-4′′′], 127.3 (d) and 127.3 (d) [C-5′′′′], 127.1 (d, 3 C, C-4′′′), 127.3 (d) and 126.9 (d) [C-6′′′′], 122.3 (s) and 122.1 (s) [C-2′′′′], 118.9 (t) and 118.4 (t) [CH=*C*H_2], 118.2 (t) and 118.0 (t) [CH=*C*H_2], 87.5 (s) and 87.0 (s) [O-*C*-trityl], 64.0 (t) and 63.6 (t) [C-1′′], 60.1 (d) and 57.6 (d) [C-1′], 49.9 (t) and 46.1 (t) [N-*C*H_2-Ar], 39.3 (t, C-2) ppm. HRMS (ESI+): calcd. for $C_{34}H_{33}{}^{79}BrNO_2^+$ [M + H]$^+$ 566.1689; found 566.1694; calcd. for $C_{34}H_{32}{}^{79}BrNO_2Na^+$ [M + Na]$^+$ 588.1509; found 588.1513.

(+)-*N*-(2-Bromobenzyl)-*N*-[(1*R*)-1-phenylprop-2-en-1-yl]but-3-enamide [(+)-(*R*)-8d]: GP2 was carried out with amine (*R*)-**6d** (920 mg, 3.04 mmol), dry dichloromethane (10 mL), DCC (753.8 mg, 3.65 mmol), DMAP (18.6 mg, 5 mol-%), and vinylacetic acid (314.5 mg, 3.65 mmol) at r.t. for 23 h. For TLC, R_f (**8d**) = 0.30, R_f (**6d**) = 0.50 (petroleum ether/ethyl acetate, 9:1; $KMnO_4$). The reaction mixture was then filtered through Celite (12 × 3 cm) with diethyl ether (50 mL), and the filtrate was concentrated in vacuo. Purification of the crude product by flash chromatography on silica (50 g; petroleum ether/ethyl acetate, from 95:5 to 6:1) gave (+)-(*R*)-**8d** (1.020 g, 90%) as a yellow oil. $[a]_D^{20}$ = +22.7 (*c* = 1.15, $CHCl_3$); 97%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$, signals from rotamers): δ = 7.47 (d, *J* = 7.7 Hz) and 7.36 (d, *J* = 8.0 Hz) [1 H, 3′′′-H], 7.40–6.86 (m, 8 H, 4′′′-H, 5′′′-H, 6′′′-H, Ar-H), 6.47 (d, *J* = 6.6 Hz) and 5.67 (d, *J* = 4.8 Hz) [1 H, 1′-H], 6.25–5.85 (m, 2 H, 2 C*H*=CH_2), 5.46–4.90 (m, 4 H, 2 CH=CH_2), 4.90–4.30 (m, 2 H, N-CH_2-Ar), 3.32 (d, *J* = 5.8 Hz) and 3.01 (d, *J* = 6.7 HZ) [2 H, 2-H] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (s, C-1), 138.7 (s) and 137.8 (s) [C-1′′], 136.8 (s) and 136.4 (s) [C-1′′′], 135.0 (d) and 134.8 (d) [*C*H=CH_2], 132.7 (d) and 132.3 (d) [C-3′′′], 131.9 (d) and 131.6 (d) [*C*H=CH_2], 128.7 (d) and 128.4 (d) [C-4′′′], 128.6 (d, 2

C, Ph-C), 128.1 (d) and 128.0 (d) [2 C, Ph-C], 127.9 (d) and 127.7 (d) [C-5′′′], 127.7 (d, C-6′′′), 127.4 (d) and 127.1 (d) [C-4′′], 122.3 (s) and 121.9 (s) [C-2′′′], 119.4 (t, CH=*C*H$_2$), 118.3 (t, CH=*C*H$_2$), 63.8 (d) and 60.1 (d) [C-1′], 49.1 (t) and 47.6 (t) [N-*C*H$_2$-Ar], 39.5 (t) and 39.2 (t) [C-2] ppm. HRMS (ESI+): calcd. for $C_{20}H_{21}{}^{79}BrNO^+$ [M + H]$^+$ 370.0801; found 370.0806; calcd. for $C_{20}H_{20}{}^{79}BrNONa^+$ [M + Na]$^+$ 392.0620; found 392.0626. $C_{20}H_{20}BrNO$ (370.28): calcd. C 64.87, H 5.44, Br 21.58, N 3.78; found C 64.88, H 5.49, Br 21.50, N 3.75.

(–)-*N*-(2-Bromobenzyl)-*N*-[(1*S*)-1-ethylprop-2-en-1-yl]pent-4-enamide [(–)-(*S*)-8bb]: GP2 was carried out with amine (*S*)-**6b** (630 mg, 2.48 mmol), dry dichloromethane (8 mL), DCC (614.2 mg, 2.98 mmol), DMAP (15.1 mg, 5 mol-%), and 4-pentenoic acid (298 mg, 2.98 mmol) at r.t. for 15 h. For TLC, R_f (**8bb**) = 0.70, R_f (**6b**) = 0.20–0.40 (petroleum ether/ethyl acetate, 4:1; $KMnO_4$). The reaction mixture was then filtered through Celite (12 × 3 cm) with diethyl ether (50 mL), and the filtrate was concentrated in vacuo. Purification of the crude product by flash chromatography on silica (50 g; petroleum ether to petroleum ether/ethyl acetate, from 9:1 to 4:1) gave (–)-(*S*)-**8bb** (764 mg, 92%) as a yellow oil. $[\alpha]_D^{20}$ = –24.9 (*c* = 0.85, $CHCl_3$); 93%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$, signals from rotamers): δ = 7.54 (d, *J* = 8.05 Hz) and 7.48 (d, *J* = 8.0 Hz) [1 H, 3′′′-H], 7.36–6.97 (m, 3 H, 4′′′-H, 5′′′-H, 6′′-H), 6.04–5.60 (m, 2 H, 2 C*H*=CH$_2$), 5.36–4.84 (m, 4 H, 2 CH=C*H*$_2$), 5.20–4.88 (m) and 4.34–4.14 (m) [1 H, 1′-H], 4.72–4.28 (m, 2 H, N-C*H*$_2$-Ar), 2.72–2.18 (m, 4 H, 2-H, 3-H), 1.73–1.44 (m, 2 H, 1′′-H), 0.89 (t, *J* = 7.1 Hz) and 0.86 (t, *J* = 6.9 Hz) [3 H, 2′′-H] ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.4 (s) and 173.2 (s) [C-1], 137.7 (d) and 137.5 (d) [*C*H=CH$_2$], 137.0 (s, C-1′′′), 136.3 (d) and 136.1 (d) [*C*H=CH$_2$], 132.9 (d) and 132.5 (d) [C-3′′′], 128.8 (d) and 128.7 (d) [C-4′′′], 128.2 (d) and 128.0 (d) [C-5′′′], 127.6 (d) and 127.4 (d) [C-6′′′], 122.4 (s) and 122.2 (s) [C-2′′′], 118.2 (t) and 117.2 (t) [CH=*C*H$_2$], 115.5 (t) [CH=*C*H$_2$], 62.0 (d) and 58.7 (d) [C-1′], 48.3 (t) and 45.8 (t) [N-*C*H$_2$-Ar], 33.2 (t, C-2), 29.6 (t) and 29.5 (t) [C-3], 25.7 (t) and 24.8 (t) [C-1′′], 11.3 (q) and 11.1 (q) [C-2′′] ppm. HRMS (ESI+): calcd. for $C_{17}H_{23}{}^{79}BrNO^+$ [M + H]$^+$ 336.0957; found 336.0959; calcd. for $C_{17}H_{22}{}^{79}BrNONa^+$ [M + Na]$^+$ 358.0777; found 358.0779. $C_{17}H_{22}BrNO$ (336.27): calcd. C 60.72, H 6.59, Br 23.76, N 4.17; found C 60.76, H 6.62, Br 23.77, N 4.18.

