Synthesis of Enantioenriched 3-Amino-3-oxindoles by Stereoselective Mannich Reaction Catalyzed by Supported Bifunctional Thioureas.

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Abstract: Enantioenriched 3-amino-3-substituted oxindoles have been obtained by addition of different nucleophiles to *N*-Boc ketimines derived from isatin catalyzed by chiral bifunctional supported thioureas. The Mannich reaction occurs with excellent enantioselection, but poor diastereoselection when prochiral nucleophiles were used. The supported catalyst were recovered and reused for five times without loss of activity. The mixture of diastereoisomers formed when a prochiral structure was used as nucleophile was converted into a single enantioenriched pyrazolyl derivative.

Keywords: Asymmetric catalysis, 3-Aminooxindoles, Chiral pyrazoles, Bifunctional thioureas, Mannich reaction, Supported thioureas.

Introduction

The properties of natural and synthetic 3-aminooxindoles as bioactive compounds[1] have done these structures targets of a great synthetic interest.[2] Specially important are oxindole derivatives with a quaternary stereocenter at C-3, and both transition-metal-mediated[3] and organocatalytic[4] procedures have been used to the preparation of these frameworks. The most interesting biological active derivatives are 3-amino-2-oxindoles with an additional substituent at C-3, and recent studies revealed that the bioactivity of these compounds is related with the stereochemistry of the C-3 stereogenic center.[5] Then, the development of enantioselective methodology for these structures is highly desirable.

Three different ways have been developed for a direct access to 3-substituted 3-amino-2-oxindoles: the addition-cyclization of 3-isothiocyanate-oxindoles to unsaturated acceptors,[4a] the electrophilic amination of oxindoles,[6] and the nucleophilic addition to ketimines derived from isatin catalyzed by chiral phosphoric acids,[7] the Morita-Baylis-Hillman reaction,[8] the addition of phenols and naphthols,[9] the asymmetric cyanation[10] or the addition of alcohols or thiols[11] catalyzed by different thioureas or squaramides.

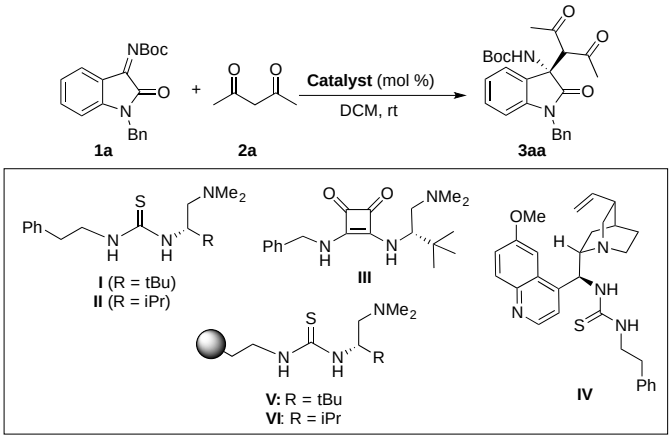
A different, but very efficient, approach to these structures is the addition of a carbon-nucleophile to ketimines derived from isatin (Mannich reaction). Recently, a few examples of organocatalyzed enantioselective Mannich reactions with these isatin-derived ketimines have been reported. Good enantioselections were obtained by using Chiral amines,[12] sulfonamides,[13] and both cinchona-derived thioureas[14] or squaramides,[15] but only moderate enantioselectivity was observed for the Manich reaction promoted by an squaramide derived from camphor.[16] All these reactions have been carried out under homogeneous conditions, but there are not antecedents on the use of supported organocatalysts in these kind of transformations.

Our research interest in developing easily recoverable supported bifunctional chiral thioureas[17] and squaramides[18] as organocatalysts led us to undertake a study on the ability of these catalysts to promote the synthesis of enantioenriched 3-aminooxindoles. We report now our results on the reaction of N-tert-butoxycarbonyl ketimines derived from isatin with different nucleophiles catalyzed by monomeric and polymer-supported thioureas.

Results and Discussion

For comparative purposes bifunctional thioureas **I** and **II**,[19] squaramide **III**,[20] a novel thiourea **IV** derived from (9*S*)-9-deoxy-9-aminoquinine, and polystyrene-supported thioureas **V** and **VI**[19] were selected as catalysts, and their activity tested in the addition of 2,4-pentanedione **2a** to isatin (*N*-Boc) ketimine **1a** as a model reaction (Table 1). The reactions were carried out by stirring at rt a mixture of 0.15 mmol of **1a** and two fold excess of **2a** in 0.4 mL of dichloromethane (DCM), in the presence of 5 mol% of the corresponding catalyst.

Table 1. Evaluation of the catalysts



Entry	Catalyst (mol %)	Time (h)	Yield(%)[a]	Er[b]
1	**I** (5%)	6	87	98:2
2[c]	**I** (5%)	8	88	98:2
3[d]	**I** (5%)	7	82	98:2
4	**II** (5%)	6	89	96:4
5	**III** (5%)	7	93	89:11
6	**IV** (5%)	6	98	88:12
7	**V** (5%)	6	84	95:5
8	**V** (10%)	3.5	90	97:3
9	**V** (2%)	17	84	94:6
10	**VI** (5%)	8	75	90:10

[a] Yields correspond to isolated compound after flash chromatography. [b] Determined by HPLC on a chiral column. [c] Reaction at 0 ºC. [d] Reaction with 1.1 equivalent of acetylacetone.

The results collected in Table 1 show that all tested catalysts provided the addition product **3aa** in excellent yields and good to excellent enantioselection, although squaramide **III** (entry 5), and thiourea **IV** derived from quinine (entry 6) were less effective than thioureas **I** and **II** (entries 1, 4), including their supported homologs **V** and **VI** (entries 7, 10). Catalysts **I** and **V**, derived from L-tert-leucine, were more enantioselective than L-valine-derived thioureas **II** and **VI** (compare entry 1 *versus* 4, and 7 *versus* 10). When the reaction was carried out at 0 ^{o}C in the presence of thiourea **I** no variation in both the yield and enantioselection was observed (entry 2), and the ratio of nucleophile can be decreasing to 1.1 equivalents without modification in the enantioselectivity (entry 3).

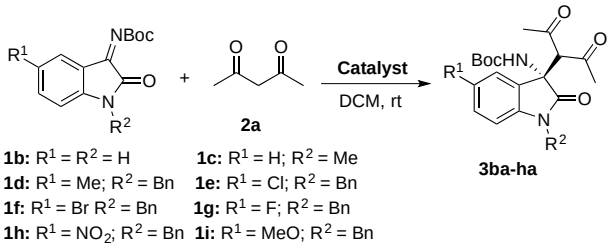
The supported homolog **V** catalyzes the reaction very efficiently, although with a slight decrease in the enantiomeric ratio with respect to **I** (entry 7), but an increase in the molar ratio of catalyst to 10 mol% yielded the addition product **3aa** in high yield and excellent enantioselectivity (entry 8). On the contrary, an increase in the reaction time and slight lowering in the stereoselectivity were observed when the ratio of catalyst was decreased to 2 mol% (entry 9). The absolute stereochemistry and the configuration at C-3 in **3aa** was assigned as (*S*) by comparison of the sign of the optical rotation with that previously described.[14c]

The reactivity of different substituted ketimines (**1b-i**) with 2,4-pentanedione (**2a**) was studied under the experimental described conditions, and taking unsupported (**I**) and supported (**V**) thioureas as the best catalysts (Table 2). In the reactions catalyzed by thiourea **I** 5 mol% of catalyst was used, but in those catalyzed by supported material 10 mol% of catalyst was employed to short the reaction time. The results summarized in Table 2 show that the substitution of the benzyl group in **1a** to a methyl group in **1c** has no effect on both the reactivity and enantioselection of the reaction (compare entries 2, 3 in Table 2 with entries 1, 7 in Table 1). On the contrary, unsubstituted ketimine **1b** yielded the addition product in excellent yield but lower enantioselection (entry 1 in Table 2).

Further attempts to diversify the ketimine structure revealed that good yields and high enantiocontrol was maintained in the reactions of 5-substituted ketimines **1d-i** with

2,4-pentanedione **2a**. Excellent enantioselectivities were observed in the reactions of ketimine with a methyl group (entries 4,5 in Table 2), or an electron-donating group (entries 14, 15) at C-5, but a high level of enantioselection was maintained with halogens (entries 6-11) or hard electron-withdrawing group (entries 12, 13). This means that the electronic character of the substituent has a little effect on the reactivity, thought longer reaction time and higher molar ratio of catalyst were required to obtain comparable results when supported thiourea **V** was used as catalyst.

