JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b00227 • Publication Date (Web): 16 Mar 2018

ACS Publications

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N-Heterocyclic Carbene Catalyzed Enantioselective [3+2] Dearomatizing Annulation of Saturated Carboxylic Esters with *N*-Imimoisoquinolinium Ylides

Pengfei Zhang, [†,‡,§] Yu Zhou, [‡,#,¶,§] Xu Han, [‡,#,¶] Jinyi Xu, [*,†] and Hong Liu[*,‡,#,¶]

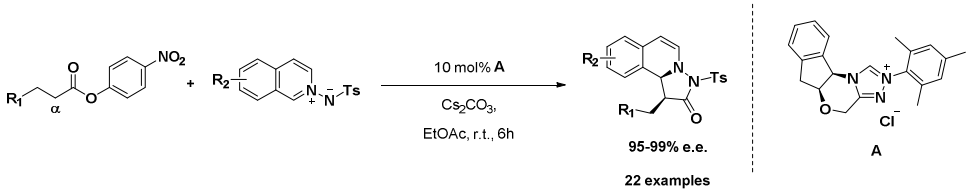
[†]State Key Laboratory of Natural Medicines and Department of Medicinal Chemistry, China Pharmaceutical University, 24 Tong Jia Xiang, Nanjing, Jiangsu 210009, China.

[‡]State key Laboratory of Drug Research and [#]Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Shanghai 201203, China.

[¶]University of Chinese Academy of Sciences, No.19A Yuquan Road, Beijing 100049, China.

Email: jinyixu@china.com (for Jinyi Xu), hliu@simm.ac.cn (for Hong Liu)

Abstract



The dearomatizing annulation reaction is a significant challenge in organic chemistry. The direct activation of α-carbons of simple saturated esters, as nucleophiles, is an important synthesis strategy. In the present study, we disclose [3+2] dearomatizing annulation reactions with direct activating α-carbons of saturated carboxylic esters and *N*-iminoisoquinolinium ylides, which possess highly enantioselective characteristics, catalyzed by *N*-heterocyclic carbenes (NHCs). The protocol achieves isoquinoline dearomatization and the construction of tricyclic chiral products under mild conditions with good yield, substrate tolerance, diastereoselectivity, and excellent enantioselectivity.

Introduction

Enantioselective dearomatization of π-conjugated heterocyclic molecules has practical significance, because most natural compounds are nonaromatic or less aromatic, and their specific configuration is required to maintain their bioactivity (Figure 1a). However, it is a significant challenge to identify suitable and mild reaction conditions to break the stabilization of large aromatic conjugated structure. Recently, transition metals, such as Pd, Ir, Fe, Rh, Ag, and Cu[1], have been frequently employed to achieve the dearomatization transformation to build intriguing nonaromatic structures, which has enlarged the scope of available substrates and obtainable

dearomatized products. Further specific bioactive chiral compounds are desired; however, traditional synthetic methods can barely realize highly enantioselective and efficient synthesis under green and mild reaction conditions. Therefore, research into enantioselective dearomatization is currently in the preliminary stage and requires further effort.

As stable and isolable cabenes, which were first reported by Arduengo *et al.*[2], *N*-heterocyclic carbenes (NHCs, Figure 1b) have exhibited an enormous capacity for C-H activation[3] and enantioselective C-C bond formation[4] to efficiently generate various chiral compounds for a wide range of application in organic chemistry[5]. Although NHCs have undergone rapid development in asymmetric organocatalysis, dearomatization reaction with NHC catalysts[6] is rare because of the difficulty of discovering suitable substrates[7]. Futher research on NHC-catalyzed dearomatization is required considering the distinctive umpolung nature and high enantioselective characteristics of NHC catalysis, which represent an excellent and convenient strategy to build diversified chiral natural-like heterocyclic compounds[8]. Recently, Glorius and co-workers[6b] reported a series of tricyclic dihydroisoquinolines with a 1,4-diamine unit, generated by isoquinoline through an NHC-dearomatization method, could be easily synthesized to indolizidine alkaloids, a class of unique scaffolds[9] that are widely present in naturally occurring molecules and have extensive biological and medicinal applications[10].

Meanwhile, varied carbonyl compounds[11] and other substrates, like alkenyl[12] have been employed to react with NHCs. Chi and co-workers[13] reported that direct activation of β-carbons of simple saturated esters, as nucleophiles, is a good strategy to synthesize cyclopentenes, offering new ideas for NHCs chemistry[14]. By contrast, activating the α-carbons of saturated esters is rarely reported[15], despite being easily accomplished in aldehyde compounds[16]. Thus, it seems that there are generally applicable barriers of common saturated carbonyl compounds with direct activating α-carbons, as nucleophiles, to participate in various NHCs-catalyzed reactions. In line with our efforts in the field of NHCs-dearomaticity crossing[8,17], we herein report novel and mild NHC-catalyzed dearomatizing [3+2] annulation reactions to synthesize highly enantioselective tricyclic dihydroisoquinolines with direct activating α-carbons of saturated carboxylic esters and *N*-imimoisoquinolinium ylides.

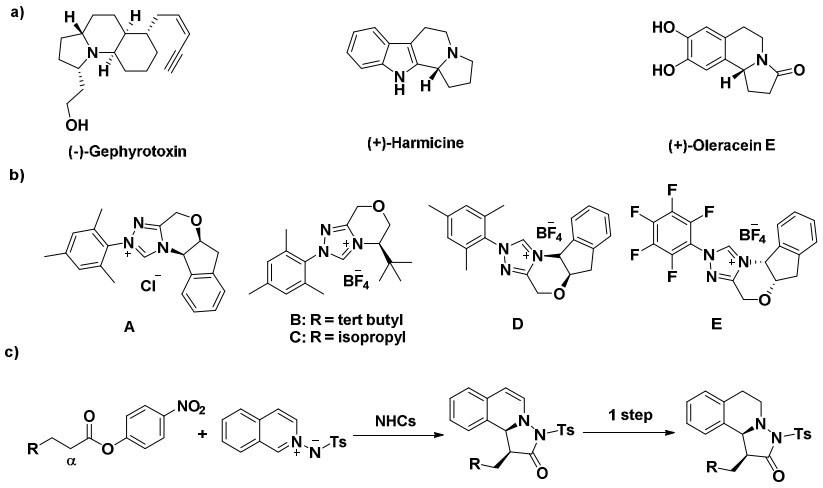
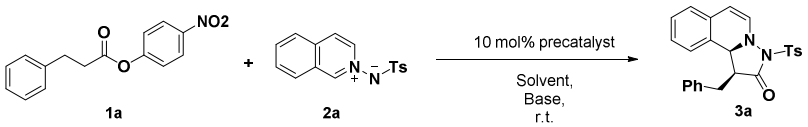


Figure 1. **a)** Examples of naturally occurring and biologically active indolizidine alkaloids. **b)** NHC precatalysts used in this work. **c)** Our current work to generate chiral indolizidine alkaloid.

Results and Discussion

Experimentally, we set out to achieve dearomatizing annulation to prepare the target tricyclic dihydroisoquinolines using saturated carboxylic ester **1a** and *N*-imimoisoquinolinium ylide **2a** as model substrates. The key experimental results of conditions screening and optimization are summarized in Table 1. With imidazolium **A** as the NHC precatalyst, K_2CO_3 as the base and tetrahydrofuran (THF) as the solvent, we observed the desired dearomatizing annulation product **3a** in a suitable yield of 80% and with a moderate enantioselectivity of 75% e.e. (Table 1, entry 1). Meanwhile, other NHC precatalysts were also tested for this transformation, but no improvements in yield and enantioselectivity were obtained (Table 1, entries 2-5). It seems that catalyst **A** is the best choice for this reaction. In addition, we further explored the influences of different solvents, and the results showed that toluene, dichloromethane and ethyl acetate gave better yields (more than 80%) and increased the enantioselectivity to 87-95% e.e. (Table 1, entries 6-9). However, when using *N,N*-dimethylformamide as the reaction solvent, the target product **3a** could barely be detected (Table 1, entry 10). Subsequently, screening of different bases revealed that the inorganic bases Cs_2CO_3 gave the best result (Table 1, entries 11-16). In brief, the optimum result could be obtained when ester **1a** (0.1 mmol, 1.0 equiv.) and ylide **2a** (0.1 mmol, 1.0 equiv.) were treated with Cs_2CO_3 (0.2 mmol, 2.0 equiv.) under 10 mol% NHC catalyst **A** at room temperature to produce **3a**.