General Procedure (GP3) for Ring-Closing Metathesis Reaction: A solution of dienamide **8** in dry dichloromethane (0.03 M) under argon was treated with Grubbs I catalyst (for six-membered ring formation) or Grubbs II catalyst (for seven-membered ring formation, 3–5 mol-%). The solution was heated at reflux for 2–5 h and was then concentrated in vacuo. The residue was subjected to flash column chromatography on silica to give **9**.

(–)-(6*S*)-1-(2-Bromobenzyl)-6-methyl-3,6-dihydropyridin-2(1*H*)-one [(–)-(*S*)-9a]: GP3 was carried out with dienamide **8a** (700 mg, 2.27 mmol), dichloromethane (76 mL, 0.03 M), and Grubbs I catalyst (56.1 mg, 3 mol-%) for 2.5 h. For TLC, R_f (**9a**) = 0.30, R_f (**8a**) = 0.60 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). Purification of the crude product by flash chromatography on silica (40 g; petroleum ether/ethyl acetate, from 4:1 to 3:2) gave (–)-(*S*)-**9a** (610 mg, 96%) as a brownish viscous liquid. $[\alpha]_D^{20}$ = –3.7 (*c* = 1.02, $CHCl_3$); 96%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (dd, *J* = 7.9, 1.0 Hz, 1 H, 3′′-H), 7.25 (ddd, *J* = 7.8, 7.0, 1.2 Hz, 1 H, 5′′-H), 7.16 (dd, *J* = 7.6, 1.2 Hz, 1 H, 6′′-H), 7.10 (ddd, *J* = 7.6, 7.5, 1.5 Hz, 1 H, 4′′-H), 5.84–5.66 (m, 2 H, 4-H, 5-H), 5.25 (d, *J* = 16.1 Hz, 1 H, N-C*H*$_{2a}$-Ar), 4.36 (d, *J* = 16.1 Hz, 1 H, N-C*H*$_{2b}$-Ar), 3.89 (dddd, *J* = 9.9, 9.9, 6.5, 3.3 Hz, 1 H, 6-H), 3.13–3.00 (m, 2 H, 3-H), 1.28 (d, *J* = 6.5 Hz, 3 H, 1′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.3 (s, C-2), 136.2 (s, C-1′′), 132.9 (d, C-3′′), 128.8 (d, C-4′′), 128.6 (d, C-6′′), 127.9 (d, C-5′′), 127.8 (d, C-5), 123.5 (s, C-2′′), 121.6 (d, C-4), 53.7 (d, C-6), 47.1 (t, N-*C*H$_2$-Ar), 32.2 (t, C-3), 20.9 (q, C-1′) ppm. HRMS (ESI+): calcd. for $C_{13}H_{15}{}^{79}BrNO^+$ [M + H]$^+$ 280.0331; found 280.0336; calcd. for $C_{13}H_{14}{}^{79}BrNONa^+$ [M + Na]$^+$ 302.0151; found 302.0156.

(–)-(6*S*)-1-(2-Bromobenzyl)-6-ethyl-3,6-dihydropyridin-2(1*H*)-one [(–)-(*S*)-9b]: GP3 was carried out with dienamide **8b** (450 mg, 1.40 mmol), dichloromethane (47 mL, 0.03 M), and Grubbs I catalyst (57.5 mg, 5 mol-%) for 2 h. For TLC, R_f (**9b**) = 0.28, R_f (**8b**) = 0.55 (petroleum ether/ethyl acetate, 7:3; $KMnO_4$). Purification of the crude product by flash chromatography on silica (35 g; petroleum ether/ethyl acetate, from 9:1 to 3:2) gave (–)-(*S*)-**9b** (410 mg, 100%) as a brownish viscous liquid. $[\alpha]_D^{20}$ = –1.2 (*c* = 1.05, $CHCl_3$); 93%*ee*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (dd, *J* = 7.9, 1.1 Hz, 1 H, 3′′-H), 7.26 (ddd, *J* = 7.8, 7.1, 1.1 Hz, 1 H, 5′′-H), 7.17 (dd, *J* = 7.8, 1.6 Hz, 1 H, 6′′-H), 7.11 (ddd, *J* = 7.5, 7.5, 1.8 Hz, 1 H, 4′′-H), 5.87 (dddd, *J* = 10.1, 3.9, 3.2, 0.8 Hz, 1 H, 4-H), 5.70 (dddd, *J* = 10.0, 4.2, 2.0, 2.0 Hz, 1 H, 5-H), 5.38 (d, *J* = 16.0 Hz, 1 H, N-C*H*$_{2a}$-Ar), 4.21 (d, *J* = 16.0 Hz, 1 H, N-C*H*$_{2b}$-Ar), 3.86 (dddd, *J* = 10.5, 6.8, 3.3, 0.6 Hz, 1 H, 6-H), 3.16–2.95 (m, 2 H, 3-H), 1.80 (dqd, *J* = 14.3, 7.2, 7.1 Hz, 1 H, 1′-H$_a$), 1.62 (dqd, *J* = 14.4, 7.3, 3.0 Hz, I H, 1′-H$_b$), 0.84 (t, *J* = 7.3 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.8 (s, C-2), 136.1 (s, C-1′′), 132.9 (d, C-3′′), 128.8 (d, C-4′′), 128.7 (d, C-6′′), 127.8 (d, C-5′′), 125.8 (d, C-5), 123.6 (s, C-2′′), 123.1 (d, C-4), 58.2 (d, C-6), 46.6 (t, N-*C*H$_2$-Ar), 32.7 (t, C-3), 26.4 (t, C-1′), 7.8 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{14}H_{17}{}^{79}BrNO^+$ [M + H]$^+$ 294.0488; found 294.0489; calcd. for $C_{14}H_{16}{}^{79}BrNONa^+$ [M + Na]$^+$ 316.0307; found 316.0309. $C_{14}H_{16}BrNO$ (294.19): calcd. C 57.16, H 5.48, Br 27.16, N 4.76; found C 57.25, H 5.45, Br 27.21, N 4.76.

