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Conjugate Addition of 2-Acetylindole Enolates to Unsaturated Oxazolopiperidone Lactams: Enantioselective Access to the Tetracyclic Ring System of Ervitsine

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Dedicated to Prof. Carmen Nájera on the occasion of her 60th birthday

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The stereochemical outcomes of the conjugate addition reactions of 2-acetylindole enolates to the unsaturated phenylglycinol-derived oxazolopiperidone lactams **1a–f** have been studied. After reduction of the 2-acylindole carbonyl group, the Michael adduct *cis*-**6** underwent a Lewis acid-promoted intramolecular α-amidoalkylation, leading enantioselectively to the tetracyclic ring system of the indole alkaloid ervitsine.

Introduction

Phenylglycinol-derived oxazolopiperidone lactams have proved to be versatile scaffolds that allow the regio- and stereocontrolled introduction of substituents at the different positions in the piperidine ring, thus providing access to enantiopure piperidines bearing virtually any type of substitution pattern and also to more complex piperidine-containing alkaloids, including indole alkaloids.[1] In particular, the stereoselective introduction of carbon appendages at the piperidine 4-position through conjugate addition reactions requires the activation of this position, which can be accomplished by generation of a conjugated C=C bond, taking advantage of the lactam carbonyl group.

In previous work we have exploited conjugate additions of lower-order alkyl and aryl cyanocuprates to unsaturated oxazolopiperidone lactams for the enantioselective synthesis of *cis*-2,4-[2] and *cis*-3,4-disubstituted piperidines,[3] as well as 2,4-bridged[2] and *cis*-3,4-fused piperidine[4] derivatives, including the antidepressant drug (–)-paroxetine[5] and synthetic intermediates en route to the indole alkaloid (–)-16-episilicine[6] and alkaloids of the madangamine group.[7]

Similarly, stereocontrolled conjugate addition reactions of sulfur-stabilized nucleophiles and indoleacetic acid ester enolates have been successfully employed as the key steps in enantioselective formal syntheses of uleine[8] and *Strychnos* alkaloids.[9,10]

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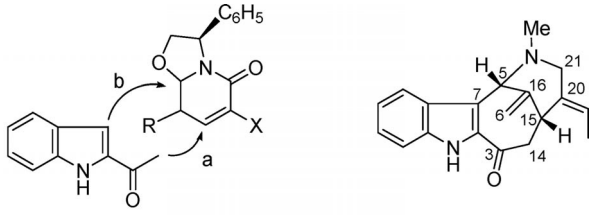
Results and Discussion

Here we report conjugate additions of 2-acetylindole enolates to unsaturated phenylglycinol-derived oxazolopiperidone lactams and the subsequent construction of the tetracyclic framework of the indole alkaloid ervitsine through closure of the seven-membered ring by intramolecular α-amidoalkylation at the indole 3-position (Scheme 1).

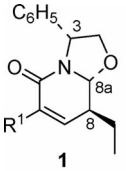


a) Stereoselective conjugate addition (bond formed: C^{14}–C^{15})
b) Intramolecular α-amidoalkylation (bond formed: C^5–C^7)

Ervitsine (biogenetic numbering)

Scheme 1. Synthetic strategy.

As the starting unsaturated lactams we selected the lactams **1a–f** (Figure 1 and Scheme 2), each bearing an ethyl substituent at the 8-position of the oxazolopiperidone system. The preparation of the 3,8a-*cis* lactams **1a–d**[3,6,8] has



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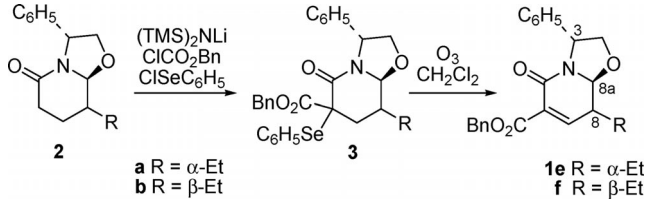
a R^1 = H
b R^1 = CO_2Bn
c R^1 = CO_2Me
d R^1 = CO_2tBu

Figure 1. Unsaturated oxazolopiperidone lactams.

been reported previously. The new 3,8a-*trans* lactams **1e** and **1f** were prepared from the known lactams **2a**[11] and **2b**[11] via the respective seleno derivatives **3a** and **3b**, as outlined in Scheme 2.



Scheme 2. Preparation of the unsaturated lactams **1e** and **1f**.

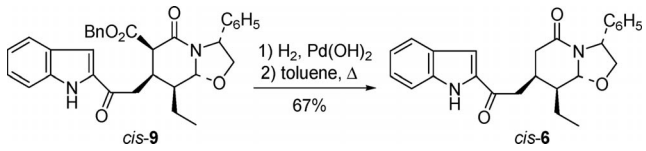
Table 1 summarizes the results obtained from the conjugate addition reactions of the 2-acetylindole enolates **4a** and **4b** to the unsaturated lactams **1a**–**d**. The initial experiments were carried out with the enolate of 2-acetyl-1-methylindole (**4a**). When starting from the unsaturated lactam **1a**, which lacks the activating electron-withdrawing benzyloxycarbonyl group, the use of a slight excess (1.2 equiv.) of the nucleophile (Entry 1) led to the expected adducts **5** in low yield (24%) as a 1:2 epimeric mixture of C-7/C-8 *cis*/*trans* isomers. A similar result was observed with the enolate of 2-acetylindole (**4b**): compound **6** was obtained in 30% yield as a C-7/C-8 *cis*/*trans* epimeric mixture in a 1:3 ratio (Entry 2). The yields grew progressively higher as the excess of the nucleophile was increased (Entries 3 and 4), reaching 68% when 5 equiv. of enolate were used.

The relative configurations of the *cis* and *trans* isomers were evident from the shielding of the oxazolopiperidone C-6 signal in the ^{13}C NMR spectrum of *cis*-**6** (δ = 37.9 ppm; compare with δ = 42.0 ppm in *trans*-**6**) resulting from the axial ethyl substituent at C-8.

The facial selectivity of the conjugate addition reactions to lactam **1a** (R^1 = H) can be accounted for by considering that the addition of stabilized anions to α,β-unsaturated carbonyl compounds is a reversible process that in the case of 5-substituted 5,6-dihydro-2-pyridones leads to the thermodynamically more stable *trans*-4,5-disubstituted derivatives.[12] Accordingly, in the reaction between the lactam **1a** and the acetylindole **4b** an increase in the proportion of the isomer *cis*-**6** was observed when the reaction was quenched after a short reaction time (Table 1, Entry 5).

In clear contrast from the stereochemical standpoint, similar conjugate addition reactions with the activated lactams **1b**–**d**, each bearing an additional activating alkoxycarbonyl substituent, led to the corresponding adducts **7**–**10** as diastereoisomeric mixtures in which the C-7/C-8 *cis* isomers predominated (Entries 6–10).[13] As in the case of lactam **1a** above, the use of excess nucleophile (5 equiv.) in these reactions resulted in higher yields, lactams **9** and **10** being formed in 90% (compare Entries 8 and 9) and 87% yields (Entry 10), respectively, even after shorter reaction times.

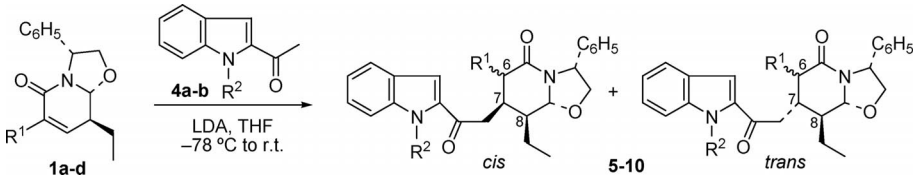
The C-7/C-8 *cis* relative configuration in the major isomer *cis*-**9** was confirmed by its conversion [H_2, $Pd(OH)_2$; then toluene at reflux] into *cis*-**6**, the minor isomer obtained from lactam **1a** (Scheme 3).



Scheme 3. Removal of the benzyloxycarbonyl substituent.

On the other hand, the predominance of the *cis* isomers in the conjugate additions to the lactams **1b**–**d** (R^1 = CO_2R) can be explained by considering that in these cases the equilibration takes place to a lesser extent, as a consequence of the greater stabilities of the initially formed adducts (1,3-dicarbonyl enolates). The process would then occur mainly under stereoelectronic control,[14] which involves an axial approach of the nucleophile to the electrophilic C atom of the conjugate double bond from the *exo* face of the bicyclic

Table 1. Conjugate addition reactions of 2-acetylindoles to the unsaturated lactams **1a**–**d**.



Entry	Lactam	Indole (equiv.)	Time	R^1	R^2	Product	H^7,H^8 *cis*/*trans* ratio	Yield [%][a]
1	**1a**	**4a** (1.2)	16 h	H	Me	**5**	1:2	24
2	**1a**	**4b** (1.2)	10 h	H	H	**6**	1:3	30
3	**1a**	**4b** (2.5)	12 h	H	H	**6**	1:2.3	56
4	**1a**	**4b** (5.0)	24 h	H	H	**6**	1:2.3	68
5	**1a**	**4b** (5.0)	3 h	H	H	**6**	1:1.3	73
6	**1b**	**4a** (1.2)	23 h	CO_2Bn	Me	**7**	3:1	42
7	**1c**	**4b** (1.2)	16 h	CO_2Me	H	**8**	3:1	38
8	**1b**	**4b** (1.2)	16 h	CO_2Bn	H	**9**	4:1	46
9	**1b**	**4b** (5.0)	5 h	CO_2Bn	H	**9**	4:1	90
10	**1d**	**4b** (5.0)	4 h	CO_2tBu	H	**10**	5:1	87

[a] For the relative configuration of the epimerizable C-6 stereocentre, see Exp. section.

system as depicted in Figure 2. In fact, irreversible conjugate additions (of organocuprates, for instance) to unsaturated oxazolopiperidone lactams (**1a**–**f** or related lactams) have been reported to occur under stereoelectronic control with complete *exo* facial selectivity.[15]

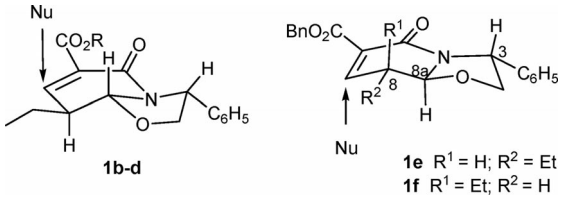
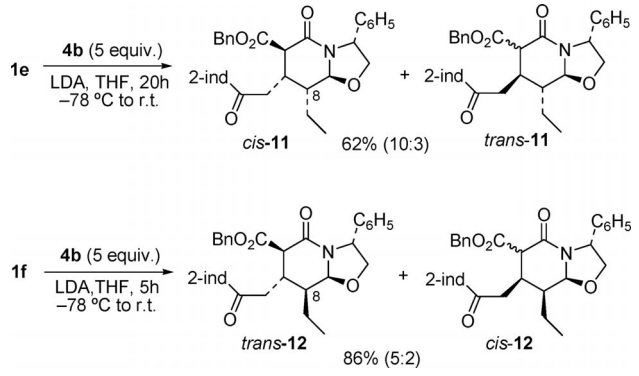


Figure 2. Stereoelectronic control in the conjugate additions.