Table 1. Optimization of reaction conditions[a]



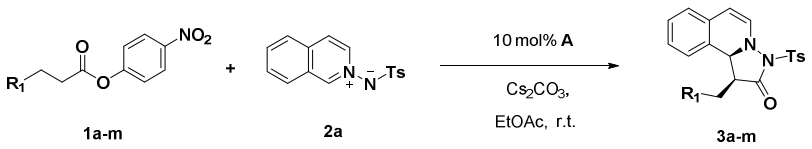
entry	catalyst[b]	base	solvent	yield(%)[c]	d.r.[d]	e.e.(%)[e]
1	**A**	K_2CO_3	THF	80	8:1	75
2	**B**	K_2CO_3	THF	75	4:1	56
3	**C**	K_2CO_3	THF	70	4:1	40
4	**D**	K_2CO_3	THF	50	2:1	6
5	**E**	K_2CO_3	THF	0	-[f]	-[f]
6	**A**	K_2CO_3	toluene	80	8:1	92
7	**A**	K_2CO_3	CH_2Cl_2	80	-[f]	87
8	**A**	K_2CO_3	EtOAc	82	10:1	95
9	**A**	K_2CO_3	dioxane	75	-[f]	76
10	**A**	K_2CO_3	DMF	2	-[f]	-[f]
11	**A**	EtONa	EtOAc	15	8:1	93
12	**A**	*t*-BuOK	EtOAc	70	10:1	95
13	**A**	TEA	EtOAc	50	-[f]	90
14	**A**	DIPEA	EtOAc	50	6:1	91
15	**A**	DBU	EtOAc	60	5:1	91
16	**A**	Cs_2CO_3	EtOAc	80	10:1	99

[a]Unless other specified, all the reactions were carried out using ester **1a** (0.1 mmol, 1.0 equiv.) and ylide **2a** (0.1 mmol, 1.0 equiv.), base (0.2 mmol, 2.0 equiv.) with 10 mol% NHC precatalyst at room temperature (r.t.) under Ar protection for 3-6 hours. [b]All NHC precatalysts in this work are showed in Figure **1b**. [c]Isolated yields after chromatography. [d]Determined by crude ^{1}H NMR spectroscopy. [e]Enantiomeric excess of **3a** determined via chiral HPLC analysis. [f]Not determined.

With the optimized catalysis condition identified, the applicability of the dearomatizing strategy was further demonstrated using a variety of esters as substrate **1**. The results are summarized in Table 2. Initially, we investigated the tolerances for different substituents on the phenyl ring of **1a**. The results showed that some electron donating (Table 2, entries 2-4) and halogens (Table 2, entries 5-9) groups on the phenyl ring could generate the desired dearomatizing annulation products **3a-3i** with excellent yield, diastereoselectivities and enantioselectivities (e.e. > 95%). In addition, the involvement of heterocyclic substituent R_1 (such as a 2-furyl group) produced **3j** with excellent yield of 80% and enantioselectivity of 97% e.e. (Table 2, entry 10). Alkly groups were also introduced into the R_1 group to explore the substrate tolerances (Table 2, entries 11-13). Although the introduction of alkyl groups led to a decrease in yields, excellent enantioselectivities

were still obtained (e.e. = 95-97%).

Table 2. Studies on the variation of substrate 1[a]



1a-m 2a 3a-m

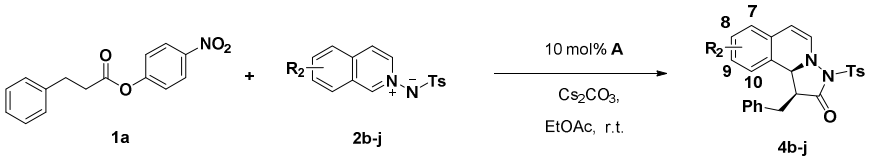
entry	R_1	product	yield (%) of **3**[b]	d.r.[c]	e.e.[d]
1	Ph	**3a**	80	10:1	99
2	4-MeC_6H_4	**3b**	80	8:1	98
3	4-$OMeC_6H_4$	**3c**	75	14:1	98
4	3-$OMeC_6H_4$	**3d**	80	14:1	96
5	4-FC_6H_4	**3e**	80	19:1	97
6	4-ClC_6H_4	**3f**	65	17:1	95
7	4-BrC_6H_4	**3g**	80	20:1	96
8	3-BrC_6H_4	**3h**	78	8:1	96
9	2-BrC_6H_4	**3i**	75	20:1	96
10	2-Furyl	**3j**	80	6:1	97
11	Me	**3k**	75	20:1	95
12	*n*-Pr	**3l**	75	7:1	98
13	Cy	**3m**	70	15:1	97

[a]Unless other specified, all the reactions were carried out using ester **1** (0.1 mmol, 1.0 equiv.) and ylide **2a** (0.1 mmol, 1.0 equiv.), Cs_2CO_3 (0.2 mmol, 2.0 equiv.) in EA with 10 mol% NHC precatalyst **A** at room temperature (r.t.) under Ar protection for 3-6 hours. [b]Isolated yields after chromatography. [c]Determined by crude ^1H NMR spectroscopy. [d]Enantiomeric excess of **3** determined via chiral HPLC analysis.

The generality of this strategy with different *N*-iminoisoquinolinium ylides **2b-j** was then investigated, as outlined in Table 3. Introducing an electron-donating group (6-Me) into the isoquinoline ring of ylide **2a** was feasible to generate 8-Me substituted product **4d** with 72% yield and 92% e.e. (Table 3, entry 3). However, when we tested 5-, 6-, or 7-methoxy substituted ylides, the dearomatizing annulation product could not be detected. We speculated that it might be caused by the weak reactive properties of methoxy-substituted ylides (not shown in Table 3). By contrast, the introduction of halogens, such as F-, Cl- and Br- substitutes, into the R_2 group (Table 3, entries 1, 2, entries 4-9) was favorable to produce the target products (**4b, 4c, 4e-4j**), which indicated good tolerance for halogen groups. We further found that 6-bromine substituted ylide **2g** generated the best yield (75%) and enantioselectivity (98% e.e.) to form the dearomatizing tricyclic compound **4g** (Table 3, entry 6), and four bromine substituted products (**4c, 4g, 4i, 4j**) with good enantioselectivities (96-98%), diastereoselectivities (11:1-20:1) and moderate yield (60-75%) (Table 3, entries 2, 6, 8, 9) demonstrated that bromine was a stable and useful group for the

dearomatizing strategy.

Table 3. Studies on the variation of substrate 2[a]



entry	R_2	product	yield (%) of **4**[b]	d.r.[c]	e.e.[d]
1	7-Cl	**4b**	60	20:1	98
2	7-Br	**4c**	65	20:1	97
3	8-Me	**4d**	72	8:1	92
4	8-F	**4e**	70	16:1	97
5	8-Cl	**4f**	71	20:1	95
6	8-Br	**4g**	75	20:1	98
7	9-Cl	**4h**	65	20:1	97
8	9-Br	**4i**	75	20:1	98
9	10-Br	**4j**	60	11:1	96

[a]Unless other specified, all the reactions were carried out using ester **1a** (0.1 mmol, 1.0 equiv.) and ylide **2** (0.1 mmol, 1.0 equiv.), Cs_2CO_3 (0.2 mmol, 2.0 equiv.) in EA with 10 mol% NHC precatalyst **A** at room temperature (r.t.) under Ar protection for 3-6 hours. [b]Isolated yields after chromatography. [c]Determined by crude ^{1}H NMR spectroscopy. [d]Enantiomeric excess of **4** determined via chiral HPLC analysis.

Indolizidine alkaloids are important structural motifs[18] (Figure 1a). In our studies, we found that some *N*-substituent tricyclic indolizidine scaffold derivatives could be easily synthesized from **3a** by a simple reduction step. As shown in Figure 2, product **3a** of the dearomatizing annulation reaction could be further transformed into *N*-substituent indolizidine derivative **5a** with treatment of $NaBH_3CN$ in 60% total yield and 95% e.e. (Figure 2). Br-substituent product **3g** also could be transformed into indolizidine derivative **5g** at the same reaction condition in 62% total yield and 97% e.e., better than the performance of **3a** (Figure 2).

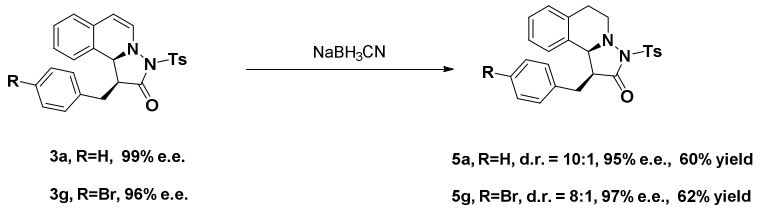


Figure 2. Derivatization of products **3** to give indolizidine derivatives **5** by one step.

A plausible mechanism is proposed in Figure 3. The addition of NHC catalyst to ester substrate **1a** gives an NHC-bound ester intermediate **I**, which bears acidic α-CHs and can undergo deprotonation to form an enolate intermediate **II**. Deprotonation of the α-CH of enolate **II**

produces the acylazolium intermediate **III**, containing the α-carbon as a nucleophilic center. Intermediate **III** then reacts with *N*-iminoisoquinolinium ylide **2a** to generate intermediate **IV**, which undergoes an intramolecular acylation in proper conformation (intermediate **V**) to give the final annulation product **3a** and regenerate the NHC catalyst.

