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Article

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(*R*)-DM-SEGPHOS-Ag(I) Catalyzed Enantioselective Synthesis of Pyrrolidines and Pyrrolizidines *via* (1,3)- and Double (1,3)-Dipolar Cycloaddition Reactions

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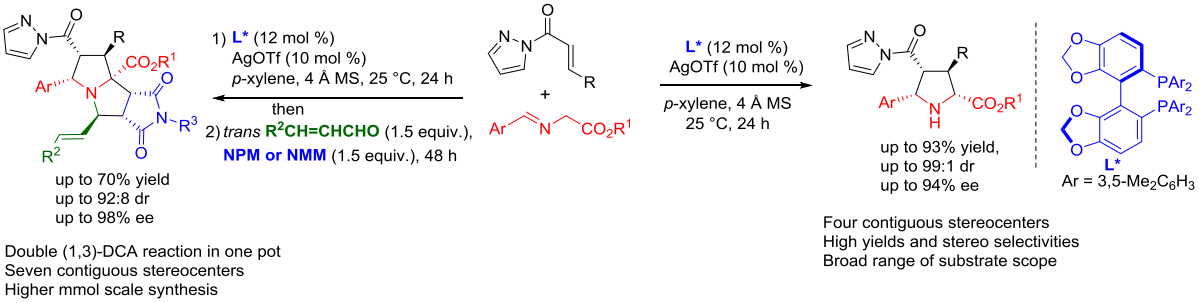
Graphical Abstract



Abstract

An efficient diastereo- and enantioselective route to access a wide range of highly substituted pyrrolidine and pyrrolizidine derivatives has been described *via* (1,3)- and double (1,3)-dipolar cycloaddition (DCA) reactions catalyzed by (*R*)-DM-SEGPHOS-Ag(I) complex. The reactions proceed smoothly at ambient temperature affording a variety of pyrrolidines and pyrrolizidines in high yields (up to 93%) with up to 99:1 dr and excellent enantioselectivities (up to 98% ee) without any additives. The newly synthesized pyrrolidine and pyrrolizidine derivatives contain four and seven contiguous stereogenic centers respectively. Moreover, the synthetic utility of enantioenriched products has been demonstrated by transforming them into various synthetically useful advanced intermediates.

Introduction

Densely functionalized pyrrolidine derivatives have been found as key structural motifs in numerous nitrogen-containing heterocycles and have evoked immense research interest due to their broad spectrum of biological properties.[1,2] Their intriguing therapeutic potential is evident from the observed analgesic,[3] antibacterial,[4] antitumor,[5] anti-inflammatory[6] and glycosidase inhibitor[7] properties (Figure 1. **1a-d**). Similarly, pyrrolizidines are privileged structural scaffolds present in many biologically active alkaloids and pharmaceuticals.[8] In fact, about 400 bioactive natural products are comprised of pyrrolizidine framework.[9] Many of them are found to be potent hepatoxic, genotoxic, carcinogenic and occasionally pneumotoxic.[10,11] Additionally, some families of pyrrolizidine display important therapeutic effects (Figure 1, **2a-d**).[12] For example, 1-hydroxymethyl substituted pyrrolizidine (-)-isoretronecanol **2a** possesses stimulant actions in the guinea-pig ileum preparation.[13]

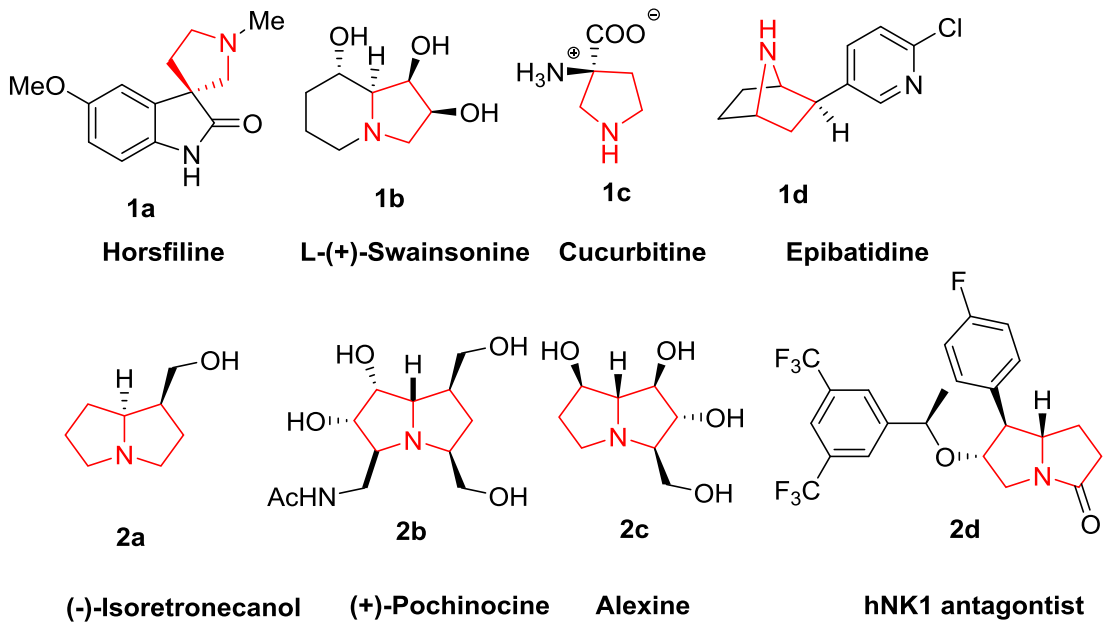


Figure 1. Representative examples of biologically active pyrrolidines and pyrrolizidines

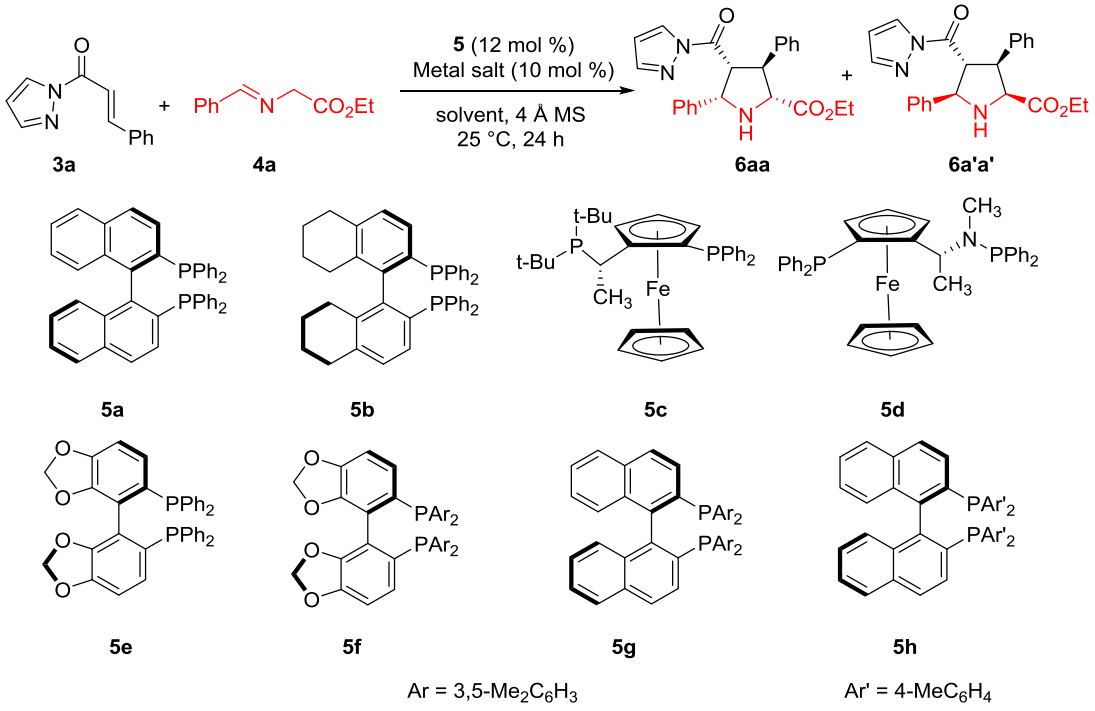
Given the synthetic value and biological potential of these two classes of compounds, many efforts have been directed towards synthesis of these *N*-heterocyclic scaffolds.[14] Among various asymmetric approaches for the construction of pyrrolidine scaffolds, transition metal catalyzed asymmetric (1,3)-DCA reaction of azomethine ylide with activated olefins has become one of the most powerful and atom-economical route.[15] The first catalytic enantioselective (1,3)-DCA reaction of azomethine ylide with activated olefins was reported by the research group of Zhang[16a]and Jørgensen[16b] independently in 2002. Since then, significant success has been achieved in enantioselective (1,3)-DCA reactions for the synthesis of pyrrolidines employing chalcones,[17a-b] alkyl cinnamates,[17a] acrylates,[17c] maleimides,[17d-e] nitroalkenes,[17f] allenoates[17g] and complicated alkenes bearing electron-withdrawing groups as dipolarophiles.[17h] Subsequently, Kobayshi *et al.* have demonstrated (*R*)-DTBM-SEGPHOS-Ag(I) catalyzed enantioselective (1,3)-DCA reactions of α- aminoester Schiff bases with various activated olefins.[18] However, to the best of our knowledge, *α,β*-unsaturated pyrazolamide has been unexplored in (1,3)-DCA reaction with azomethine ylide. The synthetic versatility of the cycloadducts having *N*-acylpyrazole moiety could be demonstrated by various functional group transformations into alcohols, esters, amides and ketones.[19] In contrast, the most common and straightforward strategy for the synthesis of enantioenriched pyrrolizidines involves multicomponent reaction of chiral proline derivatives with *α,β*-unsaturated aldehydes and various dipolarophiles.[20] In 2011, Gan and coworkers have reported the synthesis of highly functionalized pyrrolizidine derivative *via* double (1,3)-DCA reactions.[21a] Recently, Lim *et. al.* have reported Ag(I) catalyzed asymmetric double (1,3)-DCA reaction at -45 °C for the construction of enantioenriched pyrrolizidines.[21b] However, unified strategy to access both of these two important classes of compounds employing a common catalytic system in one pot is rare.

Needless to say, enantioselective construction of architecturally complex *N*-heterocyclic scaffolds having contiguous multiple stereogenic centers in one pot is still a challenging task. Herein, we report a (*R*)-DM-SEGPHOS-Ag(I) catalyzed unified approach to access highly functionalized pyrrolidines and pyrrolizidines derivatives *via* (1,3)- and double (1,3)-DCA reactions at room temperature under mild reaction conditions.

Results and Discussion

Our investigation was commenced using α,β-unsaturated pyrazolamide **3a** as a dipolarophile, azomethine ylide **4a** as a 1,3-dipole and (*R*)-BINAP-Ag(I) as the active catalyst. To our delight, the cycloaddition product was formed as a mixture of diastereomers (81:19 dr) where **6aa** was isolated as the major isomer in 68% yield with 44% ee (Table 1, entry 1). Encouraged by this preliminary outcome, an array of bis-phosphine based chiral ligands **5b-h** was examined (Table 1, entries 2-8). However, (*R*)-H_8-BINAP **5b** and ferrophos ligands **5c-d** gave disappointing results, affording **6aa** in lower enantioselectivities (Table 1, entries 2-4).

Table 1. Catalyst screening and selected entries for the optimization of reaction conditions[a]



Entry	Ligand	Metal salt	Solvent	Yield (%)[b]	dr[c]	ee (%)[d]
1	5a	AgOAc	toluene	68	81:19	44
2	5b	AgOAc	toluene	70	90:10	3
3	5c	AgOAc	toluene	73	90:10	20
4	5d	AgOAc	toluene	40	85:15	36
5	5e	AgOAc	toluene	62	87:15	55
6	5f	AgOAc	toluene	65	72:28	66
7	5g	AgOAc	toluene	55	70:30	36
8	5h	AgOAc	toluene	58	73:27	40
9	5f	AgF	toluene	52	56:44	66

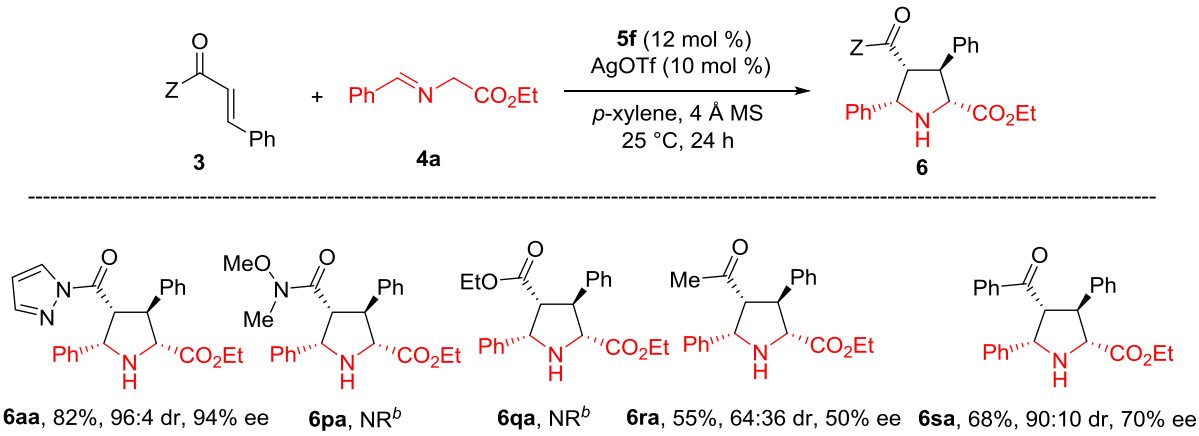
10	5f	AgOTf	toluene	75	96:4	80
11	5f	$Cu(CH_3CN)_4BF_4$	toluene	30	44:56	38
12	5f	$AgSbF_6$	toluene	60	69:31	66
13	5f	AgOTf	dioxane	89	99:1	81
14	5f	AgOTf	Et_2O	80	93:7	68
15	5f	AgOTf	THF	62	88:12	74
16	5f	AgOTf	*p*-xylene	82	96:4	94
17	5f	AgOTf	mixt. of xylene	80	99:1	92
18	5f	AgOTf	benzene	65	97:3	74
19	5f	AgOTf	mesitylene	60	94:6	93
20	5f	AgOTf	toluene + *p*-xylene	85	99:1	90
21[e]	5f	AgOTf	p-xylene	80	96:4	88
22[f]	5f	AgOTf	p-xylene	32	99:1	70

[a]Reactions were carried out using 0.2 mmol of **3a** (1 equiv) and 0.30 mmol of **4a** (1.5 equiv) in presence of 10 mol % metal salt and 12 mol % ligand **5**. [b]Yield of major diastereomer. [c]Diastereomeric ratio (dr) was determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Enantiomeric excess (ee) was determined by chiral HPLC analysis. [e]5 mol % AgOTf and 6 mol % **5f** were used. [f]Reaction was carried out without molecular sieves.