(+)-(6*R*)-1-(2-Bromobenzyl)-6-[(trityloxy)methyl]-3,6-dihydropyridin-2(1*H*)-one [(+)-(*R*)-9c]: GP3 was carried out with dienamide **8c** (950 mg, 2.56 mmol), dichloromethane (85.5 mL, 0.03 M), and Grubbs I catalyst (63.33 mg, 3 mol-%) for 5 h. For TLC, R_f (**9c**) = 0.34, R_f (**8c**) = 0.72 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). Purification of the crude product by flash chromatography on silica (40 g; petroleum ether/ethyl acetate, from 9:1 to 7:3) gave (+)-(*R*)-**9c** (800 mg, 91%) as a brownish viscous liquid. $[\alpha]_D^{20}$ = +47.5 (*c* = 1.10, $CHCl_3$); 95%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (dd, *J* = 7.9, 1.3 Hz, 1 H, 3′′-H), 7.45–7.34 (m, 6 H, trityl-Ph-H), 7.36–7.12 (m, 10 H, 5′-H, trityl-Ph-H), 7.06 (ddd, *J* = 7.7, 7.7, 1.5 Hz, 1 H, 4′′-H), 7.00 (dd, *J* = 7.5, 1.3 Hz, 1 H, 6′′-H), 5.97 (ddd, *J* = 9.9, 3.8, 2.7 Hz, 1 H, 4-H), 5.77 (ddd, *J* = 9.9, 4.6, 2.4 Hz, 1 H, 5-H), 5.27 (d, *J* = 16.5 Hz, 1 H, N-C*H*$_{2a}$-Ar), 4.04 (d, *J* = 16.5 Hz, 1 H, N-C*H*$_{2b}$-Ar), 3.90–3.70 (m, 1 H, 6-H), 3.33 (dd, *J* = 10.1, 4.2 Hz, 1 H, C*H*$_{2a}$-O), 3.25 (dd, *J* = 10.1, 4.2 Hz, 1 H, C*H*$_{2b}$-O), 3.25–2.98 (m, 2 H, 3-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.0 (s, C-2), 143.7 (s, 3 C, C-1′), 135.9 (s, C-1′′), 132.9 (d, C-3′′), 128.7 (d, 6 C, trityl-Ph-C), 128.7 (d, C-4′′), 128.2 (d, C-6′′), 128.0 (d, 6 C, trityl-Ph-C), 127.7 (d, C-5′′), 127.3 (d, 3 C, C-4′), 124.7 (d, C-5), 124.5 (d, C-4), 123.5 (s, C-2′′), 87.3 [s, (Ph)$_3$C-*C*-O], 64.0, (t, *C*H$_2$-O), 58.0 (d, C-6), 47.7 (t, N-*C*H$_2$-Ar), 33.0 (t, C-3) ppm. HRMS (ESI+): calcd. for $C_{32}H_{29}{}^{79}BrNO_2^+$ [M + H]$^+$ 538.1376; found 538.1381; calcd. for $C_{32}H_{28}{}^{79}BrNO_2Na^+$ [M + Na]$^+$ 560.1196; found 560.1200. $C_{32}H_{28}BrNO_2$ (538.47): calcd. C 71.38, H 5.24, Br 14.84, N 2.60; found C 71.68, H 5.34, Br 14.57, N 2.51.

(+)-(6*R*)-1-(2-Bromobenzyl)-6-phenyl-3,6-dihydropyridin-2(1*H*)-one [(+)-(*R*)-9d]: GP3 was carried out with dienamide **8d** (820 mg, 2.21 mmol), dichloromethane (74 mL, 0.03 M), and Grubbs I catalyst (91.1 mg, 5 mol-%) for 2.5 h. For TLC, R_f (**9d**) = 0.34, R_f (**8d**) = 0.68 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). Purification of

the crude product by flash chromatography on silica (40 g; petroleum ether/ethyl acetate, from 6:1 to 3:2) gave (+)-(*R*)-**9d** (720 mg, 95%) as a brownish viscous liquid. $[\alpha]_D^{20}$ = +92.0 (*c* = 0.92, $CHCl_3$); 97%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 7.9, 1.3 Hz, 1 H, 3′′-H), 7.43–7.20 (m, 4 H, 5′′-H, 3′-H, 4′-H, 5′-H), 7.23–7.12 (m, 3 H, 6′′-H, 2′-H, 6′-H), 7.11 (ddd, *J* = 7.7, 7.5, 1.5 Hz, 1 H, 4′′-H), 5.90–5.66 (m, 2 H, 4-H, 5-H), 5.39 (d, *J* = 16.0 Hz, 1 H, N-CH_{2a}-Ar), 4.83 (dd, *J* = 7.1, 3.5 Hz, 1 H, 6-H), 3.86 (d, *J* = 16.1 Hz, 1 H, N-CH_{2b}-Ar), 3.40–3.10 (m, 2 H, 3-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.1 (s, C-2), 139.9 (s, C-1′), 135.7 (s, C-1′′), 133.0 (d, C-3′′), 129.1 (d, 2 C, C-3′, C-5′), 128.9 (d, 2 C, C-4′′, C-6′′), 128.4 (d, C-4′), 127.7 (d, C-5′′), 127.1 (d, 2 C, C-2′, C-6′), 126.6 (d, C-5), 123.7 (s, C-2′′), 120.9 (d, C-4), 62.7 (d, C-6), 47.2 (t, N-*C*H_2-Ar), 32.3 (t, C-3) ppm. HRMS (ESI+): calcd. for $C_{18}H_{17}{}^{79}BrNO^+$ [M + H]$^+$ 342.0488; found 342.0491; calcd. for $C_{18}H_{16}{}^{79}BrNOK^+$ [M + K]$^+$ 380.0047; found 380.0050. $C_{18}H_{16}BrNO$ (342.23): calcd. C 63.17, H 4.71, Br 23.35, N 4.09; found C 63.25, H 4.83, Br 23.07, N 3.82.

