An Asymmetric Organocatalytic Quadruple Cascade to Tetraaryl-Substituted 2-Azabicyclo[3.3.0]octadienones

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Abstract: A new asymmetric organocatalytic three-component quadruple cascade of α-ketoamides with α,β-unsaturated aldehydes is described. The reaction is catalyzed by the (*S*)-diphenylprolinol TMS ether catalyst and proceeds via an aza-Michael/aldol condensation/vinylogous Michael/aldol condensation sequence to yield tetraaryl-substituted 2-azabicyclo[3.3.0]octadienone derivatives. The cascade products are obtained with good to very good yields (34–71%), virtually complete diastereoselectivities (>20:1), and very good enantioselectivities (84–97%).

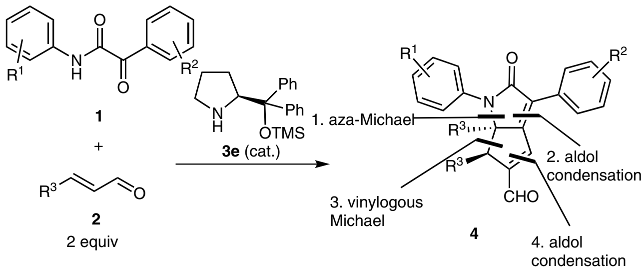
Key words: organocatalysis, domino reactions, quadruple cascade, aza-Michael addition, vinylogous Michael addition

The already huge research area of catalytic asymmetric synthesis has grown faster than ever before in the last twelve years, particularly fueled by the appearance of the new field of organocatalysis.[1] In recent years, and as part of this exciting development, organocatalytic domino reactions have come into focus for many research groups with the aim of designing efficient and highly stereoselective one-pot syntheses of functionalized more complex molecules.[2] Secondary amines like proline and its derivatives have proved their catalytic efficiency in a large number of transformations due to their possible iminium and enamine activation modes suitable for both donor or acceptor molecules.[3] To date secondary amine catalyzed asymmetric simple,[4] triple,[5] and quadruple[6] domino reactions have been developed.

Since 2005 the asymmetric organocatalytic direct vinylogous Michael addition has been studied extensively, especially using dicyanoolefins or γ-butenolides as donors.[7] It has also been demonstrated several times that γ-butyrolactams are suitable nucleophiles for the asymmetric vinylogous Michael addition.[8] In 2010, Chen et al. published a direct vinylogous addition of N-substituted γ-butyrolactams to α,β-unsaturated aldehydes with excellent yields and diastereo- and enantioselectivities employing a secondary amine catalyst.[8c]

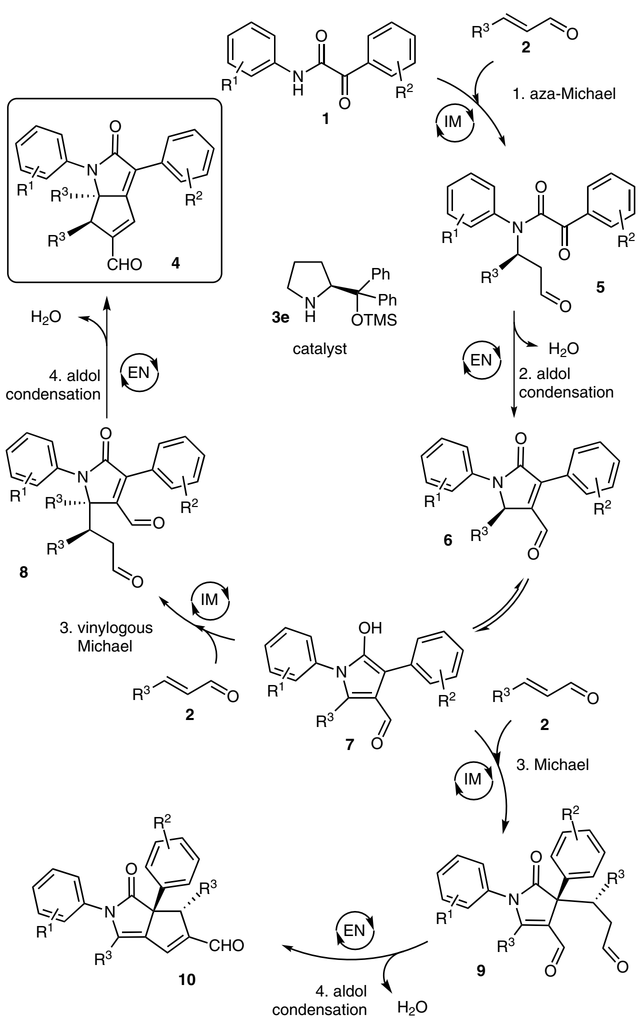
The asymmetric organocatalytic aza-Michael addition represents one possible strategy for the synthesis of chiral nitrogen-containing compounds.[9] Substrates bearing both a nucleophilic nitrogen atom and an electrophilic center were designed in order to achieve the synthesis of heterocycles via domino reactions. For example, we have recently found out that both the nucleophilicity and electrophilicity of α-ketoamides could successfully be exploited in the asymmetric synthesis of densely substituted pyrrolidin-2-ones by an aza-Michael/aldol domino reaction with α,β-unsaturated aldehydes.[10]

Herein we report the development of a new three-component quadruple domino reaction of α-ketoamides **1** with two equivalents of α,β-unsaturated aldehydes **2** yielding tetraaryl-substituted 2-azabicyclo[3.3.0]octadienones **4** with high diastereo- and enantioselectivities and proceeding via an aza-Michael addition/aldol condensation/vinylogous Michael addition/aldol condensation reaction sequence (Scheme 1).



Scheme 1 Asymmetric synthesis of tetraaryl-substituted 2-azabicyclo[3.3.0]octadienones via an organocatalytic quadruple cascade

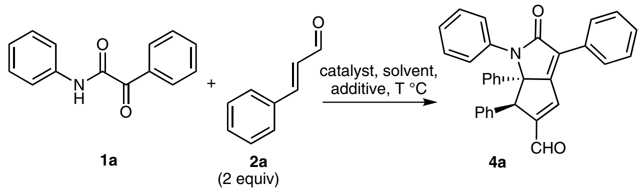
The quadruple cascade is initiated by the asymmetric aza-Michael addition of α-ketoamides **1** to different iminium-activated α,β-unsaturated aldehydes **2** leading to enamines of intermediates **5** that undergo intramolecular aldol condensation to form lactams **6**. Under the reaction conditions these pyrrolones **6** may easily tautomerize to aromatic 2-hydroxypyrroles **7**, the 5-position of which can react as a nucleophile with a second α,β-unsaturated aldehyde via iminium activation. Vinylogous 1,4-addition leads to enamines of intermediates **8** that undergo a second intramolecular aldol condensation yielding bicyclic products **4** after hydrolytic return of the catalyst. In addition, 2-hydroxypyrroles **7** can also act as nucleophiles at the 3-position with a second iminium-activated α,β-unsaturated aldehyde providing enamines of intermediates **9** that undergo an intramolecular aldol condensation to yield tetraaryl-substituted bicyclic compounds **10** after return of the catalyst. Yet the second catalytic pathway remains minor and derivatives **10** are generally obtained as minor side products of the reaction. Only traces were observed under the optimum reaction conditions, which were separated from the products **4** in the purification process (Scheme 2).