Table 2. Effect of the substitution on the ketimines.



Entry[a]	R^1	R^2	Catalyst (mol %)	Time (h)	Product	Yield (%)[b]	Er[c]
1	H	H	**I** (5%)	6	**3ba**	90	92:8
2	H	Me	**I** (5%)	6	**3ca**	94	97:3
3	H	Me	**V** (5%)	9	**3ca**	91	95:5
4	Me	Bn	**I** (5%)	4	**3da**	78	97:3
5	Me	Bn	**V** (10%)	9	**3da**	75	97:3
6	Cl	Bn	**I** (5%)	5	**3ea**	82	96:4
7	Cl	Bn	**V** (10%)	10	**3ea**	84	91:9
8	Br	Bn	**I** (5%)	5	**3fa**	77	96:4
9	Br	Bn	**V** (10%)	8	**3fa**	83	97:3
10	F	Bn	**I** (5%)	4	**3ga**	80	96:4
11	F	Bn	**V** (10%)	8	**3ga**	75	97:3
12	NO_2	Bn	**I** (5%)	2	**3ha**	90	95:5
13	NO_2	Bn	**V** (10%)	7	**3ha**	92	90:10

14	OMe	Bn	**I** (5%)	6	**3ia**	81	97:3
15	OMe	Bn	**V** (10%)	9	**3ia**	84	98:2

[a] The reaction was carried out with 0.15 mmol of ketimine, two-fold excess of acetylacetone, and **I** (5 mol%) or **V** (10 mol%) in 0.4 mL of DCM at rt. [b] Yields after purification by flash chromatography. [c] Measured by HPLC on a chiral column.

The scope of the reaction and the synthetic utility was studied by using different 1,3-difunctional compounds as nucleophiles, including symmetrical 1,3-diketones (**2b**, **c**), and diethyl malonate (**2k**) (Table 3). 3,5-Heptanedione (**2b**) easily reacted with ketimine **1a** leading to **3ab** in good yield and excellent enantioselectivity, but the reactions of **1a** with dibenzoylmethane (**2c**) or diethyl malonate (**2k**) leading to **3ac** and **3ak**, respectively, were slower and less enantioselective. The only difference in using supported catalyst **V** in these reactions was an increase in the reaction time to obtain similar results.

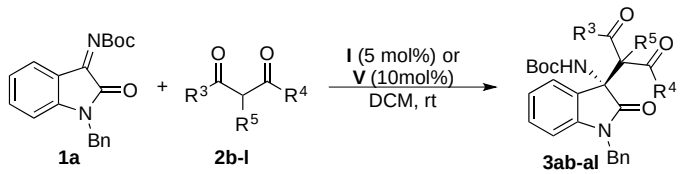
Furthermore, in an attempt to diversify the scope of the reaction we study the possibility to form two contiguous stereocenters by using prochiral nucleophiles such as unsymmetrical-substituted diketones (**2d-f**), and β-ketoesters (**2h**, **i**). 2,4-Hexanedione (**2d**), 5-methyl-2,4-hexanedione (**2e**), and benzoylacetone (**2f**) reacted easily with ketimine **1a**, in the presence of both unsupported (**I**) and supported (**V**) thioureas, leading to the Mannich adducts **3ad**, **3ae**, and **3af**, respectively, in very good yields and enantioselectivities, but without any diastereoselectivity. In a similar way, ethyl acetoacetate (**2h**) added to **1a** leading to **3ah** as a near equimolar mixture of diastereoisomers in high yield and very good enantioselection for both diastereoisomers, although the reaction of β-ketoester **2i** was less enantioselective.

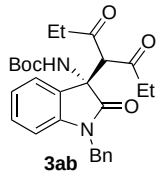
We suspect that the low diastereoselectivity observed for these transformations could be a consequence of the epimerization of the stereogenic center i□□□□□ bifunctional chain, and we decided to follow the reaction of **1a** with **2h** catalyzed by **I** every 30 min. ^{1}HNMR spectra showed that the same near equimolar mixture of diastereoisomers was formed from the beginning of the reaction. This means that the bifunctional thiourea is not able to distinguish the two pro-stereogenic faces of the nucleophile, or that the epimerization occurs too quickly to be detected.

The stereoselective formation of two tertiary-quaternary contiguous carbons was also tested in the reactions of ketimine **1a** with 3-methyl-2,4-pentanedione (**2g**), ethyl 2-

methyl-3-oxobutanoate (**2j**), and 2-ethoxycarbonylcyclopentanone (**2l**). It is interesting to compare the behavior of these tertiary nucleophiles with their unsubstituted homologs. 3-Methyl acetylacetone **2g** reacted with ketimine **1a** leading to the addition product **3ag**, but it was necessary to increase the amount of catalysts **I** to 20 mol%, and the reaction time to 168 h. In these conditions, **3ag** was obtained in moderate yield (61%) and enantioselectivity (er: 82:18). The same fact was observed for the reaction of **2j** with respect to the unsubstituted ketoester **2h**. In that case, the reaction ratio was also slower, and much longer time (120h) was required to obtain moderate yield and enantioselection but, interestingly, better diastereoselection (dr: 88:12), probably because the quaternary character of the stereocenter prevents the epimerization. Cyclic ketoester **2l** was more reactive than **2g** and **2j** towards **1a**. The addition product **3al** was formed in good yield and moderate stereoselection after stirring for 24h in the reaction catalyzed by **I** (5 mol%) or in 48 h in the presence of catalyst **V** (10 mol%).

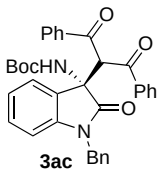
Table 3. Scope of the addition of different nucleophiles to ketimine **1a**.





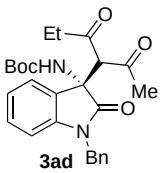
3ab

catalyst **I**, 10h, yield 96%, er: 96:4
catalyst **V**, 14h, yield 77%, er: 95:5



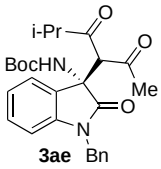
3ac

catalyst **I**, 27h, yield 88%, er: 79:21
catalyst **V**, 72h, yield 74%, er: 77:23



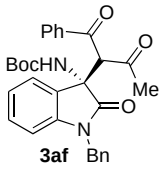
3ad

catalyst **I**, 7h, yield 82%,dr: 52:48
er: 95:5 (major; 95:5 (minor)
catalyst **V**, 8h, yield 93%,dr: 51:49
er: 89:11 (major); 89:11 (minor)



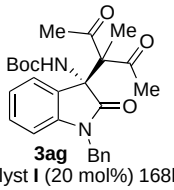
3ae

catalyst **I**, 30h, yield 75%, dr : 55:45
er: 94:6 (major); 94:6 (minor)
catalyst **V**, 48h, yield 67%, dr: 53:47
er: 94:6 (major); 91:9 (minor)



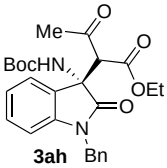
3af

catalyst **I**, 6h, yield 86%, dr: 51:49
er: 93:7 (major); 93:7 (minor)
catalyst **V**, 6h, yield 84%, dr: 52:48
er: 90:10 (major); 90:10 (minor)



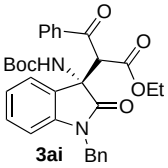
3ag

catalyst **I** (20 mol%) 168h, yield 61%,
er:82:18



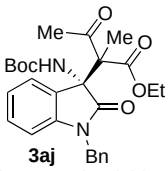
3ah

catalyst **I**, 3h, yield 82%, dr: 51:49
er: 95:5 (major); 95:5 (minor)
catalyst **V**, 24h, yield 78%, dr: 53:47
er: 93:7 (major); 93:7 (minor)



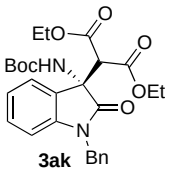
3ai

catalyst **I**, 8h, yield 95%, dr: 56:44
er: 84:16 (major); 86:14 (minor)
catalyst **V**, 24h, yield 92%, dr: 55:45
er: 79:21 (major); 80:20 (minor)



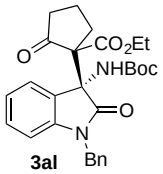
3aj

catalyst **I**, 120h, yield 68%, dr: 88:12
er: 87:13 (major); 84:16 (minor)



3ak

catalyst **I**, 48h, yield 85%, er: 87:13
catalyst **V**, 72h, yield 76%, er: 78:22



3al

catalyst **I**, 24h, yield 83%, dr: 68:32
er: 89:11 (major); 93:7 (minor)
catalyst **V**, 48h, yield 82%, dr: 65:35
er:75:25 (major); 69:31 (minor)

The comparison of the results obtained with thiourea **I**, and its supported homolog **V**, showed that the polymeric material was able to promote the stereoselective process, but it was a little less effective than the monomeric substrate. In general, the processes need longer reaction times, although maintaining the stereoselection.