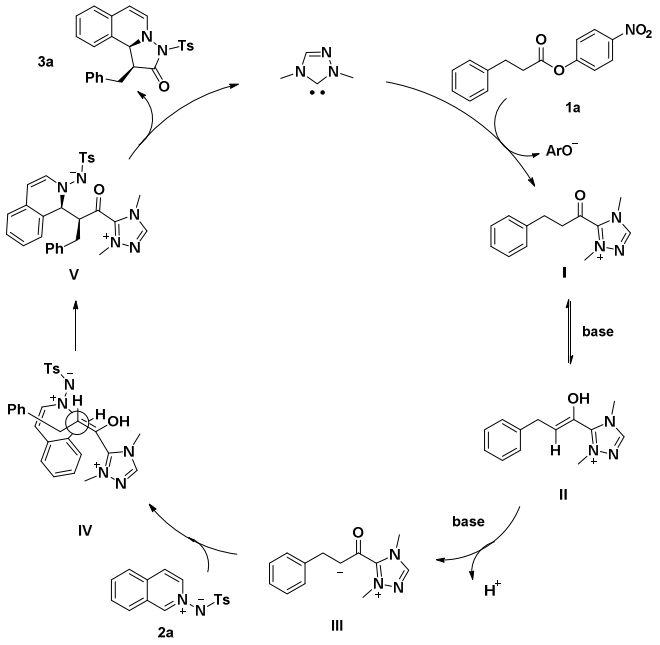


Figure 3. Postulated catalytic cycle for the NHC-catalyzed dearomatizing annulation reaction.

In summary, we developed a novel NHC-catalyzed dearomatizing [3+2] annulation reaction with direct activating α-carbons of saturated esters and *N*-iminoisoquinolinium ylides to generate chiral tricyclic products with good yield, moderate diastereoselectivity and high enantioselectivity in mild conditions. The reaction works well for different kinds of esters and has good tolerance for a diverse array of ylides. The resulting tricyclic product can be easily transformed to useful derivatives, such as indolizidine alkaloids, making this strategy potentially practical for the synthesis of bioactive molecules.

EXPERIMENTAL SECTION

General information: The reagents (chemicals) and solvents were purchased from commercial sources and used without further purification. All reactions were carried out under an atmosphere of argon in pre-dried glassware. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness), visualized by irradiation with UV light (254 nm). ^{1}H and ^{13}C-NMR spectra were recorded in deuterochloroform ($CDCl_3$) on 400, 500 and 600 MHz instruments.

Chemical shifts (δ) are given in parts per million (ppm) relative to tetramethylsilane (TMS). Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). ESI mass spectra were recorded on Agilen G6520 Q-TOF LC/MS. And EI mass spectra were recorded on Thermo-DFS high performance double focusing magnetic sector GC/MS. Optical rotations were measured on an Auto pol V PLVS matic polarimeter at 20^{o}C using a quartz glass cell (1 dm path length) and are reported as follows: $[\alpha]^{20}_{D}$ (c, in solvent). The enantiomeric ratio (e.e.) was determined by HPLC analysis using chiral column OD.

General procedure for the preparation of saturated carboxylic esters[15c]: To a solution of propionic acid (6.0 mmol, 1.0 equiv) in ethyl acetate (20 mL) was added *p*-nitrophenol (6.6 mmol, 1.1 equiv), then dicyclohexylcarbodiimide (12.0 mmol, 2.0 equiv) was added slowly to the solution. The reaction mixture was stirred overnight at room temperature. Upon filtering off the solid, ethyl acetate was removed under reduced pressure. The residue was purified by column chromatography on silica gel (Hexanes : Ethyl acetate = 20:1) to afford substrate **1.**

General procedure for the preparation of *N*-iminoisoquinolinium ylides[6b]: To a solution of isoquinoline (6.0 mmol, 1.0 equiv) in acetonitrile (25 mL) was added *O*-(2,4-dinitrophenyl)hydroxylamine (6.6 mmol, 1.1 equiv). The reaction flask was sealed and the reaction mixture was stirred for 24 h at room temperature. Upon filtering off the solvent, the orange precipitate was dissolved in THF/H_2O (30 mL, 1:1). The reaction mixture was added K_2CO_3 (21.0 mml, 3.5equiv) at room temperature, and 4-toluenesulfonyl chloride (12.0 mmol, 2.0 equiv) was slowly added. After 12 h, the reaction was diluted with 20 mL of H_2O and extracted three times with dichloromethane. The combined organic phases were dried over anhydrous Na_2SO_4, concentrated under reduced pressure and purified by column chromatography on silica gel (Ethyl acetate) to afford substrate **2**.

General procedure for enantioselective synthesis of 3 or 4 by formal [3+2] cycloaddition of saturated carboxylic esters with *N*-iminoisoquinolinium ylides: A dried and argon-filled Schlenk flask was charged with *N*-iminoisoquinolinium ylide **2** (0.1 mmol, 1.0 equiv) and Cs_2CO_3 (0.2 mmol, 2.0 equiv). Then, saturated carboxylic ester **1** (0.1 mmol, 1.0 equiv) was added quickly to the mixture. Subsequently, triazolium salt **A** (0.01 mmol, 10 mol%) in 2.5 mL EA was added to the mixture. The mixture was stirred at r.t. for 3-6 h. After purification by column chromatography on silica gel (Hexanes : Ethyl acetate = 20:1), the desired product **3** or **4** was obtained.

Synthetic Transformation of product 3 to produce 5: To a solution of **3** (0.2 mmol, 1.0 equiv) in dichloromethane (3 mL) was added acetic acid (3 mL) at room temperature. $NaBH_3CN$ (0.3 mmol, 3.0 equiv) was added and reaction mixture was stirring until the disappearance of the starting material. The mixture was quenched with aq. $NaHCO_3$ solution and extracted with dichloromethane three times. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. Purification of the residue by column chromatography on silica gel (Hexanes : Ethyl acetate = 20:1) gave the corresponding product **5**.

4-nitrophenyl 3-phenylpropanoate (**1a**): White solid (1.6g, 97% yield): mp 98-99 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 2.2 Hz, 1H), 8.16 (d, J = 2.2 Hz, 1H), 7.29-7.26 (m, 1H), 7.25 (s, 1H), 7.21-7.17 (m, 3H), 7.12 (d, J = 2.2 Hz, 1H), 7.10 (d, J = 2.2 Hz, 1H), 3.01 (t, J = 7.5 Hz, 2H), 2.89-2.83 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 155.4, 145.4, 139.6, 128.7, 128.7, 128.4, 128.4, 126.7, 125.2, 125.2, 122.4, 122.4, 35.9, 30.8. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{15}H_{13}NO_4$ 271.0845, found 271.0844.

4-nitrophenyl 3-(*p*-tolyl)propanoate (**1b**): White solid (1.6g, 96% yield): mp 105-106 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 9.2 Hz, 2H), 7.19 (d, J = 9.2 Hz, 2H), 7.15 (s, 4H), 3.04 (t, J = 7.6 Hz, 2H), 2.96-2.85 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 155.4, 145.3, 136.6, 136.2, 129.4, 129.4, 128.2, 128.2, 125.2, 125.2, 122.4, 122.4, 36.1, 30.4, 21.0. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{16}H_{15}NO_4$ 285.1001, found 285.0993.

4-nitrophenyl 3-(4-methoxyphenyl)propanoate (**1c**): White solid (1.7g, 95% yield): mp 117-119 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.34-8.14 (m, 2H), 7.22-7.14 (m, 4H), 6.90-6.83 (m, 2H), 3.80 (s, 3H), 3.03 (t, J = 7.4 Hz, 2H), 2.94-2.85 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 158.4, 155.4, 145.3, 131.7, 129.4, 129.4, 125.2, 125.2, 122.4, 122.4, 114.1, 114.1, 55.3, 36.2, 30.0. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{16}H_{15}NO_5$ 301.0950, found 301.0949.

4-nitrophenyl 3-(3-methoxyphenyl)propanoate (**1d**): White solid (1.7g, 95% yield): mp 122-123 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.33-8.17 (m, 2H), 7.25 (ddd, J = 7.6, 6.2, 2.0 Hz, 1H), 7.22-7.18 (m, 2H), 6.85 (d, J = 7.8 Hz, 1H), 6.80 (dd, J = 7.7, 1.8 Hz, 2H), 3.81 (s, 3H), 3.06 (t, J = 7.5 Hz, 2H), 2.98-2.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 159.9, 155.4, 145.4, 141.2, 129.7, 125.2, 125.2, 122.4, 122.4, 120.7, 114.3, 111.8, 55.2, 35.8, 30.8. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{16}H_{15}NO_5$ 301.0950, found 301.0959.

4-nitrophenyl 3-(4-fluorophenyl)propanoate (**1e**): White solid (1.6g, 93% yield): mp 135-137 ^oC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.20 (m, 2H), 7.25-7.16 (m, 4H), 7.06-6.96 (m, 2H), 3.06 (t, J = 7.5 Hz, 2H), 2.96-2.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.3, 162.7, 155.3, 145.4, 135.3, 129.9, 129.8, 125.2, 125.2, 122.4, 122.4, 115.6, 115.4, 36.0, 29.9. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{15}H_{12}FNO_4$ 289.0750, found 289.0742.

