Supporting Information for:

**Chiral Bisguanidine-Catalyzed Inverse-Electron-Demand Hetero-Diels—Alder
Reaction of Chalcones with Azlactones**

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A. General Information:

Reactions were carried out using commercial available reagents in oven-dried apparatus. Toluene, Et₂O and THF were dried and distilled from sodium benzophenone under nitrogen just before use. CH₂Cl₂ was dried over powdered CaH₂ and distilled under nitrogen just before use. EtOAc was purchased as analytical pure dried with K₂CO₃ and distilled. Azlatones were synthesized by the same procedure in the literature.¹ Melting points (m.p.) were measured on electrothermal digital melting point apparatus and were uncorrected. ¹H NMR spectra were recorded at 400 MHz or 600 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz), integration. ¹³C NMR data were collected at 100 MHz or 150 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel IA/IB/IC/OD-H in comparison with the authentic racemates. Optical rotations were reported as follows: $[\alpha]_D^{25} = (c: \text{g}/100 \text{ mL, in solvent})$. HRMS was recorded on a commercial apparatus (ESI Source, TOF).

B. Typical Procedure for Guanidine Preparation

2.5 M *n*-BuLi in *n*-hexane (4.2 eq., 2.5 mL, 6.3 mmol) was injected into a solution of (2*S*,2'*S*)-*N,N'*-((1*R*,2*S*)-1,2-diphenylethane-1,2-diyl)dipiperidine-2-carboxamide **A** (653.0 mg, 1.5 mmol) in THF (40 mL) dropwise over 10 mins under nitrogen atmosphere at -20 °C with well stirring. For additional 10 mins, a solution of *N,N'*-dicyclohexylcarbodiimide (2.2 eq., 700.0 mg, 3.3 mmol) in 10 mL THF was added dropwise in 10 mins. The reaction was allowed to warm to room temperature and detected by TLC. After 48 h, the mixture was evaporated under reduced pressure to get rid of THF, and the pH value of the mixture was brought into the range of 0-1 by the addition of 3 M HCl. The aqueous phase was extracted with CH₂Cl₂ (5 × 30 mL). The combined organic phase was washed with 3M HCl in brine, dried over anhydrous MgSO₄ and evaporated in vacuum and purified through flash chromatograph on silica gel (EtOAc: MeOH= 6:1, R_f 0.2 - 0.5) to produce **D**. The light yellow foam **D** in CH₂Cl₂ (16 mL) was added 4 M NaOH (15 mL) and stirred until the basification was finished (10 mins). The pH value of the mixture was kept in the range of 11-12. The aqueous phase was extracted with CH₂Cl₂ (5 × 20 mL). The combined organic phase was washed with 4 M NaOH, dried over anhydrous NaSO₄ and evaporated in vacuum. Finally a white solid **2c** was obtained. Then it was dissolved in CH₂Cl₂ and filtration through Celite to remove the silicone gel, concentrate to get a kind of white foam (762.0 mg, 60% yield). For other guanidine catalysts, this synthesis method could be applied.

C. Spectral characterization data for 1b, 2a-2f

1b: (C₃₃H₄₆N₄O₂) white solid; m.p. 100-101 °C, [α]_D²⁰ = -200.0 (c = 0.10, in CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 7.93 (t, *J* = 1.9 Hz, 1H), 7.27 – 7.13 (m, 3H), 4.47 (d, *J* = 2.9 Hz, 2H), 3.43 (d, *J* = 13.2 Hz, 2H) ppm, 3.07 – 2.89 (m, 4H), 2.82 (t, *J* = 12.3 Hz, 2H), 2.26 (d, *J* = 12.5 Hz, 2H), 2.03 – 0.93 (m, 56H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 170.66, 155.10, 138.84, 127.85, 113.29, 110.18, 56.36, 55.03, 52.80, 44.70, 34.93, 34.20, 34.06, 32.70, 25.27, 24.91, 24.63, 24.41, 24.26, 20.45 ppm. HRMS (ESI-TOF) calcd for C₃₃H₄₆N₄O₂ ([M+H]⁺) = 531.3699, Found 531.3698.

2a: (C₄₀H₇₀N₈O₂) white solid; m.p. 84-85 °C, [α]_D²⁰ = -2.35 (c = 0.34, in CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 4.07 (d, *J* = 13.5 Hz, 2H), 3.80 (dd, *J* = 19.6, 6.8 Hz, 2H), 3.71 (t, *J* = 11.2 Hz, 2H), 3.60 (s, 1H), 3.50 (dd, *J* = 11.1, 3.6 Hz, 2H), 3.06 (t, *J* = 11.6 Hz, 2H), 2.61 (tt, *J* = 10.5, 3.8 Hz, 1H),

2.08 – 0.95 (m, 56H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 172.92, 59.81, 52.92, 50.26, 44.37, 37.37, 36.82, 35.97, 35.83, 35.77, 29.69, 28.37, 27.37, 26.00, 25.69, 25.15, 24.65, 24.53, 23.08 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{40}\text{H}_{70}\text{N}_8\text{O}_2$ ($[\text{M}+\text{H}^+]$) = 695.5700, Found 695.5687.

2b: ($\text{C}_{44}\text{H}_{76}\text{N}_8\text{O}_2$) white solid; m.p. 101-103 $^\circ\text{C}$, $[\alpha]_{\text{D}}^{20} = -196.0$ ($c = 0.10$, in CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 4.25 (s, 2H), 3.72 – 3.53 (m, 2H), 3.40 (d, $J = 13.0$ Hz, 2H), 2.94 (dd, $J = 21.5, 9.9$ Hz, 4H), 2.76 (t, $J = 12.3$ Hz, 2H), 2.24 – 2.00 (m, 4H), 1.91 (dd, $J = 22.7, 12.6$ Hz, 4H), 1.83 – 0.81 (m, 56H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 172.70, 155.38, 56.65, 56.15, 53.76, 52.03, 45.30, 35.36, 34.91, 34.55, 34.17, 32.75, 26.25, 25.77, 25.66, 25.58, 25.39, 24.57, 21.66 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{44}\text{H}_{76}\text{N}_8\text{O}_2$ ($[\text{M}+\text{H}^+]$) = 749.6169, Found 749.6150.

2c: ($\text{C}_{52}\text{H}_{78}\text{N}_8\text{O}_2$) white solid; m.p. 211-213 $^\circ\text{C}$, $[\alpha]_{\text{D}}^{20} = -272.0$ ($c = 0.10$, in CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 10.38 (s, NH), 7.10 – 7.01 (m, 6H), 6.97 – 6.81 (m, 4H), 5.01 (s, 2H), 4.41 (s, 2H), 3.33 (d, $J = 12.9$ Hz, 2H), 2.96 (s, 4H), 2.41 (t, $J = 12.4$ Hz, 2H), 2.12 (d, $J = 12.4$ Hz, 2H), 1.94 (t, $J = 14.7$ Hz, 4H), 1.86 – 0.89 (m, 48H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 172.63, 155.72, 141.10, 128.02, 127.57, 126.50, 58.60, 56.46, 56.21, 53.88, 45.23, 35.63, 34.94, 34.68, 34.03, 26.08, 25.74, 25.66, 25.56, 25.44, 21.38 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{52}\text{H}_{78}\text{N}_8\text{O}_2$ ($[\text{M}+\text{H}^+]$) = 847.6362, Found 847.6342.

2d: ($\text{C}_{40}\text{H}_{62}\text{N}_8\text{O}_2$) white solid; m.p. 133-135 $^\circ\text{C}$, $[\alpha]_{\text{D}}^{20} = -312.0$ ($c = 0.10$, in CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 7.12 – 7.02 (m, 6H), 6.99 – 6.89 (m, 4H), 5.08 (s, 2H), 4.41 (d, $J = 3.3$ Hz, 2H), 3.49 – 3.28 (m, 6H), 2.53 – 2.40 (m, 2H), 2.23 – 2.12 (m, 2H), 1.76 – 1.60 (m, 2H), 1.59 – 1.06 (m, 34H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 172.58, 155.77, 140.65, 128.00, 127.69, 126.65, 58.61, 56.46, 47.48, 46.43, 45.10, 26.05, 25.61, 25.40, 24.81, 23.65, 23.55, 21.42 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{40}\text{H}_{62}\text{N}_8\text{O}_2$ ($[\text{M}+\text{H}^+]$) = 686.5074, Found 686.5067.

2e: ($\text{C}_{50}\text{H}_{74}\text{N}_8\text{O}_2$) white solid; m.p. 110-112 °C, $[\alpha]_{\text{D}}^{20} = -78.0$ ($c = 0.10$, in CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 7.11 (s, 10H), 5.27 (d, $J = 20.7$ Hz, 2H), 4.73 (s, 2H), 3.29 (d, $J = 5.5$ Hz, 4H), 2.94 (s, 4H), 2.29 – 0.60 (m, 52H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 172.65, 153.76, 139.92, 127.88, 127.70, 126.90, 59.96, 57.89, 49.71, 35.20, 25.55, 25.47, 25.32, 24.90 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{50}\text{H}_{74}\text{N}_8\text{O}_2$ ($[\text{M}+\text{H}^+]$) = 819.6013, Found 819.5997.