The main interest of supported catalysts is related with their easy recovering and recycling, and we test the recyclability of supported thiourea **V** in the reaction of isatin-derived ketimine (**1a**) with 2,4-pentanedione (**2a**). To this end, **1a** (0.3 mmol) was reacted with two-fold excess of **2a** at room temperature in the presence of **V** (10 mol%) and DCM as solvent, for a fixed time of 3.5 h. The catalyst was recovered by

filtration after each cycle, and reused after washing with DCM, and drying. The results summarized in Table 4 show that **V** was recovered by filtration after each cycle in high yield, and it can be used for five cycles without loss of enantioselectivity and chemical activity.

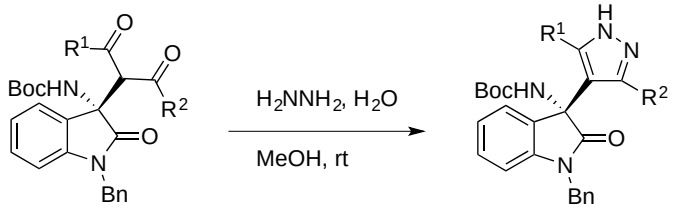
Table 4. Recyclability of catalyst **V** under the best reaction conditions

Cycle	Time (h)	Conversion (%)[a]	Recovered Catalyst	Er[b]
1	3.5	>99	89%	97:3
2	3.5	96	94%	96:4
3	3.5	>99	93%	97:3
4	3.5	>99	96%	95:5
5	3.5	94	89%	96:4

[a] Determined by ^{1}HNMR in the reaction mixture. [b] Determined by chiral HPLC analysis.

To demonstrate the utility of the method, and given the biological significance of the pyrazole nucleus,[21] we decided to prepare hybrid compounds[22] bearing the pyrazole and 3-aminooxindole components with potential pharmacological activity as summarized in Scheme 1. Similar structures have been prepared by organocatalytic addition of N-substituted pyrazoles or pyrazolones[23] to oxindole derivatives, but the direct synthesis of pyrazoles bearing an acidic N-H bond by this methodology is difficult because they always behave as N-nucleophiles.[24]

Scheme 1. Conversion of diketones **3aa**, **3ae**, and **3af** into N-unsubstituted pyrazoles.



3aa R^1= R^2 = Me, er = 98:2
3ae R^1= i-Pr, R^2 = Me, er = 94:6
3af R^1= Ph, R^2 = Me, er = 93:7

4aa 61% yield, er = >99:<1
4ae 61% yield, er = 95:5
4af 62% yield, er = 93:7

Condensation of symmetrical (**3aa**) or the mixture of diastereoisomers of unsymmetrical (**3ae**, **3af**) diketones with ten percent excess of hydrazine monohydrate in methanol occurred easily at room temperature leading to pyrazoles **4** in good yields. As expected,[25] the reaction of unsymmetrical derivatives was regioselective leading to **4ae**, and **4af** as single regioisomers. HPLC on a chiral phase of the final pyrazoles showed that the enantiomeric ratio was maintained with respect to the starting compounds, showing that there is no erosion of the enantiomeric purity during the transformation.

Conclusion

In summary, we have demonstrated that thiourea **I**, and polystyrene-supported thiourea **V**, derived from *L-tert*-Leucine, are excellent organocatalysts for the stereoselective Mannich reaction of *N-Boc*-ketimines derived from isatin. The addition products were obtained in high yields and excellent enantioselectivities, although moderate to poor diastereoselection when prochiral structures were used as nucleophiles. The use of a polymeric catalyst such as **V** is described for the first time in that kind of transformation, and it is especially important because it was easily recovered and reused maintaining the catalytic activity. Some mixtures of diastereoisomeric β-dicarbonyls were transformed into single enantioenriched N-unsubstituted pyrazolyl-3-amino oxindoles, opening a new way to the preparation of that kind of compounds.

Experimental Section

General

^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra were recorded in $CDCl_3$ as solvent. Chemical shifts for protons are reported in ppm from TMS with the residual $CHCl_3$ resonance as internal reference. Chemical shifts for carbons are reported in ppm from TMS and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants in Hertz, and integration.

Specific rotations were measured on a Perkin–Elmer 341 digital polarimeter using a 5-mL cell with a 1-dm path length, and a sodium lamp, and concentration is given in g per 100 mL. Infrared spectra were recorded on a Perkin–Elmer Spectrum One FT–

IR spectrometer and are reported in frequency of absorption (only the structurally most important peaks are given).

Flash chromatography was carried out using silica gel (230–240 mesh). TLC analysis was performed on glass-backed plates coated with silica gel 60 and F_{254} indicator, and visualized by either UV irradiation or by staining with phosphomolybdic acid solution. Chiral HPLC analysis was performed on a *J*ASCO HPLC system (JASCO PU-2089 pump and UV-2075 UV/Vis detector), a JASCO SFC system (JASCO PU-2080 pump and DAD MD-2015 detector) and a Hewlett–Packard 1090 Series II instrument equipped with a quaternary pump, using a Daicel Chiralcel OD, Chiralcel OJ, Chiralpak AD-H, Chiralpak AS-H, Chiralpak IA and Lux-amylose-1 analytical columns (250 x 4.6 mm). Detection was monitored at 220 or at 254 nm.

Elemental analyses were carried out at the Elemental Analysis Center of the Complutense University of Madrid, using a Perkin Elmer 2400 CHN.

ESI mass spectra were obtained on an Agilent 5973 inert GC/MS system.

Starting isatin (*N*-Boc) ketimines **1a-i** were prepared from the corresponding isatins as previously described.[14c] Commercially available organic and inorganic compounds were used without further purification. Solvents were dried and stored over microwave–activated 4 Å molecular sieves.

Synthesis of thiourea (IV).

To a solution of (9*S*)-9-deoxy-9-aminoquinine[26] (0.6 mmol, 194 mg) in dry CH_2Cl_2 (6 mL) was added (2-isothiocyanatoethyl) benzene[27] (108 mg, 0.66 mmol, 1.1 equiv) at 0 ºC under nitrogen atmosphere. The resulting solution was stirred overnight at room temperature. When the reaction was completed, the resulting solution was concentrated under low pressure and the residue was purified by flash chromatography (EtOAc / Methanol = 4:1) to afford **IV** as white solid (123 mg, 0.25 mmol, 42%). $[\alpha]_D^{25}$ = -78.9 (*c* = 1.04, $CHCl_3$). ^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.67 (d, *J* = 5.1 Hz, 1H), 8.00 (dd, *J* = 9.3 Hz, 1.1 Hz, 1H), 7.71 (br s, 1 H), 7.49 (m, 1H), 7.38 (ddd, J_1 = 9.2, J_2 = 2.7 Hz, J_3 = 0.9 Hz, 1H), 7.28 (m, 1H), 7.19 (m, 2H), 7.04 (d, *J* = 7.2 Hz, 2 H), 6.89 (m, 1H), 5.64 (ddd, J_1 = 17.4 Hz, J_2 = 10.1 Hz, J_3 = 7.1 Hz, 1H), 4.97 (d, *J* = 4.6 Hz, 1H), 4.95 (d, *J* = 2.1 Hz, 1H), 4.55 (br s, 1 H), 3.96 (s, 3 H), 3.64 (m, 2H); 3.25 (m, 2H), 3.10 (m, 1H), 2.70 (m, 4H), 2.29 (br s 1H), 1.68 (m, 1H), 1.62 (m, 2H), 1.36 (m, 1H), 0.91 (m, 1H) ppm. ^{13}C NMR (126 MHz, CDCl3) δ 182.4, 158.0, 147.5, 144.8, 140.5, 140.3, 138.5, 131.7, 128.7, 128.5, 126.4, 122.1, 115.2,

102.3, 60.7, 55.9, 55.1, 49.5, 45.8, 41.2, 38.8, 35.0, 27.2, 27.2, 27.1, 25.6 ppm. IR (ATR): 3234, 2940, 1620, 1530, 1506, 1473, 747, 699 cm^{-1}. HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{29}H_{35}N_4OS$ 487.2532; Found 487.2534.

General procedure for enantioselective Mannich reaction with N-Boc ketimines with nucleophiles using immobilized catalysts.