(+)-(7*S*)-1-(2-Bromobenzyl)-7-ethyl-1,3,4,7-tetrahydro-2*H*-azepin-2-one [(+)-(*S*)-9bb]: GP3 was carried out with dienamide **8bb** (700 mg, 2.08 mmol), dichloromethane (69 mL, 0.03 M), and Grubbs II catalyst (53.1 mg, 3 mol-%) for 5 h. For TLC, R_f (**9bb**) = 0.30, R_f (**8bb**) = 0.70 (petroleum ether/ethyl acetate, 7:3; $KMnO_4$). Purification of the crude product by flash chromatography on silica (40 g; petroleum ether to petroleum ether/ethyl acetate, from 6:1 to 3:2) gave (+)-(*S*)-**9bb** (630 mg, 98%) as a brownish viscous liquid. $[\alpha]_D^{20}$ = +31.8 (*c* = 1.12, $CHCl_3$); 93%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (dd, *J* = 7.9, 1.28 Hz, 1 H, 3′′-H), 7.25 (ddd, *J* = 7.3, 7.1, 0.7 Hz, 1 H, 5′′-H), 7.18 (dd, *J* = 7.9, 1.6 Hz, 1 H, 6′′-H), 7.10 (ddd, *J* = 7.8, 7.2, 1.4 Hz, 1 H, 4′′-H), 5.83 (dddd, *J* = 11.7, 5.8, 1.1, 0.8 Hz, 1 H, 5-H), 5.65 (dddd, *J* = 11.6, 7.0, 2.8, 1.4 Hz, 1 H, 6-H), 5.32 (d, *J* = 16.1 Hz, 1 H, N-CH_{2a}-Ar), 4.14 (d, *J* = 16.1 Hz, 1 H, N-CH_{2b}-Ar), 3.59 (ddd, *J* = 7.3, 7.3, 7.3 Hz, 1 H, 7-H), 2.94 (ddd, *J* = 12.9, 12.9, 3.9 Hz, 1 H, 3-H_a), 2.66 (dddd, *J* = 13.1, 5.3, 2.9, 1.0 Hz, 1 H, 3-H_b), 2.60–2.20 (m, 2 H, 4-H), 2.05–1.72 (m, 2 H, 1′-H), 1.01 (t, *J* = 7.3 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.4 (s, C-2), 136.8 (s, C-1′′), 132.7 (d, C-3′′), 129.9 (d, C-5), 128.7 (d, C-6), 128.6 (d, C-4′′), 128.3 (d, C-6′′), 127.7 (d, C-5′′), 123.3 (s, C-2′′), 60.3 (d, C-7), 52.0 (t, N-*C*H_2-Ar), 35.6 (t, C-3), 29.6 (t, C-1′), 24.6 (t, C-4), 11.9 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{30}H_{36}{}^{79}Br_2N_2O_2Na^+$ [2M + Na]$^+$ 637.1030; found 637.1045. $C_{15}H_{18}BrNO$ (308.21): calcd. C 58.45, H 5.89, Br 25.92, N 4.54; found C 58.44, H 5.93, Br 25.73, N 4.50.

General Procedure (GP4) for Intramolecular Heck Reactions: To an oven-dried microwave vial that was equipped with a magnetic stirring bar and the cyclic product **9** (1 mmol) under argon were added $Pd(PPh_3)_2Cl_2$ or Pd(dppf)Cl_2 (10–20 mol-%), triethylamine (10 mmol), and dry DMF (0.03 M). The capped vial was placed in the microwave reactor Discover CEM and irradiated at 100–120 °C for 2 min followed by a 25–120 min hold time at 100–120 °C. The reaction mixture was cooled to room temp. and was then treated with either H_2O or saturated NH_4Cl solution. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. The crude products (i.e., **10**, **11**, and **12**) were purified by flash column chromatography on silica (petroleum ether/ethyl acetate) or, if necessary, preparative HPLC (pentane/ethyl acetate).

(–)-(6*S*,11*S*)-11-Methyl-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(–)-(6*S*,11*S*)-10a], (+)-(6*R*,11*S*)-11-Methyl-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*R*,11*S*)-11a], and (+)-(6*S*,11*S*)-11-Methyl-1,4,5,6-tetrahydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*S*,11*S*)-12a]: GP4 was carried out with cyclic enamide **9a** (58.0 mg, 0.21 mmol), Pd(dppf)Cl_2 (30.4 mg, 20 mol-%), triethylamine (209.6 mg, 2.1 mmol), and dry DMF (6.9 mL, 0.03 M). The capped vial was irradiated with a microwave at 120 °C for 2 min followed by a 40 min hold time at 120 °C. For TLC, R_f (**10a**, **11a**, **12a**) = 0.60, R_f (**9a**) = 0.30 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). After cooling to room temp., water (20 mL) was added, and the resulting mixture was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash column chromatography on silica (25 g; petroleum ether/ethyl acetate, 4:1) to give a mixture of the three products (28 mg, 68%, **10a**/**11a**/**12a**, 86:10:4). Separation was accomplished by preparative HPLC (pentane/ethyl acetate, 4:1) to give first (–)-(6*S*,11*S*)-**10a** (24 mg, 58%), then (+)-(6*R*,11*S*)-**11a** (3 mg, 7%), and finally (+)-(6*S*,11*S*)-**12a** (1 mg, 2%).

(–)-(6*S*,11*S*)-10a: $[\alpha]_D^{20}$ = –356 (*c* = 0.85, $CHCl_3$); 96%*ee*. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20 (ddd, *J* = 7.4, 7.4, 1.4 Hz, 1 H, 8-H), 7.15 (dd, *J* = 7.1, 7.1 Hz, 1 H, 9-H), 7.08 (d, *J* = 7.4 Hz, 1 H, 10-H), 7.01 (d, *J* = 7.4 Hz, 1 H, 7-H), 6.98 (ddd, *J* = 9.2, 7.0, 2.1 Hz, 1 H, 5-H), 6.05 (d, *J* = 9.3 Hz, 1 H, 4-H), 4.81 (d, *J* = 16.5 Hz, 1 H, 1-H_a), 4.37 (d, *J* = 16.5 Hz, 1 H, 1-H_b), 3.85–3.71 (m, 1 H, 11-H), 3.22 (d, *J* = 6.9 Hz, 1 H, 6-H), 1.48 (d, *J* = 6.9 Hz, 3 H, 1′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.8 (s, C-3), 146.9 (d, C-5), 138.3 (s, C-10a), 135.1 (s, C-6a), 128.7 (d, C-10), 127.7 (d, C-7), 127.6 (d, C-8), 126.9 (d, C-9), 126.1 (d, C-4), 55.6 (d, C-11), 54.7 (t, C-1), 40.4 (d, C-6), 18.3 (q, C-1′) ppm. HRMS (ESI+): calcd. for $C_{13}H_{13}NONa^+$ [M + Na]$^+$ 222.0889; found 222.0889. $C_{13}H_{13}NO$ (199.25): calcd. C 78.36, H 6.58, N 7.03; found C 78.07, H 6.63, N 6.83.