4-nitrophenyl 3-(4-chlorophenyl)propanoate (**1f**): White solid (1.7g, 92% yield): mp 129-131 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-8.18 (m, 2H), 7.32-7.27 (m, 2H), 7.21 (t, J = 2.0 Hz, 2H), 7.20-7.16 (m, 2H), 3.05 (t, J = 7.4 Hz, 2H), 2.95-2.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 155.2, 145.4, 138.1, 132.5, 129.8, 129.8, 128.8, 128.8, 125.2, 125.2, 122.4, 122.4, 35.7, 30.1. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{15}H_{12}ClNO_4$ 305.0455, found 305.0452.

4-nitrophenyl 3-(4-bromophenyl)propanoate (**1g**): White solid (2.0g, 95% yield): mp 141-142 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-8.19 (m, 2H), 7.45 (d, J = 8.3 Hz, 2H), 7.22-7.16 (m, 2H), 7.14 (d, J = 8.3 Hz, 2H), 3.04 (t, J = 7.4 Hz, 2H), 2.91 (dd, J = 11.4, 4.1 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 155.2, 145.4, 138.6, 131.8, 131.8, 130.1, 130.1, 125.2, 125.2, 122.4, 122.4, 120.5, 35.6, 30.1. HRMS (EI-DF) *m/z* $[M + H]^+$ calcd for $C_{15}H_{13}BrNO_4$ 350.0028, found 349.9994.

4-nitrophenyl 3-(3-bromophenyl)propanoate (**1h**): White solid (1.9g, 94% yield): mp 140-141 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.22 (m, 2H), 7.44-7.35 (m, 2H), 7.24-7.16 (m, 4H), 3.05 (t, J = 7.3 Hz, 2H), 2.96-2.89 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 155.2, 145.4, 142.0, 131.5, 130.3, 129.8, 127.1, 125.2, 125.2, 122.7, 122.4, 122.4, 35.6, 30.3. HRMS (EI-DF) *m/z* $[M + H]^+$ calcd for $C_{15}H_{13}BrNO_4$ 350.0028, found 349.9999.

4-nitrophenyl 3-(2-bromophenyl)propanoate (**1i**): White solid (1.9g, 93% yield): mp 133-135 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30-8.21 (m, 2H), 7.58 (dd, J = 8.0, 1.1 Hz, 1H), 7.30 (ddd, J = 8.4, 7.4, 1.5 Hz, 2H), 7.27-7.20 (m, 2H), 7.17-7.08 (m, 1H), 3.20 (t, J = 7.6 Hz, 2H), 2.97 (t, J = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 155.3, 145.4, 138.9, 133.1, 130.6, 128.5, 127.7, 125.2, 125.2, 124.4, 122.4, 122.4, 34.2, 31.3. HRMS (EI-DF) *m/z* $[M + H]^+$ calcd for $C_{15}H_{13}BrNO_4$ 350.0028, found 349.9996.

4-nitrophenyl 3-(furan-2-yl)propanoate (**1j**): White solid (1.4g, 92% yield): mp 95-97 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33-8.18 (m, 2H), 7.35 (dd, J = 1.7, 0.6 Hz, 1H), 7.27-7.26 (m, 1H), 7.25-7.22 (m, 1H), 6.32 (dd, J = 3.1, 1.9 Hz, 1H), 6.11 (dd, J = 3.2, 0.8 Hz, 1H), 3.11 (t, J = 7.3 Hz, 2H), 2.95 (dd, J = 11.2, 4.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 155.4, 153.2,

145.4, 141.6, 125.2, 125.2, 122.4, 122.4, 110.4, 105.9, 33.0, 23.4. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{13}H_{11}NO_5$ 261.0637, found 261.0642.

4-nitrophenyl butyrate (**1k**): Yellow oil (1.1g, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40-8.08 (m, 2H), 7.43-7.06 (m, 2H), 2.59 (t, J = 7.4 Hz, 2H), 1.80 (dd, J = 14.8, 7.4 Hz, 2H), 1.06 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 155.5, 145.3, 125.2, 125.2, 122.4, 125.4, 36.1, 18.3, 13.6. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{10}H_{11}NO_4$ 209.0688, found 209.0688.

4-nitrophenyl hexanoate (**1l**): Yellow oil (1.3g, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37-8.13 (m, 2H), 7.37-7.17 (m, 2H), 2.60 (t, J = 7.5 Hz, 2H), 1.85-1.62 (m, 2H), 1.47-1.26 (m, 4H), 1.03-0.79 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 155.6, 145.3, 125.2, 125.2, 122.4, 122.4, 34.3, 31.2, 24.4, 22.3, 13.9. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{12}H_{15}NO_4$ 237.1001, found 237.0998.

4-nitrophenyl 3-cyclohexylpropanoate (**1m**): White solid (1.5g, 90% yield): mp 91-93 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38-8.10 (m, 2H), 7.38-7.08 (m, 2H), 2.72-2.45 (m, 2H), 1.80-1.68 (m, 5H), 1.66 (dd, J = 9.7, 5.8 Hz, 2H), 1.36-1.25 (m, 2H), 1.25-1.15 (m, 2H), 0.97 (td, J = 11.6, 2.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.6, 155.6, 145.3, 125.2, 125.2, 122.4, 122.4, 37.2, 33.0, 33.0, 32.1, 32.0, 26.5, 26.2, 26.2. HRMS (EI-DF) *m/z* $[M]^+$ calcd for $C_{15}H_{19}NO_4$ 277.1314, found 277.1309.

isoquinolin-2-ium-2-yl(tosyl)amide (**2a**): White solid (1.0g, 60% yield): mp 223-224 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.10-7.96 (m, 2H), 7.94-7.83 (m, 2H), 7.82-7.71 (m, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 8.0 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.0, 141.6, 139.0, 137.8, 134.6, 134.3, 130.5, 129.3, 129.3, 128.7, 128.1, 127.2, 127.2, 126.9, 124.6, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{15}N_2O_2S$ 299.0854, found 299.0856.

(5-chloroisoquinolin-2-ium-2-yl)(tosyl)amide (**2b**): Yellow solid (0.7g, 30% yield): mp 259-260 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.17-8.09 (m, 2H), 7.97-7.86 (m, 2H), 7.72-7.64 (m, 1H), 7.63-7.56 (m, 2H), 7.10 (d, J = 7.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.8, 141.8, 138.9, 138.3, 133.7, 132.0, 131.8, 130.8, 129.4, 129.4, 129.3, 127.4, 127.2, 127.2, 121.7, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}ClN_2O_2S$ 333.0465, found 333.0459.

(5-bromoisoquinolin-2-ium-2-yl)(tosyl)amide (**2c**): Brown solid (0.9g, 40% yield): mp 271-273 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 8.13 (d, J = 1.3 Hz, 2H), 8.09 (dd, J = 7.6, 0.9 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.60 (dt, J = 7.6, 3.8 Hz, 3H), 7.10 (d, J = 8.0 Hz, 2H), 2.29 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 141.8, 138.8, 138.4, 137.4, 133.4, 131.0, 129.4, 128.4, 129.3, 128.3, 127.2, 127.2, 124.2, 121.8, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}BrN_2O_2S$ 376.9956, found 376.9956.

(6-methylisoquinolin-2-ium-2-yl)(tosyl)amide (**2d**): Yellow solid (0.7g, 40% yield): mp 167-168 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 7.97 (dd, J = 7.0, 1.5 Hz, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.67 (d, J = 6.9 Hz, 2H), 7.62-7.48 (m, 3H), 7.07 (d, J = 7.9 Hz, 2H), 2.56 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.0, 146.2, 141.4, 139.2, 138.0, 135.0, 132.8, 129.2, 129.2, 128.5, 127.2, 127.2, 126.3, 125.9, 123.8, 22.5, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{17}H_{17}N_2O_2S$ 313.1011, found 313.1002.

(6-fluoroisoquinolin-2-ium-2-yl)(tosyl)amide (**2e**): Yellow solid (0.7g, 35% yield): mp 266-268 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 1H), 8.08 (ddd, J = 14.0, 8.0, 3.2 Hz, 2H), 7.75 (d, J = 7.1 Hz, 1H), 7.62-7.46 (m, 4H), 7.10 (d, J = 7.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 164.5, 147.0, 141.8, 138.6, 136.6, 132.2, 129.4, 129.4, 127.3, 127.3, 125.2, 123.9, 121.5, 111.2, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}FN_2O_2S$ 317.0760, found 317.0756.

(6-chloroisoquinolin-2-ium-2-yl)(tosyl)amide (**2f**): Yellow solid (0.5g, 26% yield): mp 252-253 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.14 (dd, J = 7.0, 1.5 Hz, 1H), 8.05 (d, J = 8.9 Hz, 1H), 7.95 (d, J = 1.6 Hz, 1H), 7.82–7.71 (m, 2H), 7.64 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.5, 141.8, 141.2, 138.8, 138.7, 135.0, 131.8, 130.1, 129.4, 129.4, 127.2, 127.2, 126.4, 125.9, 123.6, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}ClN_2O_2S$ 333.0465, found 333.0467.