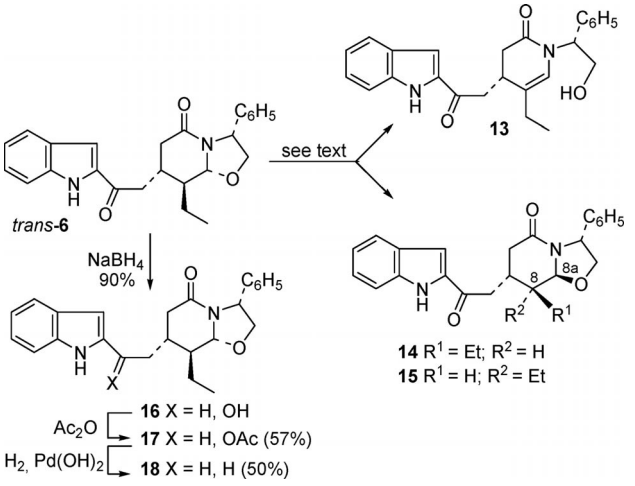
Similar stereoelectronically controlled facial stereoselectivity was observed in the conjugate additions of the enolate of **4b** to the C-8 epimeric 3,8a-*trans* lactams **1e** and **1f** (Figure 2), with the corresponding *exo* adducts *cis*-**11** and *trans*-**12** being formed as the major isomers (Scheme 4).



Scheme 4. Conjugate addition reactions between 2-acetylindole and the unsaturated lactams **1e** and **1f**; ind = indolyl.

To study the closure of the seven-membered ring characteristic of ervitsine, we initially selected the lactam *trans*-**6** (Scheme 5). However, all attempts to promote cyclization under a variety of acidic conditions ($TiCl_4$, CH_2Cl_2, reflux; $BF_3{\cdot}Et_2O$, CH_2Cl_2, reflux; HCl, MeOH or C_6H_6) resulted in failure. The enamide **13**[16] and its 8a-epimer **14** and the 8,8a-diastereoisomer **15** of *trans*-**6** were the only isolable products.[17] The stereochemistry of **14** and **15** was confirmed when these compounds were unambiguously prepared from *trans*-**12** and *cis*-**11**, respectively, by debenzylation [H_2, $Pd(OH)_2$] followed by decarboxylation.

Because the isolation of compounds **13**–**15** clearly indicated that the *N*-acyliminium cation[18] had been formed,



Scheme 5.

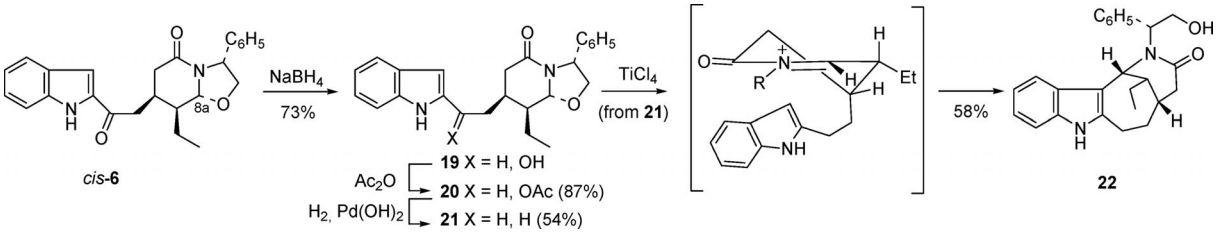
the failure of the cyclization was attributed to the deactivating effect of the carbonyl group conjugated with the indole ring. For this reason, the acylindole *trans*-**6** was converted into the alcohol **16** (Scheme 5) and then into the indolylethyl derivative **18** by hydrogenolysis of the corresponding acetate **17**.

The desired cyclization at the indole 3-position, however, did not occur from **16** or **18** either, with only extensive decomposition being observed under a variety of acidic conditions.

Bearing in mind that the closure of the seven-membered ring of ervitsine and analogues has been successfully achieved by a related intramolecular iminium ion cyclization,[19] we reasoned at this point that conformation factors could be responsible for the reluctance of the above C-7/C-8 *trans* derivatives to undergo intramolecular α-amidoalkylation: cyclization would involve an encumbered conformation in which both C-7 and C-8 substituents should be axial. To confirm this hypothesis, we decided to study related α-amidoalkylation reactions from C-7/C-8 *cis* lactams.

No cyclized products were detected, however, upon treatment of *cis*-**6** with $TiCl_4$, the only isolable product being the 8a-epimer of *cis*-**6**.[20] As in the above C-7/C-8 *trans* series, the 2-acylindole *cis*-**6** was reduced to the alcohol **19** (Scheme 6) and then converted into the indolylethyl derivative **21** via the corresponding acetate **20**.

Although the alcohol **19** underwent extensive decomposition upon acidic treatment, to our delight, when the reduced derivative **21** was treated with $TiCl_4$ in CH_2Cl_2 at reflux, the tetracycle **22** was isolated in 58% yield.



Scheme 6. Access to the tetracyclic ring system of ervitsine.

Conclusions

In conclusion, conjugate addition reactions of 2-acetylindole enolates to phenylglycinol-derived unsaturated δ-lactams allow the stereocontrolled formation of C–C bonds at the piperidine 4-position. Depending on the absence or presence of an additional electron-withdrawing substituent conjugated with the C–C double bond, the reaction predominantly leads either to *trans*- or to *cis*-4,5-disubstituted enantiopure 2-piperidone derivatives, respectively.

The synthetic potential of the resulting Michael adducts has been demonstrated with the enantioselective construction of the tetracyclic ring system of ervitsine, a minor indole alkaloid isolated from *Pandaca boiteaui*[21] that lacks the characteristic tryptamine moiety present in most monoterpenoid indole alkaloids. The strategy developed here, starting from an appropriate lactam bearing a C-8 substituent precursor of the exocyclic methylene group and involving a stereoselective conjugate addition and an intramolecular α-amidoalkylation as the key steps (see Scheme 1), may be applied to the enantioselective synthesis of ervitsine.[22]

Experimental Section

General: Flash chromatography was carried out on SiO_2 (silica gel 60, SDS, 0.04–0.06 mm) or (when indicated) with a cartridge containing amine-functionalized silica. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. High-resolution mass spectra (HMRS; LC/MSD TOF Agilent Technologies) were performed by the Serveis Científico-Tècnics, Barcelona. Microanalyses (Carlo–Erba 1106 analyzer) were performed by the Centre d'Investigació i Desenvolupament (CSIC), Barcelona. Only noteworthy IR absorptions (cm^{-1}; Perkin–Elmer 1600) are listed. NMR spectra were recorded at 200, 300, 400 or 500 MHz (^1H) and 75.4, 100.6 or 125.9 MHz (^{13}C).

(3*R*,8*R*,8a*S*)-6-(Benzyloxycarbonyl)-8-ethyl-5-oxo-3-phenyl-6-(phenylselenyl)-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (3a): Lithium bis(trimethylsilyl)amide (9.4 mL of a 1.0 M solution in THF, 9.4 mmol) was slowly added at –78 °C to a solution of lactam **2a**[11] (1.08 g, 4.24 mmol) in anhydrous THF (50 mL), and the resulting mixture was stirred for 90 min. Benzyl chloroformate (710 μL, 4.24 mmol) was then added, followed after 2 h of continuous stirring at –78 °C by a solution of C_6H_5SeCl (1.14 g, 5.09 mmol) in anhydrous THF (5 mL). The mixture was stirred for 2 h and poured into saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated. Flash chromatography (hexane to hexane/EtOAc 4:1) of the resulting oil afforded the corresponding selenides **3a** as a mixture of C-6 epimers (1.40 g, 62%).

Data for 3a: Orange oil. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.74 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 0.80 (t, J = 7.3 Hz, 3 H, CH_3 ethyl), 1.12–1.18 (m, 1 H, CH_2 ethyl), 1.12–1.22 (m, 1 H, CH_2 ethyl), 1.57–1.95 (m, 3 H, CH_2 ethyl, 7-H, 8-H), 1.61–1.72 (m, 2 H, CH_2 ethyl, 8-H), 1.83–2.00 (m, 2 H, 7-H), 2.33 (dd, J = 13.8, 2.1 Hz, 1 H, 7-H), 3.71 (dd, J = 9.0, 7.8 Hz, 1 H, 2-H), 3.78 (dd, J = 9.0, 7.5 Hz, 1 H, 2-H), 4.34 (d, J = 8.1 Hz, 1 H, 8a-H), 4.37 (dd, J = 9.0, 7.5 Hz, 1 H, 2-H), 4.46 (dd, J = 9.0, 7.8 Hz, 1 H, 2-H), 4.67 (d, J = 7.8 Hz, 1 H, 8a-H), 5.20 (d, J = 6.9 Hz, 1 H, C$H_2C_6H_5$), 5.20 (s, 2 H, C$H_2C_6H_5$), 5.24 (d, J = 6.9 Hz, 1 H, C$H_2C_6H_5$), 5.25 (d, J = 7.8 Hz, 1 H, 3-H), 5.30 (t, J = 7.5 Hz, 1 H, 3-H), 7.18–7.70 (m, 30 H, ArH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 10.5, 10.7 (CH_3 ethyl), 23.7, 24.0 (CH_2 ethyl), 32.5, 35.2 (C-7), 37.8, 39.3 (C-8), 54.2, 55.6 (C-6), 58.8 (C-3), 67.7, 67.8 (C$H_2C_6H_5$), 72.1, 72.3 (C-2), 92.0, 92.3 (C-8a), 125.7, 126.1 (C-*o*), 126.6, 126.7 (C-*m*), 127.3, 127.5 (C-*p*), 127.9, 128.0 (C-*o*), 128.0, 128.1 (C-*p*), 128.3, 128.4 (C-*m*), 128.5, 128.6 (C-*o*), 128.7, 128.8 (C-*m*), 129.3, 129.5 (C-*i*), 135.0, 135.1 (C-*i*), 138.0 (C-*p*), 138.5, 138.7 (C-*i*), 164.5, 164.9 (NCO), 169.9, 170.9 (COO) ppm.

(3*R*,8*S*,8a*S*)-6-(Benzyloxycarbonyl)-8-ethyl-5-oxo-3-phenyl-6-(phenylselenyl)-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (3b): A mixture of C-6 epimeric selenides (3.46 g, 82%) was obtained as in the above preparation of **3a**, from lactam **2b**[11] (2 g, 7.90 mmol) in THF (100 mL), LiHMDS (17.3 mL of a 1.0 M solution in THF), benzyl chloroformate (1.2 mL, 8.6 mmol) and C_6H_5SeCl (1.70 g, 8.80 mmol) in THF (20 mL). Pure isomers were isolated after subsequent flash chromatography (hexane to hexane/EtOAc 9:1).

Data for 3b (Higher R_f Epimer): Orange oil. $[\alpha]_D^{22}$ = –84.0 (c = 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.82 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.29–1.38 (m, 1 H, CH_2 ethyl), 1.53–1.63 (m, 1 H, CH_2 ethyl), 1.72–1.81 (m, 1 H, 8-H), 1.88–2.02 (m, 1 H, 7-H), 1.99 (dd, J = 12.9, 5.1 Hz, 1 H, 7-H), 3.73 (dd, J = 8.7, 6.9 Hz, 1 H, 2-H), 4.45 (t, J = 8.7 Hz, 1 H, 2-H), 4.60 (d, J = 5.4 Hz, 1 H, 8a-H), 5.09 (d, J = 12.3 Hz, 1 H, C$H_2C_6H_5$), 5.32 (d, J = 12.3 Hz, 1 H, C$H_2C_6H_5$), 5.56 (t, J = 8.1 Hz, 1 H, 3-H), 7.13–7.55 (m, 15 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 11.4 (CH_3 ethyl), 23.3 (CH_2 ethyl), 33.6 (C-7), 35.9 (C-8), 54.2 (C-6), 58.1 (C-3), 67.4 (C$H_2C_6H_5$), 70.8 (C-2), 87.8 (C-8a), 125.6 (C-*o*), 126.7 (C-*m*), 127.3 (C-*p*), 128.1 (C-*o*), 128.2 (C-*m*), 128.4 (C-*p*), 128.6 (C-*o*), 129.5 (C-*m*), 135.2 (C-*p*), 138.5 (C-*i*), 139.5 (C-*i*), 167.1 (NCO), 169.4 (COO) ppm. IR (film): $\tilde{\nu}$ = 1664, 1724 cm^{-1}. $C_{29}H_{29}NO_4Se$ (534.51): calcd. C 65.17, H 5.47, N 2.62; found C 65.19, H 5.58, N 2.54.