(+)-(6*R*,11*S*)-11a: $[\alpha]_D^{20}$ = +370 (*c* = 0.60, $CHCl_3$); 96%*ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24 (dd, *J* = 9.1, 6.6 Hz, 1 H, 5-H), 7.20 (ddd, *J* = 7.0, 7.0, 2.0 Hz, 1 H, 8-H), 7.15 (ddd, *J* = 7.1, 7.1, 1.6 Hz, 1 H, 9-H), 7.07 (dd, *J* = 7.2, 1.7 Hz, 1 H, 10-H), 6.98 (d, *J* = 6.8, 1.6 Hz, 1 H, 7-H), 6.00 (d, *J* = 9.2 Hz, 1 H, 4-H), 4.67 (d, *J* = 17.2 Hz, 1 H, 1-H_a), 4.29 (d, *J* = 17.2 Hz, 1 H, 1-H_b), 4.05 (qd, *J* = 7.0, 0.8 Hz, 1 H, 11-H), 3.05 (d, *J* = 6.7 Hz, 1 H, 6-H), 1.32 (d, *J* = 7.0 Hz, 3 H, 1′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (s, C-3), 152.8 (d, C-5), 134.5 (s, C-6a), 133.7 (s, C-10a), 130.0 (d, C-10), 127.5 (d, C-8), 127.2 (d, C-7), 127.1 (d, C-9), 125.1 (d, C-4), 54.1 (d, C-11), 46.1 (t, C-1), 40.1 (d, C-6), 16.0 (q, C-1′) ppm. HRMS (ESI+): calcd. for $C_{26}H_{26}N_2O_2Na^+$ [2M + Na]$^+$ 421.1886; found 421.1894.

(+)-(6*S*,11*S*)-12a: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.00 (m, 3 H, Ar-H), 7.03 (dd, *J* = 6.8, 1.8 Hz, 1 H, 10-H), 5.17 (d, *J* = 15.8 Hz, 1 H, 1-H_a), 4.15 (d, *J* = 15.8 Hz, 1 H, 1-H_b), 3.72 (qd, *J* = 7.1, 1.8 Hz, 1 H, 11-H), 3.12 (dd, *J* = 7.5, 2.2 Hz, 1 H, 6-H), 2.72–2.45 (m, 2 H, 4-H_a, 5-H_a), 2.44–2.23 (m, 1 H, 4-H_b), 2.10–1.85 (m, 1 H, 5-H_b), 1.48 (d, *J* = 7.0 Hz, 3 H, 1′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.3 (s, C-3), 141.9 (s, C-10a), 136.7 (s, C-6a), 129.9 (d, Ar-C), 127.2 (d, Ar-C), 126.9 (d, Ar-C), 126.7 (d, C-10), 56.6 (d, C-11), 55.7 (t, C-1), 39.5 (d, C-6), 29.8 (t, C-4), 26.9 (t, C-5), 18.2 (q, C-1′) ppm. HRMS (ESI+): calcd. for $C_{13}H_{16}NO^+$ [M + H]$^+$ 202.1226; found 202.1229; calcd. for $C_{13}H_{15}NONa^+$ [M + Na]$^+$ 224.1046; found 224.1049.

(–)-(6*S*,11*S*)-11-Ethyl-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(–)-(6*S*,11*S*)-10b], (+)-(6*R*,11*S*)-11-Ethyl-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*R*,11*S*)-11b], and (+)-(6*S*,11*S*)-11-Ethyl-1,4,5,6-tetrahydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*S*,11*S*)-12b]: GP4 was carried out with enamide **9b** (60 mg, 0.20 mmol), Pd(dppf)Cl_2 (29.9 mg, 20 mol-%), triethylamine (206.5 mg, 2.04 mmol), and dry DMF (6.8 mL, 0.03 M). The

capped vial was irradiated with a microwave at 120 °C for 2 min followed by a 40 min hold time at 120 °C. For TLC, R_f (**10b**, **11b**, **12b**) = 0.70, R_f (**9b**) = 0.35 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). The cooled reaction mixture was treated with H_2O (20 mL), and the resulting solution was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. The residue was subjected to flash column chromatography on silica (25 g; petroleum ether/ethyl acetate, 4:1) to give a mixture of the three products (32 mg, 74%, **10b/11b/12b**, 79:15:6). Separation was accomplished by preparative HPLC (pentane/ethyl acetate, 4:1) to elute first (–)-(6*S*,11*S*)-**10b** (25 mg, 59%), then (+)-(6*R*,11*S*)-**11b** (5 mg, 11%), and finally (+)-(6*S*,11*S*)-**12b** (2 mg, 4%).

(–)-(6*S*,11*S*)-10b: $[\alpha]_D^{20}$ = –317 (*c* = 0.92, $CHCl_3$); 93% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20 (ddd, *J* = 7.1, 7.1, 1.8 Hz, 1 H, 8-H), 7.15 (dd, *J* = 7.1, 6.4 Hz, 1 H, 9-H), 7.09 (dd, *J* = 7.1, 1.6 Hz, 1 H, 10-H), 7.01 (d, *J* = 8.0 Hz, 1 H, 7-H), 6.96 (ddd, *J* = 9.2, 7.0, 2.1 Hz, 1 H, 5-H), 6.03 (d, *J* = 9.15 Hz, 1 H, 4-H), 4.85 (d, *J* = 16.5 Hz, 1 H, 1-H_a), 4.34 (d, *J* = 16.5 Hz, 1 H, 1-H_b), 3.52–3.38 (m, 1 H, 11-H), 3.29 (d, *J* = 6.6 Hz, 1 H, 6-H), 2.08–1.85 (m, 1 H, 1′-H_a), 1.86–1.65 (m, 1 H, 1′-H_b), 1.01 (t, *J* = 7.5 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7 (s, C-3), 146.4 (d, C-5), 138.3 (s, C-10a), 135.5 (s, C-6a), 128.8 (d, C-10), 127.6 (d, C-7), 127.6 (d, C-8), 126.9 (d, C-9), 126.4 (d, C-4), 62.0 (d, C-11), 54.8 (t, C-1), 38.4 (d, C-6), 25.1 (t, C-1′), 11.3 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{14}H_{16}NO^+$ $[M + H]^+$ 214.1226; found 214.1227; calcd. for $C_{14}H_{15}NOK^+$ $[M + K]^+$ 252.0785; found 252.0786. $C_{14}H_{15}NO$ (213.27): calcd. C 78.84, H 7.09, N 6.57; found C 78.58, H 7.09, N 6.49.