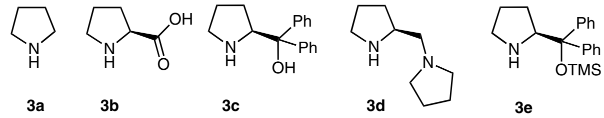


Scheme 2 Proposed mechanism for the quadruple cascade. For simplicity only the catalyst-free species are shown. IM = iminium activation, EN = enamine activation.

We initially studied the reaction between the 2-oxo-*N*,2-diphenylacetamide (**1a**) and cinnamaldehyde (**2a**) at room temperature for three days in the presence of 20 mol% of various secondary amine catalysts **3** using dichloromethane as the solvent. The (*S*)-diphenylprolinol TMS ether **3e** gave satisfactory results, while all the other tested catalysts were inefficient for the desired transformation (Table 1, entries 1–4). After increasing the reaction time to five days at room temperature in dichloromethane, propan-2-ol, or ethanol (entries 6–8), the reaction was also carried out under reflux for two days in ethanol or propan-2-ol with the result that the enantioselectivity of the reaction dropped dramatically (entries 9 and 10). The use of basic additives was also examined; performing the reaction in the presence of 20 mol% potassium or sodium carbonate did not lead to any significant improvement, the use of sodium acetate enhanced both the yield and enantioselectivity (entries 11–13). The reaction was also conducted with excess 2-oxo-*N*,2-diphenylacetamide (**1a**) as well as with excess cinnamaldehyde (**2a**) (entries 14 and 15), however without any increase in the yield. Lower catalyst loading led to a significant decrease in the yields while higher amounts did not give any remarkable improvement. Finally, we performed the cascade for three days in dichloromethane in the presence of 20 mol% of sodium acetate and obtained a remarkable decrease in the yield of the isolated product (entry 16), indicating that a reaction time of five days was, indeed, required.

Table 1 Optimization of the Reaction Conditions





3a 3b 3c 3d 3e

Entry[a]	Catalyst	Solvent	Time (d)	Additive[b]	Yield[c] (%)	ee[d] (%)
1	**3a**	CH_2Cl_2	3	–	18	n.d.
2	**3b**	CH_2Cl_2	3	–	–	n.d.
3	**3c**	CH_2Cl_2	3	–	–	n.d.
4	**3d**	CH_2Cl_2	3	–	6	n.d.
5	**3e**	CH_2Cl_2	3	–	47	97
6	**3e**	CH_2Cl_2	5	–	55	87
7	**3e**	EtOH	5	–	21	69
8	**3e**	*i*-PrOH	5	–	49	73
9	**3e**	EtOH[e]	2	–	38	32
10	**3e**	*i*-PrOH[e]	2	–	32	47
11	**3e**	CH_2Cl_2	5	NaOAc	63	97
12	**3e**	CH_2Cl_2	5	K_2CO_3	39	53
13	**3e**	CH_2Cl_2	5	Na_2CO_3	27	58
14[f]	**3e**	CH_2Cl_2	6	NaOAc	45	94
15[g]	**3e**	CH_2Cl_2	6	NaOAc	60	94
16	**3e**	CH_2Cl_2	3	NaOAc	47	93

[a] Reaction conditions: 0.3-mmol scale using **1a** (1 equiv), **2a** (2 equiv), catalyst **3a–e** (20 mol%), solvent (1 mL), r.t. Only one diastereomer was observed.
[b] 20 mol% of the additive was used.
[c] Yield of the isolated product **4a** after flash column chromatography.
[d] Determined by HPLC on a chiral stationary phase; n.d. = not detected.
[e] The reaction was heated to reflux for 2 d.
[f] A ratio 1.6:2 of **1a**/**2a** was used.
[g] A ratio 1:2.5 of **1a**/**2a** was used.

Having optimized the reaction conditions, we evaluated the scope of the quadruple cascade. Firstly, different aromatic α,β-unsaturated aldehydes were examined in the reaction and the products **4a**–**d** were obtained as single diastereomers in moderate to good yields while the enantioselectivity of the reaction remained very good (Table 2). However, neither heteroaromatic nor aliphatic α,β-unsaturated aldehydes led to satisfactory results. Next we studied extension of the scope regarding both aromatic rings (R^1, R^2) of the α-ketoamide substrate and performed the cascade reactions using the optimum conditions and the products **4e**–**i** were obtained as single diastereomers with very good yields and enantioselectivities. Other α-ketoamide derivatives bearing non-aromatic residues were also used as substrates in the reaction, but these did not react in the desired fashion.

Interestingly, α,β-unsaturated aldehydes bearing strong electron-donor groups such as 2-methoxyphenyl or 3,4,5-tris(benzyloxy)phenyl group as well as 3-[1-(*tert*-butoxycarbonyl)-1*H*-indol-2-yl]acrylaldehyde reacted in the quadruple cascade, although only by the second postulated catalytic pathway leading to the isomeric 3-azabicyclo[3.3.0]octadienones **10a**–**c** as single diastereomers in medium to good yields, but lower enantioselectivities as compared to the main catalytic pathway (Figure 1).

The relative and absolute configuration of the products **4** given is based on an X-ray crystal structure analysis of **4a** and the proposed transition state (Figure 2). As intermediates **7** are planar, there is a facial selectivity in the vinylogous Michael addition step of the cascade. The second iminium-activated α,β-unsaturated aldehyde is attacked on its *Re* face by the dienolate generating two new stereocenters and placing the two R^3 rings in a *trans* orientation (Figure 2). A different face selectivity concerning the hy-

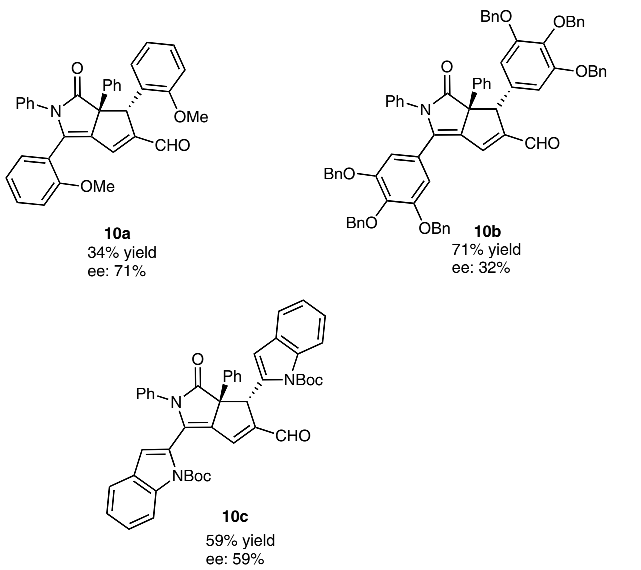
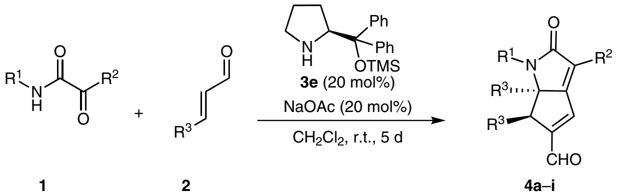