A mixture of N-Boc ketimines **1a-i** (0.15 mmol), catalyst (0.015 mmol, 0.1 equiv), and the corresponding nucleophile **2a-l** (0.3 mmol, 2 equiv) in 0.4 mL of DCM was stirred at room temperature in a Wheaton vial until consumption of the starting material (monitoring by ^{1}H-NMR). The catalyst was filtered off and washed with CH_2Cl_2 (3 x 1 mL). The solid was dried until constant weight, and reused in the next cycle. After solvent removal under reduced pressure, the crude mixture was purified by flash chromatography to afford the corresponding product. The enantiomeric excess was determined by chiral-phase HPLC analysis using mixtures of hexane/isopropanol as eluent.

General procedure to enantioselective Mannich reaction with N-Boc ketimines with nucleophiles using homogeneous catalysts.

A solution of N-Boc ketimines **1a-i** (0.15 mmol), catalyst (0.0075 mmol, 0.05 equiv), and the corresponding nucleophile **2a-l** (0.3 mmol, 2 equiv) in 0.4 mL of DCM was stirred at rt in wheaton vial until consumption of the starting material (monitoring by ^{1}H-NMR). After solvent removal under reduced pressure, the crude mixture was purified by flash column chromatography to afford the corresponding product. The enantiomeric excess was determined by chiral-phase HPLC analysis using mixtures of hexane/isopropanol as eluent.

tert-Butyl (*S*)-(1-benzyl-3-(2,4-dioxopentan-3-yl)-2-oxoindolin-3-yl)carbamate (3aa).[14c] Product **3aa** was obtained according to the general procedure using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 3:1) affording compound **3aa** as a white solid**,** (57 mg, 0.130 mmol, 87%). $[\alpha]_D^{25}$ = -14.0 (*c* = 1, $CHCl_3$) [Lit.[14c] $[\alpha]_D^{20}$ = - 2.0 (*c* = 1.0, $CHCl_3$, 94% ee) for (*S*) enantiomer]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.30-7.25 (m, 2H), 7.18 (td, *J* = 7.8, *J* = 1.3Hz, 1H), 6.98 (dt, *J* = 7.6, *J* = 1 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.57 (s, 1H), 5.04 (d, *J* = 15,7 Hz, 1H), 4.82 (br s, 1H), 4.07 (s, 1H), 2.30 (s, 3H), 2.16 (s, 3H), 1.30 (s, 9H) ppm. HPLC: Chiralpak OD-H; hexane/*i*-PrOH 95:5, 1

mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 15.30 min, minor enantiomer (*R*) t_r = 19.59 min. (er: 98:2).

tert-Butyl (*S*)-(3-(2,4-dioxopentan-3-yl)-2-oxoindolin-3-yl)carbamate (3ba).[14c] Product **3ba** was obtained according to the general procedure using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 3:1) giving compound **3ba** as a white solid, (47 mg, 0.135 mmol, 90%). $[\alpha]_D^{25}$ = +17.6 (*c* = 0.66, $CHCl_3$) [Lit.[14c] $[\alpha]_D^{20}$ = +8.0 (*c* = 1.0, $CHCl_3$, 87% ee) for (*S*) enantiomer]; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.23-7.19 (m, 2H), 6.97 (t, *J* = 7.9, 1H), 6.81 (d, *J* = 7.6, 1H), 6.72 (s, 1H), 4.09 (s, 1H), 2.33 (s, 3H), 2.15 (s, 3H), 1.31 (s, 9H) ppm. HPLC: Lux Cellulose-1; hexane/*i*-PrOH 80:20, 1 mL/min, λ = 254 nm, major enantiomer (*S*) t_r = 8.74 min, minor enantiomer (*R*) t_r = 9.77 min. (e.r: 89:11).

tert-Butyl (*S*)-(3-(2,4-dioxopentan-3-yl)-1-methyl-2-oxoindolin-3-yl)carbamate (3ca).[14c] Product **3ca** was obtained according to the general procedure, using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 3:1) affording compound **3ca** as a white solid**,** (51 mg, 0.141 mmol, 94%). $[\alpha]^{25}_D$ = -8.9 (c = 0.54, $CHCl_3$) [Lit.[14c] $[\alpha]_D^{20}$ = +11.0 (*c* = 1.0, $CHCl_3$, 95% ee) for (*R*) enantiomer]; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.30 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.27 (m, 1H), 7.02 (dt, *J* = 7.6, 1.1 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.48 (s, 1H), 4.08 (s, 1H), 3.24 (s, 3H), 2.28 (s, 3H), 2.17 (s, 3H), 1.27 (s, 9H) ppm. HPLC: Chiralpak OD, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, minor enantiomer (*R*) t_r = 24.01 min, major enantiomer (*S*) t_r = 33.25 min. (er 97:3).

tert-Butyl (*S*)-(1-benzyl-3-(2,4-dioxopentan-3-yl)-5-methyl-2-oxoindolin-3-yl) carbamate (3da). Product **3da** was obtained according to the general procedure, using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) leading to compound **3da** as a colorless solid, (53 mg, 0.117 mmol, 78%). $[\alpha]^{25}_D$ = -9.3 (*c* = 0.7, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.5 Hz), 7.33 (t, *J* = 7.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 1H), 7.07 (s, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.60 (s, 1H), 6.58 (br. s, 1H), 5.01 (d, *J* = 15.4 Hz, 1H), 4.81 (d, *J* = 10.2 Hz, 1H), 4.05 (s,

1H), 2.31 (s, 3H), 2.25 (s, 3H), 2.16 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.7; 174.1; 153.9; 140.1, 135.7; 132.5; 129.8; 128.8; 127.6; 127.5; 124.4; 109.3; 80.4; 68.6; 62.9; 44.3; 32.3; 32.3; 28.2; 21.1 ppm. IR (ATR): 3413, 2976, 1713, 1604, 1494, 729, 697 cm^{-1}. HPLC: Chiralpak OD, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 14.39 min, minor enantiomer (*R*) t_r = 18.46 min. (er 97:3). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{30}N_2NaO_5$ 473.2059; Found 473.2047.

tert-Butyl (*S*)-(1-benzyl-5-chloro-3-(2,4-dioxopentan-3-yl)-2-oxoindolin-3-yl) carbamate (3ea). Compound **3ea** was obtained according the to general procedure, using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) giving compound **3ea** as colorless oil, (58 mg, 0.123 mmol, 82%). $[\alpha]_D^{25}$ = -25.0 (*c* = 1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.30 (m, 5H), 7.28 – 7.25 (m, 2H), 7.12 (dd, *J* = 8.3, *J* = 2.0 Hz, 1H), 6.59 (d, *J* = 8.3 Hz, 1H), 6.49 (br. s, 1H), 4.97 (d, *J* = 15.6 Hz, 1H), 4.83 (d, *J* = 14.3 Hz, 1H), 4.05 (s, 1H), 2.29 (s, 3H), 2.16 (s, 3H), 1.32 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ: 201.1, 173.9, 153.8, 141.2, 135.1, 129.9, 129.4, 128.8, 128.3, 127.8, 127.4, 124.3, 110.5, 80.8, 68.4, 62.6, 44.5, 32.3, 32.0, 28.1 ppm. IR (ATR): 3405, 2976, 1713, 1608, 1482, 701 cm^{-1}; HPLC: Chiralpak OD column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 15.07 min, minor enantiomer t_r = 19.78 min (*R*). (er 96:4). HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{25}H_{28}ClN_2O_5$ 471.1687; Found 471.1681.

tert-Butyl (*S*)-(1-benzyl-5-bromo-3-(2,4-dioxopentan-3-yl)-2-oxoindolin-3-yl) carbamate (3fa). Product **3fa** was obtained according to the general procedure, using acetylacetone **2a** and catalyst **V** (25 mg, 0.015 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 4:1 to 2:1) affording compound **3fa** as a yellowish solid, (64 mg, 0.124 mmol, 83%). $[\alpha]^{25}_D$ = -31.5 (*c* = 0.9, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 1.8 Hz, 1H), 7.34 (m, 4H), 7.26 (m, 2H), 6.55 (d, *J* = 8.3 Hz, 1H), 6.49 (br. s, 1H), 4.96 (d, *J* = 15.6 Hz, 1H), 4.82 (d, *J* = 14.9 Hz, 1H), 4.04 (s, 1H), 2.29 (s, 3H), 2.16 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 173.8, 153.8, 141.7, 135.1, 132.3, 130.3, 128.8, 127.8, 127.4, 127.0, 115.6, 111.0, 80.8, 68.4, 62.6, 44.4, 32.3, 32.1, 28.2 ppm. IR (ATR): 3405, 2980, 1713, 1608, 1482, 701 cm^{-1}. HPLC: Chiralpak OD column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 17.60

min, minor enantiomer (*R*) t_r = 22.8 min. (er 97:3). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{27}BrN_2NaO_5$ 537.1001; Found 537.0996.