Among other bis-phosphine ligands screened in the reaction, sterically hindered (*R*)-DM-SEGPHOS **5f** was found to be the best, affording **6aa** in 65% yield with 72:28 dr and 66% ee (Table 1, entry 6). For further refinement of the catalytic system, a series of silver salts were assessed in chelation with ligand **5f** and silver triflate was found to be superior to the rest. Surprisingly, when silver salt was replaced by copper (I), the *exo* product **6a'a'** was formed in almost equally with endo product **6aa** (Table 1, entry 11).[22] Among various solvents screened, *p*-xylene was found to be the best solvent in terms of chemical and optical yields (82%, 94% ee) (Table 1, entry 16). Interestingly, mesitylene was equally efficient as a choice of solvent in terms of stereoselectivities, furnished **6aa** in 60% yield with 93% ee (Table 1, entry 19). Notably, use of 4 Å molecular sieves (MS) was essential to achieve the desired product **6aa** with high yield and stereoselectivities (Table 1, entry 22).

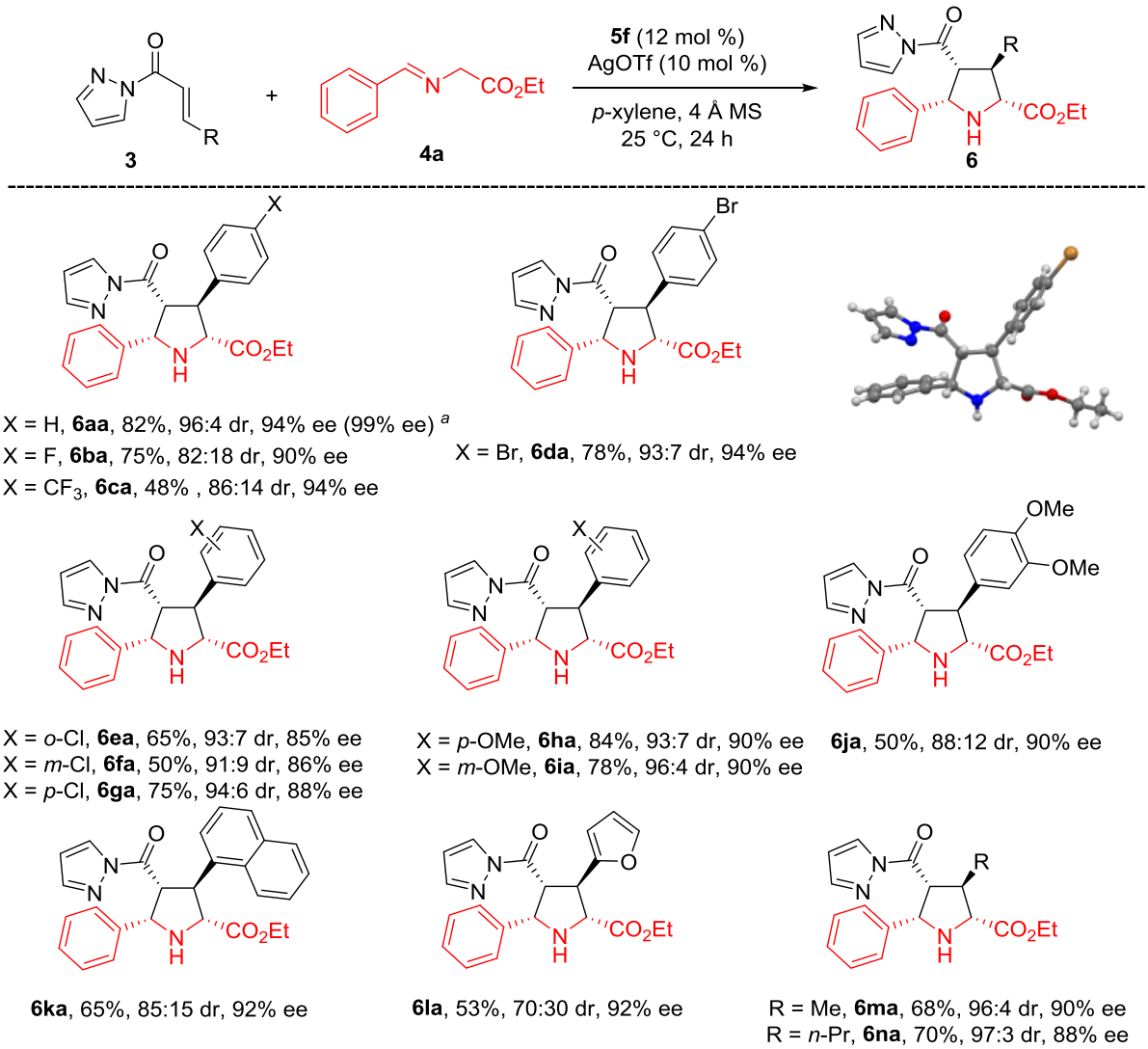
Next, to compare the reactivity and selectivity of α,β-unsaturated carbonyls as dipolarophiles, the reaction of ethyl *N*-benzylideneglycinate **4a** with a variety of activated olefins were examined in our optimized reaction conditions were. (1,3)-DCA reaction of azomethine yilide **4a** with *N*-methoxy-*N*-methylcinnamide **3p** and ethyl cinnamate **3q** did not promote this reaction. However, dipolarophiles such as benzylidene acetone **3r** and chalcone **3s** furnished the corresponding adducts **6ra-sa** in moderate yields (up to 68%) and stereoselectivities (up to 70% ee). Eventually, α,β-unsaturated pyrazolamide **3a** was found to be superior dipolarophile considering chemical and optical yields. Thus further studies were done employing **3a** (82% yield, 94% ee).

Scheme 1. Reaction of ethyl *N*-benzylideneglycinate 4a with different dipolarophile under optimized reaction conditions.[a]



[a]Reaction conditions: **3** (0.2 mmol), **4a** (0.3 mmol), **5f** (0.024 mmol), AgOTf (0.02 mmol) and 4 Å MS (50 mg) in 2 mL *p*-xylene. [b]NR = No Reaction.

Scheme 2. Scope of various *α,β*-unsaturated pyrazolamides in (1,3)-DCA reaction

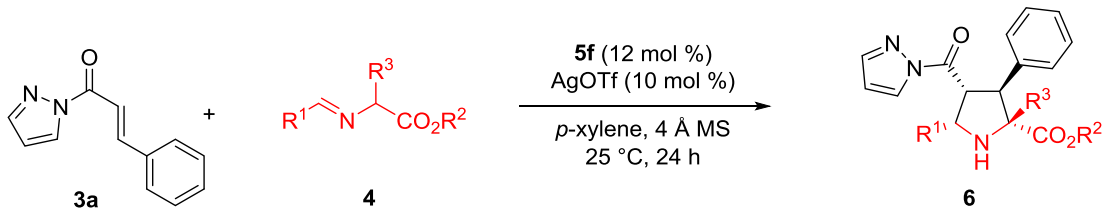


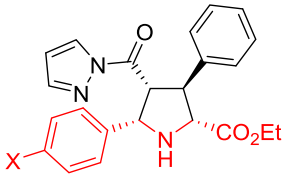
[a]ee after recrystallization

Having optimized reaction conditions in hand, a variety of α,β-unsaturated pyrazolamides **3b-n** bearing an aromatic ring or an aliphatic side chain were explored in the enantioselective (1,3)-DCA reaction (Scheme 2). Delightfully, a variety of differently substituted pyrrolidines **6ba-na** was obtained in good yields (up to 84%) with high diastereoselectivities (up to 97:3 dr) and excellent enantioselectivities (up to 94% ee). Notably, the position of substituent on the aromatic ring has a prominent effect on the chemical yields. Substrates having *para*-substituent on the aromatic ring afforded products in higher yield than that of *ortho*- and *meta*-substituents (Scheme 2, entries **6ea-ga** and **6ha-ia**). The substrates containing 1-naphthyl **3k** and 2-furyl **3l** at the β-position efficiently furnished products **6ka-la** in up to 65% yields and 92% ee. Rewardingly, α,β-unsaturated pyrazolamides having aliphatic side chain **3m-n** were well tolerated under this catalytic system, leading to pyrrolidine derivatives **6ma-na** in up to 70% yield and up to 90 % ee.

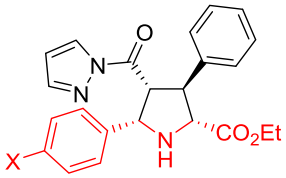
Later, the scope of the reaction was expanded to a diverse array of iminoesters **4b-o** derived from electron-poor and -rich aromatic aldehydes under optimized conditions (Scheme 3). Gratifyingly, enantioenriched products **6ab-ao** were obtained in excellent yields (up to 93%) and stereoselectivities (up to 99:1 dr, 94% ee). Noticeably, the *ortho*-substituent on the phenyl ring of iminoester has a deleterious effect in comparison to the *para*-substituent. Iminoesters **4h-i** derived from 2-naphthaldehyde and biphenyl-4-carboxaldehyde furnished pyrrolidines **6ah-6ai** in synthetically viable yields (up to 88%) and excellent enantioselectivities (up to 90% ee). Surprisingly, the azomethine ylides containing heteroaromatic ring **4j-k** also underwent (1,3)-DCA reaction to provide the corresponding pyrrolidines **6aj-ak** in moderate yields (up to 53%) and enantioselectivities (up to 68%). Iminoester derived from cinnamaldehyde **4l** afforded pyrrolidines **6al** in moderate yield (60%) with poor enantioselectivity (15% ee). Moreover, iminoesters **4m-n** were also examined towards this cycloaddition reaction. Interestingly, iminoester **4m** having a bulkier group (R^1 = *t*-Bu), afforded cycloadduct **6am** in 51% yield with 88% ee. It is noteworthy to mention that azomethine ylide derived from alanine imino ester **4o** also worked well under our optimized reaction conditions to furnish the pyrrolidine **6ao** in good yield (73%) and stereoselectivities (95:5 dr, 68% ee). Unfortunately, the reaction did not proceed with iminoesters derived from aliphatic aldehydes **4p** and **4q** even after 3 days.

Scheme 3. Scope of different azomethine ylide in (1,3)-DCA reaction

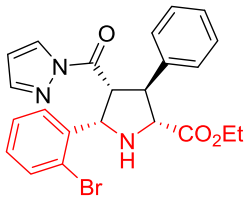




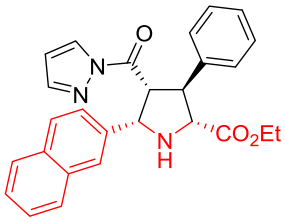
X = Me, **6ab**, 92%, 98:2 dr, 92% ee
X = OMe, **6ac**, 93%, 94:6 dr, 94% ee



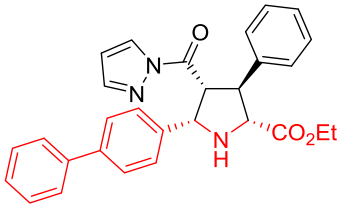
X = Cl, **6ad**, 75%, 90:10 dr, 90% ee
X = Br, **6ae**, 85%, 87:13 dr, 92% ee
X = F, **6af**, 88%, 95:5 dr, 90% ee



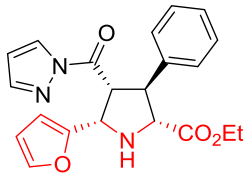
6ag, 64%, 97:3 dr, 86% ee



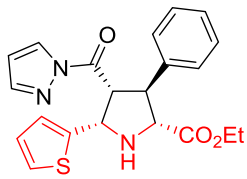
6ah, 68%, 98:2 dr, 86% ee



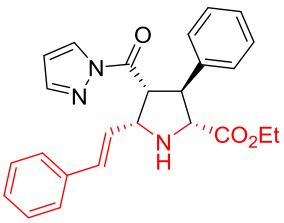
6ai, 88%, 99:1 dr, 90% ee



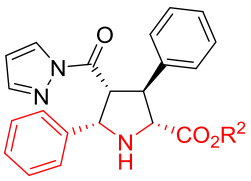
6aj, 52%, 82:18 dr, 68% ee



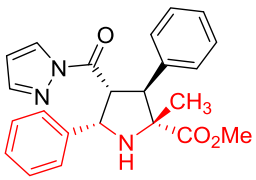
6ak, 53%, 70:30 dr, 58% ee



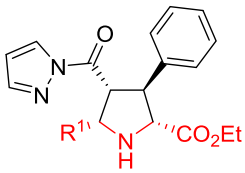
6al, 60%, 85:15 dr, 15% ee



R^2 = *t*-Bu, **6am**, 51%, 89:11 dr, 88% ee
R^2 = Me, **6an**, 91%, 93:7 dr, 88% ee