Figure 1 Quadruple cascade products obtained following the minor catalytic pathway

Table 2 Reaction of α-Ketoamides **1** with α,β-Unsaturated Aldehydes **2**



Product[a]	R^1	R^2	R^3	Yield[b] (%)	ee[c,d] (%)
4a	Ph	Ph	Ph	63	97
4b	Ph	Ph	4-$MeOC_6H_4$	51	89 (91)
4c	Ph	Ph	4-ClC_6H_4	34	85 (95)
4d	Ph	Ph	2,3-$(OCH_2O)C_6H_3$	56	84 (87)
4e	4-$MeOC_6H_4$	Ph	Ph	66	92 (91)
4f	3-ClC_6H_4	Ph	Ph	69	91 (95)
4g	4-$O_2NC_6H_4$	Ph	Ph	58	95
4h	Ph	2-MeC_6H_4	Ph	70	88
4i	Ph	4-ClC_6H_4	Ph	71	95

[a] Reaction conditions: 0.3-mmol scale using α-ketoamide **1** (1 equiv), α,β-unsaturated aldehyde **2** (2 equiv), NaOAc (20 mol%), **3e** (20 mol%), CH_2Cl_2 (1 mL), r.t. All the products were obtained as a single diastereomer.
[b] Yield of isolated **4a**–**i**.
[c] Determined by HPLC on a chiral stationary phase.
[d] Values in brackets correspond to the results obtained with the catalyst (*R*)-**3e**. For HPLC determination of the enantiomeric excess, the products **4b**–**i** were transformed into the corresponding α,β-unsaturated ethyl ester.

droxypyrrole nucleophile **7** is proposed for the Michael addition step with enals bearing electron-donor groups to form the isomeric *trans* products **10a**–**c**. This is in accordance with the X-ray structure of *ent*-**10a** obtained with catalyst (*R*)-**3e** (Figure 3).

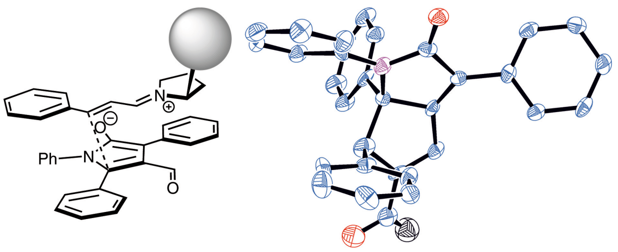


Figure 2 Proposed transition state for the vinylogous Michael addition and X-ray crystal structure of **4a**[11]

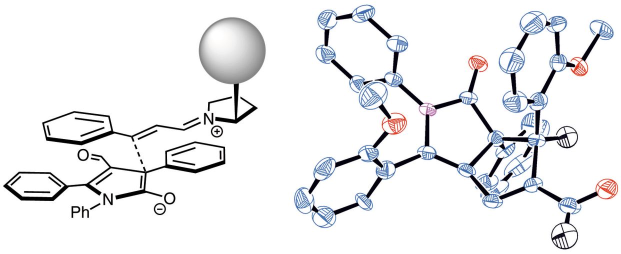


Figure 3 Proposed transition state for the Michael addition and X-ray crystal structure of *ent*-**10a**[11]

In conclusion, we have developed a new asymmetric organocatalytic quadruple cascade of various α-ketoamides with aromatic α,β-unsaturated aldehydes yielding tetraaryl-substituted 2-azabicyclo[3.3.0]octadienones in good yields, excellent diastereo- and enantioselectivities via an aza-Michael/aldol condensation/vinylogous Michael addition/aldol condensation reaction sequence. In the case of electron-rich enals isomeric 3-azabicyclo[3.3.0]octadienones are formed.

Unless otherwise noted, all commercially available compounds were used without further purification. Preparative column chromatography SIL G-25 UV252 from Macherey & Nagel, particle size 0.040–0.063 nm (230–240 mesh, flash). Visualization of the developed TLC plates was performed with UV irradiation (254 nm) and by staining with vanillin stain. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on a Finnigan SSQ7000 (EI 70 eV) spectrometer and HRMS on a Thermo Fisher Scientific Orbitrap XL spectrometer. IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum 100 using ATR-Unit. ^{1}H and ^{13}C spectra were recorded at r.t. on Varian Mercury 600 or Inova 400 instruments with TMS as an internal standard. Analytical HPLC was performed on a Hewlett-Packard 1100 Series instrument using chiral stationary phases (Daicel AD, Daicel AS, Daicel IA, Daicel OD, Diacel OJ, or Chiralpak IC). Due to their relative instability under HPLC conditions, compounds **4b**–**i** and **10j**–**l** were transformed to the corresponding α,β-unsaturated ethyl esters before determination of the enantiomeric excess. The cascade products were stirred in the presence of Wittig reagent $Ph_3P{=}CH_2CO_2Et$ (1.5 equiv) at r.t. in CH_2Cl_2 for 1 h yielding the desired α,β-unsaturated ethyl ester with 100% conversion. The α-ketoamides **1a**,**e**,**h** were prepared as described previously.[10]

Domino Reaction; General Procedure

A solution of α-ketoamide **1** (0.3 mmol, 1 equiv), α,β-unsaturated aldehyde **2** (0.6 mmol, 2 equiv), NaOAc (5 mg, 0.06 mmol, 0.2 equiv), and (*S*)-TMS-diphenylprolinol catalyst **3e** (21 mg, 0.06 mmol, 0.2 equiv) in CH_2Cl_2 (1.5 mL) was stirred at r.t. for 5 d. The crude mixture was directly purified by flash column chromatography (silica gel, *n*-pentane–Et_2O, 2:1).

***N*-(3-Chlorophenyl)-2-oxo-2-phenylacetamide (1f)**

Following the previously described general procedure[10] using 3-chloroaniline (446 mg, 3.5 mmol, 1.4 equiv) and phenylglyoxylic acid (375 mg, 2.5 mmol, 1 equiv). The crude product was purified by flash column chromatography (*n*-pentane–Et_2O, 6:1) to afford **1f** (621 mg, 96%) as a yellow solid; mp 110–112 °C; R_f = 0.35 (*n*-pentane–Et_2O, 6:1).