Data for 3b (Lower R_f Epimer): Orange oil. $[\alpha]_D^{22}$ = –22.0 (c = 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.81 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.12–1.23 (m, 1 H, CH_2 ethyl), 1.55–1.67 (m, 1 H, CH_2 ethyl), 2.04 (dd, J = 15.0, 4.2 Hz, 1 H, 7-H), 2.22–2.28 (m, 1 H, 8-H), 2.56 (dd, J = 15.0, 6.6 Hz, 1 H, 7-H), 3.84 (dd, J = 8.7, 6.3 Hz, 1 H, 2-H), 4.34 (dd, J = 8.7, 7.5 Hz, 1 H, 2-H), 4.85 (d, J = 4.8 Hz, 1 H, 8a-H), 5.18 (s, 2 H, C$H_2C_6H_5$), 5.35 (t, J = 6.8 Hz, 1 H, 3-H), 7.06–7.47 (m, 15 H, ArH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 11.6 (CH_3 ethyl), 18.7 (CH_2 ethyl), 32.5 (C-7), 37.2 (C-8), 52.7 (C-6), 58.6 (C-3), 67.9 (C$H_2C_6H_5$), 71.6 (C-2), 89.0 (C-8a), 126.5 (C-*o*), 126.7 (C-*m*), 127.6 (C-*p*), 128.1 (C-*o*), 128.4 (CHAr), 128.7 (CHAr), 129.4 (CHAr), 135.2 (C-*i*), 137.7 (C-*i*), 139.2 (C-*i*), 165.1 (NCO), 170.2 (COO) ppm. IR (film): $\tilde{\nu}$ = 1661, 1732 cm^{-1}. $C_{29}H_{29}NO_4Se$ (534.51): calcd. C 65.17, H 5.47, N 2.62; found C 64.81, H 5.64, N 2.64.

(3*R*,8*R*,8a*S*)-6-(Benzyloxycarbonyl)-8-ethyl-5-oxo-3-phenyl-3,5,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (1e): A stream of ozone gas was bubbled through a cooled (–78 °C) solution of the selenides **3a** (161 mg, 0.30 mmol) in anhydrous CH_2Cl_2 (50 mL) until the solution had turned pale blue (5 min). The solution was then purged with O_2, and the temperature was slowly raised to 25 °C. After 30 min of stirring, the mixture was poured intro brine and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated to give unsaturated lactam **1e**, which because of its instability was used in the next reaction without further purification.

Data for 1e: Yellow oil. ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.10 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.57–1.66 (m, 1 H, CH_2 ethyl), 1.81–1.90 (m, 1 H, CH_2 ethyl), 2.53–2.61 (m, 1 H, 8-H), 3.94 (dd, J = 9.0, 6.0 Hz, 1 H, 2-H), 4.44 (dd, J = 9.0, 6.9 Hz, 1 H, 2-H),

5.10 (d, J = 9.3 Hz, 1 H, 8a-H), 5.26 (d, J = 5.3 Hz, 1 H, CH_2C$_6$H$_5$), 5.29 (m, 1 H, 3-H), 5.30 (d, J = 5.3 Hz, 1 H, CH_2C$_6$H$_5$), 7.19–7.40 (m, 11 H, 7-H, ArH) ppm.

(3*R*,8*S*,8a*S*)-6-(Benzyloxycarbonyl)-8-ethyl-5-oxo-3-phenyl-3,5,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (1f): The unsaturated lactam **1f** (173 mg, 0.46 mmol) was obtained as in the above preparation of **1e**, from a mixture of selenides **3b** (246 mg, 0.46 mmol) in CH_2Cl_2 (15 mL). Because of its instability it was used in the next reaction without further purification.

Data for 1f: Orange oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.99 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.38–1.48 (m, 1 H, CH_2 ethyl), 1.83–1.92 (m, 1 H, CH_2 ethyl), 2.76–2.81 (m, 1 H, 8-H), 4.00 (dd, J = 8.4, 5.7 Hz, 1 H, 2-H), 4.47 (dd, J = 8.4, 6.9 Hz, 1 H, 2-H), 5.22–5.26 (m, 3 H, CH_2C$_6$H$_5$, 3-H), 5.50 (d, J = 5.4 Hz, 1 H, 8a-H), 7.24–7.62 (m, 11 H, 7-H, ArH) ppm.

General Procedure for the Conjugate Addition Reactions: LDA was added to a cooled (–78 °C) solution of a 2-acetylindole (**4a** or **4b**) in THF, and the mixture was stirred at this temperature for 1 h. A solution of an unsaturated lactam **1** in THF was then added to the solution (–78 °C). The resulting mixture was stirred at room temperature until the disappearance of the starting material was observed by TLC. The reaction was quenched by the addition of saturated aqueous NH_4Cl, and the mixture was extracted with EtOAc. The combined extracts were dried and concentrated to give a residue, which was purified by chromatography.

(3*R*,7*R*,8*S*,8a*R*)-8-Ethyl-7-[2-(1-methyl-2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*trans*-5) and Its 7*S* Epimer (*cis*-5): Compound **5** was obtained as a mixture of C-7 epimers as described in the General Procedure, from the lactam **1a**[3b,8] (200 mg, 0.82 mmol) in THF (30 mL), LDA (0.65 mL of a 1.5 M solution in cyclohexane, 0.98 mmol) and a solution of the indole **4a** (170 mg, 0.98 mmol) in THF (30 mL) over 16 h. Flash chromatography (hexane/EtOAc from 1:1 to 3:7) afforded *trans*-**5** (53 mg, 16%) and *cis*-**5** (27 mg, 8%).

Data for *trans*-5: Yellow foam. $[\alpha]_D^{22}$ = 13.0 (c = 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.07 (t, J = 7.4 Hz, 3 H, CH_3 ethyl), 1.65–1.89 (m, 3 H, CH_2 ethyl, 8-H), 2.16 (dd, J = 18.2, 9.2 Hz, 1 H, 6-H), 2.50–2.60 (m, 2 H, 6-H, 7-H), 2.87 (dd, J = 16.2, 7.6 Hz, 1 H, CH_2CO), 3.10 (dd, J = 16.2, 5.2 Hz, 1 H, CH_2CO), 4.05 (s, 3 H, NCH_3), 4.09 (d, J = 9.0 Hz, 1 H, 2-H), 4.18 (dd, J = 9.0, 6.8 Hz, 1 H, 2-H), 4.73 (d, J = 7.6 Hz, 1 H, 8a-H), 4.96 (dd, J = 6.8, 1.2 Hz, 1 H, 3-H), 7.11 (s, 1 H, 3-H ind), 7.13–7.20 (m, 1 H, 7-H ind), 7.26–7.40 (m, 7 H, 5-H, 6-H ind, ArH), 7.67 (dd, J = 8.2, 1.2 Hz, 1 H, 4-H ind) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 10.2 (CH_3 ethyl), 22.7 (CH_2 ethyl), 32.2 (C-7), 37.5 (C-6), 43.7 (*C*H_2CO), 44.8 (C-8), 58.4 (C-3), 73.9 (C-2), 91.1 (C-8a), 110.3 (C-3 ind), 111.8 (C-7 ind), 120.7 (C-4 ind), 122.9 (C-6 ind), 125.6 (C-5 ind), 126.2 (C-2 ind), 126.7 (C-*o*), 128.6 (C-*m*), 127.6 (C-*p*), 134.7 (C-*i*), 140.2 (C-3a ind), 141.2 (C-7a ind), 166.7 (NCO), 192.0 (CO) ppm. IR (film): $\tilde{\nu}$ = 1644, 1661 cm^{-1}. HRMS: calcd. for $C_{26}H_{29}N_2O_3$ [M + H]$^+$: 417.2178; found 417.2172.

Data for *cis*-5: Yellow foam. ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.11 (t, J = 7.4 Hz, 3 H, CH_3 ethyl), 1.38–1.63 (m, 1 H, CH_2 ethyl), 1.87–2.06 (m, 2 H, CH_2 ethyl, 8-H), 2.33–2.48 (m, 2 H, 6-H, 7-H), 2.94–3.03 (m, 3 H, 2 × CH_2CO, 6-H), 4.06–4.22 (m, 2 H, 2-H), 4.08 (s, 3 H, NCH_3), 4.68 (d, J = 9.6 Hz, 1 H, 8a-H), 4.94 (d, J = 5.8 Hz, 1 H, 3-H), 7.12–7.43 (m, 9 H, ArH, ind-H), 7.69 (d, J = 8.0 Hz, 1 H, 4-H ind) ppm.

(3*R*,7*R*,8*S*,8a*R*)-8-Ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*trans*-6) and Its 7*S* Epimer (*cis*-6): Compound **6** (Table 1, Entry 4) was obtained as a mixture of C-7 epimers as described in the General Procedure, from the unsaturated lactam **1a**[3b,8] (400 mg, 1.64 mmol) in THF (30 mL), LDA (11 mL of a 1.5 M solution in cyclohexane, 16.5 mmol) and a solution of 2-acetylindole (**4b**, 1.3 g, 8.2 mmol) in THF (50 mL) over 24 h. Flash chromatography (hexane/EtOAc 1:1 to 3:7) afforded *trans*-**6** (316 mg, 48%) and *cis*-**6** (132 mg, 20%).

The pure lactams *trans*-**6** (201 mg, 42%) and *cis*-**6** (150 mg, 31%) were also obtained after flash chromatography as above (Table 1, Entry 5), from the lactam **1a** (296 mg, 1.21 mmol) and acetylindole (**4b**, 970 mg, 6.12 mmol) after 3 h.

Data for *trans*-6: Yellow foam. $[\alpha]_D^{22}$ = –7.0 (c = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.04 (t, J = 7.2 Hz, 3 H, CH_3 ethyl), 1.64–1.88 (m, 3 H, CH_2 ethyl, 8-H), 2.16 (dd, J = 16.5, 7.6 Hz, 1 H, CH_2CO), 2.57 (m, 1 H, 7-H), 2.68 (dd, J = 16.5, 6.0 Hz, 1 H, 6-H), 2.79 (dd, J = 16.5, 9.2 Hz, 1 H, CH_2CO), 3.00 (dd, J = 16.5, 4.5 Hz, 1 H, 6-H), 4.10 (dd, J = 9.0, 1.2 Hz, 1 H, 2-H), 4.18 (dd, J = 9.0, 6.6 Hz, 1 H, 2-H), 4.71 (d, J = 8.1 Hz, 1 H, 3-H), 4.98 (d, J = 5.7 Hz, 1 H, 8a-H), 6.87 (d, J = 1.5 Hz, 1 H, 3-H ind), 7.04–7.08 (m, 1 H, 6-H ind), 7.18–7.25 (m, 1 H, 5-H ind), 7.28–7.41 (m, 7 H, ArH, 4-H ind), 10.05 (s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 10.1 (CH_3 ethyl), 22.4 (CH_2 ethyl), 30.8 (C-7), 37.2 (*C*H_2CO), 42.0 (C-6), 44.6 (C-8), 58.3 (C-3), 73.8 (C-2), 90.7 (C-8a), 109.3 (C-3 ind), 112.5 (C-7 ind), 120.3 (C-4 ind), 122.6 (C-6 ind), 125.8 (C-5 ind), 126.7 (C-*o*), 127.0 (C-3a ind), 127.5 (C-*m*), 128.5 (C-*p*), 135.0 (C-7a ind), 137.7 (C-*i*), 141.3 (C-2 ind), 167.2 (NCO), 190.4 (CO) ppm. IR (film): $\tilde{\nu}$ = 1657, 1735, 3312 cm^{-1}. $C_{25}H_{26}N_2O_3 \cdot 1/4$ EtOAc (424.52): calcd. C 73.56, H 6.65, N 6.60; found C 73.77, H 6.63, N 6.47.