6ao, 73%, 95:5 dr, 68% ee



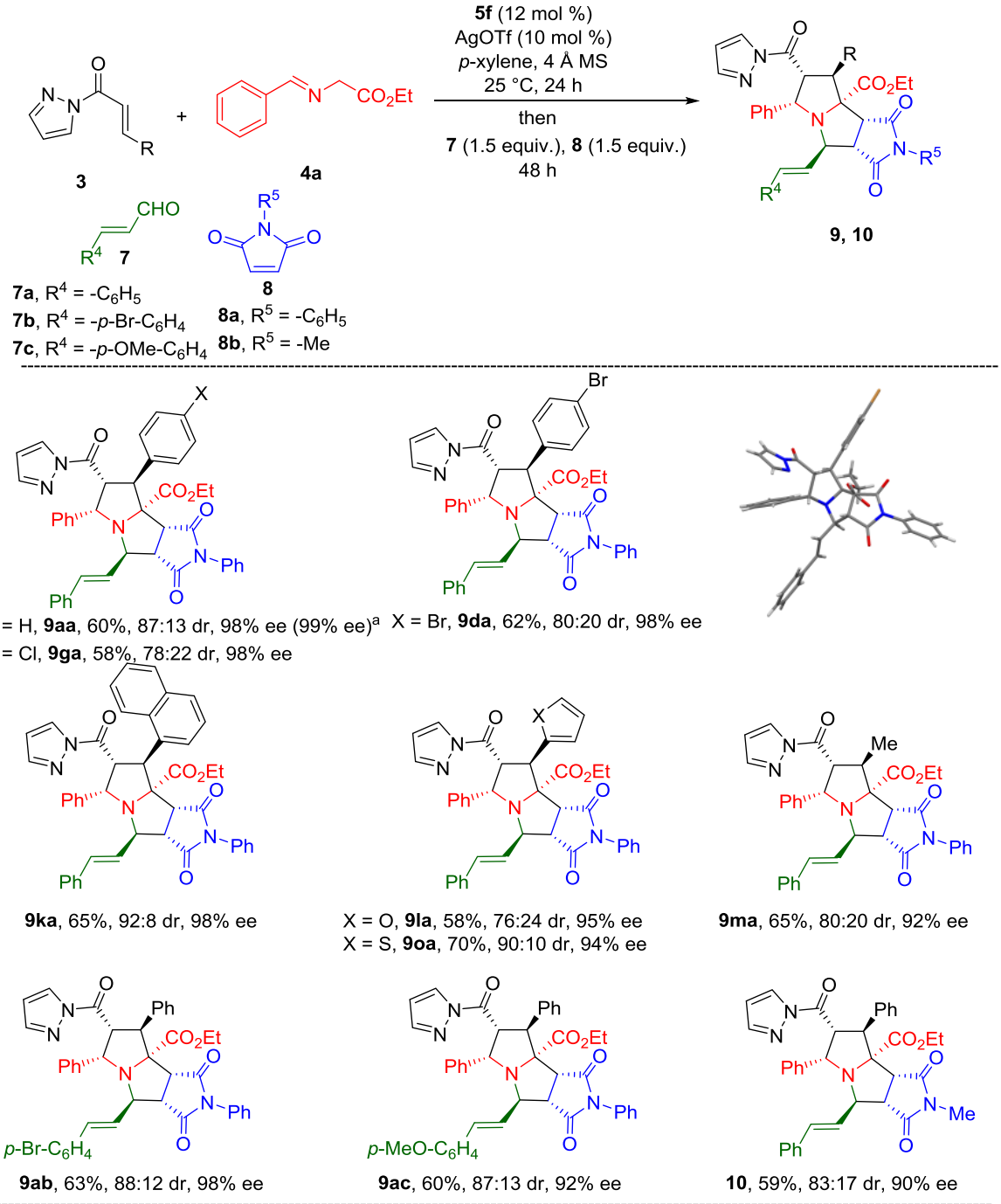
R^1 = *i*-Pr, **6ap**, NR
R^1 = Cyclohexyl, **6aq**, NR

The absolute configuration of the four contiguous stereocenters of **6da** was unambiguously determined by single crystal X-ray structure analysis. The absolute configuration of other products within this series was assigned by analogy.

Having secured the synthesis of a wide range of pyrrolidines, we turned our attention towards the construction of biologically interesting pyrrolizidine derivatives. It would be a win-win situation if the synthesis of pyrrolizidine derivatives with high enantiopurity could be achieved in one pot employing

the same catalytic system *via* a sequential double (1,3)-DCA reaction from readily and commercially available starting materials.

Scheme 4. Substrate scope in double (1,3) DCA reaction



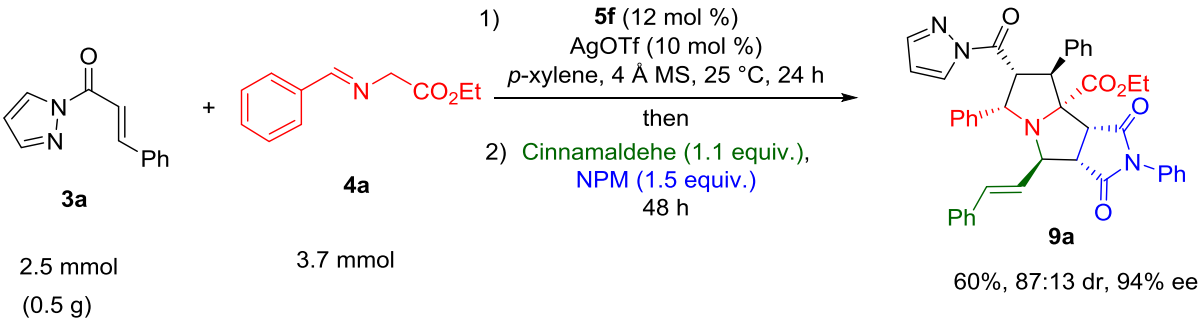
[a]ee after recrystallization

Towards this end, we studied the reaction of **3a** with azomethine ylide **4a** in our previously optimized conditions, followed by sequential addition of cinnamaldehyde 7a (1.5 equiv.) and *N*-phenylmaleimide (NPM) **8a** (1.5 equiv.) in one-pot. Delightfully, the *exo*-pyrrolizidine derivative **9aa** was obtained in 60% yield with 87:13 dr and 98% ee. This exciting outcome prompted us to further investigate the substrate scope of the double (1,3)-DCA reaction. At first, a broad range of differently substituted α,β-unsaturated pyrazolamides **3** were tested (Scheme 4). To our pleasure, pyrrolizidine

derivatives **9aa-ma** were obtained in synthetically viable yields (up to 70%), good diastereoselectivities (up to 92:8 dr) and excellent enantioselectivities (up to 98% ee). Substrates bearing 1-naphthyl and 2-heteroaryl substituted α,β-unsaturated pyrazolamides were also suitable for this reaction. Importantly, methyl substituted α,β-unsaturated pyrazolamides furnished pyrrolizidine **9ma** in 65% yield and 92% ee. Next, a variety of substituted cinnamaldehydes were examined, leading to pyrrolizidines **9ab-ac** in up to 63% yield and 98% ee. Apart from NPM, *N*-methylmaleimide (NMM) worked efficiently as a dipolarophile for the second (1,3)-DCA reaction and furnished pyrrolizidine **10** in 90% ee. It is noteworthy to mention that seven new contiguous stereogenic centers have been created in a one-pot double (1,3)-DCA reaction. Interestingly, multiple contiguous stereogenic centers exist in numerous natural and unnatural products.[23] The absolute configuration of compound **9da** was unambiguously determined on the basis of the single crystal X-ray structure analysis.

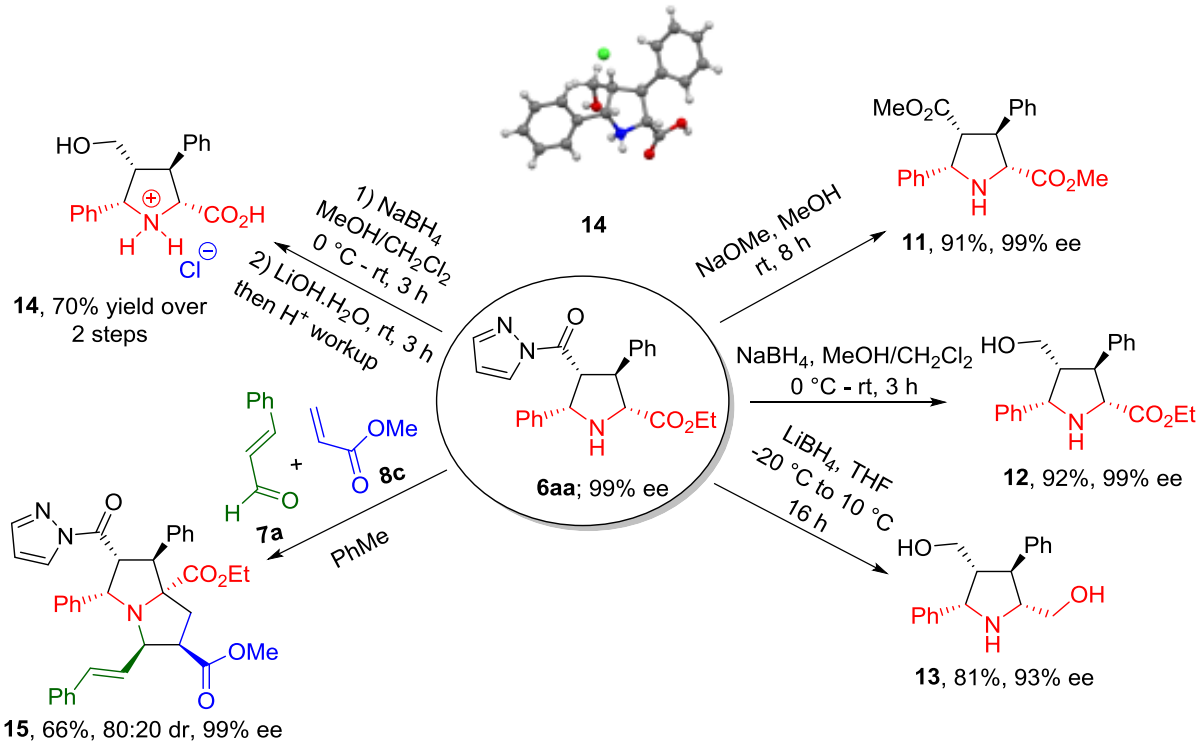
To illustrate the practical efficacy of the double (1,3)-DCA reaction, a reaction was performed with 2.5 mmol scale of the model starting material **3a** (Scheme 5).The pyrrolizidine **9aa** was obtained in 60% yield and 94% ee.

Scheme 5. Scale up of the reaction



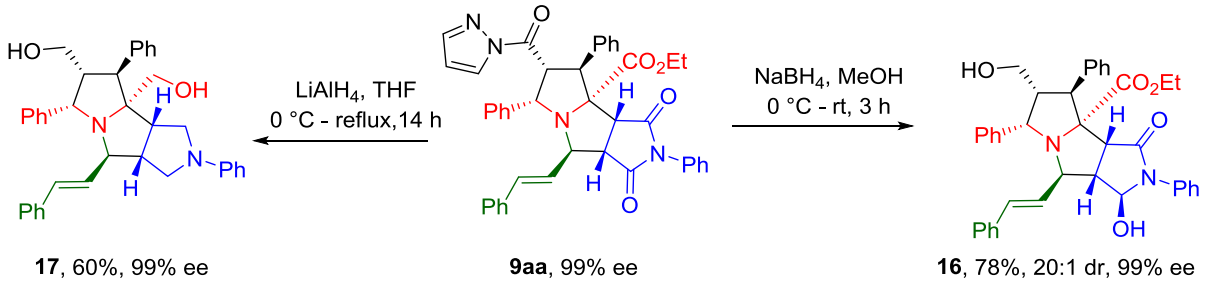
Next, the synthetic utility of this chemistry was investigated by exploiting the reactivity of *N*-acylpyrazole unit. The reaction of **6aa** (99% ee) with NaOMe in room temperature afforded methyl ester **11** without any compromise of enantiopurity (Scheme 6). Additionally, treatment of **6aa** separately with $NaBH_4$ in $MeOH/CH_2Cl_2$ (9:1) and $LiBH_4$ in THF gave the corresponding alcohol derivatives **12** and **13** in 92% and 81% yields respectively. Notably, reduction of **6aa** with $NaBH_4$ followed by saponification using $LiOH{\cdot}H_2O$ afforded optically active proline derivative **14** in 70% yield over two steps. In an interesting development, the catalyst-free three component annulation reaction of **6aa** with cinnamaldehyde **7a** and methyl acrylate **8c** in toluene afforded the product **15** in 66% yield without any erosion of enantiopurity.

Scheme 6. Synthetic elaboration of pyrrolidine derivative



Finally, the treatment of **9aa** with $NaBH_4$ and $LiAlH_4$ afforded corresponding dihydroxylated pyrrolizidines **16** and **17** respectively in good yields (Scheme 7). These hydroxylated pyrrolizidines could serve as potent inhibitors of glycosidases.[24]

Scheme 7. Synthetic transformation of pyrrolizidine derivatives



Conclusion

In conclusion, we have developed a highly stereoselective unified approach for the synthesis of a wide range of densely functionalized pyrrolidines and pyrrolizidines of immense biological importance. (*R*)-DM-SEGPHOS-Ag(I) complex has been developed as a common catalytic system for (1,3)-DCA and double (1,3)-DCA reactions. The desired pyrrolidines and pyrrolizidines were obtained in high yields (up to 93%) with remarkable stereoselectivities (up to 99:1 dr, 98% ee). Enantioselective construction of *N*-heterocyclic scaffolds containing multiple contiguous stereogenic centers is one of the salient features of this exciting chemistry. The usefulness of this synthetic protocol has also been demonstrated by converting *N*-acylpyrazole moiety into various functional groups. Further application of this unified strategy for natural product synthesis is currently underway in our laboratory.

Experimental Section

Materials and Methods

All reactions were carried out in oven dried glassware with magnetic stirring. All solventswere purified and dried according to standard methods prior to use. Starting materials *α,β*-unsaturated pyrazolamide **3a-o** and azomethine ylides **4b-k** were prepared by reported methods.[17,25] Weinreb amide **3p** was prepared according to literature known procedure.[26] *α,β*-unsaturated carbonyls **3q-s** are commercially avialable. Catalysts **5a-5h** are commercially available. Cinnamaldehyde **7a** and substituated cinnamaldehydes **7b-c** are commercially available. *N*-phenylmaleimide (**8a**) and *N*-methylmaleimide (**8b**) are commercially available. ^{1}H spectra were recorded on 400 MHz or 500 MHz in $CDCl_3$ and $^{13}C\{^{1}H\}$NMR spectra were recorded on 100 or 125 MHz in $CDCl_3$ using TMS or residual solvent signals as internal standard. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m =multiplet or unresolved, coupling constant (s) in Hz, integration). Data for $^{13}C\{^{1}H\}$NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by the ESI (Q-TOF) ionization sources. IR spectra were measured with FT/IR Vector 22 spectrometer. Optical rotations were measured on a commercial automatic polarimeter and reported as follows: $[\alpha]_D^T$ (c = g/100 mL, solvent). Routine monitoring of reactions we reperformed using precoated silica gel TLC plates from E-Merck. All the chromatographic separations were carried out by using silica gel (Acme's, 100-200 mesh). Melting points were recorded by using a melting point apparatus and are uncorrected. The enantioselectivity was determined by chiral HPLC analysis using chiralpak IA, IC and ID column chiralcel-ODH, with a 200 UV-detector by using iso-propanol and n-hexane as eluent at 25 °C.