(+)-(6*R*,11*S*)-11b: $[\alpha]_D^{20}$ = +302 (*c* = 0.91, $CHCl_3$); 93% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30 (dd, *J* = 7.4, 2.3 Hz, 1 H, 5-H), 7.21 (ddd, *J* = 7.0, 7.0, 2.0 Hz, 1 H, 8-H), 7.19 (dd, *J* = 7.3, 7.3, 1.5 Hz, 1 H, 9-H), 7.12 (dd, *J* = 7.2, 1.7 Hz, 1 H, 10-H), 7.02 (d, *J* = 6.7, 1.6 Hz, 1 H, 7-H), 6.05 (d, *J* = 9.2 Hz, 1 H, 4-H), 4.72 (d, *J* = 17.3 Hz, 1 H, 1-H_a), 4.27 (d, *J* = 17.3 Hz, 1 H, 1-H_b), 3.79 (ddd, *J* = 8.0, 7.3, 0.7 Hz, 1 H, 11-H), 3.16 (d, *J* = 6.7 Hz, 1 H, 6-H), 1.77 (ddq, *J* = 14.2, 7.6, 7.5 Hz, 1 H, 1′-H_a), 1.61 (ddq, *J* = 14.3, 7.2, 7.2 Hz, 1 H, 1′-H_b), 1.09 (t, *J* = 7.4 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3 (s, C-3), 152.8 (d, C-5), 134.8 (s, C-6a), 133.9 (s, C-10a), 129.8 (d, C-10), 127.5 (d, C-8), 127.2 (d, C-7), 127.1 (d, C-9), 125.2 (d, C-4), 60.4 (d, C-11), 46.3 (t, C-1), 38.7 (d, C-6), 22.9 (t, C-1′), 10.8 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{14}H_{16}NO^+$ $[M + H]^+$ 214.1226; found 214.1229; calcd. for $C_{28}H_{30}N_2O_2Na^+$ $[2M + Na]^+$ 449.2199; found 449.2208.

(+)-(6*S*,11*S*)-12b: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.01 (m, 3 H, Ar-H), 7.04 (dd, *J* = 6.4, 2.1 Hz, 1 H, 10-H), 5.20 (d, *J* = 15.8 Hz, 1 H, 1-H_a), 4.12 (d, *J* = 15.8 Hz, 1 H, 1-H_b), 3.40 (dd, *J* = 7.6, 7.6 Hz, 1 H, 11-H), 3.19 (dd, *J* = 7.4, 2.2 Hz, 1 H, 6-H), 2.70–2.40 (m, 2 H, 4-H_a, 5-H_a), 2.31 (dd, *J* = 15.1, 9.2 Hz, 1 H, 4-H_b), 2.10–1.60 (m, 3 H, 5-H_b, 1′-H), 1.07 (t, *J* = 7.4 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.2 (s, C-3), 142.0 (s, C-10a), 137.0 (s, C-6a), 130.0 (d, Ar-C), 127.2 (d, Ar-C), 127.0 (d, Ar-C), 126.7 (d, C-10), 63.6 (d, C-11), 56.1 (t, C-1), 38.1 (d, C-6), 30.0 (t, C-4), 27.1 (t, C-5), 25.2 (t, C-1′), 11.9 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{14}H_{18}NO^+$ $[M + H]^+$ 216.1383; found 216.1385; calcd. for $C_{28}H_{34}N_2O_2Na^+$ $[2M + Na]^+$ 453.2512; found 453.2519.

(–)-(6*S*,11*R*)-11-[(Trityloxy)methyl]-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(–)-(6*S*,11*R*)-10c], (+)-(6*R*,11*R*)-11-[(Trityloxy)methyl]-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*R*,11*R*)-11c], and (+)-(6*S*,11*R*)-11-[(Trityloxy)methyl]-1,4,5,6-tetrahydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*S*,11*R*)-12c]: GP4 was carried out with enamide **9c** (63 mg, 0.12 mmol), $Pd(dppf)Cl_2$ (17.2 mg, 20 mol-%), triethylamine (118.5 mg, 1.2 mmol), and dry DMF (3.9 mL, 0.03 M). The capped vial was irradiated with a microwave at 120 °C for 2 min followed by a 1 h hold time at 120 °C. For TLC, R_f (**10c**, **11c**, **12c**) = 0.72, R_f (**9c**) = 0.34 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). The cooled reaction mixture was diluted with H_2O (20 mL), and the resulting solution was extracted with ethyl acetate (3× 15 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. Flash column chromatography on silica (25 g; petroleum ether/ethyl acetate, 4:1) gave a mixture of the three products (40 mg, 75%, **10c/11c/12c**, 77:18:4). Separation was accomplished by reparative HPLC (pentane/ethyl acetate, 4:1) to elute first (–)-(6*S*,11*R*)-**10c** (31 mg, 58%), then (+)-(6*R*,11*R*)-**11c** (7 mg, 14%), and finally (+)-(6*S*,11*R*)-**12c** (2 mg, 3%), as brown viscous oils.

(–)-(6*S*,11*R*)-10c: $[\alpha]_D^{20}$ = –143 (*c* = 0.96, $CHCl_3$); 95% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.32 (m, 6 H, trityl-H), 7.35–7.08 (m, 12 H, 8-H, 9-H, 10-H, trityl-H), 6.98 (d, *J* = 7.2 Hz, 1 H, 7-H), 6.81 (ddd, *J* = 9.1, 6.9, 2.0 Hz, 1 H, 5-H), 5.78 (d, *J* = 9.2 Hz, 1 H, 4-H), 4.78 (d, *J* = 16.2 Hz, 1 H, 1-H_a), 4.32 (d, *J* = 16.2 Hz, 1 H, 1-H_b), 3.93–3.78 (m, 1 H, 11-H), 3.57 (dd, *J* = 9.2, 5.8 Hz, 1 H, 1′-H_a), 3.55 (d, *J* = 5.8 Hz, 1 H, 6-H), 3.37 (dd, *J* = 9.2, 9.2 Hz, 1 H, 1′-H_b) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.4 (s, C-3), 146.4 (d, C-5), 143.8 (s, 3 C, C-1′′), 137.7 (s, C-10a), 135.2 (s, C-6a), 129.0 (d, C-10), 128.7 (d, 6 C, trityl-Ph-C), 128.0 (d, 6 C, trityl-Ph-C), 127.6 (d, 2 C, C-7, C-8), 127.3 (d, 3 C, C-4′′), 126.9 (d, C-9), 125.6 (d, C-4), 86.9 [s, O-*C*(Ph)$_3$], 62.8 (t, C-1′), 59.7 (d, C-11), 54.5 (t, C-1), 36.5 (d, C-6) ppm. HRMS (ESI+): calcd. for $C_{32}H_{28}NO_2^+$ $[M + H]^+$ 458.2115; found 458.2118; calcd. for $C_{32}H_{27}NO_2Na^+$ $[M + Na]^+$ 480.1934; found 480.1940; calcd. for $C_{32}H_{27}NO_2K^+$ $[M + K]^+$ 496.1673; found 496.1680. $C_{32}H_{27}NO_2$ (457.56): calcd. C 84.00, H 5.95, N 3.06; found C 83.98, H 6.05, N 3.02.