IR (ATR): 3345, 1657, 1585, 1536, 1482, 1409, 1275, 1170, 1092, 997, 862, 775, 736, 671 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 8.4 Hz, 1 H, CH_{Ar}), 7.32 (t, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.52 (m, 3 H, CH_{Ar}), 7.67 (t, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.86 (t, *J* = 1.8 Hz, 1 H, CH_{Ar}), 8.41 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 8.98 (br s, 1 H, NH).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 117.9 (CH_{Ar}), 120.0 (CH_{Ar}), 125.3 (CH_{Ar}), 128.6 (2 C, CH_{Ar}), 130.2 (CH_{Ar}), 131.5 (2 C, CH_{Ar}), 132.8 (C), 134.8 (CH_{Ar}), 134.9 (C), 137.7 (C), 158.8 (NCO), 186.8 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 261 (11), 259 (33, M^+), 105 (100), 77 (39), 51 (16).

Anal. Calcd for $C_{14}H_{10}NO_2Cl$: C, 64.75; H, 3.88; N, 5.39. Found: C, 64.68; H, 3.61; N, 5.41.

***N*-(4-Nitrophenyl)-2-oxo-2-phenylacetamide (1g)**

Following the previously described general procedure[10] using 4-nitroaniline (1.5 g, 10.8 mmol, 1.4 equiv) and phenylglyoxylic acid (1.16 g, 7.75 mmol, 1 equiv). The crude product was purified by recrystallization (Et_2O) to afford **1g** (1.067 g, 51%) as a yellow solid; mp 215 °C; R_f = 0.5 (*n*-pentane–Et_2O, 1:1).

IR (ATR): 3327, 1701, 1650, 1593, 1499, 1409, 1330, 1273, 1153, 1103, 985, 852, 785, 741, 680 cm^{-1}.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 7.61 (t, *J* = 7.8 Hz, 2 H, CH_{Ar}), 7.76 (t, *J* = 7.2 Hz, 1 H, CH_{Ar}), 7.99 (d, *J* = 9.0 Hz, 2 H, CH_{Ar}), 8.06 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 8.28 (d, *J* = 9.0 Hz, 2 H, CH_{Ar}), 11.52 (s, 1 H, NH).

^{13}C NMR (151 MHz, DMSO-d_6): δ =120.5 (2 C, CH_{Ar}), 125.4 (2 C, CH_{Ar}), 129.5 (2 C, CH_{Ar}), 130.5 (2 C, CH_{Ar}), 132.7 (C), 133.5 (CH_{Ar}), 143.7 (C), 144.2 (C), 164.0 (NCO), 189.0 (CO).

MS (EI, 70 eV): *m*/*z* (%) = 270 (20, M^+), 105 (100), 77 (34), 51 (11).

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{10}N_2O_4Na$: 293.0533; found: 293.0533.

2-(4-Chlorophenyl)-2-oxo-*N*-phenylacetamide (1i)

Following the previously described general procedure[10] using aniline (0.7 mL, 7.6 mmol, 1.4 equiv) and 4-chlorophenylglyoxylic acid (1.0 g, 5.4 mmol, 1 equiv). The crude product was purified by flash column chromatography (*n*-pentane–Et_2O, 8:1) to afford **1i** (1.11 g, 79%) as a yellow solid, mp 118–120 °C; R_f = 0.46 (*n*-pentane–Et_2O, 8:1).

IR (ATR): 3334, 3058, 1934, 1653, 1586, 1527, 1441, 1399, 1274, 1162, 1090, 988, 875, 790, 740, 693 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.20 (t, *J* = 7.2 Hz, 1 H, CH_{Ar}), 7.39 (t, *J* = 7.8 Hz, 2 H, CH_{Ar}), 7.47 (d, *J* = 9.0 Hz, 2 H, CH_{Ar}), 7.67 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 8.40 (d, *J* = 8.4 Hz, 2 H, CH_{Ar}), 8.95 (br s, 1 H, NH).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 119.9 (2 C, CH_{Ar}), 125.4 (CH_{Ar}), 128.9 (2 C, CH_{Ar}), 129.2 (2 C, CH_{Ar}), 131.4 (C), 132.9 (2 C, CH_{Ar}), 136.4 (C), 141.5 (C), 158.5 (NCO), 186.0 (CO).

MS (EI, 70 eV): *m/z* (%) = 261 (21), 260 (16), 259 (59, M^+), 141 (32), 139 (100), 111 (13).

Anal. Calcd for $C_{14}H_{10}NO_2Cl$: C, 64.75; H, 3.88; N, 5.39; Found: C, 64.63; H, 3.91; N, 5.39.

(6*R*,6a*S*)-2-Oxo-1,3,6,6a-tetraphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4a)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4a** as a yellow solid: yield: 85 mg (63%); mp 115 °C; 97% ee [HPLC (Daicel AS)]; R_f = 0.26 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –63.5 (*c* 0.45, $CHCl_3$).

IR (ATR): 3054, 2951, 2882, 2325, 2105, 1674, 1597, 1492, 1448, 1313, 1178, 1084, 1019, 902, 744, 690 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.12 (s, 1 H, CHPh), 6.84 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 6.93–6.97 (m, 3 H, CH_{Ar}), 7.02–7.05 (m, 4 H, CH_{Ar}), 7.10 (t, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.34–7.39 (m, 5 H, CH_{Ar}), 7.46–7.52 (m, 3 H, CH_{Ar}), 7.66 (s, 1 H, C=CH), 7.98 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 9.91 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 52.9 (CHPh), 79.4 (NCPh), 121.8 (2 C, CH_{Ar}), 124.9 (CH_{Ar}), 125.6 (2 C, CH_{Ar}), 128.0 (2 C, CH_{Ar}), 128.3 (2 C, CH_{Ar}), 128.4 (2 C, CH_{Ar}), 128.5 (2 C, CH_{Ar}), 128.6 (2 C, CH_{Ar}), 129.1 (2 C, CH_{Ar}), 129.3 (2 C, CH_{Ar}), 129.8 (CH_{Ar}), 131.1 (C), 132.3 (C), 134.4 (C), 137.5 (C), 137.9 (C=*C*H), 139.5 (C), 156.5 (C), 161.4 (C), 170.9 (NCO), 187.8 (CHO).

MS (EI, 70 eV): *m/z* (%) = 454 (36), 453 (100), 425 (25), 424 (30), 396 (19), 334 (11), 215 (13), 180 (16), 78 (13), 77 (27).

Anal. Calcd for $C_{32}H_{23}NO_2$: C, 84.74; H, 5.11; N, 3.09. Found: C, 84.52; H, 5.08; N, 2.89.

(6*R*,6a*S*)-6,6a-Bis(4-methoxyphenyl)-2-oxo-1,3-diphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4b)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4b** as a yellow solid; yield: 79 mg (51%); mp 98–100 °C; 89% ee [HPLC (Daicel AS)]; R_f = 0.16 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –120.6 (*c* 0.52, $CHCl_3$).