2f: ($\text{C}_{44}\text{H}_{70}\text{N}_8\text{O}_2$) white solid; m.p. 200-202 °C, $[\alpha]_{\text{D}}^{20} = -406.0$ ($c = 0.10$, in CH_2Cl_2); ^1H NMR (400 MHz, CDCl_3) δ 7.93 (t, $J = 1.9$ Hz, 1H), 7.27 – 7.13 (m, 3H), 4.47 (d, $J = 2.9$ Hz, 2H), 3.43 (d, $J = 13.2$ Hz, 2H), 3.07 – 2.89 (m, 4H), 2.82 (t, $J = 12.3$ Hz, 2H), 2.26 (d, $J = 12.5$ Hz, 2H), 2.03 – 0.93 (m, 56H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 170.66, 155.10, 138.84, 127.85, 113.29, 110.18, 56.36, 55.03, 52.80, 44.70, 34.93, 34.20, 34.06, 32.70, 25.27, 24.91, 24.63, 24.41, 24.26, 20.45 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{44}\text{H}_{70}\text{N}_8\text{O}_2$ ($[\text{M}+\text{H}^+]$) = 743.5700, Found 743.5698.

D. General Procedure for the Asymmetric Catalytic IEDDA Reaction

To a stirred solution of chalcone **3a** (41.6 mg, 2 equiv., 0.2 mmol) and guanidine catalyst **2c** (10 mol%, 8.5 mg, 0.01 mmol) in THF/ CHCl_3 (0.7 mL, 1:1, v/v) was added slowly azlactone **4a** (25.3 mg, 0.1 mmol) in 0.3 mL THF/ CHCl_3 (1:1, v/v) at -20 °C. After being stirred for 72 h and detected via TLC, The residue was directly purified by column chromatography on silica gel (pet/EtOAc = 15/1 to 10/1 as eluent) to afford pure **6a** and the mixture of **5a** and **6a'**, then the mixture were purified by column chromatography on silica gel for the second time ($\text{CH}_2\text{Cl}_2/\text{pet} = 1.5/1$, 2:1 as eluent) to give pure adduct **5a** (33.5 mg, 73%) and Michael addition product **6a'**.

General Procedure for Attempting to Transform Michael Addition Adduct **6** to HAD Product **5a**:

To a test tube of Michael addition adduct **6** (4.0 mg, 0.09 mmol) and guanidine catalyst **2c** (8.5 mg, 0.01 mmol) was added THF/ CHCl_3 (1.0 mL, 1:1, v/v) at -20 °C. After being stirred for 72 h and detected via TLC, No HAD Product **5a** was formed. To prove this exactly, after a flash filtration, then the residue was determined by HPLC, No HAD Product **5a** was found.

E. Optimization of Conditions

Table 1. Optimization of the Reaction Conditions^a

Reaction scheme showing the reaction of **3a** and **4a** to form **5a**, **6a**, and **6a'** using catalyst **2** (10 mol%) in THF.

entry	cat.	T (°C)	yield (%)		ee of 5a (%) ^d
			5a ^{b,c}	6a and 6a' ^b	
1	1a	0	45	5	-13
2	1b	0	40	7	-11
3	2a	0	30	20	25
4	2b	0	65	18	30
5	2c	0	61	13	82
6	2d	0	64	10	80
7	2e	0	56	16	60
8	2f	0	50	20	11
9 ^e	2d	-20	78	6	89
10 ^{e,f}	2d	-20	56	24	96
11 ^{e,g}	2d	-20	73	8	96
12 ^{e,g,h}	2d	-20	63	8	96

^a Unless otherwise noted, all of the reactions were carried out with guanidine (10% mol), **3a** (0.2 mmol), and **4a** (0.1 mmol), in THF (1.0 mL) for 48 h. ^b Isolated yield. ^c Only a single diastereomer of **5a** was obtained. ^d Determined by chiral HPLC analysis. ^e For 72 h. ^f CHCl₃ was used as solvent. ^g THF/CHCl₃ [1/1 (v/v)] was used as the solvent. ^h 5 mol% catalyst was used.

Full list of substrates

Table 2. Scope of the Asymmetric IEDDA Reaction of Chalcones^a

entry	R ¹	R ²	<i>t</i> (h)	yield (%) ^{b,c}	ee (%) ^d
1	Ph	Ph	72	73 (5a)	96
2	2-ClC ₆ H ₄	Ph	72	75 (5b)	90
3	3-ClC ₆ H ₄	Ph	72	78 (5c)	92
4 ^e	4-ClC ₆ H ₄	Ph	72	75 (5d)	94
5	3,4-Cl ₂ C ₆ H ₃	Ph	72	88 (5e)	89
6	4-FC ₆ H ₄	Ph	72	78 (5f)	94
7	4-BrC ₆ H ₄	Ph	72	80 (5g)	94
8	3-BrC ₆ H ₄	Ph	72	88 (5h)	93
9	3-MeC ₆ H ₄	Ph	84	65 (5i)	94
10	4-MeC ₆ H ₄	Ph	84	68 (5j)	95
11	3-PhOC ₆ H ₄	Ph	96	64 (5k)	98
12	4-PhC ₆ H ₄	Ph	72	68 (5l)	94
13	1-naphthyl	Ph	96	40 (5m)	90
14	2-naphthyl	Ph	72	70 (5n)	94
15		Ph	96	40 (5o)	99
16	4-pyridine	Ph	96	62 (5p)	90
17	Ph	4-FC ₆ H ₄	72	67 (5q)	92
18	Ph	4-BrC ₆ H ₄	72	65 (5r)	90
19	Ph	3-MeC ₆ H ₄	84	80 (5s)	95
20	Ph	4-MeC ₆ H ₄	84	73 (5t)	96
21	Ph	2-naphthyl	72	72 (5u)	94
22	Ph		96	50 (5v)	92
23	Ph	cinnamyl	72	70 (5w)	95
24	Ph	2-furyl	84	55 (5x)	91
25	Ph	2-thienyl	84	65 (5y)	92

^a All of the reactions were carried out with 10 mol% **2c**, **3** (0.2 mmol) and **4a** (0.1 mmol) in 1.0 mL of THF/CHCl₃ [1/1 (v/v)] at -20 °C for 72–96 h. ^b Isolated yield. ^c Only a single diastereomer was obtained. ^d Determined by chiral HPLC analysis. ^e The absolute configuration was (3*S*,4*R*), as determined by X-ray analysis.

Table 3. Scope of the Asymmetric IEDDA Reaction of Azlactones^a

entry	R ³	R ⁴	<i>t</i> (h)	yield (%) ^b	ee (%) ^c
1	2-ClC ₆ H ₄	Bn	72	76 (5z)	95
2	3-ClC ₆ H ₄	Bn	72	78 (5aa)	92
3	4-ClC ₆ H ₄	Bn	72	80 (5ab)	95
4	3-MeC ₆ H ₄	Bn	84	71 (5ac)	97
5	3-MeOC ₆ H ₄	Bn	96	68 (5ad)	93
6	Ph	CH ₃	84	76 (5ae)	92
7	Ph	MeS(CH ₂) ₂	84	78 (5af)	90
8 ^d	Ph	Bn	72	70 (5a)	93
9 ^e	Ph	Bn	72	70 (5a)	93

^a Unless otherwise noted, all of the reactions were carried out with 10 mol% **2c**, **3a** (0.2 mmol) and **4** (0.1 mmol) in 1.0 mL of THF/CHCl₃ [1/1 (v/v)] at -20 °C for 72–96 h. ^b Isolated yield. ^c Determined by chiral HPLC analysis. ^d The reaction was carried out on a 5 mmol scale. ^e The catalyst was recovered in 85% yield and reused on a 4.25 mmol scale of **4a**.

F. Spectral Characterization Data and HPLC Conditions for IEDDA Products

N-(3-benzyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5a)

($C_{31}H_{25}NO_3$) a white solid; 73% yield, 96% ee. m.p. 147-149 °C, $[\alpha]_D^{20} = 214.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.8 min (minor) and 10.4 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, $J = 6.9$ Hz, 2H), 7.54 – 7.38 (m, 4H), 7.38 – 7.15 (m, 12H), 7.15 – 7.06 (m, 2H), 6.68 (s, 1H), 6.22 (d, $J = 6.8$ Hz, 1H), 4.98 (d, $J = 6.8$ Hz, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.51 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.83, 168.01, 149.12, 137.04, 135.25, 135.01, 131.45, 131.34, 130.05, 129.68, 128.86, 128.75, 128.54, 128.40, 128.26, 127.98, 127.39, 126.61, 124.71, 103.95, 65.30, 47.01, 38.83 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{25}NO_3$ ($[M+H]^+$) = 460.1913, Found 460.1918.

N-(3-benzyl-4-(2-chlorophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5b)

($C_{31}H_{24}ClNO_3$) a white solid; 75% yield, 90% ee. m.p. 177-179 °C, $[\alpha]_D^{20} = 154.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.6 min (minor) and 9.7 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, $J = 6.7$ Hz, 2H), 7.49 – 7.36 (m, 6H), 7.30 (t, $J = 7.7$ Hz, 3H), 7.24 (dd, $J = 6.6, 3.3$ Hz, 3H), 7.18 – 7.03 (m, 5H), 6.91 (s, 1H), 6.14 (s, 1H), 5.55 (s, 1H), 4.26 (d, $J = 13.8$ Hz, 1H), 3.49 (d, $J = 13.7$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.34, 166.95, 148.16, 135.68, 134.83, 134.47, 134.11, 131.43, 130.21, 129.62, 128.75, 128.59, 128.49, 128.38, 127.51, 127.11, 126.61, 124.73, 62.92, 39.91 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}ClNO_3$ ($[M+H]^+$) = 494.1523, Found 494.1513.