General procedure and characterization data of *α,β*-unsaturated pyrazolamide 3a-n. To a solution of pyrazole (5.0 g, 73.5 mmol) in CH_2Cl_2 (150 mL) was added $SOCl_2$ (8.0 mL, 110 mmol) at 0 °C, then the reaction mixture was brought to room temperature and stirred at room temperature for 1 . To the reaction mixture *trans*-Cinnamic acid (24.5 mmol) was added in one portion. The mixture was further stirred for additional 3 hours. The resulting solution was diluted with CH_2Cl_2 (150 mL), washed with aqueous NaOH solution (0.5 M, 3 x 100 mL), water (3 x 100 mL), then dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (40-50% CH_2Cl_2 in hexanes) to afford product **3a-n**.

***(E)*-3-phenyl-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3a):** White solid, 6.01 g, 90% yield. R_f = 0.62 (10% EtOAc in hexanes). **MP**: 42−45 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 2.9, 0.7 Hz, 1H), 8.06 (d, *J* = 16.0 Hz, 1H), 7.94 (d, *J* = 16.0 Hz, 1H), 7.81 (d, *J* = 1.4 Hz, 1H), 7.78 – 7.66 (m, 2H), 7.50 – 7.37 (m, 3H), 6.52 (dd, *J* = 2.8, 1.5 Hz, 1H). **$^{13}C\{^{1}H\}$NMR** (125 MHz, Chloroform-*d*) δ 163.6, 147.9, 143.8, 134.4, 131.0, 128.9, 128.8, 128.7, 115.7, 109.9. **IR** (film) ν_{max} 3621, 3132, 1954, 1705, 1623, 1385, 1351, 935, 767 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{10}N_2ONa$ 221.0685; Found 221.0700.

(*E*)-3-(4-fluorophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3b): White solid, 3.30 g, 85% yield. R_f = 0.60 (10% EtOAc in hexanes). **MP**: 117-120 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.40 (d, *J* = 2.7 Hz, 1H), 7.99 (d, *J* = 16.0 Hz, 1H), 7.84 (d, *J* = 16.0 Hz, 1H), 7.79 (d, *J* = 1.5 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.17 – 7.07 (m, 2H), 6.51 (dd, *J* = 2.9, 1.5 Hz, 1H). **$^{13}C\{^{1}H\}$NMR** (125 MHz, Chloroform-*d*) δ 165.3, 163.4, 163.3, 146.4, 143.8, 130.8, 130.7, 116.2, 116.0, 115.4, 109.8. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -108.1. **IR** (film) ν_{max} 3428, 2361, 1699, 1626, 1387, 828, 745 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9FN_2ONa$ 239.0591; Found 239.0583.

(*E*)-1-(1*H*-pyrazol-1-yl)-3-(4-(trifluoromethyl)phenyl)prop-2-e*n*-1-one (3c): White solid, 0.36 g, 55% yield. R_f = 0.63 (10% EtOAc in hexanes). **MP**: 90-93 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.7 Hz, 1H), 7.97 (d, *J* = 2.8 Hz, 2H), 7.75 (d, *J* = 8.9 Hz, 3H), 7.65 (d, *J* = 8.1 Hz, 2H), 6.52 – 6.43 (m, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.0, 145.5, 144.0, 137.6, 132.4, 132.1, 128.7, 125.9, 118.3, 110.1. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -62.9. **IR** (film) ν_{max} 3361, 2112, 1910, 1697, 1622, 1430, 1355, 801, 749 cm^{-1}; **HRMS** (ES-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_9F_3N_2ONa$ 289.0559; Found 289.0568.

(*E*)-3-(4-bromophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3d): White solid, 2.07 g, 75% yield. R_f = 0.60 (10% EtOAc in hexanes). **MP**: 104-107 °C.**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.8 Hz, 1H), 8.01 – 7.78 (m, 2H), 7.75 (d,*J* = 1.5 Hz, 1H), 7.52 (s, 4H), 6.48 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 163.3, 146.2, 143.9, 133.3, 132.2, 130.1, 128.7, 125.4, 116.4, 110.0. **IR** (film) ν_{max} 3381, 2106, 1907, 1693, 1623, 1485, 1386, 1349, 819, 762 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9BrN_2ONa$ 298.9790; Found 298.9795.

(*E*)-3-(2-chlorophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3e): White solid, 2.8 g, 60% yield. R_f = 0.60 (10% EtOAc in hexanes). **MP**: 94-97 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 16.0 Hz, 1H), 8.39 (d, *J* = 2.8 Hz, 1H), 7.91 (d, *J* = 16.0 Hz, 1H), 7.84 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.77 (d, *J* = 1.5 Hz, 1H), 7.44 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.32 (pd, *J* = 7.4, 1.7 Hz, 2H), 6.50 (dd, *J* = 2.9, 1.5 Hz, 1H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 163.1, 143.9, 143.3, 135.6, 132.6, 131.7, 130.2, 128.7, 128.1, 127.1, 118.2, 110.0. **IR** (film) ν_{max} 3443, 2361, 1706, 1621, 1387, 1350, 933, 756, 585 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9ClN_2ONa$ 255.0296; Found 255.0305.

(*E*)-3-(3-chlorophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3f): White solid, 4.18 g, 90% yield. R_f = 0.61 (10% EtOAc in hexanes). **MP**: 86-89 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 2.8 Hz, 1H), 7.91 (d, *J* = 4.7 Hz, 2H), 7.78 (d, *J* = 1.5 Hz, 1H), 7.67 (t, *J* = 1.8 Hz, 1H), 7.59 – 7.48 (m, 1H), 7.45 – 7.30 (m, 2H), 6.49 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 163.2, 146.0, 144.0, 136.2, 135.0, 130.8, 130.2, 128.7, 128.3, 127.0, 117.2, 110.0. **IR** (film) ν_{max} 3429, 2114, 1645, 1267, 752 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{12}H_{10}ClN_2O$ 233.0476; Found 233.0469.

(*E*)-3-(4-chlorophenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3g): White solid, 4.46 g, 96% yield. R_f = 0.60 (10% EtOAc in hexanes). **MP**: 104-107 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.36 (d, *J* = 2.8 Hz, 1H), 8.01 – 7.80 (m, 2H), 7.76 (d, *J* = 1.4 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.43 – 7.33 (m, 2H), 6.48 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 163.3, 146.2, 143.9, 137.0, 132.9, 129.9, 129.2, 128.7, 116.3, 109.9, 99.9. **IR** (film) ν_{max}3138, 1695, 1623, 1386, 1349, 823, 763 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9ClN_2ONa$ 255.0296; Found 255.0315.

(*E*)-3-(4-methoxyphenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3h): White solid, 5.76 g, 90% yield. R_f = 0.50 (10% EtOAc in hexanes). **MP**: 79-82 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 2.8, 0.7 Hz, 1H), 8.02 (d, *J* = 15.9 Hz, 1H), 7.82 – 7.78 (m, 2H), 7.71 – 7.67 (m, 2H), 6.99 – 6.93 (m, 2H), 6.51 (dd, *J* = 2.8, 1.5 Hz, 1H), 3.89 (s, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.8, 162.0, 147.7, 143.6, 130.7, 128.6, 127.3, 114.4, 113.0, 109.6, 55.4. **IR** (film) ν_{max} 3425, 2563, 1701, 1602, 1513, 1259, 826, 765 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{12}N_2O_2Na$ 251.0791; Found 251.0810.

(*E*)-3-(3-methoxyphenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3i): White solid, 4.7 g, 73% yield. R_f = 0.51 (10% EtOAc in hexanes). **MP**: 62-65 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 2.8, 0.7 Hz, 1H), 8.03 (d, *J* = 16.0 Hz, 1H), 7.91 (d, *J* = 16.0 Hz, 1H), 7.84 – 7.76 (m, 1H), 7.37 (t, *J* = 7.9 Hz, 1H), 7.31 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.23 (dd, *J* = 2.6, 1.7 Hz, 1H), 7.02 (ddd, *J* = 8.1, 2.6, 1.1 Hz, 1H), 6.53 (dd, *J* = 2.9, 1.5 Hz, 1H), 3.89 (s, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.6, 159.9, 147.8, 143.8, 135.7, 129.9, 128.7, 121.6, 117.1, 115.9, 113.3, 109.8, 55.4. **IR** (film) ν_{max} 3424, 2085, 1705, 1622, 1384, 774 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{12}N_2O_2Na$ 251.0791; Found 251.0787.

(*E*)-3-(3,4-dimethoxyphenyl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3j): White solid, 4.90 g, 95% yield. R_f = 0.40 (10% EtOAc in hexanes). **MP**: 105-108 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 2.9 Hz, 1H), 7.90 (d, *J* = 15.9 Hz, 1H), 7.76 – 7.59 (m, 2H), 7.23 – 7.08 (m, 2H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.41 (dd, *J* = 2.8, 1.5 Hz, 1H), 3.86 (d, *J* = 11.6 Hz, 6H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.7, 151.9, 149.2, 148.0, 143.6, 128.7, 127.5, 124.0, 113.0, 110.9, 110.0, 109.6, 56.03, 56.01. **IR** (film) ν_{max} 3658, 2938, 2037, 1701, 1593, 1515, 1267, 1027, 935, 843 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{14}H_{14}N_2O_3Na$ 281.0897; Found 281.0913.

(*E*)-3-(naphthale*n*-1-yl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3k): White solid, 1.8 g, 72% yield. R_f = 0.64 (10% EtOAc in hexanes). **MP**: 71-74 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.93 (d, *J* = 15.7 Hz, 1H), 8.47 (dd, *J* = 2.9, 0.7 Hz, 1H), 8.34 (dd, *J* = 8.5, 1.1 Hz, 1H), 8.10 – 8.05 (m, 1H), 8.05 – 8.03 (m, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.95 – 7.91 (m, 1H), 7.83 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.65 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.61 – 7.53 (m, 2H), 6.55 (dd, *J* = 2.8, 1.5 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.5, 144.5, 143.9, 133.7, 131.6, 131.5, 131.4, 128.8, 128.8, 127.1, 126.3, 125.8, 125.4, 123.2, 118.0, 109.9. **IR** (film) ν_{max} 3404, 3055, 1704, 1616, 1416, 1385, 1352, 768 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{12}N_2ONa$ 271.0842; Found 271.0863.

(*E*)-3-(fura*n*-2-yl)-1-(1*H*-pyrazol-1-yl)prop-2-e*n*-1-one (3l): White solid, 1.63 g, 87% yield. R_f = 0.55 (10% EtOAc in hexanes). **MP**: 67-70 °C. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 2.8 Hz, 1H), 7.72 (d, *J* = 6.3 Hz, 3H), 7.50 (d, *J* = 1.7 Hz, 1H), 6.73 (d, *J* = 3.4 Hz, 1H), 6.45 (ddd, *J* = 11.9, 3.2, 1.7 Hz, 2H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.6, 151.3, 145.6, 143.7, 133.3, 128.5, 116.6, 113.3, 112.6, 109.7. **IR** (film) ν_{max}3418, 3174, 2095, 1761, 1622, 1348, 759, 593 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{10}H_8N_2O_2Na$ 211.0478; Found 211.0495.

(*E*)-1-(1*H*-pyrazol-1-yl)but-2-e*n*-1-one (3m): Yellowish oil, 2.68 g, 68% yield. R_f = 0.70 (10% EtOAc in hexanes). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.35 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.76 (d, *J* = 1.2 Hz, 1H), 7.38 (dq, *J* = 15.6, 6.3 Hz, 1H), 7.34 – 7.30 (m, 1H), 6.48 (dd, *J* = 2.8, 1.5 Hz, 1H), 2.07 (dd, *J* = 6.4, 1.2 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.2, 148.8, 143.7, 128.6, 120.8, 109.6, 18.7. **IR** (film) ν_{max} 3543, 3133, 2941, 1711, 1645, 1384, 910, 809, 772 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_7H_9N_2O$ 137.07096; Found 137.0696.

(*E*)-1-(1*H*-pyrazol-1-yl)hex-2-e*n*-1-one (3n): Yellowish oil, 1.73 g, 60% yield. R_f = 0.71 (10% EtOAc in hexanes). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.29 (d, *J* = 2.8 Hz, 1H), 7.69 (s, 1H), 7.38 – 7.27 (m, 1H), 7.24 (d, *J* = 15.8 Hz, 1H), 6.41 (dd, *J* = 2.9, 1.5 Hz, 1H), 2.30 (q, *J* = 7.0 Hz, 2H), 1.54 (q, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 163.2, 153.5, 143.7, 128.6, 119.3, 109.6, 34.9, 21.2, 13.7. **IR** (film) ν_{max}3542, 3133, 2961, 2873, 1711, 1641, 1351, 1245, 933, 771 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_9H_{13}N_2O$ 165.1022; Found 165.1051.

General procedure for the synthesis of highly substituted pyrrolidine

In a round bottomed flask, silver triflate (5.14 mg, 0.02 mmol, 10 mol %) and (*R*)-DM-SEGPHOS (17.34 mg, 0.024 mmol, 12 mol %) and 4Å MS (50 mg) were taken and *p*-xylene (2.0 mL) was added to it. The mixture was stirred at room temperature (25 °C) for 1 hour under nitrogen atmosphere. Then azomethine ylide (57.3 mg, 0.3 mmol, 1.5 equiv.) was added slowly and stirred for 5 minutes followed by α,β-unsaturated pyrazolamides (40 mg, 0.2 mmol, 1.0 equiv) was added. The reaction mixture was allowed to stir for additional 24 hours at room temperature. After completion of reaction, the residue was charged over a column packed with silica gel. The cycloaddition products **6aa-6aq** were isolated by flash column chromatography using 20-30% EtOAc in hexanes as eluents.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6aa): White solid, 72 mg, 92% yield. R_f = 0.41 (20%). **MP**: 145−148 °C. dr = 96:4 $[\alpha]_D^{25}$ = +97.7 (CH_2Cl_2, c = 0.69 for 94% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 14.06 min (major), 25.84 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 2.9 Hz, 1H), 7.61 (d, *J* = 1.4 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.27 – 7.19 (m, 1H), 7.19 – 7.09 (m, 5H), 6.20 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.13 (d, *J* = 9.5 Hz, 1H), 4.94 (t, *J* = 9.6 Hz, 1H), 4.21 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.15 – 4.00 (m, 3H), 2.95 (s, 1H), 1.12 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.7, 169.6, 143.7, 139.9, 138.9, 128.6, 128.1, 128.0, 128.0, 127.7, 127.2, 127.0, 109.5, 67.6, 65.5, 61.1, 57.4, 51.8, 14.1. **IR** (film) ν_{max} 3430, 2114, 1726, 1644, 1208, 756 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}N_3O_3$ 390.1812; Found 390.1815

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(4-fluorophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ba): White solid, 61 mg, 75% yield. R_f = 0.39 (20% EtOAc in hexanes). **MP**: 86−89 °C. dr = 82:18 $[\alpha]_D^{27}$ = +71.87 (CH_2Cl_2, c = 0.34 for 90% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 11.46 min (major), 25.58 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 2.8 Hz, 1H), 7.67 (s, 1H), 7.38 (dd, *J* = 8.3, 5.3 Hz, 2H), 7.17 (s, 5H), 7.03 (t, *J* = 8.5 Hz, 2H), 6.28 – 6.19 (m, 1H), 5.15 (d, *J* = 9.5 Hz, 1H), 4.91 (t, *J* = 9.5 Hz, 1H), 4.25 (dd, *J* = 10.8, 7.0 Hz, 1H), 4.18 – 4.04 (m, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.6, 169.4, 143.8, 139.9, 134.5, 129.6, 129.5, 128.1, 128.1, 127.8, 127.0, 115.6, 115.4, 109.6, 67.4, 65.2, 61.2, 57.6, 50.8, 14.1. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -115.36. **IR** (film) ν_{max} 3429, 2114, 1645, 1514, 1267, 752 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}FN_3O_3$ 408.1718; Found 408.1741.