(6-bromoisoquinolin-2-ium-2-yl)(tosyl)amide (**2g**): Brown solid (1.0g, 45% yield): mp 282-283 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.14 (s, 2H), 7.93 (dd, J = 21.4, 8.7 Hz, 2H), 7.77 (d, J = 6.9 Hz, 1H), 7.64 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 7.8 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 141.8, 138.8, 138.7, 135.1, 134.3, 129.9, 129.8, 129.4, 129.4, 129.2, 127.2, 127.2, 126.6, 123.5, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}BrN_2O_2S$ 376.9956, found 376.9961.

(7-chloroisoquinolin-2-ium-2-yl)(tosyl)amide (**2h**): Yellow solid (0.4g, 20% yield): mp 245-247 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (s, 1H), 8.19 (d, J = 6.6 Hz, 1H), 8.03 (s, 1H), 7.97-7.75 (m, 3H), 7.66 (d, J = 7.6 Hz, 2H), 7.17 (d, J = 7.5 Hz, 2H), 2.36 (s, 3H). ^{13}C NMR (126 MHz,

$CDCl_3$) δ 144.9, 141.9, 138.7, 137.9, 136.9, 135.0, 132.5, 129.4, 129.4, 128.9, 128.4, 127.2, 127.2, 126.9, 124.6, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}ClN_2O_2S$ 333.0465, found 333.0465.

(7-bromoisoquinolin-2-ium-2-yl)(tosyl)amide (**2i**): Brown solid (0.8g, 36% yield): mp 277-278 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.20–8.08 (m, 2H), 7.90 (dd, J = 8.7, 1.9 Hz, 1H), 7.77 (dd, J = 7.9, 3.2 Hz, 2H), 7.66-7.56 (m, 2H), 7.11 (d, J = 7.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 141.9, 138.7, 138.0, 137.5, 132.6, 130.2, 129.4, 129.4, 129.2, 128.3, 127.2, 127.2, 125.0, 124.6, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}BrN_2O_2S$ 376.9956, found 376.9960.

(8-bromoisoquinolin-2-ium-2-yl)(tosyl)amide (**2j**): Brown solid (0.7g, 31% yield): mp 269-270 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 9.38 (d, J = 0.7 Hz, 1H), 8.21 (dd, J = 7.0, 1.5 Hz, 1H), 7.94 (dd, J = 7.6, 0.8 Hz, 1H), 7.83 (dd, J = 11.8, 7.6 Hz, 2H), 7.65 (dd, J = 12.1, 5.1 Hz, 3H), 7.12 (d, J = 7.9 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.0, 142.0, 138.4, 138.2, 135.5, 134.4, 134.1, 129.4, 129.4, 127.6, 127.5, 127.5, 126.5, 125.0, 122.6, 21.4. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{16}H_{14}BrN_2O_2S$ 376.9956, found 376.9947.

(1S,10bS)-1-benzyl-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3a**): White viscous oil (34.4 mg, 80% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H), 7.26 (s, 1H), 7.23 (s, 1H), 7.22-7.12 (m, 4H), 7.03 (ddd, J = 8.5, 6.5, 1.3 Hz, 3H), 6.97 (d, J = 7.5 Hz, 1H), 6.75 (d, J = 7.5 Hz, 1H), 6.27 (d, J = 7.9 Hz, 1H), 5.66 (d, J = 7.9 Hz, 1H), 3.95 (d, J = 12.4 Hz, 1H), 3.72 (ddd, J = 12.4, 6.5, 3.9 Hz, 1H), 2.93 (dd, J = 14.9, 3.9 Hz, 1H), 2.69 (dd, J = 15.0, 6.5 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 145.4, 137.9, 136.6, 134.6, 129.9, 129.9, 129.7, 129.7, 129.2, 129.0, 128.4, 128.4, 128.3, 128.1, 128.1, 126.9, 126.7, 126.6, 125.5, 107.6, 64.2, 46.9, 30.4, 21.8. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{23}N_2O_3S$ 431.1429, found 431.1422. $[\alpha]^{20}_D$ = +60 (c = 0.18, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 99% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 14.5 min, t_2 (minor) = 20.4 min.

The absolute configuration of product **3a** is deemed on three reasons. Firstly, the ^1H NMR and ^{13}C NMR spectra of product **3a** is highly consistent with the compound **4a** of Glorius's work[6b], which are the same structure theoretically. Secondly, the optical rotation of product **3a** ($[\alpha]^{20}_D$ = +60) is close to the value of compound **4a** ($[\alpha]^{26}_D$= +41) of Glorius's work. Thirdly, retention time of

product **3a** on HPLC test is t_1 (major) = 14.5 min and t_2 (minor) = 20.4 min (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), and compound **4a** of Glorius's work is t_1(major) = 13.8 min and t_2(minor) = 20.5 min (AS-H, hexane/*i*-PrOH = 70/30, detector: 230 nm, flow rate: 1mL/min). Based on comprehensive results, we deem the absolute conformation of product **3a** is (1S,10bS)-1-benzyl-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinoline-2(3*H*)-one.

(1S,10bS)-1-(4-methylbenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3b**): Yellow viscous oil (35.5 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, J = 8.3 Hz, 2H), 7.29 (s, 1H), 7.25 (dd, J = 12.5, 4.6 Hz, 2H), 7.21 (dd, J = 7.5, 1.1 Hz, 1H), 7.05 (td, J = 7.5, 1.0 Hz, 1H), 6.98 (dd, J = 16.8, 8.1 Hz, 4H), 6.79 (d, J = 7.5 Hz, 1H), 6.30 (d, J = 7.9 Hz, 1H), 5.68 (d, J = 7.9 Hz, 1H), 3.96 (d, J = 12.4 Hz, 1H), 3.71 (ddd, J = 12.4, 6.5, 3.7 Hz, 1H), 2.96 (dd, J = 15.0, 3.6 Hz, 1H), 2.65 (dd, J = 14.9, 6.5 Hz, 1H), 2.48 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 145.4, 137.9, 136.1, 134.7, 133.4, 129.8, 129.8, 129.6, 129.6, 129.1, 129.1, 129.1, 129.0, 128.4, 128.1, 128.1, 126.9, 126.7, 125.5, 107.6, 63.9, 47.0, 29.8, 21.8, 21.0. HRMS (ESI-TOF) *m/z* $[M - H]^-$ calcd for $C_{26}H_{23}N_2O_3S$ 443.1429, found 443.1436. $[\alpha]^{20}_D$ = +20 (c = 0.10, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 11.4 min, t_2 (minor) = 17.6 min.

(1S,10bS)-1-(4-methoxybenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3c**): Yellow viscous oil (34.5 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.3 Hz, 2H), 7.41-7.31 (m, 3H), 7.19 (td, J = 7.5, 1.0 Hz, 1H), 7.14 (t, J = 8.0 Hz, 3H), 6.95 (d, J = 7.5 Hz, 1H), 6.88-6.81 (m, 2H), 6.43 (d, J = 7.9 Hz, 1H), 5.81 (d, J = 7.9 Hz, 1H), 4.10 (d, J = 12.4 Hz, 1H), 3.95 (s, 3H), 3.82 (ddd, J = 12.4, 6.2, 3.8 Hz, 1H), 3.08 (dd, J = 15.0, 3.7 Hz, 1H), 2.76 (dd, J = 15.0, 6.2 Hz, 1H), 2.60 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 158.3, 145.4, 137.4, 134.7, 130.9, 130.9, 129.8, 129.8, 129.2, 129.0, 128.5, 128.3, 128.1, 128.1, 126.8, 126.7, 125.5, 113.7, 113.7, 107.6, 63.7, 55.2, 47.2, 29.4, 21.8. HRMS (ESI-TOF) *m/z* $[M - H]^-$ calcd for $C_{26}H_{23}N_2O_4S$ 459.1379, found 459.1389. $[\alpha]^{20}_D$ = +51 (c = 0.16, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 15.3 min, t_2 (minor) = 23.1 min.

(1S,10bS)-1-(3-methoxybenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3d**): Yellow viscous oil (36.8 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H), 7.25 (s, 1H), 7.24 (s, 1H), 7.19 (td, J = 7.5, 1.1 Hz, 1H), 7.07 (t, J = 7.9 Hz, 1H), 7.02 (td, J = 7.5, 1.2 Hz, 1H), 6.97 (d, J = 7.5 Hz, 1H), 6.79 (d, J = 7.3 Hz, 1H), 6.72 (dd, J = 8.2, 2.1 Hz, 1H), 6.67-6.65 (m, 1H), 6.62 (d, J = 7.6 Hz, 1H), 6.26 (d, J = 7.9 Hz, 1H), 5.66 (d, J = 7.9 Hz, 1H), 3.93 (d, J = 12.4 Hz, 1H), 3.76 (s, 3H), 3.71 (ddd, J = 12.3, 6.3, 4.0 Hz, 1H), 2.88 (dd, J = 14.9, 4.0 Hz, 1H), 2.69 (dd, J = 14.9, 6.4 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 159.6, 145.4 , 138.2, 137.8, 134.6, 129.9, 129.9, 129.3, 129.2, 129.0, 128.3, 128.1, 128.1, 126.9, 126.7, 125.5, 121.9, 115.4, 112.2, 107.7, 64.4, 55.2, 46.9, 29.7, 21.8. HRMS (ESI-TOF) *m/z* [M - H]$^-$ calcd for $C_{26}H_{23}N_2O_4S$ 459.1379, found 459.1391. $[\alpha]^{20}_D$ = +60 (c = 0.12, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 96% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 16.4 min, t_2 (minor) = 23.6 min.