***N*-(3-benzyl-4-(3-chlorophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5c)**

($C_{31}H_{24}ClNO_3$) a white solid; 78% yield, 92% ee. m.p. 169-171 °C, $[\alpha]_D^{20} = 105.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.6 min (minor) and 9.6 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, $J = 6.8$ Hz, 2H), 7.47 (ddd, $J = 24.2, 12.3, 4.9$ Hz, 6H), 7.33 (t, $J = 7.6$ Hz, 2H), 7.30 – 7.19 (m, 4H), 7.19 – 7.06 (m, 5H), 6.70 (s, 1H), 6.18 (d, $J = 6.8$ Hz, 1H), 4.98 (d, $J = 6.8$ Hz, 1H), 4.24 (d, $J = 13.9$ Hz, 1H), 3.49 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.43, 168.13, 149.60, 139.08, 135.04, 134.76, 134.56, 131.61, 131.09, 130.05, 129.95, 129.89, 128.92, 128.63, 128.53, 128.45, 128.26, 127.50, 126.61, 126.33, 124.78, 103.08, 65.09, 46.58, 38.83 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}ClNO_3$ ($[M+H]^+$) = 494.1523, Found 494.1517.

***N*-(3-benzyl-4-(4-chlorophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5d)**

(**C₃₁H₂₄ClNO₃**) a white solid; 75% yield, 94% ee. m.p. 167-169 °C, $[\alpha]_D^{20} = 266.0$ (c = 0.20, in CH₂Cl₂), HPLC DAICEL CHIRALCEL ODH, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.5 min (minor) and 7.6 min (major); ¹H NMR (400 MHz, CDCl₃) δ 7.80 (d, *J* = 7.1 Hz, 2H), 7.55 – 7.42 (m, 4H), 7.40 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.14 (m, 7H), 7.09 (dd, *J* = 6.0, 2.6 Hz, 2H), 6.72 (s, 1H), 6.19 (d, *J* = 6.8 Hz, 1H), 4.99 (d, *J* = 6.8 Hz, 1H), 4.22 (d, *J* = 13.9 Hz, 1H), 3.49 (d, *J* = 13.9 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 168.59, 167.93, 149.41, 135.55, 134.89, 134.78, 133.80, 131.69, 131.10, 130.02, 129.85, 129.65, 128.91, 128.87, 128.67, 128.45, 127.48, 126.62, 124.73, 103.43, 65.15, 46.30, 38.78 ppm. HRMS (ESI-TOF) calcd for C₃₁H₂₄ClNO₃ ([M+H⁺]) = 494.1523, Found 494.1519.

***N*-(3-benzyl-4-(3,4-dichlorophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5e)**

(**C₃₁H₂₃Cl₂NO₃**) a white solid; 88% yield, 89% ee. m.p. 149-151 °C, $[\alpha]_D^{20} = 188.0$ (c = 0.10, in CH₂Cl₂), HPLC DAICEL CHIRALCEL IC, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.7 min (minor) and 8.0 min (major); ¹H NMR (600 MHz, CDCl₃) δ 7.81 (d, *J* = 7.4 Hz, 2H), 7.44 (m, Hz, 10H), 7.25 (dd, *J* = 15.1, 8.5 Hz, 3H), 7.13 – 7.06 (m, 3H), 6.74 (s, 1H), 6.16 (d, *J* = 6.8 Hz, 1H), 4.99 (d, *J* = 6.8 Hz, 1H), 4.20 (d, *J* = 14.0 Hz, 1H), 3.48 (d, *J* = 14.0 Hz, 1H) ppm. ¹³C NMR (151 MHz, CDCl₃) δ 168.26, 168.13, 149.83, 137.26, 134.76, 134.60, 132.78, 132.11, 131.82, 130.89, 130.61, 130.39, 130.04, 128.98, 128.75, 128.51, 127.60, 127.51, 126.64, 124.80, 102.67, 45.98, 38.78 ppm. HRMS (ESI-TOF) calcd for C₃₁H₂₃Cl₂NO₃ ([M+H⁺]) = 528.1133, Found 528.1136.

***N*-(3-benzyl-4-(4-fluorophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5f)**

($C_{31}H_{24}FNO_3$) a white solid; 78% yield, 94% ee. m.p. 159-161 °C, $[\alpha]_D^{20} = 184.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IC, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.2 min (minor) and 9.3 min (major); 1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, $J = 7.5$ Hz, 2H), 7.53 – 7.03 (m, 15H), 6.89 (t, $J = 8.4$ Hz, 2H), 6.71 (s, 1H), 6.20 (d, $J = 6.8$ Hz, 1H), 4.99 (d, $J = 6.7$ Hz, 1H), 4.23 (d, $J = 14.0$ Hz, 1H), 3.49 (d, $J = 14.0$ Hz, 1H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.71, 167.96, 163.14, 161.51, 149.20, 134.97, 134.86, 132.75, 132.73, 131.66, 131.15, 130.02, 129.96, 129.90, 129.82, 128.92, 128.66, 128.45, 127.47, 126.60, 124.72, 115.69, 115.55, 103.72, 65.32, 46.16, 38.77 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}FNO_3$ ($[M+H]^+$) = 478.1818, Found 478.1822.

***N*-(3-benzyl-4-(4-bromophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5g)**

(C₃₁H₂₄BrNO₃) a white solid; 80% yield, 94% ee. m.p. 163-164 °C, $[\alpha]_D^{20} = 164.0$

(c = 0.20, in CH₂Cl₂), HPLC DAICEL CHIRALCEL IC, 2-propanol/*n*-hexane =

10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 5.3 min (minor) and 7.3

min (major); ¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.52 –

7.42 (m, 4H), 7.39 (t, *J* = 4.2 Hz, 2H), 7.37 – 7.29 (m, 4H), 7.26 – 7.10 (m, 5H),

7.08 (dt, *J* = 4.3, 3.3 Hz, 2H), 6.71 (s, 1H), 6.17 (d, *J* = 6.8 Hz, 1H), 4.97 (d, *J* = 6.8 Hz, 1H), 4.21 (d, *J*

= 13.9 Hz, 1H), 3.48 (d, *J* = 13.9 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 168.57, 167.95, 149.44,

136.08, 134.87, 134.77, 131.83, 131.71, 131.08, 130.02, 129.99, 129.87, 128.92, 128.68, 128.46, 127.50,

126.64, 124.73, 121.97, 103.35, 65.09, 46.37, 38.78 ppm. HRMS (ESI-TOF) calcd for C₃₁H₂₄BrNO₃

([M+Na⁺]) = 560.0837, Found 560.0828.

***N*-(3-benzyl-4-(3-bromophenyl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5h)**

($C_{31}H_{24}BrNO_3$) a white solid; 88% yield, 93% ee. m.p. 160-162 °C, $[\alpha]_D^{20} = 100.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 7.6 min (minor) and 8.7 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 2H), 7.54 – 7.04 (m, 17H), 6.70 (s, 1H), 6.18 (d, $J = 6.8$ Hz, 1H), 4.97 (d, $J = 6.8$ Hz, 1H), 4.24 (d, $J = 13.9$ Hz, 1H), 3.48 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.41, 168.18, 149.62, 139.31, 135.03, 134.76, 131.63, 131.51, 131.21, 131.06, 130.26, 130.06, 129.91, 128.93, 128.65, 128.47, 127.52, 126.70, 126.64, 124.78, 122.76, 103.04, 65.12, 46.53, 38.80 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}BrNO_3$ ($[M+Na^+]$) = 560.0837, Found 560.0828.

***N*-(3-benzyl-2-oxo-6-phenyl-4-*m*-tolyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5i)**

($C_{32}H_{27}NO_3$) a white solid; 65% yield, 94% ee. m.p. 142-144 °C, $[\alpha]_D^{20} = 260.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 5.9 min (minor) and 7.1 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.77 (m, 2H), 7.53 – 7.39 (m, 4H), 7.33 (dt, $J = 24.1, 7.4$ Hz, 4H), 7.26 – 7.16 (m, 3H), 7.15 – 6.94 (m, 6H), 6.65 (s, 1H), 6.20 (d, $J = 6.9$ Hz, 1H), 4.95 – 4.89 (m, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.49 (d, $J = 13.9$ Hz, 1H), 2.18 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.83, 168.09, 149.11, 138.39, 136.79, 135.36, 135.08, 131.43, 131.36, 130.06, 129.64, 129.05, 128.87, 128.76, 128.64, 128.53, 128.39, 127.37, 126.60, 125.17, 124.69, 103.95, 65.37, 46.81, 38.75, 21.37 ppm. HRMS (ESI-TOF) calcd for $C_{32}H_{27}NO_3$ ($[M+Na]^+$) = 496.1889, Found 496.1882.

***N*-(3-benzyl-2-oxo-6-phenyl-4-*p*-tolyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5j)**

($C_{32}H_{27}NO_3$) a white solid; 68% yield, 95% ee. m.p. 151-152 °C, $[\alpha]_D^{20} = 128.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 19.1 min (major) and 23.1 min (minor); 1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, $J = 8.2$ Hz, 2H), 7.46 – 7.39 (m, 1H), 7.38 – 7.15 (m, 14H), 7.11 (dd, $J = 6.6, 2.9$ Hz, 2H), 6.68 (s, 1H), 6.17 (d, $J = 6.8$ Hz, 1H), 4.96 (d, $J = 6.9$ Hz, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.51 (d, $J = 13.9$ Hz, 1H), 2.44 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.89, 167.91, 149.02, 137.66, 135.32, 135.10, 133.83, 131.40, 130.04, 129.59, 129.40, 128.83, 128.51, 128.36, 128.15, 127.34, 126.66, 124.68, 104.17, 65.38, 46.60, 38.79, 21.01 ppm. HRMS (ESI-TOF) calcd for $C_{32}H_{27}NO_3$ ($[M+H]^+$) = 474.2069, Found 474.2065.