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)-3-(4-(trifluoromethyl)phenyl)pyrrolidine-2-carboxylate (6ca): White solid, 46 mg, 48% yield. R_f = 0.40 (20% EtOAc in hexanes). **MP**: 75−78 °C. dr = 86:14 $[\alpha]_D^{26}$ = +47.46 (CH_2Cl_2, c = 0.24 for 94% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 10.17 min (major), 30.11 min (minor); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 2.9 Hz, 1H), 7.64 (s, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.13 (s, 5H), 6.22 (d, *J* = 2.2 Hz, 1H), 5.15 (d, *J* = 9.5 Hz, 1H), 4.98 – 4.85 (m, 1H), 4.21 (dd, *J* = 10.8, 7.1 Hz, 1H), 4.17 – 4.08 (m, 3H), 2.96 (s, 1H), 1.12 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.3, 169.2, 143.9, 143.1, 139.7, 128.5, 128.2, 128.1, 127.9, 127.0, 125.6, 125.6, 109.7, 67.2, 65.3, 61.3, 57.5, 51.1, 14.0. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -62.6. **IR** (film) ν_{max} 3431, 2101, 1732, 1647, 1328, 753, cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{22}F_3N_3O_3Na$ 480.1505; Found 480.1481

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(4-bromophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6da): White solid, 73 mg, 78% yield. R_f = 0.39 (20% EtOAc in hexanes). **MP**: 146−149

°C. dr = 93:7 $[\alpha]_D^{27}$ = +78.86 (CH_2Cl_2, c = 1.23 for 94% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 8.4 min (major), 22.13 min (minor); The compound was crystalized from EtOAc/pentane mixture at room temperature. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.76 – 7.57 (m, 2H), 7.43 (d, *J* = 7.9 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 7.13 (s, 5H), 6.22 (s, 1H), 5.11 (d, *J* = 9.5 Hz, 1H), 4.86 (t, *J* = 9.8 Hz, 1H), 4.18 (ddt, *J* = 19.4, 11.1, 4.1 Hz, 2H), 4.05 (dt, *J* = 20.2, 10.4 Hz, 2H), 2.92 (s, 1H), 1.14 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.4, 169.3, 143.8, 139.8, 137.9, 131.8, 129.7, 128.1, 128.1, 127.8, 127.0, 121.1, 109.7, 67.2, 65.3, 61.3, 57.5, 50.9, 14.1. **IR** (film) ν_{max} 3430, 2101, 1731, 1649, 1213, 749 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}BrN_3O_3$ 468.0917; Found 468.0937.

Ethyl (2*S*,3*S*,4*R*,5*R*)-3-(4-bromophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6d'a'): White solid, 6 mg, 5% yield. R_f = 0.39 (20% EtOAc in hexanes). **MP**: 123−126 °C. After crystalisation in EtOAc/ pentane 99 % ee . $[\alpha]_D^{24}$ = +54.58 (CH_2Cl_2, c = 0.24 for >99% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 9.39 min (major), 16.43 min (minor). The compound was crystalized from EtOAc/pentane mixture at room temperature. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 2.8 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.49 (d, *J* = 1.5 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.30 – 7.24 (m, 3H), 6.32 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.96 (t, *J* = 9.8 Hz, 1H), 4.71 (d, *J* = 9.5 Hz, 1H), 4.40 (d, *J* = 9.3 Hz, 1H), 4.25 (t, *J* = 9.7 Hz, 1H), 3.93 – 3.82 (m, 1H), 3.78 – 3.64 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 172.4, 171.7, 144.0, 139.0, 136.7, 131.3, 130.1, 128.6, 128.5, 128.1, 128.0, 127.1, 121.3, 110.2, 68.1, 65.3, 61.0, 54.2, 53.8, 13.6. **IR** (film) ν_{max} 3429, 2095, 1725, 1643, 1490, 1389, 1202, 755 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}BrN_3O_3$ 468.0917; Found 468.0904.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(2-chlorophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ea): White solid, 55 mg, 65% yield. R_f = 0.39 (20% EtOAc in hexanes). **MP**: 72−75 °C. dr = 93:7 $[\alpha]_D^{30}$ = +60.86 (CH_2Cl_2, c = 0.58 for 85% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 12.25 min (major), 29.06 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 2.9 Hz, 1H), 7.59 (d, *J* = 1.4 Hz, 1H), 7.47 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.22 – 7.07 (m, 6H), 6.18 (dd, *J* = 2.8, 1.5 Hz, 1H), 5.19 – 4.98 (m, 2H), 4.63 (t, *J* = 9.4 Hz, 1H), 4.29 – 4.18 (m, 1H), 4.18 – 4.07 (m, 2H), 3.08 (s, 1H), 1.14 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.5, 169.9, 143.7, 139.2, 136.7, 134.7, 130.0, 128.5, 128.3, 128.1, 128.1, 127.8, 127.2, 127.0, 109.5, 66.9, 65.8, 61.5, 56.4, 48.5, 13.9. **IR** (film) ν_{max} 3438, 2084, 1731, 1647, 1204, 755 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}ClN_3O_3$ 424.1422; Found 424.1437.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(3-chlorophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6fa): White solid, 42 mg, 50% yield. R_f = 0.38 (20% EtOAc in hexanes). **MP**: 110−113 °C. dr = 91:9 $[\alpha]_D^{27}$ = +69.55 (CH_2Cl_2, c = 0.69 for 86% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.10 min (major), 23.52 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.74 – 7.58 (m, 2H), 7.37 (s, 1H), 7.27 – 7.19 (m, 3H), 7.13 (s, 5H), 6.22 (s, 1H), 5.12 (d, *J* = 9.5 Hz, 1H), 4.89 (t, *J* = 9.7 Hz, 1H), 4.23 (dd, *J* = 10.8, 6.7 Hz, 1H), 4.08 (tt, *J* = 19.8, 8.7 Hz, 3H), 2.93 (s, 1H), 1.15 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.4, 169.3, 143.8, 141.1, 139.7, 134.4, 129.9, 128.2, 128.1, 128.1, 127.8, 127.5, 127.0, 126.2, 109.7, 67.3, 65.4, 61.3, 57.3, 51.2, 14.1. **IR** (film) ν_{max} 2924, 1733, 1389, 1207, 769, 699 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}ClN_3O_3$ 424.1422; Found 424.1429

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(4-chlorophenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ga): White solid, 64 mg, 75% yield. R_f = 0.39 (20% EtOAc in hexanes). **MP**: 130−133 °C. dr = 94:6 $[\alpha]_D^{26}$ = +56.49 (CH_2Cl_2, c = 1.15 for 88% ee); **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 10.34 min (major), 24.72 min (minor).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.73 – 7.59 (m, 2H), 7.30 (q, *J* = 8.4 Hz, 4H), 7.13 (s, 5H), 6.22 (d, *J* = 3.1 Hz, 1H), 5.12 (d, *J* = 9.5 Hz, 1H), 4.87 (t, *J* = 9.7 Hz, 1H), 4.26 – 4.15 (m, 1H), 4.15 – 3.99 (m, 3H), 2.92 (s, 1H), 1.14 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.5, 169.4, 143.9, 139.9, 137.4, 133.1, 129.4, 128.9, 128.2, 128.1, 127.8, 127.0, 109.7, 67.3, 65.3, 61.3, 57.6, 50.9, 14.2. **IR** (film) ν_{max} 3438, 2356, 2117, 1732, 1649, 1207, 751 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}ClN_3O_3$ 424.1422; Found 424.1401.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(4-methoxyphenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ha): White solid, 70 mg, 84% yield. R_f = 0.30 (20% EtOAc in hexanes). **MP**: 120-123 °C. dr = 93:7 $[\alpha]_D^{25}$ = +53.07 (CH_2Cl_2, c = 0.91 for 90% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 9.57 min (major), 16.56 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.73 (d, *J* = 2.8 Hz, 1H), 7.66 (d, *J* = 1.5 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.23 – 7.11 (m, 5H), 6.93 – 6.83 (m, 2H), 6.24 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.15 (d, *J* = 9.5 Hz, 1H), 4.93 (t, *J* = 9.8 Hz, 1H), 4.25 (dd, *J* = 10.8, 7.1 Hz, 1H), 4.21 – 4.02 (m, 3H), 3.80 (s, 3H), 3.02 (s, 1H), 1.18 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 172.8, 169.7, 158.8, 143.7, 140.0, 130.8, 129.0, 128.1, 128.0, 127.7, 127.0, 114.1, 109.5, 67.6, 65.4, 61.2, 57.5, 55.2, 51.1, 14.2. **IR** (film) ν_{max} 3422, 2925, 2063, 1731, 1257, 753 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{26}N_3O_4$ 420.1918; Found 420.1925.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(3-methoxyphenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ia): White solid, 65.54 mg, 78% yield. R_f = 0.30 (20% EtOAc in hexanes). **MP**: 105−108 °C. dr = 96:4 $[\alpha]_D^{25}$ = +65.58 (CH_2Cl_2, c = 1.72 for 90% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 18.18 min (major), 28.40 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 2.8 Hz, 1H), 7.56 (d, *J* = 1.4 Hz, 1H), 7.19 – 7.15 (m, 1H), 7.12 – 7.03 (m, 5H), 6.92 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.86 (t, *J* = 2.1 Hz, 1H), 6.71 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.15 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.06 (d, *J* = 9.5 Hz, 1H), 4.87 (t, *J* = 9.8 Hz, 1H), 4.23 – 4.12 (m, 1H), 4.11 – 3.95 (m, 3H), 3.72 (s, 3H), 2.93 (s, 1H), 1.09 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 172.7, 169.7, 159.7, 143.7, 140.6, 139.8, 129.6, 128.1, 128.0, 127.7, 127.0, 120.2, 113.9, 112.6, 109.6, 67.5, 65.6, 61.2, 57.4, 55.2, 51.8, 14.1. **IR** (film) ν_{max} 3436, 3385, 2926, 1734, 1608, 1264, 747, 702 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{26}N_3O_4$ 420.1918; Found 420.1920.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(3,4-dimethoxyphenyl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ja): White solid, 45 mg, 50% yield. R_f = 0.29 (20% EtOAc in hexanes). **MP**: 120−123 °C. dr = 88:12 $[\alpha]_D^{26}$ = +61.53 (CH_2Cl_2, c = 0.85 for 90% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 26.89 min (minor), 29.52 min (major); **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 2.9 Hz, 1H), 7.57 (d, *J* = 1.5 Hz, 1H), 7.08 (q, *J* = 5.4, 3.8 Hz, 5H), 6.88 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.83 (d, *J* = 2.1 Hz, 1H), 6.75 (d, *J* = 8.2 Hz, 1H), 6.16 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.06 (d, *J* = 9.5 Hz, 1H), 4.84 (t, *J* = 9.9 Hz, 1H), 4.21 – 4.10 (m, 1H), 4.10 – 3.93 (m, 3H), 3.81 (s, 3H), 3.77 (s, 3H), 2.69 (s, 1H), 1.10 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.9, 169.6, 148.9, 148.2, 143.8, 140.1, 131.3, 128.1, 128.1, 127.7, 127.0, 119.8, 111.5, 111.3, 109.6, 67.4, 65.3, 61.2, 57.5, 55.9, 55.7, 51.3, 14.2. **IR** (film) ν_{max} 3433, 2926, 2825, 2067, 1726, 1643, 1259, 1027, 744, 702 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{28}N_3O_5$ 450.2023; Found 450.2030.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-(naphthalen-1-yl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ka): White solid, 57 mg, 65% yield. R_f = 0.42 (20% EtOAc in hexanes). **MP**: 126−129 °C. dr = 85:15 $[\alpha]_D^{27}$ = +3.181 (CH_2Cl_2, c = 0.786 for 92% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 16.24 min (major), 33.95 min (minor).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 8.6 Hz, 1H), 7.83 (dd, *J* = 31.6, 8.2 Hz, 2H), 7.75 – 7.65 (m, 2H), 7.54 (ddd, *J* = 28.6, 15.6, 8.0 Hz, 4H), 7.29 (d, *J* = 7.3 Hz, 2H), 7.19 (d, *J* = 7.4 Hz, 3H), 6.20 (d, *J* = 2.8 Hz, 1H), 5.33 – 5.12 (m, 2H), 5.06 (t, *J* = 9.4 Hz, 1H), 4.26 (d, *J* = 9.4 Hz, 1H), 3.99 (q, *J* = 7.2 Hz, 2H), 3.19 (s, 1H), 0.78 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 173.1, 170.2, 143.7, 139.6, 135.7, 133.9, 132.4, 128.8, 128.2, 128.1, 127.8, 127.7, 127.1, 126.3, 125.7, 125.4, 123.2, 109.6, 68.6, 65.9, 61.2, 57.7, 13.5. **IR** (film) ν_{max} 3433, 2105, 1642, 613 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}N_3O_3$ 440.1969; Found 440.1953.

Ethyl (2*R*,3*R*,4*R*,5*S*)-3-(furan-2-yl)-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6la): White solid, 43 mg, 53% yield. R_f = 0.39 (40% EtOAc in hexanes). **MP**: 140−143 °C. dr = 70:30 $[\alpha]_D^{25}$ = +87.74 (CH_2Cl_2, c = 1.15 for 92% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 8.43 min (minor), 11.19 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 2.9 Hz, 1H), 7.64 (d, *J* = 1.4 Hz, 1H), 7.39 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.22 – 7.09 (m, 5H), 6.32 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.26 (td, *J* = 2.8, 1.1 Hz, 2H), 5.12 – 4.99 (m, 2H), 4.37 – 4.29 (m, 1H), 4.29 – 4.19 (m, 3H), 2.98 (s, 1H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 172.4, 169.9, 152.2, 143.8, 142.1, 139.2, 128.0, 127.7, 126.9, 110.3, 109.6, 107.1, 65.4, 64.9, 61.4, 54.3, 45.4, 14.2. **IR** (film) ν_{max} 3432, 2085, 1645, 1028, 697, 598 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{21}N_3O_4Na$ 402.1424; Found 402.1437.