(1S,10bS)-1-(4-fluorobenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3e**): Yellow viscous oil (35.9 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2H), 7.25 (s, 2H), 7.21 (td, J = 7.5, 1.1 Hz, 1H), 7.07-7.01 (m, 3H), 6.99 (d, J = 7.5 Hz, 1H), 6.84 (t, J = 8.7 Hz, 2H), 6.77 (d, J = 7.4 Hz, 1H), 6.28 (d, J = 7.9 Hz, 1H), 5.67 (d, J = 7.9 Hz, 1H), 3.94 (d, J = 12.4 Hz, 1H), 3.69 (ddd, J = 12.4, 6.3, 4.0 Hz, 1H), 2.90 (dd, J = 15.0, 3.8 Hz, 1H), 2.65 (dd, J = 15.0, 6.3 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 162.6, 160.7, 145.6, 137.9, 134.7, 132.1, 131.4, 131.3, 129.9, 129.9, 129.3, 129.0, 128.2, 128.0, 128.0, 126.7, 125.6, 115.2, 115.0, 107.6, 64.0, 47.0, 29.5, 21.7. HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{25}H_{22}FN_2O_3S$ 449.1335, found 449.1343. $[\alpha]^{20}_D$ = +12 (c = 0.06, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 96% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 13.8 min, t_2 (minor) = 20.4 min.

(1S,10bS)-1-(4-chlorobenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3f**): Yellow viscous oil (30.2 mg, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2H), 7.29 (s, 1H), 7.28 (s, 1H), 7.24 (td, J = 7.5, 1.1 Hz, 1H), 7.17-7.12 (m, 2H), 7.07 (td, J = 7.5, 1.1 Hz, 1H), 7.02 (t, J = 8.1 Hz, 3H), 6.79 (d, J = 7.5 Hz, 1H), 6.30 (d, J = 7.9 Hz, 1H), 5.70 (d, J = 7.9 Hz, 1H), 3.92 (d, J = 12.4 Hz, 1H), 3.72 (ddd, J = 12.5, 6.3, 3.9 Hz, 1H), 2.95 (dd, J = 15.0, 3.8 Hz, 1H), 2.65 (dd, J = 15.0, 6.2 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9,

145.7, 137.9, 134.9, 134.6, 132.6, 131.3, 131.3, 129.9, 129.9, 129.3, 129.0, 128.4, 128.4, 128.2, 128.0, 128.0, 126.8, 126.7, 125.6, 107.7, 63.8, 47.0, 29.6, 21.7. HRMS (ESI-TOF) *m/z* $[M - H]^-$ calcd for $C_{25}H_{20}ClN_2O_3S$ 463.0883, found 463.0888. $[\alpha]^{20}_D$ = +18 (c = 0.08, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 95% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 13.8 min, t_2 (minor) = 20.4 min.

(1S,10bS)-1-(4-bromobenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3g**): Yellow viscous oil (40.7 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.32-7.29 (m, 3H), 7.28-7.27 (m, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.3 Hz, 2H), 6.79 (d, *J* = 7.5 Hz, 1H), 6.30 (d, *J* = 7.9 Hz, 1H), 5.70 (d, *J* = 7.9 Hz, 1H), 3.91 (d, *J* = 12.4 Hz, 1H), 3.72 (ddd, *J* = 12.4, 6.2, 3.9 Hz, 1H), 2.94 (dd, *J* = 15.0, 3.9 Hz, 1H), 2.63 (dd, *J* = 14.9, 6.2 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 145.7, 137.9, 135.4, 134.6, 131.6, 131.6, 131.4, 131.4, 129.9, 129.9, 129.3, 129.0, 128.2, 128.0, 128.0, 126.8, 126.7, 125.6, 120.7, 107.7, 63.8, 46.9, 29.7, 21.8. HRMS (ESI-TOF) *m/z* $[M - H]^-$ calcd for $C_{25}H_{20}BrN_2O_3S$ 507.0378, found 507.0390. $[\alpha]^{20}_D$ = +22 (c = 0.10, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 96% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 14.9 min, t_2 (minor) = 22.1 min.

(1S,10bS)-1-(3-bromobenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3h**): Yellow viscous oil (39.7 mg, 78% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.35-7.32 (m, 1H), 7.31 (s, 1H), 7.30 (d, *J* = 1.6 Hz, 1H), 7.28 (d, *J* = 1.5 Hz, 1H), 7.26 (d, *J* = 6.9 Hz, 1H), 7.23 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.07 (dd, *J* = 10.1, 4.9 Hz, 2H), 7.01 (d, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.31 (d, *J* = 7.9 Hz, 1H), 5.70 (d, *J* = 7.9 Hz, 1H), 3.92 (d, *J* = 12.4 Hz, 1H), 3.73 (ddd, *J* = 12.3, 6.5, 4.2 Hz, 1H), 2.84 (dd, *J* = 14.9, 4.2 Hz, 1H), 2.70 (dd, *J* = 14.9, 6.6 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 145.6, 139.0, 137.7, 134.5, 132.7, 130.0, 130.0, 129.9, 129.8, 129.4, 129.0, 128.4, 128.1, 128.1, 128.0, 126.8, 126.8, 125.6, 122.4, 107.8, 64.6, 46.7, 29.7, 21.8. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{22}BrN_2O_3S$ 509.0535, found 509.0521. $[\alpha]^{20}_D$ = +18 (c = 0.14, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 96% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 16.3 min, t_2 (minor) = 24.4 min.

(1S,10bS)-1-(2-bromobenzyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3i**): Yellow viscous oil (38.2 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H),

7.42 - 7.38 (m, 3H), 7.30 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.18 (td, *J* = 7.5, 1.0 Hz, 1H), 7.11 (td, *J* = 7.6, 1.1 Hz, 1H), 6.99 (ddd, *J* = 11.9, 9.3, 4.6 Hz, 3H), 6.73 (d, *J* = 7.4 Hz, 1H), 6.26 (d, *J* = 7.9 Hz, 1H), 5.69 (d, *J* = 7.9 Hz, 1H), 3.94 (d, *J* = 12.4 Hz, 1H), 3.85 (ddd, *J* = 12.5, 6.9, 5.9 Hz, 1H), 2.74 (d, *J* = 6.3 Hz, 2H), 2.50 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.9, 145.8, 137.5, 136.6, 134.7, 132.7, 131.7, 130.1, 130.1, 129.3, 129.0, 128.3 , 128.3, 128.3, 127.8, 127.2, 127.2, 126.8, 125.3, 124.3, 108.0, 66.6, 44.7, 31.5, 21.9. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{22}BrN_2O_3S$ 509.0535, found 509.0531. $[\alpha]^{20}_D$ = +16 (c = 0.04, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 96% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 13.7 min, t_2 (minor) = 18.3 min.

(1S,10bS)-1-(furan-2-ylmethyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3j**): Yellow viscous oil (33.6 mg, 80% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.20 (td, *J* = 7.4, 1.4 Hz, 1H), 7.11 (d, *J* = 1.1 Hz, 1H), 7.07 (ddd, *J* = 20.9, 10.5, 3.9 Hz, 2H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.28 (d, *J* = 7.9 Hz, 1H), 6.19 (dd, *J* = 3.0, 1.9 Hz, 1H), 6.01 (d, *J* = 3.0 Hz, 1H), 5.64 (d, *J* = 7.9 Hz, 1H), 3.95 (d, *J* = 12.5 Hz, 1H), 3.61 (ddd, *J* = 12.5, 5.1, 3.6 Hz, 1H), 3.07 (dd, *J* = 15.8, 3.5 Hz, 1H), 2.66 (dd, *J* = 15.8, 5.2 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.1, 150.5, 145.3, 141.4, 137.7, 134.6, 129.9, 129.9, 129.1, 128.8, 128.4, 128.1, 128.1, 127.0, 127.0, 125.4, 110.5, 109.0, 107.4, 63.4, 46.0, 22.7, 21.8. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{23}H_{21}N_2O_4S$ 421.1222, found 421.1222. $[\alpha]^{20}_D$ = +40 (c = 0.16, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 13.2 min, t_2 (minor) = 22.6 min.