***N*-(3-benzyl-2-oxo-4-(3-phenoxyphenyl)-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide(5k)**

($C_{37}H_{29}NO_4$) a white solid; 64% yield, 98% ee. m.p. 127-129 °C, $[\alpha]_D^{20} = 200.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 15/85, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.3 min (minor) and 6.8 min (major); 1H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, $J = 7.9$ Hz, 2H), 7.54 – 7.02 (m, 16H), 6.99 – 6.94 (m, 2H), 6.82 – 6.78 (m, 1H), 6.78 – 6.73 (m, 3H), 6.19 (d, $J = 6.8$ Hz, 1H), 4.94 (d, $J = 6.8$ Hz, 1H), 4.23 (d, $J = 14.0$ Hz, 1H), 3.48 (d, $J = 14.0$ Hz, 1H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.69, 167.78, 157.50, 156.61, 149.25, 139.07, 135.04, 134.89, 131.61, 131.23, 130.05, 130.03, 129.74, 129.68, 128.85, 128.60, 128.41,

127.42, 126.74, 124.76, 123.41, 122.61, 118.98, 118.93, 118.13, 103.62, 65.14, 46.83, 38.81 ppm.
HRMS (ESI-TOF) calcd for C₃₇H₂₉NO₄ ([M+Na⁺]) = 574.1994, Found 574.1990.

***N*-(3-benzyl-4-(biphenyl-4-yl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5l)**

(C₃₇H₂₉NO₃) a white solid; 68% yield, 94% ee. m.p. 105-107 °C, $[\alpha]_D^{20} = 210.0$ (c = 0.20, in CH₂Cl₂), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 10.3 min (major) and 13.4 min(minor); ¹H NMR (400 MHz, CDCl₃) δ 7.82 (dd, *J* = 9.5, 2.6 Hz, 2H), 7.53 – 7.18 (m, 20H), 7.12 (dd, *J* = 6.6, 2.8 Hz, 2H), 6.73 (s, 1H), 6.25 (d, *J* = 6.8 Hz, 1H), 5.06 – 5.02 (m, 1H), 4.29 (d, *J* = 13.9 Hz, 1H), 3.53 (d, *J* = 13.8 Hz, 1H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 168.86, 168.11, 149.23, 140.80, 140.47, 136.01, 135.22, 135.00, 131.54, 131.31, 130.08, 129.74, 128.91, 128.78, 128.72, 128.60, 128.44, 127.42, 127.00, 126.67, 124.73, 103.86, 65.35, 46.62, 38.83 ppm. HRMS (ESI-TOF) calcd for C₃₇H₂₉NO₃ ([M+Na⁺]) = 558.2045, Found 558.2031.

***N*-(3-benzyl-4-(naphthalen-1-yl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5m)**

($C_{35}H_{27}NO_3$) a white solid, 40% yield, 90% ee. m.p. 189-190 °C, $[\alpha]_D^{20} = 97.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.9 min (minor) and 10.2 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, $J = 8.5$ Hz, 1H), 7.77 (dd, $J = 10.8, 4.4$ Hz, 3H), 7.72 – 7.55 (m, 2H), 7.50 – 7.20 (m, 10H), 7.21 – 7.04 (m, 6H), 6.65 (s, 1H), 6.29 (d, $J = 6.8$ Hz, 1H), 5.82 (d, $J = 6.6$ Hz, 1H), 4.52 (d, $J = 13.8$ Hz, 1H), 3.68 (d, $J = 13.8$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.40, 167.73, 148.55, 135.03, 134.83, 133.99, 131.53, 131.43, 131.15, 130.16, 129.60, 128.82, 128.67, 128.41, 128.34, 128.30, 127.46, 126.37, 126.22, 125.80, 125.40, 124.81, 124.66, 124.04, 104.81, 64.72, 42.33, 39.02 ppm. HRMS (ESI-TOF) calcd for $C_{35}H_{27}NO_3$ ($[M+H]^+$) = 510.2069, Found 510.2062.

***N*-(3-benzyl-4-(naphthalen-2-yl)-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5n)**

($C_{35}H_{27}NO_3$) a white solid, 70% yield, 94% ee. m.p. 205-207 °C, $[\alpha]_D^{20} = 206.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 9.6 min (minor) and 11.7 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.03 – 7.77 (m, 4H), 7.62 – 7.53 (m, 2H), 7.38 (ddd, $J = 27.2$, 14.7, 7.4 Hz, 6H), 7.28 – 7.11 (m, 9H), 6.74 (s, 1H), 6.37 (d, $J = 6.9$ Hz, 1H), 5.05 (d, $J = 6.9$ Hz, 1H), 4.32 (d, $J = 13.9$ Hz, 1H), 3.56 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.91, 168.04, 149.08, 137.08, 135.25, 135.01, 133.72, 133.18, 131.48, 130.09, 128.79, 128.73, 128.69, 128.56, 128.43, 128.30, 128.02, 127.77, 127.41, 127.12, 126.92, 126.63, 124.25, 121.91, 104.49, 65.38, 47.16, 38.93 ppm. HRMS (ESI-TOF) calcd for $C_{35}H_{27}NO_3$ ($[M+H]^+$) = 510.2069, Found 510.2071.

***N*-(4-(benzo[*d*][1,3]dioxol-5-yl)-3-benzyl-2-oxo-6-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide**

(5o)

($C_{32}H_{25}NO_5$) a white solid, 40% yield, 99% ee. m.p. 145-146 °C, $[\alpha]_D^{20} = 187.07$ ($c = 0.294$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 32.4 min (major) and 105.0 min (minor); 1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J = 6.9$ Hz, 2H), 7.56 – 7.42 (m, 6H), 7.37 (t, $J = 7.6$ Hz, 2H), 7.25 (dd, $J = 11.1, 7.6$ Hz, 3H), 7.17 – 7.08 (m, 2H), 6.84 – 6.72 (m, 3H), 6.65 (d, $J = 8.0$ Hz, 1H), 6.22 (d, $J = 6.8$ Hz, 1H), 5.88 (d, $J = 13.3$ Hz, 2H), 4.93 (d, $J = 6.8$ Hz, 1H), 4.25 (d, $J = 13.9$ Hz, 1H), 3.49 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.77, 167.97, 149.05, 147.86, 147.21, 135.24, 135.00, 131.51, 131.27, 130.49, 130.03, 129.69, 128.86, 128.59, 128.39, 127.39, 126.67, 124.70, 121.95, 108.38, 108.32, 104.01, 101.07, 65.44, 46.61, 38.75 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{25}NO_3$ ($[M+Na]^+$) = 526.1630, Found 526.1636.

***N*-(3-benzyl-2-oxo-6-phenyl-4-(pyridin-4-yl)-3,4-dihydro-2H-pyran-3-yl)benzamide (5p)**

($C_{30}H_{24}N_2O_3$) a white solid, 62% yield, 90% ee. m.p. 211-212 °C, $[\alpha]_D^{20} = 200.0$ ($c = 0.15$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 15/85, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 16.7 min (major) and 29.8min (minor); 1H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, $J = 5.6$ Hz, 2H), 7.74 (dd, $J = 7.7, 1.8$ Hz, 2H), 7.49 – 7.36 (m, 4H), 7.30 (dt, $J = 24.4, 7.4$ Hz, 4H), 7.21 – 7.11 (m, 5H), 7.02 (dd, $J = 6.5, 3.0$ Hz, 2H), 6.68 (s, 1H), 6.10 (d,

$J = 6.8$ Hz, 1H), 4.97 (d, $J = 6.8$ Hz, 1H), 4.16 (d, $J = 13.9$ Hz, 1H), 3.44 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 167.19, 166.96, 149.11, 145.42, 133.48, 133.36, 130.84, 129.79, 129.07, 128.98, 127.93, 127.69, 127.47, 126.59, 125.53, 123.77, 122.28, 101.53, 101.12, 63.45, 45.25, 37.81, 17.10 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{30}\text{H}_{24}\text{N}_2\text{O}_3$ ($[\text{M}+\text{H}^+]$) = 461.1865, Found 461.1860.

***N*-(3-benzyl-6-(4-fluorophenyl)-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5q)**

($\text{C}_{31}\text{H}_{24}\text{FNO}_3$) a white solid, 67% yield, 92% ee. m.p. 110-111 °C, $[\alpha]_{\text{D}}^{20} = 212.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 9.3 min (minor) and 11.4 min (major); ^1H NMR (400 MHz, CDCl_3) δ 7.81 – 7.75 (m, 2H), 7.46 – 7.38 (m, 1H), 7.37 – 7.27 (m, 4H), 7.27 – 7.06 (m, 12H), 6.67 (s, 1H), 6.14 (d, $J = 6.8$ Hz, 1H), 4.97 (d, $J = 6.8$ Hz, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.48 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 168.69, 168.01, 164.80, 162.31, 148.28, 136.96, 135.18, 134.91, 131.50, 130.02, 128.78, 128.55, 128.43, 128.21, 128.03, 127.44, 126.75, 126.67, 126.60, 116.07, 115.85, 103.68, 103.67, 65.24, 47.00, 38.86 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{31}\text{H}_{24}\text{FNO}_3$ ($[\text{M}+\text{H}^+]$) = 478.1818, Found 478.1830.