Data for *cis*-6: Yellow foam. $[\alpha]_D^{22}$ = –70.4 (c = 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.10 (t, J = 7.3 Hz, 3 H, CH_3 ethyl), 1.45–1.54 (m, 1 H, CH_2 ethyl), 1.89–2.03 (m, 2 H, CH_2 ethyl, 8-H), 2.45 (m, 2 H, CH_2CO), 3.00 (m, 3 H, 2 × 6-H, 7-H), 4.04 (dd, J = 9.3, 4.3 Hz, 1 H, 2-H), 4.18 (dd, J = 9.3, 6.9 Hz, 1 H, 2-H), 4.68 (d, J = 9.3 Hz, 1 H, 3-H), 4.94 (d, J = 5.7 Hz, 1 H, 8a-H), 6.87 (d, J = 1.5 Hz, 1 H, 3-H ind), 7.11–7.36 (m, 9 H, ArH, H ind), 7.68 (dd, J = 8.1, 0.9 Hz, 1 H, 4-H ind), 9.50 (s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 11.3 (CH_3 ethyl), 21.2 (CH_2 ethyl), 29.0 (C-7), 36.5 (*C*H_2CO), 37.9 (C-6), 43.6 (C-8), 59.4 (C-3), 73.8 (C-2), 90.2 (C-8a), 109.4 (C-3 ind), 112.4 (C-7 ind), 120.8 (C-4 ind), 122.8 (C-6 ind), 126.2 (C-5 ind), 126.3 (C-*o*), 127.2 (C-3a ind), 127.4 (C-*m*), 128.4 (C-*p*), 135.0 (C-7a ind), 137.6 (C-*i*), 141.3 (C-2 ind), 166.8 (NCO), 190.7 (CO) ppm. IR (film): $\tilde{\nu}$ = 1657, 1735, 3325 cm^{-1}. $C_{25}H_{26}N_2O_3 \cdot 1/2\,H_2O$ (411.19): calcd. C 73.78, H 6.56, N 6.88; found C 73.40, H 6.27, N 6.98.

(3*R*,6*R*,7*R*,8*S*,8a*R*)-6-(Benzyloxycarbonyl)-8-ethyl-7-[2-(1-methyl-2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*cis*-7): Compound **7** was obtained as a mixture of diastereoisomers as described in the General Procedure, from the crude product obtained from the unsaturated lactam **1b**[3a] (500 mg, 1.32 mmol) in THF (10 mL), LDA (0.8 mL of a 2.0 M solution in THF/diethyl ether, 1.6 mmol) and a solution of the indole **4a** (274 mg, 1.58 mmol) in THF (20 mL) over 23 h. Flash chromatography (hexane/EtOAc 9:1 to 1:1) afforded *cis*-**7** (228 mg, 32%) and *trans*-**7** (mixture of C-6 epimers; 76 mg, 10%).

Data for *cis*-7: Yellow foam. $[\alpha]_D^{22}$ = –69.8 (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.02 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.40–1.50 (m, 1 H, CH_2 ethyl), 1.85–1.94 (m, 1 H, CH_2 ethyl), 2.42–2.51 (m, 1 H, 8-H), 2.95 (dd, J = 16.2, 11.1 Hz, 1 H, CH_2CO), 3.13 (dd, J = 16.2, 2.4 Hz, 1 H, CH_2CO), 3.15–3.19 (m, 1 H, 7-H), 3.45 (d, J = 0.3 Hz, 1 H, 6-H), 4.01–4.12 (m, 1 H, 2-H), 4.05 (s, 3 H, NCH_3), 4.18 (dd, J = 9.0, 6.9 Hz, 1 H, 2-H), 4.67 (d, J = 9.6 Hz, 1 H, 8a-H), 4.95 (t, J = 5.7 Hz, 1 H, 3-H), 5.06 (d,

J = 12.3 Hz, 1 H, C$H_2C_6H_5$), 5.13 (d, J = 12.3 Hz, 1 H, C$H_2C_6H_5$), 7.15–7.40 (m, 14 H, ArH, ind-H), 7.68 (dd, J = 7.8 Hz, 1 H, ind-H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 11.1 (CH_3 ethyl), 20.8 (CH_2 ethyl), 32.2 (NCH_3), 33.1 (C-7), 37.4 (*C*H_2CO), 40.2 (C-8), 53.4 (C-6), 59.7 (C-3), 66.9 (*C*$H_2C_6H_5$), 74.0 (C-2), 90.3 (C-8a), 110.5 (C-3 ind), 114.4 (C-7 ind), 120.9 (C-5 ind), 122.9 (C-4 ind), 125.6 (CAr), 126.3 (CHAr), 126.4 (CHAr), 127.5 (CAr), 127.8 (CHAr), 128.0 (CAr), 128.4 (CHAr), 128.5 (CHAr), 134.5 (C-*i*), 135.6 (C-2 ind), 140.3 (C-3a ind), 140.6 (C-7a ind), 162.1 (NCO), 169.5 (COO), 190.8 (CO) ppm. IR (film): $\tilde{\nu}$ = 1660, 1735 cm^{-1}. $C_{34}H_{34}N_2O_5$·1/3 EtOAc (579.73): calcd. C 73.18, H 6.37, N 4.83; found C 72.97, H 6.24, N 5.06.

(3*R*,6*S*,7*R*,8*S*,8a*R*)-8-Ethyl-7-[2-(2-indolyl)-2-oxoethyl]-6-(methoxycarbonyl)-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo-[3,2-*a*]pyridine (*cis*-8) and Its 6*R*,7*S* Diastereoisomer (*trans*-8): Compound **8** was obtained as a mixture of diastereoisomers as described in the General Procedure, from the crude product obtained from the unsaturated lactam **1c**[3a] (657 mg, 2.18 mmol) in THF (10 mL), LDA (3.84 mL of a 1.5 M solution in THF, 5.76 mmol) and a solution of 2-acetylindole (**4b**, 417 mg, 2.61 mmol) in THF (30 mL) over 16 h. Flash chromatography (hexane to hexane/EtOAc 9:1) afforded *cis*-**8** (290 mg, 29%) and *trans*-**8** (90 mg, 9%).

Data for *cis*-8: Yellow foam. $[\alpha]_D^{22}$ = –65.3 (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.11 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.44–1.54 (m, 1 H, CH_2 ethyl), 1.89–1.99 (m, 1 H, CH_2 ethyl), 2.46–2.55 (m, 1 H, 8-H), 2.93 (dd, J = 16.2, 11.1 Hz, 1 H, CH_2CO), 3.12 (dd, J = 16.2, 2.7 Hz, 1 H, CH_2CO), 3.17–3.21 (m, 1 H, 7-H), 3.41 (d, J = 10.5 Hz, 1 H, 6-H), 3.60 (s, 3 H, OCH_3), 4.06 (dd, J = 9.0, 1.5 Hz, 1 H, 2-H), 4.20 (dd, J = 9.0, 7.2 Hz, 1 H, 2-H), 4.68 (d, J = 9.9 Hz, 1 H, 8a-H), 4.97 (dd, J = 7.2, 1.5 Hz, 1 H, 3-H), 7.13–7.40 (m, 9 H, ArH, ind-H), 7.68 (dd, J = 8.1, 0.9 Hz, 1 H, 4-H ind), 9.27 (s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 11.2 (CH_3 ethyl), 20.0 (CH_2 ethyl), 33.4 (C-7), 35.8 (*C*H_2CO), 40.1 (C-8), 52.4 (C-6), 53.1 (OCH_3), 59.7 (C-3), 74.0 (C-2), 90.3 (C-8a), 109.6 (C-3 ind), 112.5 (C-7 ind), 121.0 (C-4 ind), 122.9 (C-5 ind), 126.5 (C-6 ind), 126.6 (C-*o*), 127.3 (C-2 ind), 127.5 (C-*m*), 128.3 (C-*p*), 134.8 (C-*i*), 137.7 (C-3a ind), 140.6 (C-7a ind), 162.4 (NCO), 170.2 (COO), 190.1 (CO) ppm. IR (film): $\tilde{\nu}$ = 1655, 1736, 3324 cm^{-1}. $C_{27}H_{28}N_2O_5$·1/2 EtOAc (504.58): calcd. C 69.03, H 6.39, N 5.55; found C 68.99, H 6.16, N 5.59.

Data for *trans*-8: Yellow foam. $[\alpha]_D^{22}$ = +3.6 (c = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.11 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.63–1.75 (m, 1 H, CH_2 ethyl), 1.75–1.87 (m, 1 H, CH_2 ethyl), 1.96–2.01 (m, 1 H, 8-H), 2.89–2.98 (m, 1 H, 7-H), 3.02–3.06 (m, 2 H, CH_2CO), 3.52 (d, J = 7.2 Hz, 1 H, 6-H), 3.69 (s, 3 H, OCH_3), 4.12 (dd, J = 9.3, 1.2 Hz, 1 H, 2-H), 4.21 (dd, J = 9.3, 6.6 Hz, 1 H, 2-H), 4.83 (d, J = 8.4 Hz, 1 H, 8a-H), 4.98–5.00 (m, 1 H, 3-H), 7.01 (d, J = 1.8 Hz, 1 H, 3-H ind), 7.11–7.45 (m, 8 H, ArH, ind-H), 7.66 (d, J = 8.1 Hz, 1 H, 4-H ind), 9.32 (s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 10.3 (CH_3 ethyl), 23.1 (CH_2 ethyl), 33.7 (C-7), 41.1 (*C*H_2CO), 44.7 (C-8), 52.6 (OCH_3), 54.9 (C-6), 59.0 (C-3), 73.8 (C-2), 90.4 (C-8a), 109.6 (C-3 ind), 112.3 (C-7 ind), 120.9 (C-4 ind), 122.9 (C-5 ind), 126.8 (C-6 ind), 126.6 (C-*o*), 127.3 (C-2 ind), 127.5 (C-*p*), 128.5 (C-*m*), 134.8 (C-*i*), 137.6 (C-3a ind), 140.8 (C-7a ind), 162.7 (NCO), 170.0 (COO), 190.1 (CO) ppm. IR (film): $\tilde{\nu}$ = 1656, 1737, 3310 cm^{-1}. $C_{27}H_{28}N_2O_5$·3/4 H_2O (474.04): calcd. C 68.41, H 6.27, N 5.91; found C 68.12, H 6.10, N 5.64.

(3*R*,6*R*,7*R*,8*S*,8a*R*)-6-(Benzyloxycarbonyl)-8-ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*cis*-9) and Its 6*S*,7*S* Diastereoisomer (*trans*-9): Compound **9** was obtained as a mixture of diastereoisomers as described in the General Procedure, from the crude product obtained from the unsaturated lactam **1b**[3a] (1.55 g, 4.11 mmol) in THF (50 mL), LDA (27.4 mL of a 1.5 M solution in THF, 41.1 mmol) and a solution of 2-acetylindole (**4b**, 3.27 g, 20.5 mmol) in THF (100 mL) over 5 h. Flash chromatography (hexane to hexane/EtOAc 1:1) afforded *cis*-**9** (accompanied by trace amounts of the C-6 epimer; 1.53 g, 69%) and *trans*-**9** (457 mg, 21%).