(1S,10bS)-1-ethyl-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3k**): Yellow viscous oil (27.6 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 7.7 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.10-6.86 (m, 2H), 6.69 (d, *J* = 7.2 Hz, 1H), 6.27 (d, *J* = 7.7 Hz, 1H), 5.63 (d, *J* = 7.7 Hz, 1H), 3.94 (d, *J* = 12.5 Hz, 1H), 3.38-3.21 (m, 1H), 2.47 (s, 3H), 1.54 (d, *J* = 3.7 Hz, 1H), 1.45-1.30 (m, 1H), 1.26 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 145.7, 137.9, 135.0, 129.9, 129.9, 129.2, 129.0, 128.6, 128.2, 128.2, 126.7, 126.5, 125.4, 107.2, 64.3, 46.3, 21.8, 17.5, 9.6. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{20}H_{21}N_2O_3S$ 369.1273, found 369.1275. $[\alpha]^{20}_D$ = +130 (c = 0.20, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 95% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm,

flow rate: 1 mL/min), t_1 (major) = 9.7 min, t_2 (minor) = 12.8 min.

(1S,10bS)-1-butyl-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3l**): Yellow viscous oil (29.7 mg, 75% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.23-7.16 (m, 1H), 7.05 (td, J = 7.5, 1.1 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 6.70 (d, J = 7.5 Hz, 1H), 6.27 (d, J = 7.9 Hz, 1H), 5.63 (d, J = 7.9 Hz, 1H), 3.94 (d, J = 12.5 Hz, 1H), 3.31 (ddd, J = 12.5, 6.5, 3.9 Hz, 1H), 2.47 (s, 3H), 1.44 - 1.35 (m, 2H), 1.24-1.14 (m, 2H), 0.96-0.86 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 145.7, 137.9, 135.0, 129.9, 129.9, 129.2, 129.0, 128.6, 128.2, 128.2, 126.7, 126.5, 125.4, 107.1, 64.9, 45.5, 27.5, 24.4, 22.8, 21.8, 13.8. HRMS (ESI-TOF) *m/z* $[M - H]^-$ calcd for $C_{22}H_{23}N_2O_3S$ 395.1429, found 395.1431. $[\alpha]^{20}_D$ = +142 (c = 0.16, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 7.9 min, t_2 (minor) = 10.2 min.

(1S,10bS)-1-(cyclohexylmethyl)-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**3m**): Yellow viscous oil (30.5 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.23 (td, J = 7.5, 1.1 Hz, 1H), 7.06 (td, J = 7.5, 1.1 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 6.77 (d, J = 7.5 Hz, 1H), 6.31 (d, J = 7.9 Hz, 1H), 5.67 (d, J = 7.9 Hz, 1H), 3.85 (d, J = 12.4 Hz, 1H), 3.41 (ddd, J = 12.1, 7.8, 4.1 Hz, 1H), 2.49 (s, 3H), 1.67-1.49 (m, 5H), 1.47-1.32 (m, 4H), 1.13-1.01 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 145.6, 137.9, 134.8, 130.0, 130.0, 129.2, 129.0, 128.4, 128.2, 128.2, 126.8, 126.6, 125.4, 107.4, 66.7, 42.7, 34.4, 33.7, 33.0, 32.5, 26.3, 26.0, 25.9, 21.8. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{29}N_2O_3S$ 437.1899, found 437.1905. $[\alpha]^{20}_D$ = +180 (c = 0.14, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 7.5 min, t_2 (minor) = 9.3 min.

(1S,10bS)-1-benzyl-7-chloro-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4b**): Yellow viscous oil (27.9 mg, 60% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 1H), 7.27 (s, 1H), 7.26 (s, 1H), 7.22 (d, J = 8.1 Hz, 1H), 7.16 (dt, J = 5.4, 4.1 Hz, 3H), 7.05-7.00 (m, 2H), 6.92 (t, J = 7.8 Hz, 1H), 6.61 (d, J = 7.5 Hz, 1H), 6.36 (d, J = 8.1 Hz, 1H), 6.05 (d, J = 8.1 Hz, 1H), 3.95 (d, J = 12.4 Hz, 1H), 3.74 (ddd, J = 12.3, 6.4, 4.1 Hz, 1H), 2.92 (dd, J = 15.0, 4.0 Hz, 1H), 2.70 (dd, J = 15.1, 6.4 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.7, 145.6, 139.3, 136.3, 134.5, 130.6, 130.0, 130.0, 130.0, 129.9, 129.5, 129.5, 128.4, 128.4, 128.1, 128.1,

127.3, 127.0, 126.7, 125.4, 103.6, 64.2, 46.6, 30.4, 21.8. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{22}ClN_2O_3S$ 465.1040, found 465.1043. $[\alpha]^{20}_D$ = +8.0 (c = 0.06, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 23.7 min, t_2 (minor) = 31.0 min.

(1S,10bS)-1-benzyl-7-bromo-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4c**): Yellow viscous oil (33.1 mg, 65% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.29 (s, 1H), 7.28-7.26 (m, 1H), 7.18 (d, *J* = 6.8 Hz, 3H), 7.10-6.99 (m, 2H), 6.86 (t, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.36 (d, *J* = 8.1 Hz, 1H), 6.04 (d, *J* = 8.1 Hz, 1H), 3.94 (d, *J* = 12.4 Hz, 1H), 3.77 (ddd, *J* = 12.3, 6.4, 4.1 Hz, 1H), 2.94 (dd, *J* = 15.1, 4.0 Hz, 1H), 2.71 (dd, *J* = 15.1, 6.5 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 145.2, 139.2, 135.9, 134.0, 132.9, 129.6, 129.5, 129.5, 129.1, 129.1, 128.2, 128.0, 128.0, 127.7, 127.7, 127.1, 126.3, 125.7, 120.6, 105.7 , 63.8, 46.1, 30.0, 21.4. HRMS (ESI-TOF) *m/z* $[M - H]^-$ calcd for $C_{25}H_{20}BrN_2O_3S$ 507.0378, found 507.0383. $[\alpha]^{20}_D$ = +10 (c = 0.08, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 19.5 min, t_2 (minor) = 25.8 min.

(1S,10bS)-1-benzyl-8-methyl-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4d**): Yellow viscous oil (32.0 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.19 (dd, *J* = 5.0, 2.1 Hz, 3H), 7.08 (dd, *J* = 7.2, 2.1 Hz, 2H), 6.90-6.79 (m, 2H), 6.69 (d, *J* = 7.6 Hz, 1H), 6.29 (d, *J* = 7.9 Hz, 1H), 5.65 (d, *J* = 7.9 Hz, 1H), 3.94 (d, *J* = 12.4 Hz, 1H), 3.69 (ddd, *J* = 12.3, 6.6, 3.7 Hz, 1H), 2.96 (dd, *J* = 14.9, 3.7 Hz, 1H), 2.68 (dd, *J* = 14.9, 6.6 Hz, 1H), 2.47 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.4, 145.4, 139.0, 137.8, 136.7, 134.6, 129.9, 129.9, 129.7, 129.7, 128.8, 128.4, 128.4, 128.1, 128.1, 127.2, 126.8, 126.6, 126.3, 125.4, 107.7, 64.0, 47.0, 30.3, 21.8, 21.1. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{26}H_{25}N_2O_3S$ 445.1586, found 445.1584. $[\alpha]^{20}_D$ = +30 (c = 0.16, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 92% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 14.9 min, t_2 (minor) = 18.2 min

(1S,10bS)-1-benzyl-8-fluoro-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4e**): Yellow viscous oil (31.4 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.30 (s, 2H), 7.19 (t, *J* = 5.7 Hz, 3H), 7.04 (dd, *J* = 7.4, 1.8 Hz, 2H), 6.74-6.65 (m, 3H), 6.36 (d, *J* = 7.9 Hz, 1H), 5.64 (d, *J* = 7.9 Hz, 1H), 3.97 (d, *J* = 12.3 Hz, 1H), 3.72 (ddd, *J* = 12.3, 6.4, 4.2 Hz,

1H), 2.92 (dd, *J* = 15.0, 4.2 Hz, 1H), 2.74 (dd, *J* = 15.0, 6.4 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 145.6, 139.0, 136.4, 134.6, 131.3, 131.2, 130.0, 130.0, 129.5, 129.5, 128.5, 128.5, 128.4, 128.1, 128.1, 126.7, 123.8, 112.9, 112.5, 106.8, 64.0, 46.8, 30.5, 21.8. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{22}FN_2O_3S$ 449.1335, found 449.1319. $[\alpha]^{20}_D$ = +10 (c = 0.04, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 21.5 min, t_2 (minor) = 25.6 min.