[(+)-(6*R*,11*R*)-11c]: $[\alpha]_D^{20}$ = +110 (*c* = 1.08, $CHCl_3$); 95% *ee*. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–6.98 (m, 19 H, trityl-H, Ar-H, 5-H), 6.86–6.73 (m, 1 H, Ar-H), 6.01 (d, *J* = 9.2 Hz, 1 H, 4-H), 4.53 (d, *J* = 17.3 Hz, 1 H, 1-H_a), 4.12 (dd, *J* = 7.6 and 6.1 Hz, 1 H, 11-H), 3.86 (d, *J* = 17.3 Hz, 1 H, 1-H_b), 3.44 (d, *J* = 8.9 Hz, 1 H, 6-H), 3.38 (dd, *J* = 9.1, 3.5 Hz, 1 H, 1′-H_a), 3.33 (dd, *J* = 8.9, 8.9 Hz, 1 H, 1′-H_b) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.8 (s, C-3), 152.6 (d, C-5), 143.6 (s, 3 C, C-1′′), 134.2 (s, C-6a), 133.6 (s, C-10a), 129.7 (d, C-7), 128.6 (d, 6 C, trityl-Ph-C), 127.9 (d, 6 C, trityl-Ph-C), 127.5 (d, C-10), 127.2 (d, 3 C, C-4′′), 127.1 (d, Ar-C), 127.1 (d, Ar-C), 125.2 (d, C-4), 86.9 [s, O-*C*(Ph)$_3$], 61.8 (t, C-1′), 58.4 (d, C-11), 47.3 (t, C-1), 36.8 (d, C-6) ppm. HRMS (ESI+): calcd. for $C_{32}H_{28}NO_2^+$ $[M + H]^+$ 458.2115; found 458.2125; calcd. for $C_{64}H_{54}N_2O_4Na^+$ $[2M + Na]^+$ 937.3976; found 937.3997.

[(+)-(6*S*,11*R*)-12c]: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.39 (m, 6 H, trityl-Ph-H), 7.40–7.03 (m, 12 H, Ar-H, trityl-Ph-H), 7.03 (dd, *J* = 6.9, 2.0 Hz, 1 H, Ar-H), 5.17 (d, *J* = 15.9 Hz, 1 H, 1-H_a), 4.19 (d, *J* = 15.9 Hz, 1 H, 1-H_b), 3.87 (dd, *J* = 6.4, 6.4 Hz, 1 H, 11-H), 3.57 (dd, *J* = 9.2, 5.5 Hz, 1 H, 1′-H_a), 3.38–3.21 (m, 2 H, 1′-H_b, 6-H), 2.30–1.87 (m, 3 H, 5-H_a, 4-H), 1.90–1.88 (m, 1 H, 5-H_b) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 183.9 (s, C-3), 143.8 (s, 3 C, C-1′′), 141.6 (s, C-10a), 136.7 (s, C-6a), 130.1 (d, Ar-C), 128.7 (d, 6 C, trityl-C), 128.1 (d, 6 C, trityl-C), 127.4 (d, 3 C, C-4′′), 127.2 (d, Ar-C), 126.9 (d, Ar-C), 126.8 (d, C-10), 86.9 [s, O-*C*(Ph)$_3$], 63.9 (t, C-1′), 61.6 (d, C-11), 55.8 (t, C-1), 36.8 (d, C-6), 30.1 (t, C-4), 27.1 (t, C-5) ppm. HRMS (ESI+): calcd. for $C_{32}H_{30}NO_2^+$ $[M + H]^+$ 460.2271; found 460.2279; calcd. for $C_{32}H_{29}NO_2Na^+$ $[M + Na]^+$ 482.2090; found 482.2100.

(–)-(6*S*,11*R*)-11-Phenyl-1,6-dihydro-3*H*-2,6-methano-2-benzazocin-3-one [(–)-(6*S*,11*R*)-10d] and (+)-(6*S*,11*R*)-11-Phenyl-1,4,5,6-tetra-

hydro-3*H*-2,6-methano-2-benzazocin-3-one [(+)-(6*S*,11*R*)-12d]: GP4 was carried out with enamide **9d** (62 mg, 0.18 mmol), $Pd(dppf)Cl_2$ (26.6 mg, 20 mol-%), triethylamine (183.4 mg, 1.8 mmol), and dry DMF (6.04 mL, 0.03 M). The capped vial was irradiated with a microwave at 120 °C for 2 min followed by a 1 h hold time at 120 °C. For TLC, R_f (**10d**, **11d**, **12d**) = 0.70, R_f (**9d**) = 0.34 (petroleum ether/ethyl acetate, 3:2; $KMnO_4$). The cooled reaction mixture was treated with H_2O (20 mL), and the resulting solution was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. Flash column chromatography on silica (25 g; petroleum ether/ethyl acetate, 4:1) gave a mixture of the three products (36 mg, 76%, **10d/11d/12d**, 92:2:6). Preparative HPLC (pentane/ethyl acetate, 4:1) gave first (–)-(6*S*,11*R*)-**10d** (33 mg, 70%) as solid (recrystallized from petroleum ether/dichloromethane) followed by (+)-(6*S*,11*R*)-**12d** (2 mg, 4%), as a semisolid.

(–)-(6*S*,11*R*)-10d: M.p. 171–172 °C; $[\alpha]_D^{20}$ = –187 (*c* = 0.96, $CHCl_3$); 97%*ee*. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.28 (m, 4 H, Ar-H, Ph-H), 7.32–7.14 (m, 4 H, Ar-H, Ph-H), 7.08 (d, *J* = 6.7 Hz, 1 H, 7-H), 6.84 (ddd, *J* = 9.2, 6.8, 1.9 Hz, 1 H, 5-H), 5.87 (d, *J* = 9.4 Hz, 1 H, 4-H), 5.04 (d, *J* = 16.5 Hz, 1 H, 1-H_a), 4.92 (s, 1 H, 11-H), 4.49 (d, *J* = 16.5 Hz, 1 H, 1-H_b), 3.92 (dd, *J* = 6.8, 1.9 Hz, 1 H, 6-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7 (s, C-3), 146.8 (d, C-5), 139.5 (s, C-1′), 137.3 (s, C-10a), 135.5 (s, C-6a), 129.0 (d, C-10), 128.6 (d, 2 C, Ph-C), 127.8 (d, C-4′), 127.7 (d, C-7), 127.1 (d, C-8), 127.0 (d, C-9), 126.9 (d, C-4), 126.6 (d, 2 C, Ph-C), 61.8 (d, C-11), 54.3 (t, C-1), 39.5 (d, C-6) ppm. HRMS (ESI+): calcd. for $C_{18}H_{16}NO^+$ $[M + H]^+$ 262.1226; found 262.1229; calcd. for $C_{18}H_{15}NONa^+$ $[M + Na]^+$ 284.1046; found 284.1049. $C_{18}H_{15}NO$ (261.32): calcd. C 82.73, H 5.79, N 5.36; found C 82.43, H 5.77, N 5.43.