IR (ATR): 2934, 2836, 1674, 1603, 1502, 1453, 1308, 1250, 1176, 1027, 833, 788, 749, 690 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 5.03 (s, 1 H, CHPh), 6.55 (d, *J* = 8.4 Hz, 2 H, CH_{Ar}), 6.75 (d, *J* = 8.4 Hz, 2 H, CH_{Ar}), 6.82 (d, *J* = 8.8 Hz, 2 H, CH_{Ar}), 6.93–7.07 (m, 5 H, CH_{Ar}), 7.26 (d, *J* = 9.2 Hz, 2 H, CH_{Ar}), 7.44–7.49 (m, 3 H, CH_{Ar}), 7.61 (s, 1 H, C*H*=CCHO), 7.96 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 9.86 (s, 1 H, CHO).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 52.1 (CHPh), 55.1 (OCH_3), 55.3 (OCH_3), 78.9 (NCPh), 113.7 (2 C, CH_{Ar}), 114.4 (2 C, CH_{Ar}), 121.7 (2 C, CH_{Ar}), 124.7 (CH_{Ar}), 126.4 (C), 126.7 (2 C, CH_{Ar}), 128.2 (2 C, CH_{Ar}), 128.4 (2 C, CH_{Ar}), 128.9 (2 C, CH_{Ar}), 129.1 (2 C, CH_{Ar}), 129.5 (CH_{Ar}), 130.9 (C), 131.0 (C), 131.8 (C), 137.5 (*C*H=CCHO), 137.5 (C), 156.7 (C), 159.0 (C), 159.5 (C), 161.4 (C), 170.8 (NCO), 187.8 (CHO).

MS (EI, 70 eV): *m/z* (%) = 514 (35), 513 (100, M^+), 486 (13), 485 (39), 484 (34), 456 (14), 405 (13), 366 (13), 364 (12), 351 (12), 210 (20), 202 (11), 77 (21).

HRMS: *m/z* $[M + H]^+$ calcd for $C_{34}H_{28}NO_4$: 514.2013; found: 514.2012.

(6*R*,6a*S*)-6,6a-Bis(4-chlorophenyl)-2-oxo-1,3-diphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4c)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4c** as a yellow solid; yield: 54 mg (34%); mp 110–112 °C; 85% ee [HPLC (Daicel AS)]; R_f = 0.33 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –122.8 (*c* 0.25, $CHCl_3$).

IR (ATR): 1676, 1596, 1491, 1314, 1181, 1094, 1011, 833, 783, 748, 692 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.03 (s, 1 H, CHPh), 6.74 (d, *J* = 8.4 Hz, 2 H, CH_{Ar}), 6.98–7.01 (m, 4 H, CH_{Ar}), 7.06–7.10 (m, 2 H, CH_{Ar}), 7.25–7.32 (m, 5 H, CH_{Ar}), 7.47–7.54 (m, 3 H, CH_{Ar}), 7.65 (s, 1 H, C*H*=CCHO), 7.94 (dd, *J* = 8.0, 1.6 Hz, 2 H, CH_{Ar}), 9.89 (s, 1 H, CHO).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 52.0 (CHPh), 78.6 (NCPh), 121.1 (2 C, CH_{Ar}), 124.9 (CH_{Ar}), 126.7 (2 C, CH_{Ar}), 128.5 (6 C, CH_{Ar}), 129.0 (2 C, CH_{Ar}), 129.3 (2 C, CH_{Ar}), 129.5 (2 C, CH_{Ar}), 129.9 (CH_{Ar}), 130.6 (C), 132.5 (C), 132.6 (C), 133.9 (C), 134.7 (C), 137.1 (C), 137.8 (C), 137.9 (*C*H=CCHO), 155.8 (C), 160.4 (C), 170.4 (NCO), 187.4 (CHO).

MS (EI, 70 eV): *m/z* (%) = 524 (17), 523 (73), 522 (34), 521 (100, M^+), 494 (17), 493 (17), 492 (24), 216 (18), 215 (48), 214 (46), 213 (26), 77 (83).

HRMS: *m/z* $[M + H]^+$ calcd for $C_{32}H_{22}NO_2Cl_2$: 522.1022; found: 522.1021.

(6*R*,6a*S*)-6,6a-Bis(1,3-benzodioxol-5-yl)-2-oxo-1,3-diphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4d)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4d** as a yellow solid; yield: 91 mg (56%); mp 119–121 °C; 84% ee [HPLC (Daicel AS)]; R_f = 0.14 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –117.8 (*c* 0.5, $CHCl_3$).

IR (ATR): 2893, 1676, 1598, 1491, 1441, 1371, 1311, 1190, 1099, 1035, 928, 855, 812, 778, 748, 691 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.95 (s, 1 H, CHPh), 5.80 (dd, *J* = 11.2, 1.6 Hz, 2 H, OCH_2O), 5.92 (s, 2 H, OCH_2O), 6.26 (d, *J* = 1.6 Hz, 1 H, CH_{Ar}), 6.33 (dd, *J* = 8.0, 1.6 Hz, 1 H, CH_{Ar}), 6.46 (d, *J* = 8.0 Hz, 1 H, CH_{Ar}), 6.73 (d, *J* = 8.4 Hz, 1 H, CH_{Ar}), 6.78 (d, *J* = 2 Hz, 1 H, CH_{Ar}), 6.83 (dd, *J* = 8.4, 2 Hz, 1 H, CH_{Ar}), 6.98–7.12 (m, 5 H, CH_{Ar}), 7.44–7.51 (m, 3 H, CH_{Ar}), 7.61 (s, 1 H, C*H*=CCHO), 7.94 (d, *J* = 6.8 Hz, 2 H, CH_{Ar}), 9.86 (s, 1 H, CHO).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 52.6 (CHPh), 78.9 (NCPh), 101.0 (OCH_2O), 101.5 (OCH_2O), 106.1 (CH_{Ar}), 107.9 (CH_{Ar}), 108.0 (CH_{Ar}), 108.5 (CH_{Ar}), 119.1 (CH_{Ar}), 121.8 (2 C, CH_{Ar}), 122.1 (CH_{Ar}), 124.9 (CH_{Ar}), 127.8 (C), 128.3 (2 C, CH_{Ar}), 128.5 (2 C, CH_{Ar}), 128.9 (2 C, CH_{Ar}), 129.7 (CH_{Ar}), 130.8 (C), 132.1 (C), 133.0 (C), 137.4 (C), 137.7 (*C*H=CCHO), 147.2 (C), 147.6 (C), 147.8 (C), 148.5 (C), 156.3 (C), 161.1 (C), 170.6 (NCO), 187.6 (CHO).

MS (EI, 70 eV): *m/z* (%) = 542 (37), 541 (97, M^+), 513 (26), 512 (19), 395 (19), 394 (23), 383 (15), 365 (28), 355 (25), 354 (66), 268 (36), 255 (25), 253 (32), 235 (10), 231 (16), 230 (100), 228 (37), 225 (78), 224 (30), 182 (23), 161 (17), 105 (92), 77 (52).