Ethyl (2*R*,3*R*,4*R*,5*S*)-3-methyl-5-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ma): Viscous colourless oil, 48 mg, 68% yield. R_f = 0.42 (20% EtOAc in hexanes). dr = 96:4 $[\alpha]_D^{25}$ = +107.36 (CH_2Cl_2, c = 0.38 for 90% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 8.32 min (major), 19.76 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 2.8 Hz, 1H), 7.77 – 7.67 (m, 1H), 7.20 – 7.04 (m, 5H), 6.31 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.95 (d, *J* = 9.2 Hz, 1H), 4.45 – 4.27 (m, 3H), 3.66 (d, *J* = 9.7 Hz, 1H), 3.03 – 2.85 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.30 (d, *J* = 6.6 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 173.3, 170.3, 143.8, 140.3, 128.1, 128.1, 127.6, 126.8, 109.6, 67.1, 64.9, 61.3, 57.1, 40.9, 16.9, 14.3. **IR** (film) ν_{max} 3425, 2088, 1645, 1266, 1034, 750 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{21}N_3O_3Na$ 350.1475; Found 350.1487

Ethyl (2*R*,3*R*,4*R*,5*S*)-5-phenyl-3-propyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6na): Viscous colourless oil, 50 mg, 70% yield. R_f = 0.43 (20% EtOAc in hexanes). dr = 97:3 $[\alpha]_D^{25}$ = +62.86 (CH_2Cl_2, c = 0.41 for 88% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 10.26 min (major), 13.42 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 2.8 Hz, 1H), 7.62 (d, *J* = 1.4 Hz, 1H), 7.23 – 7.04 (m, 5H), 6.25 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.81 (d, *J* = 8.7 H z, 1H), 4.56 (dd, *J* = 8.7, 6.9 Hz, 1H), 4.33 (dd, *J* = 7.2, 3.9 Hz, 2H), 3.69 (d, *J* = 8.3 Hz, 1H), 3.03 (s, 1H), 2.93 (qd, *J* = 8.1, 5.9 Hz, 1H), 1.84 – 1.70 (m, 1H), 1.69 – 1.55 (m, 1H), 1.41 (ddt, *J* = 10.1, 6.9, 2.9 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 173.1, 171.6, 143.6, 138.7, 127.9, 127.9, 127.4, 126.8, 109.5, 66.4, 65.7, 61.2, 54.3, 47.7, 35.7, 20.9, 14.3, 14.2. **IR** (film) ν_{max} 3438, 2100, 1645, 1456, 1198, 752 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{26}N_3O_3$ 356.1969; Found 356.1982

Ethyl (2*R*,3*S*,4*R*,5*S*)-4-acetyl-3,5-diphenylpyrrolidine-2-carboxylate (6ra): Viscous gel, 37 mg, 55% yield. R_f = 0.41 (20% EtOAc in hexanes). dr = 64:36 $[\alpha]_D^{24}$ = +4.68 (CH_2Cl_2, c = 1.68 for 50% ee). **HPLC** (Chiralpak IA , *n*-hexane/*iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 8.55 min (minor), 12.55 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.29 – 7.26 (m, 4H), 7.25 (d, *J* = 2.6 Hz, 3H), 7.24 – 7.16 (m, 3H), 4.81 (d, *J* = 8.7 Hz, 1H), 4.17 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.06 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.93 (d, *J* = 8.5 Hz, 1H), 3.84 (dd, *J* = 8.6, 7.2 Hz, 1H), 3.57 (dd, *J* = 8.7, 7.2 Hz, 1H), 2.74 (s, 1H), 1.46 (s, 3H), 1.10 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 207.4, 172.6, 140.9, 139.0, 128.8, 128.7, 128.1, 127.7, 127.3, 127.1, 67.9, 66.0, 65.7, 61.2, 52.2, 31.3, 14.1. **IR** (film) ν_{max} 3379, 3059, 2985, 2928, 2306, 1730, 1266, 1213, 731, 704 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{24}NO_3$ 338.1751; Found 338.1763.

Ethyl (2*R*,3*S*,4*R*,5*S*)-4-benzoyl-3,5-diphenylpyrrolidine-2-carboxylate (6sa): White solid, 54 mg, 68% yield. R_f = 0.41 (20% EtOAc in hexanes). **MP**: 126−129 °C. dr = 90:10 $[\alpha]_D^{24}$ = +38.47 (CH_2Cl_2, c = 1.91 for 70% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 50/50, 1.0 mL/min, 254 nm): t_R = 9.25 min (major), 12.17 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.60 – 7.54 (m, 2H), 7.45 – 7.40 (m, 3H), 7.38 – 7.33 (m, 2H), 7.31 – 7.26 (m, 3H), 7.17 – 7.07 (m, 5H), 5.03 (d, *J* = 8.8 Hz, 1H), 4.57 (dd, *J* = 8.8, 7.7 Hz, 1H), 4.35 – 4.23 (m, 1H), 4.23 – 4.07 (m, 3H), 3.11 (s, 1H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 198.5, 172.9, 140.6, 139.2, 137.5, 132.8, 128.7, 128.2, 128.1, 128.0, 127.8, 127.6, 127.4, 127.1, 67.8, 66.7, 61.2, 60.7, 52.8, 14.2. **IR** (film) ν_{max} 2927, 1885, 1732, 1675, 1262, 1211, 752, 698 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{26}H_{25}NO_3$ 400.1907; Found 400.1926.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)-5-(*p*-tolyl)pyrrolidine-2-carboxylate (6ab): White solid, 78 mg, 92% yield. R_f = 0.42 (20% EtOAc in hexanes). **MP**: 159−162 °C. dr = 98:2 $[\alpha]_D^{26}$ = +92.73 (CH_2Cl_2, c = 0.87 for 92% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 250 nm): t_R = 11.09 min (major), 31.18 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 2.8 Hz, 1H), 7.66 (d, *J* = 1.4 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.24 (m, 1H), 7.12 – 7.02 (m, 2H), 6.97 (d, *J* = 7.8 Hz, 2H), 6.25 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.14 (d, *J* = 9.5 Hz, 1H), 4.96 (t, *J* = 9.9 Hz, 1H), 4.30 – 4.19 (m, 1H), 4.19 – 4.04 (m, 3H), 2.92 (s, 1H), 2.25 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 172.8, 169.7, 143.7, 138.9, 137.4, 136.9, 128.8, 128.6, 128.1, 128.1, 127.3, 126.9, 109.5, 67.6, 65.3, 61.2, 57.5, 51.8, 21.1, 14.1. **IR** (film) ν_{max} 3433, 1728, 1651, 1389, 1206, 758 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{25}N_3O_3Na$ 426.1788; Found 426.1805l.

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(4-methoxyphenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ac): White solid, 78 mg, 93% yield. R_f = 0.30 (20% EtOAc in hexanes). **MP**: 108−111 °C. dr = 94:6 $[\alpha]_D^{23}$ = +98.01 (CH_2Cl_2, c = 0.60 for 94% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 25.49 min (major), 36.31 min (minor).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 2.8 Hz, 1H), 7.62 (s, 1H), 7.37 (d, *J* = 7.5 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.3 Hz, 2H), 6.25 – 6.15 (m, 1H), 5.09 (d, *J* = 9.5 Hz, 1H), 4.89 (t, *J* = 9.7 Hz, 1H), 4.20 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.15 – 3.99 (m, 3H), 3.70 (s, 3H), 2.91 (s, 1H), 1.11 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.8, 169.7, 158.9, 143.7, 138.9, 132.1, 128.6, 128.2, 128.1, 128.0, 127.2, 67.5, 65.0, 61.1, 57.6, 55.1, 51.8, 14.1. **IR** (film) ν_{max} 3428, 2925, 2308, 2122, 1729, 1644, 1512, 1260, 1029, 745 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{24}H_{26}N_3O_4$ 420.1918; Found 420.1939.

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(4-chlorophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ad): White solid, 64 mg, 75% yield. R_f = 0.39 (20% EtOAc in hexanes). **MP**: 138−141

°C. dr = 90:10 $[\alpha]_D^{25}$ = +103.06 (CH_2Cl_2, c = 0.62 for 90% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 95/5, 1.0 mL/min, 254 nm): t_R = 19.13 min (major), 28.02 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 2.8 Hz, 1H), 7.61 – 7.53 (m, 1H), 7.36 – 7.21 (m, 4H), 7.19 – 7.14 (m, 1H), 7.04 (s, 4H), 6.18 (dd, *J* = 2.7, 1.4 Hz, 1H), 5.05 (d, *J* = 9.5 Hz, 1H), 4.86 (t, *J* = 9.8 Hz, 1H), 4.21 – 4.10 (m, 1H), 4.10 – 3.95 (m, 3H), 2.84 (s, 1H), 1.06 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.7, 169.4, 143.9, 138.7, 138.7, 133.5, 128.7, 128.5, 128.2, 128.2, 128.0, 127.4, 109.8, 67.4, 64.6, 61.2, 57.2, 51.3, 14.0. **IR** (film) ν_{max} 3111, 2928, 1727, 1391, 1208, 758 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}ClN_3O_3$ 424.1422; Found 424.1437.

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(4-bromophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ae): White solid, 78 mg, 85% yield. R_f = 0.38 (20% EtOAc in hexanes). **MP**: 133−136 °C. dr = 87:13 $[\alpha]_D^{26}$ = +103.44 (CH_2Cl_2, c = 1.68 for 92% ee). **HPLC** (Chiralcel OD-H, *n*-hexane/ *iso*-propanol = 95/5, 1.0 mL/min, 254 nm): t_R = 20.92 min (major), 31.01 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 2.8 Hz, 1H), 7.63 (s, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 4.3 Hz, 3H), 7.05 (d, *J* = 8.2 Hz, 2H), 6.25 (t, *J* = 2.1 Hz, 1H), 5.10 (d, *J* = 9.5 Hz, 1H), 4.91 (t, *J* = 9.8 Hz, 1H), 4.26 – 4.15 (m, 1H), 4.15 – 3.99 (m, 3H), 2.90 (s, 1H), 1.12 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.7, 169.3, 143.9, 139.3, 138.6, 131.2, 128.8, 128.7, 128.2, 128.0, 127.4, 121.7, 109.8, 67.4, 64.6, 61.2, 57.1, 51.3, 14.1. **IR** (film) ν_{max} 3426, 2982, 2303, 1726, 1650, 1208, 933, 752 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}BrN_3O_3$ 468.0917; Found 468.0944

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(4-fluorophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6af): White solid, 72 mg, 88% yield. R_f = 0.40 (20% EtOAc in hexanes). **MP**: 139−142 °C. dr = 90:10 $[\alpha]_D^{26}$ = +69.24 (CH_2Cl_2, c = 0.94 for 90% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 15.14 min (major), 20.74 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 2.8 Hz, 1H), 7.66 (s, 1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.31 – 7.23 (m, 1H), 7.18 (dd, *J* = 8.4, 5.4 Hz, 2H), 6.85 (t, *J* = 8.5 Hz, 2H), 6.30 – 6.22 (m, 1H), 5.16 (d, *J* = 9.5 Hz, 1H), 4.94 (t, *J* = 9.7 Hz, 1H), 4.24 (ddd, *J* = 14.2, 8.9, 5.4 Hz, 1H), 4.19 – 4.05 (m, 3H), 2.74 (s, 1H), 1.16 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.7, 169.5, 163.4, 160.9, 143.9, 138.7, 135.8, 128.9, 128.8, 128.7, 128.1, 128.0, 127.3, 115.1, 114.9, 109.7, 67.4, 64.6, 61.2, 57.3, 51.4, 14.1. **^{19}F NMR** (470 MHz, Chloroform-*d*) δ -114.50. **IR** (film) ν_{max} 3434, 1716, 1647, 1511, 1265, 754, 689, 620 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}FN_3O_3$ 408.1718; Found 408.1739

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(2-bromophenyl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ag): White solid, 60 mg, 64% yield. R_f = 0.38 (20% EtOAc in hexanes). **MP**: 130−133 °C. dr = 97:3 $[\alpha]_D^{26}$ = -6.09 (CH_2Cl_2, c = 0.16 for 86% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 90/10, 1.0 mL/min, 254 nm): t_R = 17.72 min (major), 23.45 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 2.7 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.52 (s, 1H), 7.43 (d, *J* = 7.7 Hz, 2H), 7.40 – 7.32 (m, 3H), 7.25 (t, *J* = 7.7 Hz, 2H), 7.00 (t, *J* = 7.7 Hz, 1H), 6.18 (d, *J* = 2.8 Hz, 1H), 5.48 (d, *J* = 8.5 Hz, 1H), 5.16 (t, *J* = 7.4 Hz, 1H), 4.34 – 4.18 (m, 2H), 4.13 (d, *J* = 7.0 Hz, 2H), 3.08 (s, 1H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.3, 143.6, 140.1, 132.4, 129.0, 128.8, 128.4, 127.8, 127.7, 127.3, 109.7, 68.0, 64.8, 61.3, 54.7, 52.9, 14.2. **IR** (film) ν_{max} 3441, 2113, 1729, 1647, 1390, 1264, 1027, 740 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}BrN_3O_3$ 468.0917; Found 468.0924

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(naphthalen-2-yl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ah):White solid, 60 mg, 68% yield. R_f = 0.42 (20% EtOAc in hexanes). **MP**: 164−167

°C. dr = 98:2 $[\alpha]_D^{23}$ = +70.48 (CH_2Cl_2, c =0.59 for 86% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 18.24 min (major), 25.88 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.72 (ddd, *J* = 15.1, 6.2, 3.4 Hz, 2H), 7.69 – 7.58 (m, 4H), 7.48 – 7.39 (m, 4H), 7.35 (q, *J* = 8.3, 7.9 Hz, 3H), 7.26 (d, *J* = 7.3 Hz, 1H), 6.19 – 6.12 (m, 1H), 5.38 – 5.29 (m, 1H), 5.07 (t, *J* = 9.3 Hz, 1H), 4.33 – 4.23 (m, 1H), 4.23 – 4.13 (m, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.8, 169.6, 143.8, 139.0, 137.4, 132.9, 132.8, 128.7, 128.2, 128.1, 128.0, 127.8, 127.5, 127.3, 126.2, 125.9, 125.8, 124.9, 109.6, 67.7, 65.6, 61.2, 57.4, 51.8, 14.1. **IR** (film) ν_{max} 3431, 2106, 1718, 1645, 1264, 1201, 751 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{27}H_{26}N_3O_3$ 440.1969; Found 440.1994

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-([1,1'-biphenyl]-4-yl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ai): White solid, 82 mg, 88% yield. R_f = 0.43 (20% EtOAc in hexanes). **MP**: 149−152 °C. dr = 99:1 $[\alpha]_D^{22}$ = +119.47 (CH_2Cl_2, c = 0.60 for 90% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 19.08 min (major), 20.90 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 2.8 Hz, 1H), 7.67 (s, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.42 (td, *J* = 8.6, 8.1, 2.7 Hz, 6H), 7.36 (t, *J* = 7.7 Hz, 3H), 7.28 (q, *J* = 1.8 Hz, 3H), 6.28 – 6.19 (m, 1H), 5.22 (d, *J* = 9.5 Hz, 1H), 5.00 (t, *J* = 9.5 Hz, 1H), 4.26 (ddd, *J* = 14.2, 8.9, 5.3 Hz, 1H), 4.20 – 4.08 (m, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.7, 169.7, 143.8, 140.6, 140.4, 138.9, 128.7, 128.2, 128.1, 127.5, 127.3, 127.3, 126.9, 126.8, 109.6, 67.6, 65.2, 61.2, 57.5, 51.8, 14.1. **IR** (film) ν_{max} 3418, 2117, 1728, 1645, 1388, 1207, 1029, 739 cm^{-1};**HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{29}H_{28}N_3O_3$ 466.2125; Found 466.2155.