***N*-(3-benzyl-6-(4-bromophenyl)-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5r)**

($C_{31}H_{24}BrNO_3$) a white solid, 65% yield, 90% ee. m.p. 127-129 °C, $[\alpha]_D^{20} = 182.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.8 min (minor) and 12.4 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, $J = 21.4, 8.7$ Hz, 4H), 7.45 – 7.37 (m, 1H), 7.32 (dt, $J = 15.0, 7.4$ Hz, 4H), 7.26 – 7.03 (m, 10H), 6.66 (s, 1H), 6.22 (d, $J = 6.8$ Hz, 1H), 4.97 (d, $J = 6.8$ Hz, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.46 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.57, 168.01, 148.23, 136.77, 135.14, 134.85, 132.08, 131.52, 130.22, 130.01, 128.81, 128.57, 128.45, 128.21, 128.08, 127.47, 126.60, 126.22, 123.93, 104.51, 65.23, 47.05, 38.87 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}BrNO_3$ ($[M+Na^+]$) = 560.0837, Found 560.0825.

***N*-(3-benzyl-2-oxo-4-phenyl-6-*m*-tolyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5s)**

(C₃₂H₂₇NO₃) a white solid; 80% yield, 95% ee. m.p. 154-155 °C, $[\alpha]_D^{20} = 242.0$ ($c = 0.20$, in CH₂Cl₂), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 7.4 min (minor) and 8.3 min (major); ¹H NMR (400 MHz, CDCl₃) δ 7.65 – 7.57 (m, 2H), 7.36 (ddd, $J = 21.6, 15.4, 7.2$ Hz, 5H), 7.26 (d, $J = 9.4$ Hz, 4H), 7.18 (dt, $J = 13.1, 3.4$ Hz, 6H), 7.14 – 7.07 (m, 2H), 6.68 (s, 1H), 6.20 (d, $J = 6.8$ Hz, 1H), 4.97 (d, $J = 6.8$ Hz, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.51 (d, $J = 13.9$ Hz, 1H), 2.44 (s, 3H) ppm. ¹³C NMR (101 MHz, CDCl₃) δ 168.91, 168.01, 149.23, 138.62, 137.09, 135.26, 135.03, 131.44, 131.27, 130.45, 130.06, 128.76, 128.73, 128.53, 128.39, 128.26, 127.95, 127.37, 126.61, 125.34, 121.89, 103.81, 65.30, 47.02, 38.84, 21.54 ppm. HRMS (ESI-TOF) calcd for C₃₂H₂₇NO₃ ($[M+H]^+$) = 474.2069, Found 474.2062.

***N*-(3-benzyl-2-oxo-4-phenyl-6-*m*-tolyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5t)**

(C₃₂H₂₇NO₃) a white solid; 73% yield, 96% ee. m.p. 154-155 °C, $[\alpha]_D^{20} = 240.0$ ($c = 0.20$, in CH₂Cl₂), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 9.3 min (minor) and 11.6 min (major); ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, $J = 8.2$ Hz, 2H), 7.46 – 7.38 (m, 1H), 7.37 –

7.14 (m, 14H), 7.10 (dd, $J = 6.5, 2.8$ Hz, 2H), 6.68 (s, 1H), 6.16 (d, $J = 6.8$ Hz, 1H), 4.96 (d, $J = 6.8$ Hz, 1H), 4.26 (d, $J = 13.9$ Hz, 1H), 3.50 (d, $J = 13.8$ Hz, 1H), 2.42 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 168.93, 168.00, 149.21, 139.86, 137.17, 135.28, 135.06, 131.44, 130.06, 129.54, 128.72, 128.53, 128.38, 128.26, 127.92, 127.36, 126.61, 124.64, 103.00, 65.33, 46.94, 38.78, 21.37 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{32}\text{H}_{27}\text{NO}_3$ ($[\text{M}+\text{H}^+]$) = 474.2069, Found 474.2059.

***N*-(3-benzyl-6-(naphthalen-2-yl)-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5u)**

($\text{C}_{35}\text{H}_{27}\text{NO}_3$) a white solid, 72% yield, 94% ee. m.p. 226-227 °C, $[\alpha]_{\text{D}}^{20} = 301.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 11.8 min (minor) and 14.1min (major); ^1H NMR (400 MHz, CDCl_3) δ 8.36 (s, 1H), 8.01 – 7.85 (m, 3H), 7.79 (dd, $J = 8.7, 1.8$ Hz, 1H), 7.62 – 7.51 (m, 2H), 7.33 (m, 7H), 7.27 – 7.09 (m, 8H), 6.72 (s, 1H), 6.36 (d, $J = 6.9$ Hz, 1H), 5.03 (d, $J = 6.9$ Hz, 1H), 4.30 (d, $J = 13.9$ Hz, 1H), 3.55 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 167.91, 167.03, 148.08, 136.08, 134.25, 134.01, 132.72, 132.18, 130.48, 129.08, 127.79, 127.73, 127.69, 127.55, 127.42, 127.30, 127.01, 126.76, 126.41, 126.12, 125.92, 125.63, 123.25, 120.91, 103.49, 64.37, 46.15, 37.93 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{35}\text{H}_{27}\text{NO}_3$ ($[\text{M}+\text{Na}^+]$) = 459.1834, Found 325.1031.

***N*-(6-(benzo[d][1,3]dioxol-5-yl)-3-benzyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5v)**

($C_{32}H_{25}NO_5$) a white solid, 50% yield, 92% ee. m.p. 122-123°C, $[\alpha]_D^{20} = 182.00$ ($c = 0.08$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.2 min (minor) and 10.1min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.42 (t, $J = 7.0$ Hz, 1H), 7.37 – 7.15 (m, 15H), 7.14 – 7.05 (m, 2H), 6.91 (d, $J = 8.2$ Hz, 1H), 6.66 (s, 1H), 6.05 (d, $J = 4.4$ Hz, 2H), 4.94 (d, $J = 6.9$ Hz, 1H), 4.26 (d, $J = 13.9$ Hz, 1H), 3.48 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.77, 168.00, 148.91, 148.79, 148.28, 137.17, 135.24, 135.01, 131.45, 130.04, 128.72, 128.53, 128.39, 128.22, 127.93, 127.38, 126.60, 125.49, 119.08, 108.53, 105.24, 102.56, 101.60, 65.28, 46.91, 38.79 ppm. HRMS (ESI-TOF) calcd for $C_{32}H_{25}NO_5$ ($[M+Na]^+$) = 526.1630, Found 526.1599.

(E)-N-(3-benzyl-2-oxo-4-phenyl-6-styryl-3,4-dihydro-2H-pyran-3-yl)benzamide (5w)

($C_{33}H_{27}NO_3$) a white solid, 70% yield, 95% ee. m.p. 137-139°C, $[\alpha]_D^{20} = 358.0$ (c = 0.20, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90 flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.8 min (minor) and 12.6 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, $J = 7.4$ Hz, 2H), 7.40 (td, $J = 7.3, 4.0$ Hz, 3H), 7.36 – 7.26 (m, 5H), 7.26 – 7.08 (m, 10H), 6.72 – 6.60 (m, 2H), 5.76 (d, $J = 6.8$ Hz, 1H), 4.92 (d, $J = 6.8$ Hz, 1H), 4.26 (d, $J = 13.9$ Hz, 1H), 3.45 (d, $J = 13.8$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.69, 167.99, 148.52, 137.14, 135.89, 135.23, 135.00, 131.48, 130.73, 130.08, 128.92, 128.77, 128.71, 128.55, 128.43, 128.24, 127.98, 127.42, 127.04, 126.62, 119.09, 108.41, 65.49, 47.23, 38.97 ppm. HRMS (ESI-TOF) calcd for $C_{33}H_{27}NO_3$ ($[M+H]^+$) = 486.2069, Found 486.2077.

N-(3-benzyl-6-(furan-2-yl)-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-3-yl)benzamide(5x)

(**C₂₉H₂₃NO₄**) a white solid, 55% yield, 91% ee. m.p. 187-189 °C, $[\alpha]_D^{20} = 201.59$ ($c = 0.126$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 3/97, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 10.8 min (major) and 11.9 min (minor); ^1H NMR (600 MHz, CDCl_3) δ 7.50 (d, $J = 3.0$ Hz, 1H), 7.45 – 7.37 (m, 2H), 7.32 (dt, $J = 14.9, 7.4$ Hz, 4H), 7.28 – 7.16 (m, 8H), 7.15 – 7.07 (m, 3H), 6.65 (s, 1H), 6.06 (d, $J = 6.8$ Hz, 1H), 4.95 (d, $J = 6.8$ Hz, 1H), 4.28 (d, $J = 14.0$ Hz, 1H), 3.51 (d, $J = 14.0$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 168.33, 167.94, 145.10, 137.04, 135.21, 134.91, 134.78, 131.43, 130.06, 128.73, 128.51, 128.38, 128.23, 127.97, 127.84, 127.38, 126.58, 126.48, 125.19, 102.94, 65.42, 47.07, 38.97 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{29}\text{H}_{23}\text{NO}_4$ ($[\text{M}+\text{H}^+]$) = 450.1705, Found 450.1698.