HRMS: *m/z* $[M + H]^+$ calcd for $C_{34}H_{24}NO_6$: 542.1598; found: 542.1593.

(6*R*,6a*S*)-1-(4-Methoxyphenyl)-2-oxo-3,6,6a-triphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4e)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4e** as a yellow solid; yield: 64 mg (66%); mp 88–90 °C; 92% ee [HPLC (Daicel AS)]; R_f = 0.24 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –55.2 (*c* 0.5, $CHCl_3$).

IR (ATR): 3058, 2834, 1674, 1506, 1447, 1300, 1246, 1176, 1027, 873, 826, 786, 749, 693 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 3 H, OCH_3), 5.04 (s, 1 H, CHPh), 6.53–6.59 (m, 4 H, CH_{Ar}), 6.90 (d, *J* = 6.8 Hz, 2 H, CH_{Ar}), 7.08–7.52 (m, 11 H, CH_{Ar}), 7.68 (s, 1 H, C*H*=CCHO), 7.99 (d, *J* = 6.8 Hz, 2 H, CH_{Ar}), 9.84 (s, 1 H, CHO).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 52.8 (CHPh), 55.2 (OCH_3), 79.6 (NCPh), 113.5 (2 C, CH_{Ar}), 124.8 (2 C, CH_{Ar}), 125.9 (2 C, CH_{Ar}), 127.9 (CH_{Ar}), 128.2 (2 C, CH_{Ar}), 128.4 (2 C, CH_{Ar}), 128.5 (3 C, CH_{Ar}), 128.9 (2 C, CH_{Ar}), 129.0 (2 C, CH_{Ar}), 129.6 (CH_{Ar}), 130.1 (C), 131.1 (C), 132.5 (C), 134.9 (C), 137.9 (*C*H=CCHO), 139.6 (C), 156.4 (C), 157.0 (C), 160.7 (C), 170.8 (NCO), 187.6 (CHO).

MS (EI, 70 eV): m/z (%) = 484 (37), 483 (100, M^+), 455 (24), 454 (27), 426 (17), 369 (13), 340 (18), 306 (11), 215 (27), 210 (35), 189 (10), 167 (12), 92 (11), 77 (17).

HRMS: m/z [M + H]$^+$ calcd for $C_{33}H_{26}NO_3$: 484.1907; found: 484.1913.

(6*R*,6a*S*)-1-(3-Chlorophenyl)-2-oxo-3,6,6a-triphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4f)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4f** as a yellow solid; yield: 101 mg (69%); mp 98–100 °C; 91% ee [HPLC (Daicel AS)]; R_f = 0.42 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –72.9 (*c* 0.49, $CHCl_3$).

IR (ATR): 1676, 1590, 1482, 1444, 1324, 1179, 1082, 1036, 1008, 872, 834, 777, 692 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 5.13 (s, 1 H, CHPh), 6.80–6.84 (m, 3 H, CH_{Ar}), 6.92–6.96 (m, 2 H, CH_{Ar}), 7.05 (t, *J* = 7.8 Hz, 2 H, CH_{Ar}), 7.11–7.13 (m, 2 H, CH_{Ar}), 7.38 (m, 5 H, CH_{Ar}), 7.46–7.52 (m, 3 H, CH_{Ar}), 7.65 (s, 1 H, C*H*=CCHO), 7.94 (d, *J* = 6.6 Hz, 2 H, CH_{Ar}), 9.91 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 52.7 (CHPh), 79.1 (NCPh), 119.0 (CH_{Ar}), 121.6 (CH_{Ar}), 124.6 (CH_{Ar}), 125.3 (2 C, CH_{Ar}), 128.0 (2 C, CH_{Ar}), 128.1 (CH_{Ar}), 128.4 (2 C, CH_{Ar}), 128.5 (2 C, CH_{Ar}), 128.7 (CH_{Ar}), 129.0 (2 C, CH_{Ar}), 129.1 (CH_{Ar}), 129.4 (2 C, CH_{Ar}), 129.8 (C), 130.7 (C), 131.8 (C), 133.8 (C), 134.0 (*C*H=CCHO), 137.6 (C), 138.5 (C), 139.0 (C), 156.3 (C), 161.6 (C), 170.7 (NCO), 187.6 (CHO).

MS (EI, 70 eV): m/z (%) = 490 (12), 489 (35), 488 (35), 487 (100), 460 (15), 459 (20), 458 (24), 430 (14), 216 (11), 215 (21), 214 (19), 111 (11).

HRMS: m/z [M + H]$^+$ calcd for $C_{32}H_{23}NO_2Cl$: 488.1412; found: 488.1411.

(6*R*,6a*S*)-1-(4-Nitrophenyl)-2-oxo-3,6,6a-triphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4g)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4g** as a yellow solid; yield: 87 mg (58%); mp 132 °C; 95% ee [HPLC (Daicel AS)]; R_f = 0.31 (*n*-pentane–Et_2O, 1:1); $[\alpha]_D^{22}$ –134.4 (*c* 0.57, $CHCl_3$).

IR (ATR): 1678, 1593, 1501, 1447, 1310, 1169, 1113, 1004, 849, 800, 748, 692 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 5.18 (s, 1 H, CH), 6.80 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 7.00 (t, *J* = 7.8 Hz, 2 H, CH_{Ar}), 7.07 (t, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.34–7.40 (m, 7 H, CH_{Ar}), 7.48–7.53 (m, 3 H, CH_{Ar}), 7.65 (s, 1 H, C*H*=CCHO), 7.91–7.94 (m, 4 H, CH_{Ar}), 9.96 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 52.8 (CHPh), 78.9 (NCPh), 119.5 (2 C, CH_{Ar}), 124.1 (2 C, CH_{Ar}), 124.9 (2 C, CH_{Ar}), 127.9 (2 C, CH_{Ar}), 128.3 (CH_{Ar}), 128.4 (2 C, CH_{Ar}), 128.5 (2 C, CH_{Ar}), 129.0 (CH_{Ar}), 129.1 (2 C, CH_{Ar}), 129.7 (2 C, CH_{Ar}), 130.0 (CH_{Ar}), 130.3 (C), 131.3 (C), 133.2 (C), 137.3 (*C*H=CCHO), 138.2 (C), 143.1 (C), 143.1 (C), 156.3 (C), 162.4 (C), 171.0 (NCO), 187.4 (CHO).

MS (EI, 70 eV): m/z (%) = 499 (26), 498 (75, M^+), 470 (14), 469 (24), 441 (12), 355 (22), 255 (15), 225 (16), 215 (25), 207 (13), 205 (14), 179 (34), 116 (15), 115 (40), 105 (100), 77 (69).

HRMS: m/z [M + H]$^+$ calcd for $C_{32}H_{23}O_4N_2$: 499.1652; found: 499.1653.