Data for *cis*-9: Yellow foam. $[\alpha]_D^{22}$ = –87.0 (c = 0.2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.02 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.40–1.50 (m, 1 H, CH_2 ethyl), 1.83–1.94 (m, 1 H, CH_2 ethyl), 2.42–2.51 (m, 1 H, 8-H), 2.92 (dd, J = 16.2, 11.1 Hz, 1 H, CH_2CO), 3.10 (dd, J = 16.2, 2.7 Hz, 1 H, CH_2CO), 3.16 (m, 1 H, 7-H), 3.47 (d, J = 1.2 Hz, 1 H, 6-H), 4.03 (dd, J = 9.0, 1.5 Hz, 1 H, 2-H), 4.19 (dd, J = 9.0, 7.2 Hz, 1 H, 2-H), 4.67 (d, J = 9.6 Hz, 1 H, 8a-H), 4.97 (dd, J = 7.2, 1.5 Hz, 1 H, 3-H), 5.03 (d, J = 16.8 Hz, 1 H, C$H_2C_6H_5$), 5.08 (d, J = 16.8 Hz, 1 H, C$H_2C_6H_5$), 7.12–7.41 (m, 14 H, ArH), 7.69 (dd, J = 8.4, 1.2 Hz, 1 H, 4-H ind), 9.22 (s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 11.1 (CH_3 ethyl), 20.7 (CH_2 ethyl), 33.4 (C-7), 35.8 (*C*H_2CO), 40.1 (C-8), 53.1 (C-6), 59.5 (C-3), 66.7 (*C*$H_2C_6H_5$), 73.8 (C-2), 90.0 (C-8a), 109.3 (C-3 ind), 112.6 (C-7 ind), 120.6 (C-2 ind), 122.5 (C-6 ind), 126.1 (C-5 ind), 126.2 (C-4 ind), 126.9, 127.2, 127.5, 127.7, 127.9, 128.1 (C-*o*, *m*, *p*), 134.6 (C-3a ind), 135.2 (C-7a ind), 140.5 (C-*i*), 137.7 (C-*i*), 162.2 (COO), 169.2 (NCO), 189.9 (CO) ppm. IR (film): $\tilde{\nu}$ = 1655, 1735, 3320 cm^{-1}. $C_{33}H_{32}N_2O_5$·1/4 EtOAc (558.65): calcd. C 73.10, H 6.13, N 5.01; found C 73.08, H 6.00, N 4.99.

Data for *trans*-9: Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.99 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.71–2.04 (m, 3 H, CH_2 ethyl, 8-H), 2.87–3.18 (m, 3 H, 2 × CH_2CO, 7-H), 3.56 (d, J = 5.6 Hz, 1 H, 6-H), 4.01–4.20 (m, 2 H, 2-H), 4.71 (d, J = 8.4 Hz, 1 H, 8a-H), 4.97 (d, J = 6.0 Hz, 1 H, 3-H), 5.09 (d, J = 11.6 Hz, 1 H, C$H_2C_6H_5$), 5.14 (d, J = 11.6 Hz, 1 H, C$H_2C_6H_5$), 6.95 (d, J = 1.6 Hz, 1 H, 3-H ind), 7.12–7.41 (m, 13 H, ArH), 7.65 (d, J = 7.6 Hz, 1 H, 4-H ind), 9.09 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 10.4 (CH_3 ethyl), 23.1 (CH_2 ethyl), 34.9 (C-7), 41.1 (*C*H_2CO), 44.7 (C-8), 55.0 (C-6), 58.9 (C-3), 67.3 (*C*$H_2C_6H_5$), 73.8 (C-2), 90.4 (C-8a), 109.7 (C-3 ind), 112.3 (C-7 ind), 120.9 (C-2 ind), 123.0 (C-6 ind), 126.4 (C-5 ind), 126.5 (C-4 ind), 126.9–128.6 (C-*o*, *m*, *p*), 134.8 (C-3a ind), 137.5 (C-7a ind), 140.6 (C-*i*), 140.8 (C-*i*), 162.7 (COO), 169.9 (NCO), 190.0 (CO) ppm.

(3*R*,6*R*,7*R*,8*S*,8a*R*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*cis*-10): Compound **10** was obtained as a mixture of diastereoisomers as described in the General Procedure, from the crude unsaturated lactam **1d**[6] (1.0 g, 2.90 mmol) in THF (50 mL), LDA (19.5 mL of a 1.5 M solution in cyclohexane, 29 mmol) and a solution of 2-acetylindole (**4b**, 2.3 g, 14.5 mmol) in THF (100 mL) over 4 h. Flash chromatography (hexane to hexane/EtOAc 1:1) afforded *cis*-**10** (1.17 g, 80%) and *trans*-**10** (mixture of C-6 epimers; 230 mg, 7%).

Data for *cis*-10: Yellow foam. $[\alpha]_D^{22}$ = –21.5 (c = 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.11 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.34 [s, 9 H, $(CH_3)_3C$], 1.43–1.52 (m, 1 H, CH_2 ethyl), 1.88–1.96 (m, 1 H, CH_2 ethyl), 2.56 (ddd, J = 13.6, 9.2, 4.8 Hz, 1 H, 8-H), 2.91 (dd, J = 16.0, 10.8 Hz, 1 H, CH_2CO), 3.08 (dd, J = 16.0, 2.4 Hz, 1 H, CH_2CO), 3.20 (m, 1 H, 7-H), 3.30 (s, 1 H, 6-H), 4.04 (d, J = 8.4 Hz, 1 H, 2-H), 4.19 (dd, J = 8.4, 7.2 Hz, 1 H, 2-H), 4.66 (d, J = 9.6 Hz, 1 H, 8a-H), 4.97 (d, J = 6.4 Hz, 1 H, 3-H), 7.12–7.40 (m, 9 H, ArH), 7.68 (d, J = 8.4 Hz, 1 H, 4-H ind), 9.36 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.2 (CH_3 ethyl), 20.8 (CH_2 ethyl), 27.8 [C(*C*H_3)$_3$], 32.9 (C-7), 36.0

(CH_2CO), 40.3 (C-8), 54.4 (C-6), 59.6 (C-3), 74.1 (C-2), 81.9 [$C(CH_3)_3$], 90.3 (C-8a), 109.5 (C-3 ind), 112.3 (C-7 ind), 121.0 (C-5 ind), 123.0 (C-6 ind), 126.5 (C-*o*), 126.6 (C-2 ind), 127.4 (C-*m*), 128.4 (C-*p*), 134.9 (C-3a ind), 137.5 (C-7a ind), 140.8 (C-*i*), 162.5 (NCO), 168.3 (COO), 190.1 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 1662, 1728, 2958 cm^{-1}. HRMS: calcd. for $C_{30}H_{35}N_2O_5$ $[M + H]^+$: 503.2540; found 503.2541.

(3*R*,6*R*,7*S*,8*R*,8a*S*)-6-(Benzyloxycarbonyl)-8-ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*cis*-11): Compound **11** was obtained as a mixture of diastereoisomers as described in the General Procedure, from the crude unsaturated lactam **1e** (161 mg, 0.43 mmol) in THF (10 mL), LDA (2.86 mL of a 1.5 M solution in THF, 4.3 mmol) and a solution of 2-acetylindole (**4b**, 342 mg, 2.15 mmol) in THF (15 mL) over 20 h. Flash chromatography (hexane/EtOAc 9:1 to EtOAc) afforded *cis*-**11** (110 mg, 48%) and *trans*-**11** (1:1 mixture of C-6 epimers; 32 mg, 14%).

Data for *cis*-11: Yellow foam. $[\alpha]_D^{22}$ = –101.1 (*c* = 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.98 (t, *J* = 7.5 Hz, 3 H, CH_3 ethyl), 1.61 (m, 1 H, CH_2 ethyl), 1.76 (m, 1 H, CH_2 ethyl), 1.91 (m, 1 H, 8-H), 2.91 (m, 1 H, 7-H), 3.12 (dd, *J* = 5.4, 2.4 Hz, 2 H, CH_2CO), 3.67 (d, *J* = 9.3 Hz, 1 H, 6-H), 3.73 (dd, *J* = 9.0, 7.8 Hz, 1 H, 2-H), 4.49 (dd, *J* = 9.0, 7.8 Hz, 1 H, 2-H), 4.93 (d, *J* = 8.4 Hz, 1 H, 8a-H), 5.04 (d, *J* = 12.3 Hz, 1 H, $CH_2C_6H_5$), 5.13 (d, *J* = 12.3 Hz, 1 H, $CH_2C_6H_5$), 5.29 (t, *J* = 7.8 Hz, 1 H, 3-H), 7.12–7.37 (m, 14 H, ArH, ind-H), 7.67 (d, *J* = 8.1 Hz, 1 H, 4-H ind), 9.21 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 9.9 (CH_3 ethyl), 21.5 (CH_2 ethyl), 33.4 (C-7), 38.6 (CH_2CO), 40.3 (C-8), 55.4 (C-6), 58.7 (C-3), 67.4 ($CH_2C_6H_5$), 72.6 (C-2), 90.6 (C-8a), 109.4 (C-3 ind), 112.3 (CH ind), 121.0 (CH ind), 123.1 (CH ind), 125.7 (CHAr), 126.5 (CHAr), 127.4 (C-*i*), 127.6 (CHAr), 128.0 (CHAr), 128.2 (CHAr), 128.4 (CHAr), 128.8 (CHAr), 134.8 (C-*i*), 135.2 (C-2 ind), 137.4 (C-3a ind), 138.6 (C-7a), 164.1 (NCO), 170.1 (COO), 190.0 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 1656, 1735 cm^{-1}. $C_{33}H_{32}N_2O_5$ (536.62): calcd. C 73.86, H 6.01, N 5.22; found C 73.46, H 6.08, N 5.34.

[3*R*,6*R*/6*S*),7*S*,8*S*,8a*S*]-6-(Benzyloxycarbonyl)-8-ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (*trans*-12): Compound **12** was obtained as a mixture of diastereoisomers as described in the General Procedure, from the crude product obtained from the unsaturated lactam **1f** (1 g, 2.65 mmol) in THF (50 mL), LDA (26.5 mL of a 1 M solution in THF, 26.5 mmol) and a solution of 2-acetylindole (**4b**, 2.11 g, 13.25 mmol) in THF (100 mL) over 5 h. Flash chromatography (hexane/EtOAc 9:1 to EtOAc) afforded *trans*-**12** (9:1 mixture of C-6 epimers; 1.02 g, 72%) and *cis*-**12** (mixture of C-6 epimers; 211 mg, 14%).

Data for *trans*-12 (Major 6*S* Epimer): Yellow foam. ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, *J* = 7.2 Hz, 3 H, CH_3 ethyl), 1.26–1.41 (m, 1 H, CH_2 ethyl), 1.64–1.71 (m, 1 H, CH_2 ethyl), 2.23–2.31 (m, 1 H, 8-H), 2.98–3.04 (m, 1 H, 7-H), 3.09 (dd, *J* = 12.4, 6.0 Hz, 1 H, CH_2CO), 3.13 (dd, *J* = 12.4, 6.4 Hz, 1 H, CH_2CO), 3.66 (d, *J* = 8.8 Hz, 1 H, 6-H), 3.86 (dd, *J* = 8.8, 6.8 Hz, 1 H, 2-H), 4.45 (dd, *J* = 8.8, 8.0 Hz, 1 H, 2-H), 5.09 (d, *J* = 9.2 Hz, 1 H, 8a-H), 5.16 (d, *J* = 12.5 Hz, 1 H, $CH_2C_6H_5$), 5.19 (d, *J* = 12.5 Hz, 1 H, $CH_2C_6H_5$), 5.33 (t, *J* = 7.6 Hz, 1 H, 3-H), 7.10 (d, *J* = 1.4 Hz, 1 H, 3-H ind), 7.15–7.42 (m, 13 H, ArH, ind-H), 7.69 (t, *J* = 8.0 Hz, 1 H, ind-H), 9.09 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.3 (CH_3 ethyl), 19.9 (CH_2 ethyl), 33.1 (C-7), 40.5 (CH_2CO), 42.1 (C-8), 53.8 (C-6), 58.8 (C-3), 67.2 ($CH_2C_6H_5$), 72.3 (C-2), 88.0 (C-8a), 109.5 (C-3 ind), 112.2 (C-7 ind), 121.1 (C-4 ind), 123.2 (C-5 ind), 125.6 (C-6 ind), 126.3, 126.7, 127.8, 128.1, 128.3, 128.4, 128.8, (C-*o*, C-*m*, C-*p*, C-3a ind), 134.7 (C-2 ind), 135.5 (C-7a ind), 139.1 (C-*i*), 166.0 (NCO), 169.6 (COO), 190.3 (CO) ppm. IR (film): $\tilde{\nu}$ = 1655, 1736, 3324 cm^{-1}. HRMS: calcd. for $C_{33}H_{32}N_2NaO_5$ $[M + Na]^+$: 559.2203; found 559.2207.