tert-Butyl (*S*)-(1-benzyl-3-(2,4-dioxopentan-3-yl)-5-fluoro-2-oxoindolin-3-yl)carbamate (3ga). Product **3ga** was obtained according to the general procedure, using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) leading to compound **3ga** ascolorless solid, (55 mg, 0.121 mmol, 80%). $[\alpha]^{25}_D$= -20.4 (*c* = 1.0, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 4H), 7.25 (m, 1H), 7.06 (dd, *J* = 7.9, *J* = 2.5 Hz, 1H), 6.89 – 6.85 (dt, *J* = 8.8, 2.5 Hz, 1H),6.60 (dd, *J* = 8.5, *J* = 4.0 Hz, 1H), 6.48 (br s, 1H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.82 (d, *J* = 13.6 Hz, 1H), 4.08 (s, 1H), 2.29 (s, 3H), 2.16 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 174.1, 160.4, 158.0, 153.8, 138.6, 135.3, 128.8, 127.8, 127.4, 115.9, 112.3, 110.1, 80.7, 68.4, 62.8, 44.5, 32.3, 32.0, 28.1 ppm. IR (ATR): 3413, 2976, 1713, 1620, 1486, 697 cm^{-1}. HPLC: Chiralpak OD column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 17.05 min, minor enantiomer (*R*) t_r = 23.93 min. (er 96:4). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{27}FN_2NaO_5$ 477.1802; Found 477.1796.

tert-Butyl (*S*)-(1-benzyl-3-(2,4-dioxopentan-3-yl)-5-nitro-2-oxoindolin-3-yl)carbamate (3ha). Compound **3ha** was obtained according to the general procedure, using acetylacetone **2a** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) affording compound **3ha** as yellow oil, (65 mg, 0.135 mmol, 90%). $[\alpha]^{25}_D$= -122.0 (*c* = 0.7, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 2.3 Hz, 1H), 8.12 (dd, *J* = 8.9, *J* = 2.0 Hz, 1H), 7.40 (d, *J* = 7.3 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.1 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 1H), 6.51 (br. s, 1H), 5.01 (m, 2H), 4.14 (s, 1H), 2.29 (s, 1H), 2.20 (s, 1H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.1, 200.8, 174.7, 153.8, 148.6, 143.5, 134.4, 129.2, 129.0, 128.1, 127.4, 126.5, 119.8, 109.2, 81.2, 68.4, 62.0, 44.8, 32.2, 31.9, 28.1 ppm. IR (ATR): 3405, 2976, 1713, 1608, 1486, 729 cm^{-1}. HPLC: Chiralpak AD column, CO_2/methanol = 85:15, 2.0 mL/min, λ = 220 nm, minor enantiomer (*R*) t_r = 4.41 min, major enantiomer (*S*) t_r = 6.08 min. (er 95:5). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{27}N_3NaO_7$ 504.1747; Found 504.1741.

tert-Butyl (*S*)-(1-benzyl-3-(2,4-dioxopentan-3-yl)-5-methoxy-2-oxoindolin-3-yl)carbamate (3ia). Product **3ia** was obtained according to the general procedure, using acetylacetone **2a** and catalyst **V** (25 mg, 0.015 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) yielding compound **3ia** as colorless oil, (59 mg, 0.126 mmol, 84%). $[\alpha]_D^{25}$ = -12.6 (*c* = 0.9, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.26 (d, *J* = 7.1 Hz, 1H), 6.88 (d, *J* = 2.4 Hz, 1H), 6.68 (dd, *J* = 8.5, *J* = 2.5 Hz, 1H), 6.57 (d, *J* = 17.2 Hz, 1H), 6.57 (br. s, 1H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.79 (d, *J* = 13.1 Hz, 1H), 4.05 (s, 1H), 3.69 (s, 3H), 2.29 (s, 1H), 2.15 (s, 1H), 1.30 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 201.5, 173.9, 156.1, 153.9, 135.8, 135.7, 129.6, 128.8, 127.5, 113.8, 111.2, 109.9, 80.5, 68.5, 63.1, 55.7, 44.4, 32.4, 32.2, 28.2 ppm. IR (ATR): 3413, 2980, 1713, 1604, 733, 697 cm^{-1}. HPLC: Chiralpak OD column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 22.65 min, minor enantiomer (*R*) t_r = 28.18 min. (er 98:2). HRMS (ESI-QTOF) m/z: $[M + H]^+$ Calcd. for $C_{26}H_{31}N_2O_6$ 467.2182; Found:467.2177.

tert-Butyl (*S*)-(1-benzyl-3-(3,5-dioxoheptan-4-yl)-2-oxoindolin-3-yl)carbamate (3ab). Product **3ab** was obtained according to the general procedure, using heptane-3,5-dione **2b** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 3:1) affording compound **3ab** as colorless solid, (67 mg, 0.144 mmol, 96%). $[\alpha]_D^{25}$ = -8.1 (*c* = 1.1, $CHCl_3$); $[\alpha]_D$ = -52.55 (*c* = 1.1, EtOAc). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.81 (br. s, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 5.01 (d, *J* = 15.6 Hz, 1H), 4.81 (d, *J* = 13.3 Hz, 1H), 3.94 (s, 1H), 2.69 – 2.42 (m, 2H), 2.27 – 2.13 (m, 2H), 1.28 (s, 9H), 1.01 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 203.8, 203.5, 174.4, 153.8, 142.4, 135.7, 129.4, 128.7, 127.6, 127.5, 123.3, 122.8, 109.5, 80.3, 66.6, 63.1, 44.3, 38.6, 38.7, 28.1, 7.4, 7.2 ppm. IR (ATR): 3409, 2976, 1713, 1612, 754, 697 cm^{-1}; HPLC: Chiralpak OD column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 8.89 min, minor enantiomer (*R*) t_r = 12.35 min. (er 96:4). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{27}H_{32}N_2NaO_5$ 487.2209; Found 487.2216.

tert-Butyl (*S*)-(1-benzyl-3-(1,3-dioxo-1,3-diphenylpropan-2-yl)-2-oxoindolin-3-yl)carbamate (3ac). Product **3ac** was obtained according to the general procedure,

using 1,3-diphenylpropane-1,3-dione **2c** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 8:1 to 4:1) to yield compound **3ac** as colorless solid, (74 mg, 0.132 mmol, 88%). $[\alpha]_D^{25}$ = +14.2 (*c* = 0.5, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 6.94 (t, *J* = 7.5 Hz, 1H), 5.79 (br. s, 1H), 4.85 (d, *J* = 14.4 Hz, 1H), 4.68 (d, *J* = 12.8 Hz, 1H), 1.30 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 192.1, 191.9, 174.5, 153.9, 142.5, 136.8, 136.6, 136.1, 133.8, 133.7, 128.8, 128.7, 128.6, 128.5, 127.7, 127.6, 125.2, 122.9, 109.1, 80.1, 66.1, 64.1, 56.0, 44.2, 28.2 ppm. IR (ATR): 3441, 2972, 1717, 1616, 749, 685, 567 cm^{-1}; HPLC: Chiralpak OD column, hexane/*iso*-propanol = 95:5, 0.5 mL/min, λ = 254 nm, major enantiomer (*S*) t_r = 29.08 min, minor enantiomer (*R*) t_r = 32.46 min. (er 79:21). HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{35}H_{33}N_2O_5$ 561.2389; Found 561.2388.