Ethyl (2*R*,3*S*,4*R*,5*S*)-5-(furan-2-yl)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6aj): White solid, 40 mg, 52% yield. R_f = 0.42 (20% EtOAc in hexanes). **MP**: 89−92 °C. dr = 82:18 $[\alpha]_D^{25}$ = +371.95 (CH_2Cl_2, c = 0.16 for 68% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 250 nm): t_R = 10.9 min (major), 24.20 min (minor).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.9 (d, *J* = 2.8 Hz, 1H), 7.6 (s, 1H), 7.3 (d, *J* = 7.7 Hz, 2H), 7.2 (t, *J* = 7.5 Hz, 2H), 7.2 – 7.1 (m, 3H), 6.2 (d, *J* = 2.6 Hz, 1H), 6.1 (d, *J* = 3.2 Hz, 1H), 6.0 (d, *J* = 3.3 Hz, 1H), 5.1 (d, *J* = 8.6 Hz, 1H), 4.7 (t, *J* = 9.4 Hz, 1H), 4.2 (dd, *J* = 10.9, 7.1 Hz, 1H), 4.1 – 4.0 (m, 3H), 1.1 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.8, 168.9, 152.8, 143.9, 142.4, 139.2, 128.6, 128.2, 128.1, 127.3, 110.2, 109.5, 107.6, 67.2, 61.2, 59.4, 56.5, 51.0, 14.1. **IR** (film) ν_{max} 3415, 2923, 2855, 1735, 1654, 1385, 1199, 741 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{21}H_{22}N_3O_4$ 380.1605; Found 380.1602.

Ethyl (2*R*,3*S*,4*R*,5*S*)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)-5-(thiophen-2-yl)pyrrolidine-2-carboxylate (6ak) White solid, 42 mg, 53% yield. R_f = 0.42 (20% EtOAc in hexanes). **MP**: 92−95 °C. dr = 70:30 $[\alpha]_D^{25}$ = +26.17 (CH_2Cl_2, c = 0.25 for 58% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 260 nm): t_R = 8.98 min (major), 31.78 min (minor).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.8 (d, *J* = 2.9 Hz, 1H), 7.6 (d, *J* = 1.5 Hz, 1H), 7.3 (d, *J* = 7.1 Hz, 2H), 7.2 (t, *J* = 7.5 Hz, 2H), 7.2 – 7.1 (m, 1H), 7.0 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.7 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.6 (d, *J* = 3.5 Hz, 1H), 6.2 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.4 (d, *J* = 8.9 Hz, 1H), 4.8 (dt, *J* = 8.8, 5.3 Hz, 1H), 4.2 – 4.1 (m, 1H), 4.1 – 4.0 (m, 3H), 2.9 (s, 1H), 1.1 (t, *J* = 7.1 Hz, 3H).**^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.6, 168.7, 144.7, 144.0, 138.6, 128.6, 128.3, 128.2, 127.3, 126.7, 124.9, 124.6, 109.8, 67.0, 61.2, 60.5, 57.4, 50.3, 14.1. **IR** (film) ν_{max} 3360, 2924, 1733, 1389, 1267, 1205, 755 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{21}N_3O_3SNa$ 418.1196; Found 418.1202.

Ethyl (2*R*,3*S*,4*R*,5*R*)-3-phenyl-4-(1*H*-pyrazole-1-carbonyl)-5-((*E*)-styryl)pyrrolidine-2-carboxylate (6al): White solid, 50 mg, 60% yield. R_f = 0.32 (20% EtOAc in hexanes). **MP**: 52−55

°C. dr = 85:15 $[\alpha]_D^{25}$ = +26.82 (CH_2Cl_2, c = 0.49 for 15% ee). **HPLC** (Chiralpak IA, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 24.05 min (major), 44.68 min (minor).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 2.8 Hz, 1H), 7.71 (s, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.26 (dd, *J* = 14.4, 7.5 Hz, 3H), 7.22 (d, *J* = 6.8 Hz, 1H), 7.19 – 7.14 (m, 2H), 6.38 – 6.29 (m, 2H), 6.08 (dd, *J* = 15.7, 8.3 Hz, 1H), 4.85 (t, *J* = 8.5 Hz, 1H), 4.69 (t, *J* = 8.5 Hz, 1H), 4.25 (ddd, *J* = 14.2, 8.8, 5.3 Hz, 1H), 4.20 – 4.09 (m, 1H), 4.05 (d, *J* = 7.1 Hz, 2H), 2.75 (s, 1H), 1.18 (t, *J* = 7.1 Hz, 3H).. **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 173.1, 169.9, 144.1, 139.7, 136.4, 132.7, 128.7, 128.4, 128.4, 127.9, 127.7, 127.3, 126.8, 126.5, 109.8, 67.6, 64.1, 61.3, 56.6, 51.8, 14.1. **IR** (film) ν_{max} 3423, 2926, 1733, 1653, 1388, 1199, 1097, 752 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{26}N_3O_3$ 416.1969; Found 416.1991.

***tert*-butyl (2*R*,3*S*,4*R*,5*S*)-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6am):** White solid, 43 mg, 51% yield. R_f = 0.43 (20% EtOAc in hexanes). **MP**: 169−172 °C. dr = 89:11 $[\alpha]_D^{27}$ = +65.84 (CH_2Cl_2, c = 0.77 for 88% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 5.35 min (major), 8.25 min (minor). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 2.9 Hz, 1H), 7.66 (d, *J* = 1.4 Hz, 1H), 7.42 (d, *J* = 7.4 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 6.1 Hz, 1H), 7.17 (q, *J* = 5.0 Hz, 5H), 6.24 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.15 (d, *J* = 9.6 Hz, 1H), 4.95 (t, *J* = 10.0 Hz, 1H), 4.10 – 3.94 (m, 2H), 2.97 (s, 1H), 1.34 (s, 9H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 171.8, 169.6, 143.7, 140.1, 139.1, 128.5, 128.2, 128.2, 128.1, 127.7, 127.2, 127.1, 109.5, 68.1, 65.6, 57.9, 52.3, 27.9. **IR** (film) ν_{max} 3428, 2925, 1722, 1652, 1161, 745, 700 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{25}H_{28}N_3O_3$ 418.2125; Found 418.2131

Methyl (2*R*,3*S*,4*R*,5*S*)-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6an):White solid, 72 mg, 91% yield. R_f = 0.42 (20% EtOAc in hexanes). **MP**: 140−143 °C. dr = 93:7 $[\alpha]_D^{26}$ = +51.01 (CH_2Cl_2, c = 0.64 for 88% ee). **HPLC** (Chiralpak IC, *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 8.39 min (major), 13.90 min (minor).**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 2.9 Hz, 1H), 7.65 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.28 (d, *J* = 6.9 Hz, 1H), 7.18 (ddd, *J* = 11.7, 5.6, 3.1 Hz, 5H), 6.28 – 6.15 (m, 1H), 5.17 (d, *J* = 9.4 Hz, 1H), 4.97 (t, *J* = 9.6 Hz, 1H), 4.17 (dt, *J* = 19.6, 9.9 Hz, 2H), 3.74 (s, 3H), 2.99 (s, 1H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 173.2, 169.7, 143.7, 139.8, 139.0, 128.7, 128.1, 128.1, 127.9, 127.7, 127.3, 127.1, 109.6, 67.5, 65.5, 57.4, 52.3, 51.6. **IR** (film) ν_{max} 3426, 2924, 2854, 2113, 1736, 1650, 1389, 1209, 750 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{22}H_{21}N_3O_3Na$ 398.1475; Found 398.1499

Methyl (2*R*,3*S*,4*R*,5*S*)-2-methyl-3,5-diphenyl-4-(1*H*-pyrazole-1-carbonyl)pyrrolidine-2-carboxylate (6ao): White solid, 57 mg, 73% yield. R_f = 0.35 (20% EtOAc in hexanes). **MP**: 85−88 °C. dr = 95:5 $[\alpha]_D^{25}$ = +28.33 (CH_2Cl_2, c = 0.36 for 68% ee). **HPLC** (Chiralpak ID, *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 18.45 min (minor), 19.82 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.7 (dd, *J* = 18.9, 2.1 Hz, 2H), 7.3 (d, *J* = 4.4 Hz, 4H), 7.3 – 7.3 (m, 1H), 7.2 (dd, *J* = 7.3, 2.5 Hz, 2H), 7.2 – 7.1 (m, 3H), 6.2 (dd, *J* = 2.8, 1.5 Hz, 1H), 5.4 – 5.3 (m, 1H), 5.2 (d, *J* = 10.0 Hz, 1H), 4.5 (d, *J* = 12.0 Hz, 1H), 3.8 (s, 3H), 3.3 (s, 1H), 1.4 (s, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.2, 169.5, 143.8, 139.7, 136.4, 128.7, 128.4, 128.2, 128.1, 127.8, 127.5, 127.2, 109.6, 68.9, 63.2, 54.2, 53.0, 52.6, 20.5. **IR** (film) ν_{max} 3361, 2925, 2343, 1733, 1419, 1388, 1258, 746 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{23}H_{24}N_3O_3$ 390.1812; Found 390.1814.

General procedure for the synthesis of highly substituted pyrrolizidine.

In a round bottomed flask, silver triflate (5.14 mg, 0.02 mmol, 10 mol %) and (*R*)-DM-SEGPHOS (17.34 mg, 0.024 mmol, 12 mol %) and 50 mg 4Å MS (50 mg) were taken and *p*-xylene (2.0 mL) was added to it. The mixture was stirred at room temperature (25 °C) for 1 hour under nitrogen

atmosphere. Then azomethine ylide (57.3 mg, 0.3 mmol, 1.5 equiv.) was added slowly and stirred for 5 minutes followed by *α,β*-unsaturated pyrazolamides (40 mg, 0.2 mmol, 1.0 equiv) was added. The reaction mixture was allowed to stir for additional 24 hours at room temperature. After this, cinnamaldehyde (39 mg, 0.3 mmol, 1.5 equiv.) and *N*-phenylmaleimide (NPM) (52 mg, 0.3 mmol, 1.5 equiv.) were added to the reaction mixture. The reaction mixture was allowed to stirr for additional 48 hours. After completion of reaction, the residue was charged over a column packed with silica gel. The highly substituted pyrrolizidine derivative **9a** was isolated by flash column chromatography using 25-30% EtOAc in hexanes as eluent.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-1,3-dioxo-2,6,8-triphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9aa): White solid, 81 mg, 60% yield. R_f = 0.45 (20% EtOAc in hexanes). **MP**: 207-210 °C. dr = 87:13 $[\alpha]_D^{25}$ = +126.95 (CH_2Cl_2, c = 0.52 for 98% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 10.49 min (minor), 24.09 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 1.4 Hz, 1H), 7.64 (d, *J* = 2.7 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.28 – 7.20 (m, 5H), 7.18 – 7.12 (m, 3H), 7.08 (td, *J* = 5.6, 4.9, 2.0 Hz, 5H), 7.00 (dt, *J* = 7.0, 3.1 Hz, 2H), 6.87 (dd, *J* = 16.3, 2.2 Hz, 1H), 6.24 (dd, *J* = 2.8, 1.5 Hz, 1H), 6.08 (dt, *J* = 16.3, 3.2 Hz, 1H), 5.40 (dd, *J* = 13.1, 2.4 Hz, 1H), 5.21 (s, 1H), 5.14 (ddd, *J* = 12.9, 10.5, 2.4 Hz, 1H), 4.93 (dd, *J* = 10.8, 2.4 Hz, 1H), 4.58 (dt, *J* = 8.8, 2.9 Hz, 1H), 4.46 – 4.36 (m, 2H), 3.93 (td, *J* = 9.8, 9.0, 1.6 Hz, 1H), 3.67 (dd, *J* = 10.5, 2.1 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.0, 173.7, 170.3, 167.5, 144.3, 140.8, 136.5, 135.2, 133.8, 132.2, 128.9, 128.9, 128.5, 128.5, 128.3, 128.1, 128.0, 127.8, 127.8, 127.6, 127.5, 126.6, 126.5, 124.8, 110.0, 82.9, 67.0, 64.4, 62.7, 50.8, 50.7, 49.3, 47.8, 14.4. **IR** (film) ν_{max} 3471, 3060, 2927, 2258, 1955, 1888, 1777, 1715, 1601, 1381, 1204, 743 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{42}H_{36}N_4O_5Na$ 699.2578; Found 699.2592.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-8-(4-chlorophenyl)-1,3-dioxo-2,6-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9ga): White solid, 83 mg, 58% yield. R_f = 0.46 (20% EtOAc in hexanes). **MP**: 162-165 °C. dr = 78:22 $[\alpha]_D^{27}$ = +92.85 (CH_2Cl_2, c = 0.89 for 98% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 8.34 min (minor), 25.70 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 1.4 Hz, 1H), 7.75 (d, *J* = 2.8 Hz, 1H), 7.48 – 7.41 (m, 4H), 7.39 – 7.35 (m, 1H), 7.35 – 7.31 (m, 4H), 7.29 – 7.23 (m, 4H), 7.18 (td, *J* = 6.1, 5.4, 2.4 Hz, 4H), 7.10 – 7.02 (m, 2H), 6.97 (dd, *J* = 16.3, 2.3 Hz, 1H), 6.36 (dd, *J* = 2.8, 1.5 Hz, 1H), 6.18 (dd, *J* = 16.3, 3.9 Hz, 1H), 5.44 (d, *J* = 13.0 Hz, 1H), 5.17 (dd, *J* = 13.0, 10.7 Hz, 1H), 5.03 (d, *J* = 10.6 Hz, 1H), 4.71 (ddd, *J* = 9.0, 3.9, 2.3 Hz, 1H), 4.51 (dddd, *J* = 17.9, 10.8, 7.1, 3.6 Hz, 2H), 4.05 (dd, *J* = 10.6, 8.9 Hz, 1H), 3.73 (d, *J* = 10.5 Hz, 1H), 1.49 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 174.9, 170.1, 167.4, 144.4, 140.5, 136.4, 133.9, 133.8, 133.7, 129.3, 129.1, 129.0, 128.5, 128.5, 128.5, 128.1, 127.8, 127.7, 127.4, 126.6, 126.5, 124.6, 110.1, 82.5, 67.0, 64.3, 62.7, 50.8, 50.8, 49.5, 47.3, 14.3. **IR** (film) ν_{max} 3426, 2116, 1713, 1646, 1497, 1385, 748 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{42}H_{36}ClN_4O_5$ 711.2369; Found 711.2376.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-8-(4-bromophenyl)-1,3-dioxo-2,6-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9da): White solid, 94 mg, 62% yield. R_f = 0.44 (20% EtOAc in hexanes). **MP**: 116−119 °C. dr = 80:20 $[\alpha]_D^{25}$ = +126.18 (CH_2Cl_2, c = 0.76 for 98% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.42 min (minor), 31.23 min (major). The compound was crystalized from ethanol at room temperature. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.67 (dd, *J* = 24.8, 2.1 Hz, 2H),