(6*R*,6a*S*)-2-Oxo-1,6,6a-triphenyl-3-(2-tolyl)-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4h)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4h** as a yellow solid; yield: 98 mg (70%); mp 83–85 °C; 88% ee [HPLC (Daicel AS)]; R_f = 0.41 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –35.6 (*c* 0.5, $CHCl_3$).

IR (ATR): 2322, 2065, 1989, 1676, 1597, 1492, 1449, 1313, 1173, 1032, 880, 750, 691 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 2.45 (s, 3 H, CH_3), 5.10 (s, 1 H, CHPh), 6.83 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 6.92–6.96 (m, 3 H, CH_{Ar}), 7.02 (t, *J* = 8.4 Hz, 4 H, CH_{Ar}), 7.09 (t, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.27–7.41 (m, 7 H, CH_{Ar}), 7.66 (s, 1 H, CH_{Ar}), 7.74 (d, *J* = 7.8 Hz, 1 H, CH_{Ar}), 7.81 (s, 1 H, C=CH), 9.90 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 21.5 (CH_3), 52.7 (CHPh), 79.2 (NCPh), 121.6 (2 C, CH_{Ar}), 124.7 (CH_{Ar}), 125.4 (2 C, CH_{Ar}), 125.6 (CH_{Ar}), 126.0 (C), 127.8 (CH_{Ar}), 128.1 (2 C, CH_{Ar}), 128.2 (2 C, CH_{Ar}), 128.3 (2 C, CH_{Ar}), 128.8 (CH_{Ar}), 129.0 (CH_{Ar}), 129.2 (2 C, CH_{Ar}), 130.5 (CH_{Ar}), 130.9 (C), 132.3 (C), 134.3 (C), 137.4 (C), 137.9 (C=*C*H), 138.7 (C), 139.4 (C), 156.2 (C), 161.1 (C), 170.8 (NCO), 187.7 (CHO).

MS (EI, 70 eV): m/z (%) = 468 (40), 467 (100, M^+), 439 (20), 438 (30), 410 (15), 348 (11), 335 (11), 307 (11), 215 (11), 180 (23), 77 (28).

HRMS: m/z [M + H]$^+$ calcd for $C_{33}H_{26}NO_2$: 468.1958; found: 468.1954.

(6*R*,6a*S*)-3-(4-Chlorophenyl)-2-oxo-1,6,6a-triphenyl-1,2,6,6a-tetrahydrocyclopenta[*b*]pyrrole-5-carbaldehyde (4i)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **4i** as a yellow solid; yield: 104 mg (71%); mp 102–104 °C; 95% ee [HPLC (Daicel AS)]; R_f = 0.42 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ +26.7 (*c* 0.52, $CHCl_3$).

IR (ATR): 1675, 1594, 1555, 1491, 1450, 1401, 1357, 1315, 1179, 1138, 1090, 1033, 1008, 871, 837, 748, 694 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 5.11 (s, 1 H, CHPh), 6.80 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 6.91 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 6.96 (t, *J* = 7.2 Hz, 1 H, CH_{Ar}), 7.01–7.04 (m, 4 H, CH_{Ar}), 7.10 (t, *J* = 7.2 Hz, 1 H, CH_{Ar}), 7.33–7.37 (m, 5 H, CH_{Ar}), 7.48 (d, *J* = 8.4 Hz, 2 H, CH_{Ar}), 7.63 (s, 1 H, C*H*=CCHO), 7.93 (d, *J* = 9.0 Hz, 2 H, CH_{Ar}), 9.91 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 52.7 (CHPh), 79.3 (NCPh), 121.6 (2 C, CH_{Ar}), 124.8 (CH_{Ar}), 125.4 (2 C, CH_{Ar}), 127.9 (CH_{Ar}), 128.1 (2 C, CH_{Ar}), 128.3 (2 C, CH_{Ar}), 128.3 (2 C, CH_{Ar}), 128.6 (CH_{Ar}), 129.9 (2 C, CH_{Ar}), 129.3 (2 C, CH_{Ar}), 129.4 (C), 129.7 (2 C, CH_{Ar}), 130.8 (C), 134.0 (C), 135.7 (C), 137.2 (C), 137.2 (*C*H=CCHO), 139.1 (C), 156.2 (C), 161.5 (C), 170.5 (NCO), 187.5 (CHO).

MS (EI, 70 eV): m/z (%) = 490 (12), 489 (40), 488 (40), 487 (100, M^+), 461 (11), 460 (19), 459 (30), 458 (31), 430 (18), 368 (13).

HRMS: m/z [M + Na]$^+$ calcd for $C_{32}H_{22}NO_2ClNa$: 510.1231; found: 510.1237.

(6*R*,6a*S*)-3,6-Bis(2-methoxyphenyl)-1-oxo-2,6a-diphenyl-1,2,6,6a-tetrahydrocyclopenta[*c*]pyrrole-5-carbaldehyde (10a)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **10a** as a yellow solid; yield: 53 mg (34%); mp 92–94 °C; 71% ee [HPLC (Daicel AS)]; R_f = 0.39 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ +169.3 (*c* 0.44, $CHCl_3$)

IR (ATR): 1729, 1667, 1627, 1595, 1547, 1491, 1459, 1340, 1246, 1154, 1107, 1025, 834, 735, 695 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 3.49 (s, 3 H, OCH_3), 4.08 (s, 3 H, OCH_3), 5.13 (s, 1 H, CH), 6.67 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 6.77–6.80 (m, 2 H, CH_{Ar}), 6.85 (d, *J* = 7.2 Hz, 1 H, CH_{Ar}), 6.94–7.04 (m, 5 H, CH_{Ar}), 7.23–7.29 (m, 2 H, CH_{Ar}), 7.32–7.38 (m, 4 H, CH_{Ar}), 7.47 (s, 1 H, C*H*=CCHO), 7.88 (d, *J* = 13.8 Hz, 2 H, CH_{Ar}), 9.58 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 49.4 (CH), 55.0 (OCH_3), 55.9 (OCH_3), 65.8 (CCO), 111.1 (CH_{Ar}), 111.1 (CH_{Ar}), 118.6 (C), 120.2 (CH_{Ar}), 120.6 (C), 125.1 (2 C, CH_{Ar}), 125.7 (CH_{Ar}), 126.1 (CH_{Ar}), 126.6 (C), 127.3 (2 C, CH_{Ar}), 127.8 (CH_{Ar}), 127.8 (2 C, CH_{Ar}), 128.4 (CH_{Ar}), 128.6 (2 C, CH_{Ar}), 129.0 (C), 130.6 (CH_{Ar}), 131.5 (CH_{Ar}), 135.7 (2 C, C), 142.1 (C), 142.7 (*C*H=CCHO), 149.3 (C), 156.8 (C), 157.8 (C), 174.9 (NCO), 187.4 (CHO).

MS (EI, 70 eV): m/z (%) = 514 (39), 513 (99, M^+), 486 (18), 484 (36), 482 (13), 456 (11), 406 (34), 405 (100), 364 (17), 340 (16), 210 (31), 202 (11), 195 (13), 167 (16), 91 (11), 77 (32).