(+)-(6*S*,11*R*)-12d: ^1H NMR (300 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.0 Hz, 2 H, 2′-H, 6′-H), 7.42 (dd, *J* = 7.5, 7.5 Hz, 2 H, 3′-H, 5′-H), 7.40–7.03 (m, 5 H, Ar-H, Ph-H), 5.41 (d, *J* = 16.1 Hz, 1 H, 1-H_a), 4.81 (s, 1 H, 11-H), 4.30 (d, *J* = 16.1 Hz, 1 H, 1-H_b), 3.93 (dd, *J* = 8.8, 1.8 Hz, 1 H, 6-H), 2.70–2.38 (m, 1 H, 5-H_a), 2.30–1.70 (m, 3 H, 5-H_b, 4-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 184.1 (s, C-3), 141.6 (s, C-10a), 139.6 (s, C-1′), 136.6 (s, C-6a), 130.1 (d, Ar-C), 129.1 (d, 2 C, C-2′, C-6′), 127.4 (d, Ar-C), 127.3 (d, C-4′), 127.0 (d, C-10), 127.0 (d, Ar-C), 125.2 (d, 2 C, C-3′, C-5′), 62.6 (d, C-11), 54.5 (t, C-1), 37.9 (d, C-6), 30.7 (t, C-4), 27.9 (t, C-5) ppm. HRMS (ESI+): calcd. for $C_{18}H_{18}NO^+$ $[M + H]^+$ 264.1383; found 264.1386; calcd. for $C_{18}H_{17}NOK^+$ $[M + K]^+$ 302.0942; found 302.0946; calcd. for $C_{36}H_{34}N_2O_2K^+$ $[2M + K]^+$ 565.2252; found 565.2262.

(+)-(7*S*,12*S*)-12-Ethyl-4,7-dihydro-2,7-methano-2-benzazonin-3(1*H*)-one [(+)-(7*S*,12*S*)-10bb] and (+)-(7*R*,12*S*)-12-Ethyl-4,7-dihydro-2,7-methano-2-benzazonin-3(1*H*)-one [(+)-(7*R*,12*S*)-11bb]: GP4 was carried out with enamide **9bb** (72 mg, 0.23 mmol), $Pd(dppf)Cl_2$ (17.1 mg, 10 mol-%), triethylamine (236 mg, 2.34 mmol), and dry DMF (7.79 mL, 0.03 M). The capped vial was irradiated with a microwave at 100 °C for 2 min followed by a 2 h hold time at 100 °C. For TLC, R_f (**10bb**, **11bb**) = 0.65, R_f (**9bb**) = 0.30 (petroleum ether/ethyl acetate, 7:3; $KMnO_4$). The cooled reaction mixture was diluted with H_2O (20 mL), and the resulting solution was extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in vacuo. The residue was subjected to flash column chromatography on silica (25 g; petroleum ether/ethyl acetate, from 6:1 to 3:1) to give first the major isomer (+)-(7*S*,12*S*)-**10bb** (38 mg, 72%) and then (+)-(7*R*,12*S*)-**11bb** (8 mg, 15%) as brown viscous oils.

(+)-(7*S*,12*S*)-10bb: $[\alpha]_D^{20}$ = +190 (*c* = 1.2, $CHCl_3$); 93%*ee*. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–6.98 (m, 4 H, Ar-H), 5.85 (ddd, *J* = 11.1, 5.7, 3.3 Hz, 1 H, 6-H), 5.62 (dddd, *J* = 11.0, 8.9, 2.0, 2.0 Hz, 1 H, 5-H), 5.40 (d, *J* = 16.8 Hz, 1 H, 1-H_a), 4.35 (dd, *J* = 8.9, 6.4 Hz, 1 H, 12-H), 3.98 (d, *J* = 16.6 Hz, 1 H, 1-H_b), 3.81 (ddd, *J* = 16.4, 5.7, 2.7 Hz, 1 H, 4-H_a), 3.22 (br. s, 1 H, 7-H), 2.87 (dd, *J* = 16.5, 8.7 Hz, 1 H, 4-H_b), 1.73 (ddq, *J* = 16.1, 7.2, 7.2 Hz, 1 H, 1′-H_a), 1.56 (ddq, *J* = 13.9, 7.0, 6.9 Hz, 1 H, 1′-H_b), 1.03 (t, *J* = 7.4 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.3 (s, C-3), 134.7 (s, d, C-11a, C-5), 134.2 (s, C-7a), 129.5 (d, Ar-C), 126.9 (d, Ar-C), 126.7 (d, Ar-C), 126.4 (d, Ar-C), 120.5 (d, C-6), 56.1 (d, C-12), 42.1 (d, C-7), 40.9 (t, C-1), 35.9 (t, C-4), 23.5 (t, C-1′), 11.2 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{15}H_{18}NO^+$ $[M + H]^+$ 228.1383; found 228.1386; calcd. for $C_{30}H_{34}N_2O_2Na^+$ $[2M + Na]^+$ 477.2512; found 477.2522.

(+)-(7*R*,12*S*)-11bb: ^1H NMR (300 MHz, $CDCl_3$): δ = 7.28–6.99 (m, 4 H, Ar-H), 6.23–6.00 (m, 2 H, 5-H, 6-H), 5.40 (d, *J* = 16.7 Hz, 1 H, 1-H_a), 4.23–4.01 (m, 1 H, 12-H), 4.12 (dd, *J* = 16.7 Hz, 1 H, 1-H_b), 3.11 (dd, *J* = 10.2, 2.9 Hz, 1 H, 7-H), 2.94 (ddd, *J* = 18.2, 10.3, 6.0 Hz, 1 H, 4-H_a), 2.50–2.30 (m, 1 H, 4-H_b), 1.70 (ddq, *J* = 14.4, 9.0, 7.2 Hz, 1 H, 1′-H_a), 1.53 (ddq, *J* = 14.0, 7.1, 7.0 Hz, 1 H, 1′-H_b), 0.98 (t, *J* = 7.4 Hz, 3 H, 2′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.0 (s, C-3), 139.1 (s, C-11a), 136.6 (d, C-6), 133.4 (s, C-7a), 130.1 (d, Ar-C), 127.2 (d, Ar-C), 126.6 (d, Ar-C), 126.5 (d, Ar-C), 126.4 (d, C-6), 57.0 (d, C-12), 42.4 (d, C-1), 41.0 (t, C-7), 36.1 (t, C-4), 23.4 (t, C-1′), 11.4 (q, C-2′) ppm. HRMS (ESI+): calcd. for $C_{30}H_{34}N_2O_2Na^+$ $[2M + Na]^+$ 477.2512; found 477.2519.

Supporting Information (see footnote on the first page of this article): Copies of HPLC data for compounds **5b–5d** and **8a** as well as X-ray crystal data for **10d** and ^1H and ^{13}C NMR spectra.

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