Data for *trans*-12 (Minor 6*R* Epimer): ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.00 (t, *J* = 7.4 Hz, 3 H, CH_3 ethyl), 1.30–1.42 (m, 2 H, CH_2 ethyl), 3.15–3.20 (m, 2 H, 7-H, 8-H), 3.25 (dd, *J* = 16.0, 7.2 Hz, 1 H, CH_2CO), 3.30 (dd, *J* = 16.0, 5.6 Hz, 1 H, CH_2CO), 3.74 (dd, *J* = 8.7, 7.6 Hz, 1 H, 2-H), 3.78 (d, *J* = 5.6 Hz, 1 H, 6-H), 4.52 (t, *J* = 8.4 Hz, 1 H, 2-H), 5.07 (d, *J* = 12.4 Hz, 1 H, $CH_2C_6H_5$), 5.13 (d, *J* = 12.4 Hz, 1 H, $CH_2C_6H_5$), 5.16 (masked, 1 H, 8a-H), 5.38 (t, *J* = 7.6 Hz, 1 H, 3-H), 7.00 (d, *J* = 1.4 Hz, 1 H, 3-H ind), 7.10–7.42 (m, 13 H, ArH, ind-H), 7.68 (t, *J* = 8.6 Hz, 1 H, ind-H), 9.07 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.6 (CH_3 ethyl), 19.5 (CH_2 ethyl), 32.0 (C-7), 38.4 (CH_2CO), 39.6 (C-8), 50.5 (C-6), 58.1 (C-3), 67.3 ($CH_2C_6H_5$), 71.9 (C-2), 87.6 (C-8a), 109.5 (C-3 ind), 112.2 (C-7 ind), 121.1 (C-4 ind), 123.2 (C-5 ind), 125.6 (C-6 ind), 126.6, 127.5, 128.4, 128.5, 128.6, 128.8, 128.9 (C-*o*, C-*m*, C-*p*, C-3a ind), 135.1 (C-2 ind), 134.8 (C-7a ind), 137.3 (C-*i*), 164.8, (NCO), 169.2 (COO), 190.1 ppm.

Conversion of *cis*-9 into *cis*-6: A solution of *cis*-**9** (200 mg, 0.43 mmol) in EtOAc (10 mL) containing $Pd(OH)_2$ (20 mg) was hydrogenated with vigorous stirring at room temperature and atmospheric pressure for 24 h. The catalyst was removed by filtration, and the solvent was evaporated to give an oil, which was dissolved in toluene (30 mL). The resulting solution was heated at reflux for 16 h and concentrated to dryness. The residue was chromatographed (hexane/EtOAc 4:1 to EtOAc) to give *cis*-**6** (97 mg, 65%).

(3*R*,7*R*,8*S*,8a*S*)-8-Ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (14): Compound **14** (452 mg, 67%) was obtained as above, from *trans*-**12** (900 mg, 1.68 mmol) and $Pd(OH)_2$ (30%, 270 mg) in EtOAc (50 mL), with subsequent heating at reflux in toluene (100 mL), after column chromatography (hexane to hexane/EtOAc 1:1).

Data for 14: Yellow foam. $[\alpha]_D^{22}$ = –21.6 (*c* = 0.5, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.01 (t, *J* = 7.4 Hz, 3 H, CH_3 ethyl), 1.21–1.28 (m, 1 H, CH_2 ethyl), 1.71–1.79 (m, 1 H, CH_2 ethyl), 2.18 (ddd, *J* = 14.0, 6.0, 4.8 Hz, 1 H, 8-H), 2.36 (dd, *J* = 18.4, 3.2 Hz, 1 H, CH_2CO), 2.63 (dd, *J* = 18.4, 6.4 Hz, 1 H, CH_2CO), 2.84 (m, 1 H, 7-H), 3.09–3.11 (m, 2 H, 6-H), 3.79 (dd, *J* = 8.8, 7.6 Hz, 1 H, 2-H), 4.48 (t, *J* = 8.8 Hz, 1 H, 2-H), 5.23 (d, *J* = 4.4 Hz, 1 H, 8a-H), 5.30 (t, *J* = 7.6 Hz, 1 H, 3-H), 7.14–7.41 (m, 9 H, ArH), 7.69 (d, *J* = 8.0 Hz, 1 H, 4-H ind), 9.35 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.6 (CH_3 ethyl), 18.7 (CH_2 ethyl), 29.6 (C-7), 33.7 (CH_2CO), 40.7 (C-8), 41.9 (C-6), 58.3 (C-3), 72.2 (C-2), 88.0 (C-8a), 109.5 (C-3 ind), 112.3 (C-7 ind), 121.1 (C-5 ind), 123.1 (C-6 ind), 126.0 (C-*o*), 126.7 (C-2 ind), 127.7 (C-*m*), 128.9 (C-*p*), 134.9 (C-3a ind), 137.5 (C-7a ind), 139.6 (C-*i*), 168.1 (NCO), 190.7 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 1649, 3312 cm^{-1}. HRMS: calcd. for $C_{25}H_{27}N_2O_3$ $[M + H]^+$: 403.2016; found 403.2014.

(3*R*,7*R*,8*R*,8a*S*)-8-Ethyl-7-[2-(2-indolyl)-2-oxoethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (15): Compound **15** (288 mg, 62%) was obtained as above, from *cis*-**11** (620 mg, 1.15 mmol) and $Pd(OH)_2$ (20%, 124 mg) in MeOH (40 mL), with subsequent heating at reflux in toluene (70 mL), after column chromatography (hexane to hexane/EtOAc 1:1).

Data for 15: Yellow foam. $[\alpha]_D^{22}$ = –74.7 (*c* = 0.67, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.08 (t, *J* = 7.6 Hz, 3 H, CH_3 ethyl), 1.45–1.54 (m, 1 H, CH_2 ethyl), 1.75–1.90 (m, 2 H, CH_2 ethyl, 8-H), 2.54–2.66 (m, 2 H, 6-H, 7-H), 2.90 (m, 1 H, 6-H), 2.97 (d, *J* = 11.8 Hz, 1 H, CH_2CO), 3.08 (d, *J* = 11.8 Hz, 1 H, CH_2CO), 3.80

(t, J = 8.4 Hz, 1 H, 2-H), 4.56 (t, J = 8.4 Hz, 1 H, 2-H), 4.78 (d, J = 9.2 Hz, 1 H, 8a-H), 5.35 (t, J = 8.0 Hz, 1 H, 3-H), 7.12–7.41 (m, 9 H, ArH, H ind), 7.66 (d, J = 8.4 Hz, 1 H, ind-H), 9.26 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.5 (CH_3 ethyl), 22.1 (CH_2 ethyl), 29.0 (C-7), 36.1 (*C*H_2CO), 37.4 (C-6), 44.0 (C-8), 58.3 (C-3), 72.4 (C-2), 90.9 (C-8a), 109.4 (C-3 ind), 112.3 (C-7 ind), 121.1 (C-4 ind), 123.0 (C-5 ind), 125.9 (C-*o*), 126.7 (C-6 ind), 127.4 (C-2 ind), 127.8 (C-*m*), 129.0 (C-*p*), 135.0 (C-*i*), 137.5 (C-3a), 139.7 (C-7a), 168.3 (NCO), 190.9 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 1648 cm^{-1}. HRMS: calcd. for $C_{25}H_{27}N_2O_3$ [M + H]$^+$: 403.2016; found 403.2018. $C_{25}H_{26}N_2O_3 \cdot 1/2\,H_2O$ (411.50): calcd. C 72.97, H 6.61, N 6.81; found C 72.94, H 6.61, N 6.45.

(3*R*,7*R*,8*S*,8a*R*)-8-Ethyl-7-[2-hydroxy-2-(2-indolyl)ethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (16): $NaBH_4$ (117 mg, 3.11 mmol) was slowly added at 0 °C to a solution of *trans*-**6** (128 mg, 0.31 mmol) in MeOH (11 mL). The mixture was stirred at 0 °C for 1 h and the temperature was slowly raised to 25 °C. The mixture was concentrated, water was added, and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried and concentrated to give a foam, which was chromatographed (hexane/EtOAc 1:1 to EtOAc) to afford the alcohol **16** as a mixture of epimers (115 mg, 90%).

Data for 16 (Higher R_f Epimer): Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.80 (t, J = 7.4 Hz, 3 H, CH_3 ethyl), 1.37–1.62 (m, 5 H, CH_2 ethyl, C*H*$_2$CHOH, 7-H, 8-H), 1.88 (dd, J = 16.8, 7.2 Hz, 1 H, 6-H), 1.97 (dd, J = 10.4, 8.0 Hz, 1 H, C*H*$_2$CHOH), 2.22 (br. s, 1 H, OH), 2.43 (dd, J = 16.8, 4.4 Hz, 1 H, 6-H), 3.92 (dd, J = 8.8, 1.6 Hz, 1 H, 2-H), 3.96 (dd, J = 8.8, 6.0 Hz, 1 H, 2-H), 4.20 (d, J = 7.6 Hz, 1 H, 8a-H), 4.59 (m, 1 H, C*H*OH), 4.77 (d, J = 5.2 Hz, 1 H, 3-H), 6.20 (s, 1 H, 3-H ind), 7.02–7.27 (m, 8 H, ArH, ind-H), 7.50 (d, J = 7.2 Hz, 1 H, 4-H ind), 9.16 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 9.5 (CH_3 ethyl), 21.2 (CH_2 ethyl), 31.2 (C-7), 37.4 (C-6), 40.5 (*C*H_2CHOH), 44.4 (C-8), 58.7 (C-3), 66.6 (CHOH), 73.7 (C-2), 90.5 (C-8a), 98.9 (C-3 ind), 111.3 (C-7 ind), 119.6 (C-5 ind), 120.3 (C-4 ind), 121.7 (C-6 ind), 126.5 (C-*o*), 127.6 (C-*p*), 128.0 (C-2 ind), 128.5 (C-*m*), 136.0 (C-3a ind), 140.8 (C-7a ind), 141.2 (C-*i*), 167.6 (NCO) ppm.