***N*-(3-benzyl-2-oxo-4-phenyl-6-(thiophen-2-yl)-3,4-dihydro-2H-pyran-3-yl)benzamide (5y)**

(**C₂₉H₂₃NO₃S**) a white solid, 65% yield, 92% ee. m.p. 120-121 °C, $[\alpha]_D^{20} = 164.00$ ($c = 0.08$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.8 min (minor) and 7.8 min (major); ^1H NMR (400 MHz, CDCl_3) δ 7.84 – 7.79 (m, 2H), 7.56 – 7.43 (m, 6H), 7.37 (t, $J = 7.6$ Hz, 2H), 7.28 – 7.19 (m, 3H), 7.17 – 7.05 (m, 3H), 6.96 (d, $J = 3.5$ Hz, 1H), 6.86 (dd, $J = 4.9, 3.8$ Hz, 1H), 6.81 (s, 1H), 6.29 (d, $J = 6.9$ Hz, 1H), 5.36 (d, $J = 6.9$ Hz, 1H), 4.20 (d, $J = 13.9$ Hz, 1H), 3.49 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 168.34, 168.01, 149.24, 139.36, 135.11, 134.93, 131.65, 131.21, 130.03, 129.84, 128.89, 128.63, 128.43, 127.44, 127.02, 126.93, 126.83, 125.56, 124.83, 103.81, 77.37,

77.25, 77.05, 76.73, 65.85, 41.40, 38.53 ppm. HRMS (ESI-TOF) calcd for $C_{29}H_{23}NO_3S$ ($[M+H]^+$) = 466.1477, Found 466.1475.

***N*-(3-benzyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)-2-chlorobenzamide (5z)**

($C_{31}H_{24}ClNO_3$) a white solid; 76% yield, 95% ee. m.p. 150-151°C, $[\alpha]_D^{20}$ = 150.0 ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.5 min (minor) and 7.8 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.77 (m, 2H), 7.51 – 7.41 (m, 3H), 7.32 – 7.19 (m, 12H), 7.09 (td, $J = 7.5, 1.4$ Hz, 1H), 6.76 (dd, $J = 7.7, 1.5$ Hz, 1H), 6.72 (s, 1H), 6.21 (d, $J = 6.8$ Hz, 1H), 4.95 (d, $J = 6.8$ Hz, 1H), 4.24 (d, $J = 14.0$ Hz, 1H), 3.53 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.62, 165.20, 147.77, 136.19, 133.70, 133.59, 130.33, 130.24, 129.48, 129.23, 128.64, 128.33, 127.88, 127.81, 127.53, 127.37, 127.05, 126.41, 125.68, 123.65, 64.41, 46.29, 38.09 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}ClNO_3$ ($[M+H]^+$) = 494.1523, Found 494.1919.

***N*-(3-benzyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)-3-chlorobenzamide (5aa)**

($C_{31}H_{24}ClNO_3$) a white solid; 78% yield, 92% ee. m.p. 147-149 °C, $[\alpha]_D^{20} = 222.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 5.7 min (minor) and 6.7 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.78 (m, 2H), 7.53 – 7.42 (m, 3H), 7.38 (d, $J = 7.1$ Hz, 2H), 7.27 – 7.19 (m, 9H), 7.14 – 7.06 (m, 3H), 6.65 (s, 1H), 6.22 (d, $J = 6.8$ Hz, 1H), 4.94 (d, $J = 6.8$ Hz, 1H), 4.22 (d, $J = 13.9$ Hz, 1H), 3.51 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.74, 165.53, 148.11, 135.91, 135.81, 133.81, 133.76, 130.58, 130.22, 128.97, 128.84, 128.73, 127.87, 127.82, 127.46, 127.18, 127.08, 126.50, 126.08, 123.70, 123.51, 102.80, 64.33, 46.00, 37.85 ppm. HRMS (ESI-TOF) calcd for $C_{31}H_{24}ClNO_3$ ($[M+H]^+$) = 494.1523, Found 494.1519.

***N*-(3-benzyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)-4-chlorobenzamide (5ab)**

($C_{31}H_{24}ClNO_3$) a white solid; 80% yield, 95% ee m.p. 187-189 °C, $[\alpha]_D^{20} = 190.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 7.5 min (minor) and 8.6 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, $J = 6.9$ Hz, 2H), 7.53 – 7.42 (m, 3H), 7.31 – 7.15 (m, 12H), 7.08 (dd, $J = 6.4, 2.8$ Hz, 2H), 6.64 (s, 1H), 6.21 (d, $J = 6.8$ Hz, 1H), 4.94 (d, $J = 6.8$ Hz, 1H),

4.23 (d, $J = 13.9$ Hz, 1H), 3.51 (d, $J = 13.9$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 168.81, 166.82, 149.13, 137.77, 136.95, 134.88, 133.45, 131.24, 129.98, 129.73, 128.88, 128.82, 128.78, 128.44, 128.20, 128.05, 127.46, 124.70, 103.82, 65.32, 46.99, 38.85 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{31}\text{H}_{24}\text{ClNO}_3$ ($[\text{M}+\text{Na}^+]$) = 516.1342, Found 516.1331.

***N*-(3-benzyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)-4-methylbenzamide (5ac)**

($\text{C}_{32}\text{H}_{27}\text{NO}_3$) a white solid; 71% yield, 97% ee. m.p. 204-205 $^{\circ}\text{C}$, $[\alpha]_{\text{D}}^{20} = 186.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 7.5 min (minor) and 8.6 min (major); ^1H NMR (400 MHz, CDCl_3) δ 7.81 (d, $J = 7.0$ Hz, 2H), 7.55 – 7.41 (m, 3H), 7.31 – 7.15 (m, 10H), 7.10 (t, $J = 7.7$ Hz, 4H), 6.66 (s, 1H), 6.22 (d, $J = 6.8$ Hz, 1H), 4.98 (d, $J = 6.8$ Hz, 1H), 4.28 (d, $J = 13.9$ Hz, 1H), 3.50 (d, $J = 13.8$ Hz, 1H), 2.34 (s, 6H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 168.87, 167.89, 149.09, 141.91, 137.04, 135.06, 132.37, 131.35, 130.06, 129.65, 129.17, 128.86, 128.71, 128.37, 128.26, 127.93, 127.34, 126.64, 124.70, 104.00, 65.26, 46.97, 38.78, 21.43 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{32}\text{H}_{27}\text{NO}_3$ ($[\text{M}+\text{H}^+]$) = 474.2069, Found 474.2060.

***N*-(3-benzyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)-4-methoxybenzamide (5ad)**

($C_{32}H_{27}NO_4$) a white solid; 68% yield, 95% ee. m.p. 207-208 °C, $[\alpha]_D^{20} = 218.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 8.3 min (minor) and 9.0 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, $J = 6.9$ Hz, 2H), 7.45 (m, 5H), 7.30 – 7.04 (m, 10H), 6.80 (d, $J = 8.7$ Hz, 2H), 6.61 (s, 1H), 6.22 (d, $J = 6.8$ Hz, 1H), 4.97 (d, $J = 6.8$ Hz, 1H), 4.27 (d, $J = 13.9$ Hz, 1H), 3.79 (s, 3H), 3.49 (d, $J = 13.8$ Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.93, 167.38, 162.18, 149.09, 137.06, 135.10, 131.36, 130.07, 129.64, 128.85, 128.69, 128.47, 128.35, 128.27, 127.89, 127.47, 127.32, 113.71, 104.02, 65.25, 55.37, 46.97, 38.81 ppm. HRMS (ESI-TOF) calcd for $C_{32}H_{27}NO_4$ ($[M+H]^+$) = 490.2018, Found 490.2010.

***N*-(3-methyl-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5ae)**

($C_{25}H_{21}NO_3$) a white solid; 76% yield, 92% ee. m.p. 146-147 °C, $[\alpha]_D^{20} = 389.0$ ($c = 0.10$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 6.9 min (minor) and 11.4 min (major); 1H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, $J = 7.7, 1.7$ Hz, 2H), 7.45 (ddd, $J = 10.6, 5.8, 2.4$ Hz, 6H), 7.34 (t, $J = 7.6$ Hz, 2H), 7.23 (d, $J = 23.7$ Hz, 5H), 6.89 (s, 1H), 6.12 (d, $J = 6.9$ Hz, 1H), 4.80 (d, $J = 6.9$ Hz, 1H), 3.39 – 3.28 (m, 1H), 2.61 – 2.34 (m, 3H), 2.04 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.61, 166.33, 148.24, 135.81, 133.61, 130.62, 130.05, 128.62, 127.77, 127.74, 127.55, 127.10, 126.99, 125.62, 123.63, 62.42, 45.82, 32.10, 27.87, 14.61 ppm. HRMS (ESI-TOF) calcd for $C_{25}H_{21}NO_3$ ($[M+Na^+]$) = 384.1600, Found 384.1612.