tert-Butyl ((*S*)-1-benzyl-3-(2,4-dioxohexan-3-yl)-2-oxoindolin-3-yl)carbamate (3ad). Product **3ad** was obtained according to the general procedure, using hexane-2,4-dione **2d** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was subjected to flash chromatography (hexane/ethyl acetate: 8:1 to 4:1) affording compound **3ad** as an inseparable mixture (52:48) of diastereoisomers. Colorless oil, (55 mg, 0.123 mmol, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.24 (m, 1H), 7.21 – 7.13 (m, 1H), 6.97 (m, 1H), 6.79 (br. s, 0.52H) (major diastereoisomer), 6.71 (dd, *J* = 7.5, *J* = 5.0 Hz, 1H), 6.61 (br. s, 0.48H) (minor diastereoisomer), 5.07 – 4.98 (m, 1H), 4.93 – 4.77 (m, 1H), 4.05 (s, 0.48H) (minor), 3.96 (s, 0.52H) (major), 2.59 (m, 0.52H) (major), 2.51 (m, 1H), 2.33 (s, 1.56H) (major), 2.30 – 2.22 (m, 0.48H) (minor), 2.16 (s, 1.44H) (minor), 1.30 (s, 9H), 1.02 (t, *J* = 7.1 Hz, 1.44H) (minor), 0.97 (t, *J* = 7.1 Hz, 1.56H) (major) ppm. ^{13}C NMR. (101 MHz, $CDCl_3$) δ 204.3, 203.9, 201.3, 201.0, 174.4, 174.2, 153.8, 142.5, 142.4, 135.6, 129.4, 129.4, 128.8, 128.8, 127.6, 127.5, 127.5, 123.7, 123.2, 122.9, 122.8, 109.5, 80.4, 67.8, 67.6, 62.9, 44.3, 44.3, 38.9, 38.8, 32.1, 28.1, 7.4, 7.2 ppm. IR (ATR): 3409, 2976, 1713, 1612, 754, 733, 697 cm^{-1}. HPLC: Lux-i-Amylose-1 column, hexane/*iso*-propanol = 90:10, 1 mL/min, λ = 254 nm. Major diastereoisomer: t_r = 9.98 min (minor enantiomer), t_r = 21.31 min (major enantiomer) (er: 95:5). Minor diastereoisomer: t_r = 11.04 min (minor enantiomer), t_r = 28.44 min (major

enantiomer). (er 95:5). HRMS (ESI-QTOF) m/z: [M Na]$^+$ Calcd. for $C_{26}H_{30}N_2NaO_5$ 473.2052; Found 473.2047.

tert-Butyl ((*S*)-1-benzyl-3-(5-methyl-2,4-dioxohexan-3-yl)-2-oxoindolin-3-yl)carbamate (3ae). Product **3ae** was obtained according to general procedure, using 5-methylhexane-2,4-dione **2e** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was subjected to flash chromatography (hexane/ethyl acetate: 8:1 to 4:1) leading to compound **3ae** as an inseparable mixture (55:45) of diastereoisomers. Colorless oil, (52 mg, 0.113 mmol, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.37 (m, 2H), 7.35 – 7.23 (m, 4H), 7.15 (t, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 8.2 Hz, 0.45H), 6.98 (br. s, 0.45H) (minor diastereoisomer), 6.96 – 6.90 (m, 1H), 6.69 (dd, *J* = 12.8, 7.9 Hz, 1H), 6.42 (br. s, 0.55H) (major diastereoisomer), 5.11 – 5.00 (m, 0.45H) (minor), 4.93 (s, 1H), 4.79 (s, 0.55H) (major), 4.28 (s, 0.55H) (major), 3.96 (s, 0.45H) (minor), 2.54 – 2.46 (m, 0.55H) (major), 2.42 – 2.34 (m, 0.45H) (minor), 2.37 (s, 1.35H) (minor), 2.20 (s, 1.65H) (major), 1.29 (s, 9H), 1.00 (d, *J* = 7.1 Hz, 1.65H) (major), 0.97 (d, *J* = 6.9 Hz, 1.35H) (minor), 0.90 (d, *J* = 6.7 Hz, 1.65H) (major), 0.83 (d, *J* = 6.8 Hz, 1.35H) (minor) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.4, 207.3, 201.4, 200.3, 174.5, 174.1, 154.0, 153.7, 142.8, 142.1, 135.7, 135.6, 129.5, 129.5, 128.8, 128.7, 128.0, 127.7, 127.6, 127.5, 127.5, 123.9, 123.2, 122.7, 109.5, 80.4, 80.3, 66.3, 65.7, 63.3, 63.1, 44.4, 44.3, 43.5, 43.2, 32.0, 31.8, 28.1, 17.7, 17.4, 17.1 ppm. IR (ATR): 3405, 2976, 1713, 1612, 754, 697 cm^{-1}. HPLC: Lux-i-Amylose-1 column, hexane/*iso*-propanol = 90:10, 1 mL/min, λ = 254 nm. Major diastereoisomer: t_r = 7.51 min (minor enantiomer), t_r = 11.74 min (major enantiomer) (er 94:6). Minor diastereoisomer: t_r = 9.22 min (minor enantiomer), t_r = 17.70 min (major enantiomer). (er 94:6). HRMS (ESI-QTOF) m/z: [M+Na]$^+$ Calcd. for $C_{27}H_{32}N_2NaO_5$ 487.2209; Found 487.2203.

tert-Butyl ((*S*)-1-benzyl-3-(1,3-dioxo-1-phenylbutan-2-yl)-2-oxoindolin-3-yl)carbamate (3af). Product **3af** was obtained according to the general procedure, using 1-phenylbutane-1,3-dione **2f** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was subjected to flash column chromatography (hexane/ethyl acetate: 8:1 to 4:1) affording compound **3af** asan inseparable mixture (51:49) of diastereoisomers. Orange oil, (64 mg, 0.129 mmol, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 7.55 (q, *J* = 7.3 Hz, 1H), 7.46 – 7.22 (m, 7.51H), 7.18 – 7.07 (m, 2H), 6.90 (t, *J* = 7.6 Hz, 0.51H) (major

diastereoisomer), 6.84 (t, *J* = 7.6 Hz, 0.49H) (minor diastereoisomer), 6.72 (d, *J* = 7.8 Hz, 0.51H) (major), 6.67 (d, *J* = 7.8 Hz, 0.49H) (minor), 6.38 (br s, 0.49H) (minor), 5.13 (s, 0.51H) (major), 4.99 (m, 1H), 4.87 (m, 0.51H) (major), 4.79 (s, 0.49H) (minor), 4.71 (s, 0.49H) (minor), 2.35 (s, 1.47H) (minor), 2.13 (s, 1.53H) (major), 1.31 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.8, 200.8, 193.9, 193.8, 174.6, 174.1, 154.0, 153.8, 143.1, 142.3, 136.9, 136.6, 135.8, 135.7, 134.3, 134.0, 129.4, 129.3, 128.9, 128.7, 128.7, 128.4, 127.7, 127.6, 127.5, 124.6, 123.9, 122.8, 122.7, 109.3, 80.3, 63.5, 63.2, 62.5 , 44.5, 44.3, 31.4, 28.2 ppm. IR (ATR): 3417, 2976, 1713, 1612, 733, 693 cm^{-1}. HPLC: Lux-Amylose-1 column, hexane/*iso*-propanol = 90:10, 1.0 mL/min, λ = 254 nm. Major diastereoisomer: t_r = 15.95 min (major enantiomer), t_r = 48.98 min (minor enantiomer) (er: 93:7). Minor diastereoisomer: t_r = 17.72 min (major enantiomer), t_r = 74.87 min (minor enantiomer). (er 93:7). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{30}H_{30}N_2NaO_5$ 521.2052; Found 521.2047.

tert-Butyl (*R*)-(1-benzyl-3-(3-methyl-2,4-dioxopentan-3-yl)-2-oxoindolin-3-yl)carbamate (3ag). Product **3ag** was obtained according to the general procedure, using 3-methylpentane-2,4-dione **2g** and catalyst **I** (10 mg, 0.03 mmol). The crude reaction mixture was purified by flash chromatography (hexane/ethyl acetate: 8:1 to 4:1) affording compound **3ag** as a yellowish solid,(41 mg, 0.092 mmol, 61%). $[\alpha]_D^{25}$ = -13.7 (*c* = 0.5, $CHCl_3$). ^{1}H-NMR (400 MHz, Chloroform-d) δ 7.43 (d, *J* = 7.4 Hz, 2H), 7.37 – 7.30 (m, 3H), 7.29 – 7.25 (m, 2H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.88 (s, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 15.7 Hz, 1H), 4.76 (m, 1H), 2.40 (s, 3H), 2.06 (s, 3H), 1.28 (s, 9H), 1.21 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.3, 174.2, 153.9, 144.0, 135.8, 129.2, 128.7, 127.8, 127.6, 124.9, 122.9, 108.9, 80.1, 68.3, 44.5, 30.3, 28.7, 28.1, 15.8 ppm. IR (ATR): 3421, 2980, 1713, 1612, 754, 697 cm^{-1}. HPLC: Lux-Amylose-1 column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm, minor enantiomer (*S*) t_r = 27.14 min, major enantiomer (*R*) t_r = 49.35 min. (er 82:18). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{26}H_{30}N_2NaO_5$ 473.2052; Found 473.2047.