Data for 16 (Lower R_f Epimer): Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.91 (t, J = 7.3 Hz, 3 H, CH_3 ethyl), 1.19–1.26 (m, 1 H, C*H*$_2$CHOH), 1.41–1.45 (m, 1 H, 8-H), 1.49–1.59 (m, 1 H, CH_2 ethyl), 1.68 (ddd, J = 14.4, 7.2, 4.0 Hz, 1 H, CH_2 ethyl), 1.88–1.92 (m, 1 H, 6-H), 1.95–2.04 (m, 2 H, C*H*$_2$CHOH, 7-H), 2.21 (br. s, 1 H, OH), 2.55 (dd, J = 16.4, 4.8 Hz, 1 H, 6-H), 3.91–3.97 (m, 2 H, 2-H), 4.29 (d, J = 9.2 Hz, 1 H, 8a-H), 4.73 (d, J = 9.2 Hz, 1 H, C*H*OH), 4.78 (d, J = 4.8 Hz, 1 H, 3-H), 6.18 (s, 1 H, 3-H ind), 7.04 (dd, J = 6.4, 1.2 Hz, 1 H, 7-H ind), 7.08 (dd, J = 7.6, 1.6 Hz, 1 H, 5-H ind), 7.09–7.24 (m, 6 H, ArH, 6-H ind), 7.53 (d, J = 8.0 Hz, 1 H, 4-H ind), 9.24 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 9.3 (CH_3 ethyl), 20.5 (CH_2 ethyl), 29.2 (C-7), 36.5 (C-6), 39.7 (*C*H_2CHOH), 44.2 (C-8), 59.0 (C-3), 64.4 (CHOH), 73.7 (C-2), 90.6 (C-8a), 97.5 (C-3 ind), 111.1 (C-7 ind), 119.4 (C-5 ind), 120.2 (C-4 ind), 121.3 (C-6 ind), 126.4 (C-*o*), 127.6 (C-*p*), 128.2 (C-2 ind), 128.6 (C-*m*), 135.8 (C-3a ind), 141.2 (C-7a ind), 142.4 (C-*i*), 167.7 (NCO) ppm.

(3*R*,7*R*,8*S*,8a*R*)-7-[2-Acetyl-2-(2-indolyl)ethyl]-8-ethyl-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (17): DMAP (8 mg, 0.06 mmol) and Ac_2O (140 μL, 1.48 mmol) were added to a cooled (0 °C) solution of the alcohols **16** (135 mg, 0.34 mmol) in CH_2Cl_2 and pyridine (2 mL, 4:1). The mixture was stirred at room temp. for 4 h, diluted with $CHCl_3$ and successively washed with aqueous HCl (1 N) and saturated aqueous $NaHCO_3$. The organic solution was dried and concentrated to afford an epimeric mixture of acetates **17** (86 mg, 57%), which was used in the next reaction without further purification.

Data for 17: Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.87 (t, J = 7.2 Hz, 3 H, CH_3 ethyl), 1.04 (t, J = 7.4 Hz, 3 H, CH_3 ethyl), 1.12–1.17 (m, 2 H, 7-H), 1.23–2.21 (m, 8 H, CH_2 ethyl, C*H*$_2$CHO, 8-H), 2.20 (s, 3 H, CH_3CO), 2.25 (s, 3 H, CH_3CO), 2.55–2.63 (m, 2 H, C*H*$_2$CHO), 2.34 (dd, J = 14.0, 6.8 Hz, 1 H, 6-H), 3.32–3.49 (m, 3 H, 6-H), 4.01 (d, J = 9.0 Hz, 1 H, 2-H), 4.05 (d, J = 8.8 Hz, 1 H, 2-H), 4.07 (d, J = 8.8 Hz, 1 H, 2-H), 4.17 (dd, J = 9.0, 6.8 Hz, 1 H, 2-H), 4.47–4.54 (m, 3 H, CH_2C*H*O, 8a-H), 4.70 (d, J = 8.4 Hz, 1 H, 8a-H), 4.90 (d, J = 6.4 Hz, 1 H, 3-H), 4.95 (d, J = 6.0 Hz, 1 H, 3-H), 6.33 (s, 1 H, 3-H ind), 6.44 (s, 1 H, 3-H ind), 7.10 (dd, J = 14.8, 7.2 Hz, 1 H, ind-H), 7.17 (dd, J = 14.8, 7.2 Hz, 1 H, ind-H), 7.07–7.59 (m, 18 H, ArH, ind-H), 8.30 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 9.6, 9.9 (CH_3 ethyl), 15.2, 15.3 (CH_2 ethyl), 21.5, 21.6 (CO*C*H$_3$), 30.3, 30.9 (C-7), 36.9, 37.4 (C-6), 44.8, 44.9 (*C*H_2CO), 58.7, 58.7 (C-3), 64.3, 64.5 (CHOAc), 73.9, 74.0 (C-2), 90.7, 91.1 (C-8a), 100.4, 102.1 (C-3 ind), 110.9, 111.0 (C-7 ind), 119.8, 119.9 (C-5 ind), 120.4, 120.5 (C-4 ind), 121.8, 122.1 (C-6 ind), 126.4, 126.5 (C-*o*), 127.5 (C-*p*), 128.0, 128.2 (C-2 ind), 128.6 (C-*m*), 135.9, 136.2 (C-3a ind), 137.7, 139.4 (C-3a ind), 141.2, 141.3 (C-*i*), 166.6 (NCO), 166.8 (COO) ppm.

(3*R*,7*R*,8*S*,8a*R*)-8-Ethyl-7-[(2-indolyl)ethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (18): A solution of acetates **17** (160 mg, 0.36 mmol) in EtOAc (25 mL) containing Pd-C (20%, 17 mg) was hydrogenated at room temp. for 4 d at atmospheric pressure. The catalyst was removed by filtration, and the solvent was evaporated to give an oil. Flash chromatography (hexane/EtOAc 9:1 to 4:1) afforded **18** (70 mg, 50%).

Data for 18: Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.99 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.63–2.18 (m, 7 H, CH_2 ethyl, 7-H, 8-H, indC*H*$_2$CH$_2$, indCH$_2$C*H*$_2$), 2.49–2.64 (m, 1 H, indC*H*$_2$CH$_2$), 2.53 (dd, J = 15.0, 6.0 Hz, 1 H, 6-H), 2.77 (ddd, J = 15.0, 9.6, 4.8 Hz, 1 H, 6-H), 4.06 (dd, J = 9.2, 1.2 Hz, 1 H, 2-H), 4.16 (dd, J = 9.2, 6.8 Hz, 1 H, 2-H), 4.63 (d, J = 8.4 Hz, 1 H, 8a-H), 4.94 (d, J = 5.6 Hz, 1 H, 3-H), 6.20 (s, 1 H, 3-H ind), 7.03–7.57 (m, 9 H, ArH, ind-H), 8.22 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 10.0 (CH_3 ethyl), 22.0 (CH_2 ethyl), 24.9 (C-6), 33.2 (C-7, indCH$_2$*C*H$_2$), 36.8 (ind*C*H$_2$), 45.1 (C-8), 58.7 (C-3), 74.0 (C-2), 91.0 (C-8a), 99.5 (C-3 ind), 110.4 (C-7 ind), 119.5 (C-5 ind), 119.7 (C-4 ind), 121.0 (C-6 ind), 126.4, 126.6 (C-*o*), 127.6 (C-*p*), 128.6 (C-*m*), 128.7 (C-2 ind), 135.9 (C-3a ind), 138.6 (C-7a ind), 141.2 (C-*i*), 167.0 (NCO) ppm.

(3*R*,7*S*,8*S*,8a*R*)-8-Ethyl-7-[2-hydroxy-2-(2-indolyl)ethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (19): As in the above reduction of *trans*-**6**, a foam was obtained from a solution of *cis*-**6** (1.05 mg, 2.60 mmol) in THF (50 mL) and $NaBH_4$ (148 mg, 3.91 mmol) for 3 h. Flash chromatography (hexane/EtOAc 1:1 to EtOAc) gave two epimeric alcohols **19** (higher R_f epimer: 462 mg, 44%; lower R_f epimer: 308 mg, 29%).

Data for 19 (Higher R_f Epimer): Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.03 (t, J = 7.4 Hz, 3 H, CH_3 ethyl), 1.38–2.49 (m, 8 H, CH_2 ethyl, C*H*$_2$CHOH, 6-H, 7-H, 8-H), 3.14 (br. s, 1 H, OH), 3.94–4.04 (m, 2 H, 2-H), 4.50 (d, J = 8.4 Hz, 1 H, 8a-H), 4.81 (m, 2 H, C*H*OH, 3-H), 6.29 (s, 1 H, 3-H ind), 7.07 (t, J = 7.4 Hz, 1 H, ind-H), 7.13 (t, J = 7.4 Hz, 1 H, ind-H), 7.21–7.31 (m, 6 H, ArH, ind-H), 7.54 (d, J = 7.6 Hz, 1 H, 4-H ind), 8.78 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.2 (CH_3 ethyl), 20.7 (CH_2 ethyl), 28.6 (C-7), 35.4 (C-6), 36.9 (*C*H_2CHOH), 43.8 (C-8), 59.3 (*C*HOH), 65.3 (C-3), 73.8 (C-2), 90.3 (C-8a), 98.1 (C-3 ind), 111.0 (C-7 ind), 119.7 (C-5 ind), 120.4

(C-4 ind), 121.7 (C-6 ind), 126.3 (C-*o*), 127.6 (C-*p*), 128.2 (C-2 ind), 128.6 (C-*m*), 135.7 (C-3a ind), 141.4 (C-7a ind), 141.6 (C-*i*), 167.7 (NCO) ppm.

Data for 19 (Lower R_f Epimer): Yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.83 (t, J = 7.4 Hz, 3 H, CH_3 ethyl), 1.34–2.72 (m, 8 H, CH_2 ethyl, CH_2CHOH, 6-H, 7-H, 8-H), 3.87–4.00 (m, 2 H, 2-H), 4.51 (d, J = 6.8 Hz, 1 H, 8a-H), 4.62–4.78 (m, 2 H, C*H*OH, 3-H), 6.27 (s, 1 H, 3-H ind), 7.66–7.28 (m, 8 H, ArH, ind-H), 7.54 (d, J = 7.6 Hz, 1 H, 4-H ind), 9.20 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.2 (CH_3 ethyl), 20.8 (CH_2 ethyl), 29.7 (C-7), 30.8 (C-6), 38.0 (*C*H_2CHOH), 44.2 (C-8), 59.3 (*C*HOH), 68.2 (C-3), 73.8 (C-2), 90.3 (C-8a), 99.2 (C-3 ind), 111.3 (C-7 ind), 119.6 (C-5 ind), 120.3 (C-4 ind), 121.8 (C-6 ind), 126.3 (C-*o*), 127.6 (C-*p*), 127.9 (C-2 ind), 128.6 (C-*m*), 136.2 (C-3a ind), 141.0 (C-7a ind), 141.4 (C-*i*), 170.2 (NCO) ppm.

(3*R*,7*S*,8*S*,8a*R*)-7-[2-Acetyl-2-(2-indolyl)ethyl]-8-ethyl-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (20): The two epimeric acetates **20** (higher R_f epimer: 440 mg, 52%; lower R_f epimer: 300 mg, 35%) were obtained as in the above preparation of **17** (reaction time 14 h), from the alcohols **19** (770 mg, 1.90 mmol), DMAP (8 mg, 0.06 mmol) and Ac_2O (0.8 mL, 7.61 mmol) in CH_2Cl_2 and pyridine (12.5 mL, 4:1), after column chromatography (hexane to hexane/EtOAc 9:1).