***N*-(3-(2-(methylthio)-ethyl)-2-oxo-4,6-diphenyl-3,4-dihydro-2H-pyran-3-yl)benzamide (5af)**

(**C₂₇H₂₅NO₃S**) a white solid; 78% yield, 90% ee. m.p. 160-161 °C, $[\alpha]_{\text{D}}^{20} = 306.0$ ($c = 0.20$, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, $\lambda = 254$ nm, retention time: 7.3 min (minor) and 7.8 min (major); ^1H NMR (400 MHz, CDCl_3) δ 7.71 (dd, $J = 7.7, 1.4$ Hz, 2H), 7.49 – 7.38 (m, 6H), 7.33 (t, $J = 7.7$ Hz, 2H), 7.27 – 7.14 (m, 5H), 7.03 (s, 1H), 6.13 (d, $J = 6.9$ Hz, 1H), 4.80 (d, $J = 6.9$ Hz, 1H), 2.08 (s, 3H) ppm. ^{13}C NMR (101 MHz, CDCl_3) δ 169.96, 166.31, 148.15, 136.26, 133.90, 130.44, 130.24, 128.52, 127.70, 127.46, 126.93, 126.88, 125.64, 123.61, 102.95, 58.80, 45.57, 21.40 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{27}\text{H}_{25}\text{NO}_3\text{S}$ ($[\text{M}+\text{Na}^+]$) = 466.1453, Found 466.1357.

The two diastereoisomers of Michael addition product **6** were isolated. The dr of **6** was determined by ^1H NMR of the crude product and the ee of two diastereoisomers were determined respectively by HPLC. The data was follows: dr: **6a**:**6a'**=2.5:1; ee: **6a** (96% ee), **6a'** (30% ee). The absolute configuration of **6a** was determined by X-ray analysis.

4-benzyl-4-(3-oxo-1,3-diphenylpropyl)-2-phenyloxazol-5(4H)-one (**6a**)

($\text{C}_{31}\text{H}_{25}\text{NO}_3$) a white solid; ^1H NMR (600 MHz, CDCl_3) δ 7.82 (t, J = 6.6 Hz, 4H), 7.58 – 7.47 (m, 4H), 7.41 (dt, J = 22.7, 7.6 Hz, 4H), 7.30 (t, J = 7.5 Hz, 2H), 7.22 (t, J = 7.2 Hz, 1H), 4.12 (dd, J = 10.2, 3.2 Hz, 1H), 3.60 (dd, J = 16.6, 10.3 Hz, 1H), 3.18 (dd, J = 16.7, 3.2 Hz, 1H), 3.07 (d, J = 13.4 Hz, 1H), 2.91 (d, J = 13.4 Hz, 1H) ppm. HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane =5/95, flow rate = 1.0 mL/min, λ = 254 nm, retention time: 8.9 min (minor) and 8.3 min (major).

4-benzyl-4-(3-oxo-1,3-diphenylpropyl)-2-phenyloxazol-5(4H)-one (6a')

($C_{31}H_{25}NO_3$) a white solid; 1H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.95

(m, 2H), 7.74 – 7.68 (m, 2H), 7.58 – 7.35 (m, 6H), 7.30 – 7.24 (m, 2H),

7.17 – 7.06 (m, 8H), 4.29 – 4.20 (m, 1H), 3.86 – 3.79 (m, 2H), 3.30 (dd, J

= 48.2, 13.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.60, 177.90,

160.60, 138.55, 136.86, 134.12, 133.26, 132.49, 130.29, 129.27, 128.64,

128.61, 128.21, 128.13, 128.12, 127.73, 127.54, 127.21, 125.62, 78.49,

46.90, 42.05, 39.74. HPLC DAICEL CHIRALCEL IB, 2-propanol/n-hexane = 5/95, flow rate = 1.0

mL/min, λ = 254 nm, retention time: 8.0 min (minor) and 9.0 min (major).

G. Experimental Procedure for Scale-up IEDDA Reaction and Recycling Chiral Guanidines **2c**

To a stirred solution of chalcone **3a** (2.08 g, 2 equiv., 10 mmol) and guanidine catalyst **2c** (10 mol%, 425 mg, 0.5 mmol) in THF/CHCl₃ (40 mL, 1:1, v/v) was added slowly azlactone **4a** (1.765 g, 5 mmol) in 10 mL THF/CHCl₃ (1:1, v/v) at -20 °C. After being stirred for 72 h and detected via TLC, the reaction mixture was concentrated in vacuum. The residue was purified by column chromatography on Al₂O₃ gel to afford the crude product (pet/EtOAc = 1/1) and chiral guanidine **2c** (MeOH/EtOAc = 1/1 to 1/0). chiral guanidines **2c** in CH₂Cl₂ (16 mL) was added 4 M NaOH (15 mL) and stirred until the basification was finished (10 mins). The pH value of the mixture was kept in the range of 11-12. The aqueous phase was extracted with CH₂Cl₂ (5 × 20 mL). The combined organic phase was washed with 4 M NaOH, dried over anhydrous NaSO₄ and evaporated in vacuum. Finally a white solid **2c** was obtained (362 mg, 85% yield). The crude product were purified by column chromatography on silica gel (pet/EtOAc = 30/1 to 10/1 as eluent) to afford the mixture of **5a** and **6a**, then the mixture were purified by column chromatography on silica gel for the second time (CH₂Cl₂/pet = 1/1 to 2:1, as eluent) to give pure adduct **5a** (1.511g, 70%).

H. Copies of NMR Spectra for 1b-2f ,IEEDA Products and Michael Addition Adduct 6

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2009-12-16T11:51:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8012.8 Hz
 AQ: undefined
 TE: 296.9 C

CHANNEL f1

NUC1: 1H
 P1: 12 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 0.60 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 7.08
 Ph1: 15.01

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2009-12-16T12:21:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 300.1 C

CHANNEL f1

NUC1: 13C
 P1: 15.5 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 2.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -101.76
 Ph1: 73.63

Ph0: 6.56
Ph1: 1.3 1.5 Ph0: -97.11
Ph1: 62.00

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-21T16:04:00
F2PROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 293.4 C

===== CHANNEL f1 =====

NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 2.56
Ph1: 12.29

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-21T16:34:00
F2PROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 294.6 C

===== CHANNEL f1 =====

NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -109.07
Ph1: 81.53

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-21T16:58:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 293.2 C

CHANNEL f1

NUC1: 1H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: -0.20 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -5.70
Ph1: 20.50

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-21T17:28:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 294.5 C

CHANNEL f1

NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -103.22
Ph1: 71.86

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-19T10:17:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 12335.5 Hz
 AQ: undefined
 TE: 293.1 C

===== CHANNEL f1 =====
 NUC1: 1H
 P1: 7.2 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.20 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 77.38
 Ph1: 30.70

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-19T10:43:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 36057.7 Hz
 AQ: undefined
 TE: 293.1 C

===== CHANNEL f1 =====
 NUC1: 13C
 P1: 11.5 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -286.00
 Ph1: 40.20

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-21T15:27:00
PULPROG: zg30
TD: 32768
Solvent: CDCl₃
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 293.2 C

===== CHANNEL f1 =====

NUC1: ¹H
P1: 12 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: -0.40 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -2.30
Ph1: 18.26

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-21T15:56:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl₃
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 294.6 C

===== CHANNEL f1 =====

NUC1: ¹³C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -99.08
Ph1: 61.81

```
F2 - Acquisition Parameters
DATE: 2010-01-20T11:53:00
PULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 293.3 C
```

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 0.30 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 0.54
Ph1: 20.17

```
F2 - Acquisition Parameters
DATE: 2010-01-20T12:22:00
PULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 294.3 C
```

F2 - Processing Parameters
SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -114.04
Ph1: 77.97

DATE: 2009-12-18T22:00:00
FULPROG: zg30
TD: 32768
Solvent: CDC13
NS: 16
DS: undefined
SWH: 8223.7 Hz
AQ: undefined
TE: 296.2 C

```
NUC1: 1H
P1: 12 usec
SFO1: undefined MHz
```

SI: 65536
DC: 0.05
LB: -0.40 Hz
Gauss: 1.00
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 3.29
Ph1: 16.59

DATE: 2009-12-18T22:31:00
PULPROG: zgpg30
TD: 32768
Solvent: CDC13
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 297.7 C

```
NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz
```

SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -103.84
Ph1: 69.01

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-22T15:23:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 294.1 C

CHANNEL f1
 NUC1: 1H
 P1: 12 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.20 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 4.96
 Ph1: 19.28

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-22T15:53:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 295 C

CHANNEL f1
 NUC1: 13C
 P1: 15.5 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -101.82
 Ph1: 73.37

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-22T15:59:00
 FULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 294 C

CHANNEL f1

NUC1: 1H
 P1: 12 usec
 SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
 DC: 0.05
 LB: -0.20 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 4.91
 Ph1: 15.72

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-22T16:51:00
 FULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 295.3 C

CHANNEL f1

NUC1: 13C
 P1: 15.5 usec
 SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -90.73
 Ph1: 60.52

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2009-12-16T16:19:00
 FULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8012.8 Hz
 AQ: undefined
 TE: 296.1 C

CHANNEL f1

NUC1: 1H
 P1: 12 usec
 SF01: undefined MHz

F2 - Processing Parameters

SI: 65536
 DC: 0.05
 LB: 0.60 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 4.78
 Ph1: 12.21

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-03-11T11:29:00
 FULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 295.7 C

CHANNEL f1

NUC1: 13C
 P1: 15.5 usec
 SF01: undefined MHz

F2 - Processing Parameters

SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -105.88
 Ph1: 54.48

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-01-19T13:29:00
FULPROG: zg30
TD: 32768
Solvent: CDCl3
NS: 16
DS: undefined
SWH: 12335.5 Hz
AQ: undefined
TE: 292.7 C

CHANNEL f1

NUC1: 1H
P1: 7.2 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: 2.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: 81.07
Ph1: 25.73