Ethyl (*S*)-2-(1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-3-oxobutanoate (3ah). Product **3ah** was obtained according to the general procedure fromethyl 3-oxobutanoate **2h** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was subjected to flash chromatography (hexane/ethyl acetate: 8:1 to 4:1) affording compound **3ah** as an inseparable mixture (51:49) of diastereoisomers.

Yellow oil,(55 mg, 0.117 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.37 (m, 2.51H) (major diastereoisomer), 7.31 (dt, *J* = 7.7, *J* = 4.0 Hz, 2.49H) (minor diastereoisomer), 7.24 (dt, *J* = 7.8, *J* = 3.6 Hz, 1H), 7.15 (dt, *J* = 7.7, *J* = 1.3 Hz, 1H), 6.99 – 6.88 (m, 1H), 6.68 (t, *J* = 7.8 Hz, 1H), 6.47 (br. s, 0.49H) (minor), 6.39 (br. s, 0.51H) (major), 4.99 (dd, *J* = 15.4, *J* = 6.1 Hz, 1H), 4.83 (d, *J* = 15.3 Hz, 1H), 4.19 – 4.06 (m, 2H), 4.02 (s, 0.49H) (minor), 3.92 (s, 0.51H) (major), 2.25 (s, 1.53H) (major), 2.15 (s, 1.47H) (minor), 1.29 (s, 9H), 1.16 (t, *J* = 7.2 Hz, 1.53H) (major), 1.12 (t, *J* = 7.1 Hz, 1.47H) (minor) ppm.^{13}C NMR (101 MHz, $CDCl_3$) δ 200.6, 200.3, 174.3, 174.2, 166.6, 166.0, 154.0, 153.7, 143.1, 142.9, 135.7, 129.4, 129.4, 128.7, 128.7, 128.3, 128.0, 127.6, 127.5, 124.2, 124.0, 122.8, 122.7, 109.3, 80.3, 80.3, 62.1, 62.1, 61.9, 61.8, 60.6, 44.4, 44.4, 32.1, 31.1, 28.1, 13.8, 13.8 ppm. IR (ATR): 3417, 2980, 1713, 1612, 754, 733, 697 cm^{-1}. HPLC: Lux-i-Amylose-1 column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 254 nm. Major diastereoisomer: t_r = 15.96 min (major enantiomer), t_r = 38.75 min (minor enantiomer) (er 95:5). Minor diastereoisomer: t_r = 26.60 min (major enantiomer), t_r = 53.92 min (minor enantiomer). (er 95:5). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{26}H_{30}N_2NaO_6$ 489.2002; Found: 489.1996.

Ethyl (*S*)-2-(1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-3-oxo-3-phenylpropanoate (3ai). Product **3ai** was obtained according to the general procedure, using ethyl 3-oxo-3-phenylpropanoate **2i** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was subjected to flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) giving compound **3ai** as an inseparable mixture (56:44) of diastereomers. Yellow oil, (45 mg, 0.142 mmol, 95%). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.4, *J* = 1.3 Hz, 1H), 7.78 (dd, *J* = 8.4, *J* = 1.2 Hz, 1H), 7.57 – 7.51 (m, 2H), 7.43 – 7.35 (m, 4H), 7.33 – 7.22 (m, 3H), 7.17 (dt, *J* = 7.7, *J* = 1.2 Hz, 0.56H) (major diastereoisomer), 7.15 – 7.10 (m, 0.44H) (minor diastereoisomer), 6.97 (m, 0.56Hz) (major), 6.92 (br. s, 0.44H) (minor), 6.87 (t, *J* = 7.6 Hz, 0.44H) (minor), 6.74 (d, *J* = 7.8 Hz, 0.56H) (major), 6.70 (d, *J* = 7.8 Hz, 0.44H) (minor), 6.60 (br. s, 0.56H) (major), 5.02 (m, 1H), 4.98 (s, 0.56H) (major), 4.79 (m, 1H), 4.66 (s, 0.44H) (minor), 4.28 – 4.22 (m, 2H), 4.13 – 4.04 (m, 2H), 1.33 (s, 9H), 1.23 (t, *J* = 7.2 Hz, 1.32H) (minor), 1.06 (t, *J* = 7.1 Hz, 1.68H) (major) ppm.^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 191.6, 174.4, 174.2, 166.2, 165.9, 154.1, 153.7, 143.0, 142.7, 137.0, 136.3, 135.9, 135.9, 134.0, 133.6, 129.4, 129.2, 128.7,

128.7, 128.7, 128.5, 128.4, 127.7, 127.5, 127.5, 124.7, 124.2, 122.7, 122.6, 109.2, 109.2, 80.2, 62.4, 62.1, 56.6, 55.2, 44.4 , 44.3, 28.2, 13.8, 13.8 ppm. IR (ATR): 3421, 2976, 1713, 1612, 754, 733, 697 cm^{-1}. HPLC: Lux-Amylose-1 column, hexane/*iso*-propanol = 80:20, 1.0 mL/min, λ = 254 nm. Major diastereoisomer: t_r = 7.85 min (minor enantiomer), t_r = 26.56 min (major enantiomer) (er 84:16). Minor diastereoisomer: t_r = 9.25 min (minor enantiomer), t_r = 21.02 min (major enantiomer). (er 86:14). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{31}H_{32}N_2NaO_6$ 551.2158; Found: 551.2153.

Ethyl (*R*)-2-(1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-2-methyl-3-oxobutanoate (3aj). Product **3aj** was obtained according to the general procedure, using ethyl 2-methyl-3-oxobutanoate **2j** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was subjected to flash chromatography (hexane/ethyl acetate: 8:1 to 4:1) leading to compound **3aj** asan inseparable mixture (88:12) of diastereoisomers. Orange oil, (49 mg, 0.102 mmol, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.0 Hz, 3H), 7.33 – 7.27 (m, 2H), 7.23 (dt, *J* = 7.3, *J* = 3.8 Hz, 1H), 7.14 (dt, *J* = 7.7, *J* = 1.1 Hz, 1H), 6.99 – 6.90 (m, 1H), 6.90 (br. s, 0.12H) (minor diastereoisomer), 6.67 (d, *J* = 7.8 Hz, 1H), 6.61 (br. s, 0.88H) (major diastereoisomer), 4.98 (d, *J* = 15.5 Hz, 1H), 4.78 (d, *J* = 15.8 Hz, 1H), 4.31 (m, 1H), 4.25 – 4.18 (m, 1H), 2.32 (s, 0.36H) (minor), 2.09 (s, 2.64H) (major), 1.30-1.21 (m, 12H), 1.27 (t, *J* = 7.3 Hz, 2.64H) (major), 1.12 (t, *J* = 7.0 Hz, 0.36H) (minor) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 174.1, 169.8, 169.4, 153.9, 153.8, 144.2, 144.1, 138.2, 135.8, 129.2, 129.0, 128.6, 128.6, 127.9, 127.8, 127.6, 127.5, 127.5, 125.4, 124.6, 122.8, 122.6, 108.8, 108.8, 79.9, 65.1, 63.6, 62.4, 62.1, 44.6, 44.5, 29.3, 28.1, 16.1, 15.9, 13.8, 13.7. IR (ATR): 3421, 2980, 1713, 1612, 754, 729, 697 cm^{-1}. HPLC: Lux-Amylose-1 column, hexane/*iso*-propanol = 95:5, 1.0 mL/min, λ = 220 nm. Major diastereoisomer: t_r = 16.60 min (minor enantiomer), t_r = 32.94 min (major enantiomer) (er 87:13). Minor diastereoisomer: t_r = 22.60 min (minor enantiomer), t_r = 42.45 min (major enantiomer). (er 84:16). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{27}H_{32}N_2NaO_6$ 503.2158; Found: 503.2195.