Data for 20 (Higher R_f Epimer): Yellow foam. $[\alpha]_D^{22}$ = +47.5 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.11 (t, J = 7.3 Hz, 3 H, CH_3 ethyl), 1.54–1.63 (m, 1 H, CH_2 ethyl), 1.79 (dd, J = 11.2, 2.8 Hz, 1 H, 6-H), 1.92–1.99 (m, 2 H, CH_2 ethyl, 8-H), 2.10 (s, 3 H, CH_3CO), 2.26–2.31 (m, 1 H, 7-H), 2.35–2.45 (m, 3 H, CH_2CHO, 6-H), 2.54 (d, J = 17.6 Hz, 1 H, CH_2CHO), 3.99 (dd, J = 9.2, 1.2 Hz, 1 H, 2-H), 4.12 (dd, J = 9.2, 6.8 Hz, 1 H, 2-H), 4.62 (d, J = 9.2 Hz, 1 H, 8a-H), 4.89 (d, J = 6.8 Hz, 1 H, 3-H), 6.03 (dd, J = 10.8, 2.4 Hz, 1 H, CH_2C*H*O), 6.49 (d, J = 2.4 Hz, 1 H, 3-H ind), 7.08–7.32 (m, 8 H, ArH, ind-H), 7.58 (d, J = 7.2 Hz, 1 H, ind-H), 9.18 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.0 (CH_3 ethyl), 20.6 (CH_2 ethyl), 21.1 (OCH_3), 28.9 (C-7), 32.3 (C-6), 37.1 (*C*H_2CHO), 43.7 (C-8), 59.4 (C-3), 67.5 (CH_2*C*HO), 73.9 (C-2), 90.1 (C-8a), 100.2 (C-3 ind), 111.4 (C-4 ind), 119.8 (C-5 ind), 120.6 (C-4 ind), 122.3 (C-6 ind), 126.3 (C-*o*); 127.5, 127.6 (C-*p*, C-2 ind), 128.6 (C-*m*), 136.0 (C-3a ind), 137.0 (C-3a ind), 141.5 (C-*i*), 166.8 (NCO), 171.2 (COO) ppm. IR (KBr): $\tilde{\nu}$ = 1641, 1739, 3267 cm^{-1}. HRMS: calcd. for $C_{27}H_{31}N_2O_4$ [M + H]$^+$: 447.2278; found 447.2300.

Data for 20 (Lower R_f Epimer): Yellow foam. $[\alpha]_D^{22}$ = +4.6 (c = 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, J = 7.3 Hz, 3 H, CH_3 ethyl), 1.48–1.52 (m, 1 H, CH_2 ethyl), 1.83–1.95 (m, 3 H, CH_2 ethyl, 6-H, 8-H), 2.05 (s, 3 H, CH_3CO), 2.05–2.11 (m, 1 H, 7-H), 2.31–2.38 (m, 1 H, 6-H), 2.35 (d, J = 17.6, 5.6 Hz, 1 H, CH_2CHO), 2.59 (d, J = 17.6 Hz, 1 H, CH_2CHO), 3.40 (dd, J = 8.8, 1.2 Hz, 1 H, 2-H), 4.13 (dd, J = 9.2, 8.8 Hz, 1 H, 2-H), 4.65 (d, J = 9.2 Hz, 1 H, 8a-H), 4.92 (d, J = 6.8 Hz, 1 H, 3-H), 5.96 (dd, J = 9.2, 6.0 Hz, 1 H, CH_2C*H*O), 6.52 (d, J = 2.0 Hz, 1 H, 3-H ind), 7.11 (td, J = 7.6, 0.8 Hz, 1 H, ind-H), 7.17–7.32 (m, 7 H, ArH, ind-H), 7.59 (d, J = 8.4 Hz, 1 H, ind-H), 8.98 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.4 (CH_3 ethyl), 20.9 (CH_2 ethyl), 21.2 (OCH_3), 30.2 (C-7), 31.8 (C-6), 37.5 (*C*H_2CHO), 44.2 (C-8), 59.4 (C-3), 69.2 (CH_2*C*HO), 73.9 (C-2), 90.1 (C-8a), 101.0 (C-3 ind), 111.4 (C-4 ind), 120.0 (C-5 ind), 120.8 (C-4 ind), 122.6 (C-6 ind), 126.3 (C-*o*), 127.5, 127.6 (C-*p*, C-2 ind), 128.6 (C-*m*), 135.8 (C-3a ind), 135.9 (C-3a ind), 141.4 (C-*i*), 166.7 (NCO), 171.0 (COO) ppm. IR (KBr): $\tilde{\nu}$ = 1645, 1732, 3261 cm^{-1}. HRMS: calcd. for $C_{27}H_{30}N_2NaO_4$ [M + Na]$^+$: 469.2098; found 469.2113.

(3*R*,7*S*,8*S*,8a*R*)-8-Ethyl-7-[(2-indolyl)ethyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (21): A solution of the acetates **20** (150 mg, 0.34 mmol) in EtOAc (20 mL) containing $Pd(OH)_2$ (20%, 30 mg) was hydrogenated at room temp. (400 psi pressure) for 2 d. The catalyst was removed by filtration, and the solvent was evaporated to give a foam. Flash chromatography (hexane/EtOAc 9:1 to 1:1) afforded **21** (71 mg, 54%).

Data for 21: Yellow foam. $[\alpha]_D^{22}$ = –42.5 (c = 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.98 (t, J = 7.6 Hz, 3 H, CH_3 ethyl), 1.45–1.56 (m, 2 H, CH_2 ethyl, indCH_2CH_2), 1.82–1.93 (m, 2 H, CH_2 ethyl, indCH_2CH_2), 1.95–2.02 (m, 1 H, 8-H), 2.09–2.14 (m, 1 H, 7-H), 2.40 (dd, J = 18.0, 5.2 Hz, 1 H, indCH_2), 2.52 (dd, J = 18.0, 2.0 Hz, 1 H, indCH_2), 2.66 (ddd, J = 14.8, 10.0, 7.2 Hz, 1 H, 6-H), 2.95 (ddd, J = 14.8, 10.0, 4.8 Hz, 1 H, 6-H), 3.99 (dd, J = 9.2, 1.2 Hz, 1 H, 2-H), 4.11 (dd, J = 9.2, 7.2 Hz, 1 H, 2-H), 4.61 (d, J = 9.6 Hz, 1 H, 1 H, 8a-H), 4.89 (d, J = 6.0 Hz, 1 H, 3-H), 6.24 (d, J = 1.2 Hz, 1 H, 3-H ind), 7.05–7.53 (m, 9 H, ArH, ind-H), 8.07 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 11.3 (CH_3 ethyl), 20.9 (CH_2 ethyl), 26.5 (C-6), 27.5 (indCH_2*C*H_2), 32.4 (C-7), 36.8 (ind*C*H_2), 44.1 (C-8), 59.3 (C-3), 73.8 (C-2), 90.3 (C-8a), 99.9 (C-3 ind), 110.4 (C-7 ind), 119.7 (C-5 ind), 119.8 (C-4 ind), 121.2 (C-6 ind), 126.3 (C-*o*), 127.5 (C-*p*), 128.6 (C-*m*), 128.7 (C-2 ind), 135.9 (C-3a ind), 138.3 (C-7a ind), 141.5 (C-*i*), 171.5 (NCO) ppm. IR (KBr): $\tilde{\nu}$ = 1642 cm^{-1}. HRMS: calcd. for $C_{25}H_{29}N_2O_2$ [M + H]$^+$: 389.2224; found 389.2224.

(1*R*,5*S*,13*S*)-13-Ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-3-oxo-2,3,4,5,6,7-hexahydro-3*H*-1,5-methanoazocine[4,3-*b*]indole (22): $TiCl_4$ (1 mL of a 1.0 M solution in CH_2Cl_2, 1.0 mmol) was added at room temp. to a solution of **21** (38 mg, 0.10 mmol) in CH_2Cl_2 (2 mL), and the resulting mixture was heated at reflux for 24 h. $TiCl_4$ (1 mL of a 1.0 M solution in CH_2Cl_2, 1.0 mmol) was then once again added after a further 24 h, and the mixture was maintained at reflux for an additional 48 h. The mixture was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the resulting residue was chromatographed with a cartridge containing amine functionalized silica (hexane/EtOAc 1:1 to EtOAc/MeOH 1:1) to give **22** (22 mg, 58%).

Data for 22: Yellow foam. $[\alpha]_D^{22}$ = –88.2 (c = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 0.72 (t, J = 7.5 Hz, 3 H, CH_3 ethyl), 1.11 (td, J = 7.5, 7.5, 2.0 Hz, 2 H, CH_2 ethyl), 1.73 (ddd, J = 14.0, 7.0, 5.0 Hz, 1 H, 6-H), 1.95 (dt, J = 14.0, 2.5 Hz, 1 H, 6-H), 2.05–2.10 (m, 1 H, 13-H), 2.42–2.50 (m, 1 H, 5-H), 2.55 (ddd, J = 16.0, 5.0, 3.0 Hz, 1 H, 7-H), 2.75 (d, J = 18.5 Hz, 1 H, 4-H), 3.00 (dd, J = 18.5, 8.5 Hz, 1 H, 4-H), 3.12 (m, 1 H, 7-H), 3.54 (m, 1 H, $C_6H_5CHCH_2$), 3.80–3.83 (m, 1 H, $C_6H_5CHCH_2$), 4.51 (d, J = 5.0 Hz, 1 H, 1-H), 5.74 (m, 1 H, $C_6H_5CHCH_2$), 6.98–7.31 (m, 9 H, ArH, ind-H), 8.03 (br. s, 1 H, NH) ppm. ^{13}C NMR (125.9 MHz, $CDCl_3$, 25 °C): δ = 11.7 (CH_3 ethyl), 23.0 (CH_2 ethyl), 23.4 (C-6), 26.9 (C-7), 33.8 (C-5), 38.4 (C-4), 41.7 (C-13), 53.0 (C-1), 60.5 ($C_6H_5CHCH_2$), 63.2 ($C_6H_5CHCH_2$), 110.6 (C-12b), 110.8 (C-9), 117.4 (C-12), 119.6 (C-11), 121.0 (C-10), 127.6 (C-*m*), 128.1 (C-*o*), 128.2 (C-7a), 128.3 (C-*p*), 133.9 (C-12a), 136.9 (C-8a), 138.5 (C-*i*), 172.1 (NCO) ppm. IR (KBr): $\tilde{\nu}$ = 1608, 2926 cm^{-1}. HRMS: calcd. for $C_{25}H_{29}N_2O_2$ [M + H]$^+$: 389.2224; found 389.2222.

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[13] For the relative configuration at the epimerizable C-6 stereocenter, see the Exp. Section. The relative configuration at C-6 was deduced from the 6-H/7-H coupling constant of 6-H in the NMR spectra.

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[16] Data for **13**: Yellow foam. $[\alpha]_D^{22}$ = –14.4 (*c* = 0.35, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.95 (t, *J* = 7.6 Hz, 3 H, CH_3 ethyl), 1.94–1.99 (m, 2 H, CH_2 ethyl), 2.62 (dd, *J* = 16.0, 2.2 Hz, 1 H, CH_2CO), 2.76 (dd, *J* = 16.0, 6.0 Hz, 1 H, CH_2CO), 2.76–2.82 (m, 2 H, 3-H), 2.89–2.95 (m, 1 H, 4-H), 4.11–4.17 (m, 2 H, 2′-H), 5.85 (t, *J* = 7.2 Hz, 1 H, 1′-H), 5.94 (s, 1 H, 6-H), 6.75 (d, *J* = 1.6 Hz, 1 H, 3-H ind), 7.25–7.42 (m, 8 H, ArH, H ind), 7.58 (d, *J* = 8.4 Hz, 1 H, 4-H ind), 9.53 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 12.6 (CH_3 ethyl), 25.5 (CH_2 ethyl), 31.2 (C-4), 37.3 (CH_2CO), 39.5 (C-3), 57.9 (C-1′), 62.1 (C-2′), 110.0 (C-3 ind), 112.2 (C-7 ind), 120.5 (C-6), 120.8 (C-4 ind), 123.0 (C-5 ind), 125.9 (C-5), 126.4 (C-6 ind), 127.3 (C-3a ind), 127.6 (C-*o*), 127.9 (C-*p*), 128.8 (C-*m*), 135.2 (C-*i*), 137.6 (C-2 ind), 137.7 (C-7a ind), 169.5 (NCO), 191.2 (CO) ppm. IR (KBr): $\tilde{\nu}$ = 1635 cm^{-1}. HRMS: calcd. for $C_{25}H_{27}N_2O_3$ $[M + H]^+$: 403.2016; found 403.2016.

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