(1S,10bS)-1-benzyl-8-chloro-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4f**): Yellow viscous oil (33.0 mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.29 (s, 1H), 7.28 (s, 1H), 7.19 (q, *J* = 5.9 Hz, 3H), 7.04 (d, *J* = 6.2 Hz, 2H), 7.01 - 6.95 (m, 2H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.34 (d, *J* = 7.9 Hz, 1H), 5.62 (d, *J* = 7.9 Hz, 1H), 3.96 (d, *J* = 12.4 Hz, 1H), 3.72 (ddd, *J* = 12.3, 6.4, 4.1 Hz, 1H), 2.93 (dd, *J* = 15.0, 4.0 Hz, 1H), 2.71 (dd, *J* = 15.0, 6.4 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.3, 145.1, 138.6, 135.8, 134.5, 134.0, 130.3, 129.5, 129.5, 129.0, 129.0, 128.0, 128.0, 127.6, 127.6, 127.6, 126.2, 126.0, 125.9, 124.8, 106.0, 63.3, 46.3, 29.9, 21.3. HRMS (ESI-TOF) *m/z* $[M + H]^+$ calcd for $C_{25}H_{22}ClN_2O_3S$ 465.1040, found 465.1039. $[\alpha]^{20}_D$ = +14 (c = 0.12, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 95% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 21.5 min, t_2 (minor) = 25.6 min.

(1S,10bS)-1-benzyl-8-bromo-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4g**): Yellow viscous oil (38.2 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 2H), 7.28 (s, 1H), 7.27-7.26 (m, 1H), 7.22-7.15 (m, 3H), 7.15-7.10 (m, 2H), 7.03 (d, *J* = 6.7 Hz, 2H), 6.59 (d, *J* = 8.6 Hz, 1H), 6.33 (d, *J* = 7.9 Hz, 1H), 5.60 (d, *J* = 7.9 Hz, 1H), 3.94 (d, *J* = 12.4 Hz, 1H), 3.72 (ddd, *J* = 12.3, 6.4, 4.1 Hz, 1H), 2.93 (dd, *J* = 15.0, 3.9 Hz, 1H), 2.70 (dd, *J* = 15.0, 6.4 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 145.2, 138.7, 135.8, 134.1, 130.6, 129.5, 129.5, 129.1, 129.1, 128.9, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 126.6, 126.3, 122.7, 106.0, 63.4, 46.3, 29.3, 21.4. HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{25}H_{21}BrN_2O_3SNa$ 531.0354, found 531.0354. $[\alpha]^{20}_D$ = +7.5 (c = 0.04, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 22.1 min, t_2 (minor) = 26.1 min.

(1S,10bS)-1-benzyl-9-chloro-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4h**): Yellow viscous oil (30.2 mg, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.19 (dd, J = 5.0, 1.9 Hz, 3H), 7.15 (dd, J = 8.1, 2.1 Hz, 1H), 7.04 (dd, J = 6.5, 2.9 Hz, 2H), 6.90 (d, J = 8.1 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H), 6.31 (d, J = 7.9 Hz, 1H), 5.65 (d, J = 7.9 Hz, 1H), 3.91 (d, J = 12.4 Hz, 1H), 3.75 (ddd, J = 12.4, 6.2, 4.5 Hz, 1H), 2.92 (dd, J = 15.1, 4.5 Hz, 1H), 2.78 (dd, J = 15.1, 6.2 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 145.7, 138.2, 136.2, 134.5, 131.9, 130.0, 130.0, 129.9, 129.4, 129.4, 129.1, 128.5, 128.5, 128.1, 128.1, 127.5, 127.2, 126.8, 126.5, 106.7, 64.1, 46.6, 30.6, 21.8. HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{25}H_{22}ClN_2O_3S$ 465.1040, found 465.1035. $[\alpha]^{20}_D$ = +10 (c = 0.12, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 17.5 min, t_2 (minor) = 28.6 min.

(1S,10bS)-1-benzyl-9-bromo-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4i**): Yellow viscous oil (38.2 mg, 75% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, J = 8.2 Hz, 2H), 7.32-7.28 (m, 3H), 7.19 (dd, J = 5.0, 1.7 Hz, 3H), 7.06-6.97 (m, 2H), 6.82 (dd, J = 18.3, 4.7 Hz, 2H), 6.32 (d, J = 7.8 Hz, 1H), 5.63 (d, J = 7.9 Hz, 1H), 3.89 (d, J = 12.4 Hz, 1H), 3.82-3.68 (m, 1H), 2.91 (dd, J = 15.1, 4.4 Hz, 1H), 2.78 (dd, J = 15.1, 6.2 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 145.3, 137.9, 135.7, 134.1, 131.6, 129.7, 129.6, 129.6, 129.5, 129.0, 129.0, 128.1, 128.1, 127.6, 127.6, 127.5, 126.4, 126.3, 119.3, 106.3, 63.5, 46.2, 30.1, 21.4. HRMS (ESI-TOF) *m/z* [M - H]$^-$ calcd for $C_{25}H_{20}BrN_2O_3S$ 507.0378, found 507.0386. $[\alpha]^{20}_D$ = +9.5 (c = 0.10, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 98% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 14.4 min, t_2 (minor) = 22.2 min.

(1S,10bS)-1-benzyl-10-bromo-3-tosyl-1,10b-dihydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**4j**): Yellow viscous oil (30.5 mg, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.09 (dd, J = 7.7, 2.3 Hz, 3H), 7.04 (dd, J = 8.0, 1.1 Hz, 1H), 6.99 (t, J = 7.7 Hz, 1H), 6.91-6.83 (m, 3H), 6.57 (d, J = 7.8 Hz, 1H), 5.49 (d, J = 7.9 Hz, 1H), 4.66 (d, J = 6.2 Hz, 1H), 3.17 (dd, J = 13.8, 7.8 Hz, 1H), 3.03 (dd, J = 13.8, 7.3 Hz, 1H), 2.94 (dd, J = 13.9, 7.1 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9, 146.1, 139.4, 136.9, 134.4, 133.5, 130.8, 130.3, 130.1, 130.1, 128.6, 128.6, 128.3, 128.3, 128.2, 128.2, 126.4, 126.3, 124.2, 122.8,

105.0, 63.2, 49.4, 33.2, 21.8. HRMS (ESI-TOF) *m/z* [M - H]$^-$ calcd for $C_{25}H_{20}BrN_2O_3S$ 507.0378, found 507.0373. $[\alpha]^{20}_D$ = +8.5 (c = 0.06, $CHCl_3$). The product was analyzed by HPLC to determine the enantiomeric excess: 96% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 13.8 min, t_2 (minor) = 35.2 min.

(1S,10bS)-1-benzyl-3-tosyl-1,5,6,10b-tetrahydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**5a**): White viscous oil (51.9 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.23 (s, 1H), 7.19 (dd, *J* = 7.1, 4.0 Hz, 4H), 7.17-7.12 (m, 2H), 7.10 (dd, *J* = 9.9, 4.5 Hz, 3H), 4.05 (d, *J* = 12.3 Hz, 1H), 3.74-3.59 (m, 1H), 3.37-3.11 (m, 4H), 3.00-2.80 (m, 2H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 144.9, 136.4, 135.1, 133.5, 133.3, 129.9, 129.9, 129.7, 129.7, 129.0, 128.4, 128.4, 128.0, 128.0, 127.5, 126.8, 126.6, 126.2, 61.2, 51.1, 48.1, 31.7, 29.1, 21.7. HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{25}H_{25}N_2O_3S$ 433.1586, found 433.1579. The product was analyzed by HPLC to determine the enantiomeric excess: 95% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 12.5 min, t_2 (minor) = 16.9 min.

(1S,10bS)-1-(4-bromobenzyl)-3-tosyl-1,5,6,10b-tetrahydropyrazolo[5,1-*a*]isoquinolin-2(3*H*)-one (**5g**): White viscous oil (63.4 mg, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.26 (s, 1H), 7.25 (s, 1H), 7.19 (dd, *J* = 11.4, 4.5 Hz, 5H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 3.96 (d, *J* = 12.4 Hz, 1H), 3.76-3.58 (m, 1H), 3.23 (dddd, *J* = 12.5, 10.1, 9.3, 3.4 Hz, 4H), 2.98-2.78 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 145.2, 135.2, 135.0, 133.6, 133.2, 131.9, 131.9, 131.4, 131.4, 129.7, 129.7, 129.2, 129.2, 127.9, 127.7, 126.6, 126.3, 120.8, 60.8, 51.2, 48.0, 31.0, 29.2, 21.8. HRMS (ESI-TOF) *m/z* [M + H]$^+$ calcd for $C_{25}H_{24}BrN_2O_3S$ 511.0691, found 511.0693. The product was analyzed by HPLC to determine the enantiomeric excess: 97% e.e. (OD-H, hexane/*i*-PrOH = 70/30, detector: 254 nm, flow rate: 1 mL/min), t_1 (major) = 14.8 min, t_2 (minor) = 33.8 min.

ASSOCIATED CONTENT

Supporting Information

Information not shown in table 3, ^{1}H NMR and ^{13}C NMR spectra, HPLC spectra of products.

AUTHOR INFORMATION

Corresponding Author

*E-mail: jinyixu@china.com.

*E-mail: hliu@simm.ac.cn.

Author Contributions

[§]Pengfei Zhang and Yu Zhou contributed equally to this work.

Notes:

The authors declare no competing financial interest.

ACKNOWLEDGMENT

We are grateful to the National Natural Science Foundation of China (No. 21672232, 81673306, 81703348) for financial support.

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