Diethyl (*S*)-2-(1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)malonate (3ak). Product **3ak** was obtained according to the general procedure, using diethyl malonate **2k** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 4:1)

afforded compound **3ak** as yellow oil, (63 mg, 0.128 mmol, 85%). $[\alpha]_D^{25}$ = -11.3 (*c* = 0.9, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 (d, *J* = 7.6 Hz, 2H), 7.39 (m, *J* = 6.3 Hz, 1H), 7.35-7.30 (m, 2H), 7.26 (m, 1H), 7.17 (dt, *J* = 7.7 Hz, *J* = 1.3 Hz, 1H), 6.97 (dt, *J* = 7.6 Hz, *J* = 1.0 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 6.45 (s, 1H), 5.00 (d, *J* = 15,7 Hz, 1H), 4.86 (d, *J* = 16.1 Hz, 1H), 4.16 (m, 4H), 3.92 (s, 1H), 1.30 (s, 9H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$); 174.1, 166.8, 166.7, 153.9, 143.2, 135.7, 159.5, 128.9, 127.6, 127.5, 124.1, 122.6, 109.2, 80.4, 62.1(2C), 60.9, 55.6, 44.4, 28.1, 25.3, 13.9, 13.8 ppm. IR (ATR): 3417, 2980, 1717, 1612, 749, 697 cm^{-1}. HPLC: Lux-Amylose-1 column, hexane/*iso*-propanol = 90:10, 1.0 mL/min, λ = 220 nm, major enantiomer (*S*) t_r = 24.33 min, minor enantiomer (*R*), t_r = 34.67 min. (er 87:13). HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{27}H_{33}N_2O_7$ 497.2288; Found: 497.2282.

Ethyl (*R*)-1-(1-benzyl-3-((tert-butoxycarbonyl)amino)-2-oxoindolin-3-yl)-2-oxocyclopentane-1-carboxylate (3al). Product **3al** was obtained according to the general procedure, using ethyl 2-oxocyclopentane-1-carboxylate **2l** and catalyst **I** (2.5 mg, 0.0075 mmol). The crude reaction mixture subjected to flash chromatography (hexane/ethyl acetate: 4:1 to 2:1) giving compound **3al** as an inseparable mixture (68:32) of diastereoisomers. Colorless oil, (59 mg, 0.123 mmol, 82%). $[\alpha]_D^{25}$ = -13.9 (*c* = 0.8, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.27 (m, 5H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.06 (br. s, 0.69H) (major diastereoisomer), 7.01 (br. s, 0.31H) (minor diastereoisomer), 6.95 (t, *J* = 7.4 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 0.69H) (major), 6.68 (d, *J* = 7.5 Hz, 0.31H) (minor), 5.05 (m, 0.31H) (minor), 4.93 (m, 1.38H) (major), 4.75 (m, 0.31H) (minor), 4.41-4.24 (m, 2H), 2.48 (m, 0.31H) (minor), 2.37 – 2.31 (m, 1.69H) (major), 2.27 – 2.22 (m, 0.69H) (major), 1.93 (m, 0.31H) (minor), 1.89 – 1.60 (m, 3H), 1.31 (m, 12H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 217.4, 217.3, 210.4, 210.3, 174.7, 173.5, 153.8, 153.5, 144.0, 143.8, 135.9, 135.7, 129.4, 129.4, 128.6, 127.8, 127.6, 124.2, 122.8, 122.7, 109.1, 79.9, 62.8, 62.4, 44.5,44.5, 39.4, 39.2, 28.1, 19.5, 19.3, 13.9 ppm. IR (ATR): 3421, 2976, 1749, 1713, 1612, 754, 733, 697 cm^{-1}. HPLC: Lux-Cellulose-1 column, hexane/*iso*-propanol = 97:3, 0.5 mL/min, λ = 254 nm. Minor diastereoisomer: t_r = 28.38 min (major enantiomer), t_r = 33.33 min (minor enantiomer) (er 89:11). Major diastereoisomer: t_r = 29.90 min (major enantiomer), t_r = 37.08 min (minor

enantiomer). (er 93:7). HRMS (ESI-QTOF) m/z: $[M+Na]^+$ Calcd. for $C_{28}H_{32}N_2NaO_6$ 515.2158; Found: 515.2211.

General procedure for the preparation of pyrazole derivatives.

A solution of dicarbonyl derivative (0.15 mmol), hydrazine monohydrate (8 µL, 0.165 mmol, 1,1 equiv) in methanol (3.5 mL) was stirred at room temperature for 2 h. The reaction was monitored by TLC until consumption of the starting material. After solvent removal under reduced pressure, the crude mixture was purified by flash column chromatography on silica gel (hexane/ethyl acetate: 4:1 to 2:1) to afford the corresponding products.

tert-Butyl (R)-(1-benzyl-3-(3,5-dimethyl-1H-pyrazol-4-yl)-2-oxoindolin-3-yl)carbamate(4aa). Compound **4aa** was obtained according to general procedure using compound **3aa** (65 mg, 0.15 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 4:1 to 2:1) afforded compound **4aa** as colorless oil, (40 mg, 0.092 mmol, 61%). $[\alpha]_D^{25}$ = +101.6 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 (s, 1H), 7.39 (d, J = 6.7 Hz, 1H), 7.29 – 7.17 (m, 6H), 7.06 – 7.01 (m, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.70 (s, 1H), 5.10 (m, 1H), 4.66 (m, 1H), 1.99 (s, 6H), 1.28 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2, 154.0, 143.0, 135.8, 129.2, 128.7, 127.6, 127.2, 124.6, 122.7, 109.1, 44.0, 28.1, 12.8 ppm. IR (ATR): 3672, 3314, 1714, 1614, 1489, 1364, 749, 699 cm^{-1}. HPLC: Lux-i-Amylose-1 column, hexane/*iso*-propanol = 90:10, 1.0 mL/min, λ = 254 nm, t_r =32.73 min (major enantiomer), t_r = 20.14 (minminor enantiomer) (er >99:<1). HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{25}H_{29}N_4O_3$ 433.2241; Found 433.2234.

tert-Butyl (R)-(1-benzyl-3-(5-isopropyl-3-methyl-1H-pyrazol-4-yl)-2-oxoindolin-3-yl)carbamate(4ae). Compound **4ae** was obtained according to general procedureusing compound **3ae** (70 mg, 0.15 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 4:1 to 2:1) afforded compound **4ae** as colorless oil, (42 mg, 0.091 mmol, 61%). $[\alpha]_D^{25}$ = +217.0 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.40 (d, J = 7.1 Hz, 1H), 7.29 – 7.20 (m, 6H), 7.06 – 7.00 (m, 1H), 6.72 (d, J = 7.8 Hz, 1H), 5.55 (s, 1H), 5.08 (m, 1H), 4.67 (m, 1H), 2.88 (dt, J_1 = 13.8, J_2 = 6.9 Hz), 2.03 (s, 3H), 1.28 (s, 9H), 1.16 (d, J = 6.9 Hz, 3H), 1.11 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 153.8, 143.0, 135.7, 129.4, 128.7, 127.6, 127.3, 124.5, 122.7, 109.1, 44.1, 28.1, 25.4, 23.2, 23.0, 13.2 ppm. IR (ATR): 3272, 1708, 1612, 1487, 1366, 1253, 747, 730, 697,

cm^{-1}. HPLC: Lux-i-Amylose-1 column, hexane/*iso*- propanol = 90:10, 1.0 mL/min, λ = 254 nm, t_r =17.92 min (major enantiomer), t_r = 13.76 min (minor enantiomer), (er 95:5). HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{30}H_{31}N_4O_3$ 495.2398; Found 495.2391.

tert-Butyl (R)-(1-benzyl-3-(3-methyl-5-phenyl-1H-pyrazol-4-yl)-2-oxoindolin-3-yl)carbamate(4af). Compound **4ae** was obtained according to general procedureusing compound **3ae** (75 mg, 0.15 mmol). The crude reaction mixture was purified by flash column chromatography (hexane/ethyl acetate: 4:1 to 2:1) afforded compound **4ae** as colorless oil, (46 mg, 0.093 mmol, 62%). $[\alpha]_D^{25}$ = +126.8 (*c* = 0.2, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.56 (s, 2H), 7.41 – 7.37 (m, 2H), 7.31 (m, 3H), 7.26 (m, 4H), 7.11 (dt, J_1 = 7.8, J_2 = 1.2 Hz, 1H), 6.84 (t, J = 7.4 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 5.33 (s, 1H), 4.99 (m, 1H), 4.72 (m, 1H), 1.63 (s, 3H), 1.19 (s, 9H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.5, 153.4, 143.1, 135.9, 130.7, 130.4, 130.0, 129.2, 128.9, 128.8, 128.1, 127.7, 124.9, 122.9, 112.3, 109.0, 44.4, 28.1, 11.9 ppm. IR (ATR): 3239, 1717, 1612, 1487, 1366, 1244, 747, 697 cm^{-1}. HPLC: Lux-i-Amylose-1 column, hexane/*iso*- propanol = 90:10, 1.0 mL/min, λ = 254 nm, t_r =27.48 min (major), t_r = 18.42 min (minor), (er 93:7). HRMS (ESI-QTOF) m/z: $[M+H]^+$ Calcd. for $C_{27}H_{33}N_4O_3$ 461.2553; Found 461.2547.

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