HRMS: m/z [M + Na]$^+$ calcd for $C_{34}H_{27}NO_4Na$: 536.1832; found: 536.1832.

(6*R*,6a*S*)-1-Oxo-2,6a-diphenyl-3,6-bis[3,4,5-tris(benzyloxy)phenyl]-1,2,6,6a-tetrahydrocyclopenta[*c*]pyrrole-5-carbaldehyde (10b)

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **10b** as a yellow solid; yield: 232 mg (71%); mp 62–64 °C; 32% ee [HPLC (Daicel AS)]; R_f = 0.44 (*n*-pentane–Et_2O, 1:1); $[\alpha]_D^{22}$ –36.7 (*c* 0.52, $CHCl_3$)

IR (ATR): 3040, 2322, 2191, 2095, 1678, 1586, 1495, 1438, 1315, 1219, 1100, 993, 837, 733 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 4.44 (d, *J* = 11.4 Hz, 2 H, OCH_2Ph), 4.71 (m, 3 H, OCH_2Ph, CH), 4.91 (s, 2 H, OCH_2Ph), 4.99 (s, 4 H, OCH_2Ph), 5.07–5.12 (m, 2 H, OCH_2Ph), 5.91 (d, *J* = 1.8 Hz, 2 H, CH_{Ar}), 6.50 (d, *J* = 1.8 Hz, 2 H, CH_{Ar}), 6.93 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 6.98 (t, *J* = 7.2 Hz, 1 H, CH_{Ar}), 7.05 (t, *J* = 7.2 Hz, 2 H, CH_{Ar}), 7.17–7.43 (m, 30 H, C*H*=CCHO, CH_{Ar}), 7.50–7.53 (m, 3 H, CH_{Ar}), 7.66 (d, *J* = 7.2 Hz, 1 H, CH_{Ar}), 7.91 (d, *J* = 7.8 Hz, 2 H, CH_{Ar}), 9.59 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 52.1 (CH), 71.1 (4 C, CH_2Ph), 71.3 (C), 75.1 (CH_2Ph), 75.1 (CH_2Ph), 105.7 (2 C, CH_{Ar}), 107.9 (2 C, CH_{Ar}), 121.3 (2 C, CH_{Ar}), 124.6 (CH_{Ar}), 126.1 (CH_{Ar}), 126.8 (CH_{Ar}), 127.2 (4 C, CH_{Ar}), 127.3 (2 C, CH_{Ar}), 127.5 (4 C, CH_{Ar}), 127.7 (2 C, CH_{Ar}), 127.8 (2 C, CH_{Ar}), 127.9 (2 C, CH_{Ar}), 128.1 (2 C, CH_{Ar}), 128.2 (2 C, CH_{Ar}), 128.4 (4 C, CH_{Ar}), 128.5 (4 C, CH_{Ar}), 128.5 (2 C, CH_{Ar}), 128.6 (2 C, CH_{Ar}), 128.9 (C), 129.0 (2 C, CH_{Ar}), 129.9 (CH_{Ar}), 131.0 (C), 131.9 (C), 134.1 (C), 136.6 (2 C, C), 137.0 (2 C, C), 137.6 (C), 137.7 (C), 137.8 (*C*H=CCHO), 137.9 (C), 138.5 (C), 152.5 (2 C, C), 152.8 (2 C, C), 153.0 (C), 155.8 (C), 160.9 (C), 170.3 (NCO), 187.4 (CHO).

MS (ESI): m/z (%) = 1090 ([M + H]$^+$), 999 (16), 908 (95), 628 (100), 600 (12), 538 (24), 510 (11).

HRMS: m/z [M + H]$^+$ calcd for $C_{74}H_{60}NO_8$: 1090.4313; found: 1090.4313.

***tert*-Butyl 3-{(3a*S*,4*R*)-4-[1-(*tert*-Butoxycarbonyl)-1*H*-indol-2-yl]-5-formyl-3-oxo-2,3a-diphenyl-2,3,3a,4-tetrahydrocyclopenta[*c*]pyrrol-1-yl}-1*H*-indole-1-carboxylate (10c)**

Flash chromatography (*n*-pentane–Et_2O, 2:1) gave **10c** as a yellow solid; yield: 130 mg (59%); mp 133–135 °C; 59% ee [HPLC (Daicel AS)]; R_f = 0.26 (*n*-pentane–Et_2O, 2:1); $[\alpha]_D^{22}$ –60.8 (*c* 0.5, $CHCl_3$).

IR (ATR): 1735, 1679, 1494, 1452, 1365, 1310, 1250, 1153, 1083, 1021, 853, 745, 691 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.54 [s, 9 H, $(CH_3)_3$], 1.70 [s, 9 H, $(CH_3)_3$], 5.26 (s, 1 H, CH), 6.86 (s, 5 H, CH_{Ar}), 7.04–7.08 (m, 3 H, CH_{Ar}), 7.21–7.26 (m, 2 H, CH_{Ar}), 7.39–7.52 (m, 5 H, CH_{Ar}), 7.59 (s, 1 H, C*H*=CCHO), 7.77 (s, 1 H, CH_{Ar}), 7.95 (d, *J* = 7.2 Hz, 2 H, CH_{Ar}), 8.05–8.10 (m, 2 H, CH_{Ar}), 9.60 (s, 1 H, CHO).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 28.1 (3 C, CH_3), 28.2 (3 C, CH_3), 44.8 (CH), 76.6 (CCO), 83.8 [$C(CH_3)_3$], 84.8 [$C(CH_3)_3$], 114.2 (C), 115.0 (CH_{Ar}), 115.4 (CH_{Ar}), 118.7 (CH_{Ar}), 119.4 (C), 120.6 (CH_{Ar}), 122.7 (CH_{Ar}), 123.1 (CH_{Ar}), 123.2 (CH_{Ar}), 123.4 (CH_{Ar}), 124.3 (CH_{Ar}), 124.4 (CH_{Ar}), 124.8 (CH_{Ar}), 125.6 (CH_{Ar}), 127.7 (C), 128.3 (2 C, CH_{Ar}), 128.6 (2 C, CH_{Ar}), 129.0 (2 C, CH_{Ar}), 129.7 (C), 129.8 (2 C, CH_{Ar}), 130.7 (C), 133.8 (C), 135.0 (C), 135.6 (C), 136.7 (*C*H=CCHO), 137.1 (C), 149.1 (C), 149.3 (C), 157.0 (CO), 158.8 (CO), 170.4 (NCO), 187.5 (CHO).

MS (ESI): m/z (%) = 764 ([M + Na]$^+$), 732 ([M + H]$^+$), 676 (100), 663 (55), 662 (36), 632 (26), 550 (14), 549 (66), 548 (24), 532 (19), 476 (25), 475 (16), 407 (11), 236 (45).

HRMS: m/z [M + H]$^+$ calcd for $C_{46}H_{42}N_3O_6$: 732.3068; found: 732.3068.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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