Current Data Parameters

F2 - Acquisition Parameters

DATE: 2010-03-18T21:50:00
FULPROG: zgpg30
TD: 32768
Solvent: CDCl3
NS: 512
DS: undefined
SWH: 24038.5 Hz
AQ: undefined
TE: 299.4 C

CHANNEL f1

NUC1: 13C
P1: 15.5 usec
SFO1: undefined MHz

F2 - Processing Parameters

SI: 65536
DC: 0.05
LB: 1.00 Hz
First Point: 0.50
FT: Hyper Quadrature
Phase: Manual
Ph0: -102.59
Ph1: 65.89

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2009-12-18T21:54:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 297.5 C

CHANNEL f1

NUC1: 13C
 P1: 15.5 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -95.57
 Ph1: 61.45

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2009-12-18T21:23:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 295.8 C

CHANNEL f1

NUC1: 1H
 P1: 12 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.20 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 4.58
 Ph1: 16.98

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-02-02T09:49:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 295.1 C

CHANNEL f1

NUC1: 1H
 P1: 12 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.60 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -7.79
 Ph1: 17.27

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-02-02T10:19:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 296.1 C

CHANNEL f1

NUC1: 13C
 P1: 15.5 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 2.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -133.23
 Ph1: 58.99

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-02-02T13:13:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 294.9 C

CHANNEL f1

NUC1: 1H
 P1: 12 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.60 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 8.01
 Ph1: 15.83

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-02-02T13:42:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 295.6 C

CHANNEL f1

NUC1: 13C
 P1: 15.5 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 2.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -106.94
 Ph1: 70.72

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-29T15:46:00
 FULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 294.5 C

CHANNEL f1
 NUC1: 1H
 P1: 12 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.20 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 0.42
 Ph1: 19.44

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-29T16:16:00
 FULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 295.4 C

CHANNEL f1
 NUC1: 13C
 P1: 15.5 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -98.67
 Ph1: 70.63

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-29T14:34:00
 FULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 294.8 C

===== CHANNEL f1 =====
 NUC1: 1H
 P1: 12 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: -0.20 Hz
 Gauss: 1.00
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 5.87
 Ph1: 15.48

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-01-29T15:03:00
 FULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 295.6 C

===== CHANNEL f1 =====
 NUC1: 13C
 P1: 15.5 usec
 SFO1: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 1.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -95.40
 Ph1: 67.53

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-02-04T09:38:00
 PULPROG: zg30
 TD: 32768
 Solvent: CDCl3
 NS: 16
 DS: undefined
 SWH: 8223.7 Hz
 AQ: undefined
 TE: 294.8 C

CHANNEL f1
 NUC1: 1H
 P1: 12 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 0.60 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: 1.55
 Ph1: 15.95

Current Data Parameters

F2 - Acquisition Parameters
 DATE: 2010-02-04T10:08:00
 PULPROG: zgpg30
 TD: 32768
 Solvent: CDCl3
 NS: 512
 DS: undefined
 SWH: 24038.5 Hz
 AQ: undefined
 TE: 296.4 C

CHANNEL f1
 NUC1: 13C
 P1: 15.5 usec
 SF01: undefined MHz

F2 - Processing Parameters
 SI: 65536
 DC: 0.05
 LB: 2.00 Hz
 First Point: 0.50
 FT: Hyper Quadrature
 Phase: Manual
 Ph0: -116.86
 Ph1: 78.73

I. X-ray Structure and Mechanism Evidence and Corresponding NMR Spectra²

1. X-ray Structure of Chiral Guanidine 2c

Table S-1. Crystal Data and Structure Refinement for Guanidine 2c

Empirical formula	C ₅₂ H ₇₈ N ₈ O ₂
Formula weight	847.22
Temperature	173 (2)
Wavelength	0.71073 Å
Crystal system	Hexagonal
Space group	P6 (1)
Unit cell dimensions	a = 10.7895 (5) Å α = 90.00° b = 10.7895 (5) Å β = 90.00° c = 72.850 (7) Å γ = 120.00 °
Volume	7344.5(8) Å ³
Z	6
Density (calculated)	1.149 g/cm ³
Absorption coefficient	0.71 cm ⁻¹
F(000)	2772
S35	
Theta range for data collection	2.34 to 24.99°
Index ranges	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -78 ≤ l ≤ 86
Reflections collected	42033
Independent reflections	4327
Completeness to theta = 24.99°	99.8 %
Absorption correction	numerical
Refinement method	Full-matrix least-squares on F

Data/restraints/parameters	4185 / 0 / 559
Goodness-of-fit	1.236
Final R indices [$I > 2 \sigma(I)$]	$R1 = 0.0830$, $wR2 = 0.2034$
Absolute structure parameter	10 (10)
Largest diff. Peak and hole	0.266 and -0.243 e. Å ⁻³

2. X-ray Structure of the Product 5d

Table S-2. Crystal Data and Structure Refinement for 5d

Empirical formula	$C_{31}H_{24}ClNO_3, CH_2Cl_2$	
Formula weight	578.89	
Temperature	173.15 (2)	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2 (1)$	
Unit cell dimensions	$a = 11.845 (3) \text{ Å}$	$\alpha = 90.00^\circ$
	$b = 10.783 (2) \text{ Å}$	$\beta = 117.80^\circ (3)$
	$c = 12.350 (3) \text{ Å}$	$\gamma = 90.00^\circ$

Volume	1395.3 (6) Å ³
Z	2
Density (calculated)	1.378 g/cm ³
Absorption coefficient	3.63 cm ⁻¹
F (000)	600
Theta range for data collection	2.71 to 27.48°
Index ranges	-14 ≤ h ≤ 15, -14 ≤ k ≤ 11, -16 ≤ l ≤ 16
Reflections collected	12515
Independent reflections	5713
Completeness to theta = 27.48°	99.8 %
Absorption correction	numerical
Refinement method	Full-matrix least-squares on F
Data/restraints/parameters	4959 / 0 / 352
Goodness-of-fit	1.098
Final R indices [I > 2σ(I)]	R1 = 0.0636, wR2 = 0.1265
Absolute structure parameter	-0.03 (7)
Largest diff. Peak and hole	0.252 and -0.271 e. Å ⁻³

3. X-ray Structure of the Michael Addition Adduct 6a

Empirical formula	C ₃₁ H ₂₅ NO ₃
Formula weight	459.52
Temperature	173.15 (2)
Radiation type	CuKα
Wavelength	1.54186
Crystal system	orthorhombic

Space group	<i>P</i> 2 (1)2(1)2(1)
Unit cell dimensions	<i>a</i> = 9.3195(11) Å α = 90.00° <i>b</i> = 10.5990(12) Å β = 90.00° <i>c</i> = 24.308(3) Å γ = 90.00°
Volume	2401.1(5) Å ³
<i>Z</i>	4
Density (calculated)	1.271 g/cm ³
Absorption coefficient	6.48 cm ⁻¹
<i>F</i> (000)	968
Theta range for data collection	3.64 to 68.23°
Index ranges	-11 ≤ <i>h</i> ≤ 11, -12 ≤ <i>k</i> ≤ 10, -28 ≤ <i>l</i> ≤ 29
Reflections collected	16859
Independent reflections	4325
Completeness to theta = 27.48°	99.6 %
Absorption correction	numerical
Refinement method	Full-matrix least-squares on <i>F</i>
Data/restraints/parameters	4153 / 0 / 317
Goodness-of-fit	1.143
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> 1 = 0.0310, <i>wR</i> 2 = 0.0737
Absolute structure parameter	-0.03(19)
Largest diff. Peak and hole	0.161 and -0.131 e. Å ⁻³

4. Mechanism Evidence and Corresponding NMR Spectra²

The two diastereoisomers of Michael addition product **6** were isolated. The dr of **6** was determined by ¹H NMR of the crude product and the ee of two diastereoisomers were determined respectively by HPLC. The data was follows: dr: **6a**:**6a'**=2.5: 1; ee: **6a** (95 % ee), **6a'** (30% ee). The absolute configuration of **6a** was determined by *X-ray* analysis.

We have isolated Michael addition adduct **6a** and **6a'** and re-subjected them to the reaction condition, neither diastereoisomer could perform intramolecular nucleophilic addition to give **5a**. Furthermore, we also tried to use other methods to transform **6** into **5a**, such as TFA, NaOH, K₂CO₃, TMG (1,1,3,3-tetramethylguanidine), but we failed.

In the presence of basic guanidine catalyst, there might be equilibrium between intermediate II and Michael addition adducts. So based on the experimental data mentioned above, we thought that the pathway for obtaining the cyclic product **5a** was **cycloaddition** mechanism rather than **stepwise mechanism**.

In addition, we had also analyzed the spectrograph of the mixture of guanidine **2c** with chalcone **3a** and azlactone **4a** (mol/mol, 1:1). On the basis of the X-ray structure of guanidine **2c** and product **5d**, a bifunctionally activated transition state for IEDDA reaction of chalcone **3a** with azlactone **4a** is proposed. As shown in Figure 1, the N—H moiety of the amide could act as a Brønsted acid to activate the chalcone and lower its LUMO energy through a hydrogen bond. Azlactone **4a** could be enolized and recognized by the guanidine moiety, associating with the N—H proton of the amide on the other side via dual intermolecular hydrogen bonds. The enolized azlactone could attack only from the *Re* face of chalcone to form the major (*3S,4R*)-product, in accordance with the experimental results.

Figure 1. Proposed transition state for the IEDDA reaction of chalcone **3a** with azlactone **4a**

J. References

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