7.43 – 7.14 (m, 13H), 7.07 (dd, *J* = 5.1, 2.0 Hz, 3H), 7.00 – 6.95 (m, 2H), 6.94 – 6.90 (m, 2H), 6.25 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.06 (dd, *J* = 16.3, 3.9 Hz, 1H), 5.40 (d, *J* = 12.9 Hz, 1H), 5.20 – 5.09 (m, 1H), 4.88 (d, *J* = 10.7 Hz, 1H), 4.55 (ddd, *J* = 9.1, 3.9, 2.2 Hz, 1H), 4.48 – 4.36 (m, 2H), 3.92 (dd, *J* = 10.5, 8.9 Hz, 1H), 3.67 (d, *J* = 10.5 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.0, 173.7, 170.3, 167.5, 144.3, 140.6, 135.4, 135.1, 132.6, 131.6, 128.9, 128.9, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 126.6, 125.7, 121.6, 110.0, 82.9, 66.9, 64.5, 62.7, 50.8, 50.7, 49.2, 47.9, 14.3. **IR** (film) ν_{max} 3443, 2115, 1954, 1776, 1714, 1648, 1384, 1201, 739, 697 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{42}H_{36}BrN_4O_5$ 755.1864; Found 755.1892.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-8-(naphthal*e*n-1-yl)-1,3-dioxo-2,6-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9ka): White solid, 95 mg, 65% yield. R_f = 0.46 (20% EtOAc in hexanes). **MP**: 88−91 °C. dr = 92:8 $[\alpha]_D^{23}$ = +41.80 (CH_2Cl_2, c = 0.5 for 98% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 10.16 min (minor), 16.87 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.82 (d, *J* = 8.7 Hz, 1H), 7.89 – 7.78 (m, 3H), 7.71 (d, *J* = 1.5 Hz, 1H), 7.63 (dd, *J* = 5.9, 2.4 Hz, 2H), 7.51 (q, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.34 – 7.26 (m, 6H), 7.26 – 7.18 (m, 5H), 7.11 (dd, *J* = 7.6, 1.8 Hz, 2H), 6.91 (dd, *J* = 16.2, 2.2 Hz, 1H), 6.28 – 6.20 (m, 2H), 6.13 (dd, *J* = 16.2, 4.3 Hz, 1H), 5.51 (t, *J* = 11.1 Hz, 1H), 5.11 (d, *J* = 10.6 Hz, 1H), 4.56 (ddd, *J* = 8.7, 4.4, 2.1 Hz, 1H), 4.40 (dd, *J* = 10.7, 7.2 Hz, 1H), 4.35 – 4.25 (m, 2H), 4.13 (dd, *J* = 10.7, 8.5 Hz, 1H), 1.48 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.3, 173.3, 170.7, 168.1, 144.0, 136.4, 133.6, 131.9, 129.2, 128.9, 128.9, 128.5, 128.3, 128.3, 128.0, 127.8, 127.7, 127.6, 126.7, 126.5, 126.0, 125.8, 125.2, 125.0, 124.5, 124.3, 109.9, 83.7, 65.9, 64.7, 62.7, 52.6, 51.3, 49.9, 43.6, 14.2. **IR** (film) ν_{max} 3432, 2116, 1647, 149+9, 1264, 1082, 751, 625 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{46}H_{39}N_4O_5$ 727.2915; Found 727.2905.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*R*,8a*S*,8b*R*)-8-(fura*n*-2-yl)-1,3-dioxo-2,6-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9la): White solid, 77 mg, 58% yield. R_f = 0.43 (20% EtOAc in hexanes). **MP**: 115−118 °C. dr = 76:24 $[\alpha]_D^{23}$ = +105.50 (CH_2Cl_2, c = 0.8 for 95% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 11.89 min (minor), 19.33 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.64 (dd, *J* = 6.2, 2.1 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.23 (m, 4H), 7.17 – 7.10 (m, 3H), 7.05 (dt, *J* = 5.8, 1.9 Hz, 5H), 6.97 – 6.91 (m, 2H), 6.85 (dd, *J* = 16.3, 2.3 Hz, 1H), 6.33 (d, *J* = 3.4 Hz, 1H), 6.26 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.21 (dd, *J* = 2.8, 1.5 Hz, 1H), 6.03 (dd, *J* = 16.3, 4.0 Hz, 1H), 5.31 (d, *J* = 12.7 Hz, 1H), 5.05 (dd, *J* = 12.8, 10.9 Hz, 1H), 4.86 (d, *J* = 10.9 Hz, 1H), 4.63 (ddd, *J* = 6.8, 3.8, 2.2 Hz, 1H), 4.45 – 4.36 (m, 1H), 4.31 (dd, *J* = 10.8, 7.2 Hz, 1H), 3.99 – 3.91 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.1, 174.1, 169.9, 167.5, 149.5, 144.2, 142.6, 140.4, 136.5, 133.7, 132.2, 128.9, 128.5, 128.4, 128.4, 128.0, 127.8, 127.6, 127.6, 126.6, 126.5, 124.9, 110.6, 109.9, 108.8, 81.6, 67.3, 64.6, 62.6, 51.4, 50.7, 49.0, 43.5, 14.3. **IR** (film) ν_{max} 3434, 2925, 2116, 1712, 1497, 1385, 1260, 1197, 744 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{40}H_{35}N_4O_6$ 667.2551; Found 667.2575.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*R*,8a*R*,8b*R*)-1,3-dioxo-2,6-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)-8-(thiophe*n*-2-yl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9oa): White solid, 96 mg, 70% yield. R_f = 0.43 (20% EtOAc in hexanes). **MP**: 112−115 °C. dr = 90:10 $[\alpha]_D^{24}$ = +102.29 (CH_2Cl_2, c = 0.96 for 94% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.97 min(minor), 21.58 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.78 (dd, *J* = 10.9, 2.2 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.32 (m, 3H), 7.32 – 7.22 (m, 4H), 7.22 – 7.15 (m, 5H), 7.15 – 7.11 (m, 1H), 7.11 – 7.04 (m, 2H), 7.03 – 6.94 (m, 2H), 6.35 (dd, *J* = 2.9,

1.5 Hz, 1H), 6.17 (dd, *J* = 16.3, 3.8 Hz, 1H), 5.63 (d, *J* = 12.8 Hz, 1H), 5.16 (dd, *J* = 12.9, 10.8 Hz, 1H), 5.00 (d, *J* = 10.8 Hz, 1H), 4.80 (ddd, *J* = 9.0, 3.9, 2.2 Hz, 1H), 4.58 – 4.43 (m, 2H), 4.08 (dd, *J* = 10.6, 8.9 Hz, 1H), 3.89 (d, *J* = 10.5 Hz, 1H), 1.52 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.0, 173.9, 170.0, 167.2, 144.4, 140.3, 138.6, 136.5, 133.8, 132.1, 128.9, 128.5, 128.5, 128.4, 128.1, 127.8, 127.7, 127.5, 127.0, 126.6, 126.5, 125.5, 125.2, 124.8, 110.1, 82.5, 67.6, 64.5, 62.8, 51.5, 51.2, 50.6, 44.5, 14.3. **IR** (film) ν_{max} 3427, 2926, 2361, 2101, 1712, 1498, 1262, 751 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{40}H_{35}N_4O_5S$ 683.2323; Found 683.2300.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*R*,8a*S*,8b*R*)-8-methyl-1,3-dioxo-2,6-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9ma): White solid, 80 mg, 65% yield. ***R*$_f$** = 0.45 (20% EtOAc in hexanes). **MP**: 84−87 °C. dr = 80:20 $[\alpha]_D^{23}$ = +96.30 (CH_2Cl_2, c = 0.49 for 92% ee). **HPLC**(Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 9.54 min (minor), 12.84 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 2.8 Hz, 1H), 7.62 (d, *J* = 1.4 Hz, 1H), 7.41 (dd, *J* = 8.5, 7.1 Hz, 2H), 7.33 (dd, *J* = 8.0, 2.1 Hz, 3H), 7.16 – 7.10 (m, 3H), 7.07 – 7.00 (m, 5H), 6.90 – 6.86 (m, 2H), 6.82 (dd, *J* = 16.3, 2.2 Hz, 1H), 6.21 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.02 (dd, *J* = 16.2, 3.9 Hz, 1H), 4.70 (s, 1H), 4.67 (ddd, *J* = 8.8, 3.9, 2.3 Hz, 1H), 4.34 – 4.23 (m, 2H), 4.20 (dd, *J* = 12.7, 10.9 Hz, 1H), 3.97 – 3.90 (m, 2H), 3.66 (d, *J* = 10.5 Hz, 1H), 1.32 – 1.28 (m, 6H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.5, 175.0, 170.5, 168.3, 144.0, 140.7, 136.5, 133.3, 132.3, 129.1, 128.5, 128.5, 128.3, 127.9, 127.7, 127.6, 127.4, 126.7, 126.5, 125.3, 109.8, 82.7, 67.2, 65.1, 62.3, 52.8, 50.7, 50.7, 38.3, 14.2, 13.9. **IR** (film) ν_{max} 3430, 2360, 2101, 1710, 1646, 1495, 1188, 750 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{37}H_{35}N_4O_5$ 615.2602; Found 615.2615.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-4-((*E*)-4-bromostyryl)-1,3-dioxo-2,6,8-triphenyl-7-(1*H*-pyrazole-1-carbonyl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9ab): White solid, 95 mg, 63% yield. ***R*$_f$** = 0.44 (20% EtOAc in hexanes). **MP**: 115−118 °C. dr = 88:12 $[\alpha]_D^{24}$ = +80.81 (CH_2Cl_2, c = 0.82 for 98% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 11.43 min (minor), 28.47 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 1.4 Hz, 1H), 7.64 (d, *J* = 2.8 Hz, 1H), 7.37 (d, *J* = 7.4 Hz, 2H), 7.32 (dd, *J* = 8.3, 7.0 Hz, 2H), 7.29 – 7.23 (m, 5H), 7.23 – 7.18 (m, 3H), 7.07 (dd, *J* = 5.1, 2.0 Hz, 3H), 6.99 – 6.95 (m, 2H), 6.94 – 6.90 (m, 2H), 6.79 (dd, *J* = 16.4, 2.2 Hz, 1H), 6.25 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.06 (dd, *J* = 16.3, 3.9 Hz, 1H), 5.40 (d, *J* = 12.9 Hz, 1H), 5.19 – 5.10 (m, 1H), 4.88 (d, *J* = 10.7 Hz, 1H), 4.55 (ddd, *J* = 9.1, 3.9, 2.2 Hz, 1H), 4.47 – 4.36 (m, 2H), 3.92 (dd, *J* = 10.5, 8.9 Hz, 1H), 3.67 (d, *J* = 10.5 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.0, 173.7, 170.3, 167.5, 144.3, 140.6, 135.4, 135.1, 132.6, 131.6, 128.9, 128.9, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 126.6, 125.7, 121.6, 110.0, 82.9, 66.9, 64.5, 62.7, 50.8, 50.7, 49.3, 47.8, 14.3. **IR** (film) ν_{max} 3441, 3058, 2926, 2855, 2122, 1712, 1495, 1264, 743, 622 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{42}H_{36}BrN_4O_5$ 755.184; Found 755.1887.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-4-((*E*)-4-methoxystyryl)-1,3-dioxo-2,6,8-triphenyl-7-(1*H*-pyrazole-1-carbonyl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (9ac): White solid, 85 mg, 60% yield. ***R*$_f$** = 0.42 (20% EtOAc in hexanes). **MP**: 249−252 °C. dr = 87:13 $[\alpha]_D^{25}$ = +107.47 (CH_2Cl_2, c = 1.15 for 92% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 8.47 min (minor), 21.76 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 (d, *J* = 1.5 Hz, 1H), 7.64 (d, *J* = 2.9 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.32 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.16 (m, 6H), 7.07 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.03 – 7.00 (m, 2H), 6.99 (dd, *J* = 6.6, 3.0 Hz, 2H), 6.80 (dd, *J* = 16.2, 2.2 Hz, 1H), 6.72 – 6.68 (m, 2H), 6.24 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.93 (dd, *J* = 16.3, 4.0 Hz, 1H), 5.40 (d, *J* = 13.0 Hz, 1H), 5.13 (dd, *J* = 13.0, 10.7 Hz, 1H), 4.94 (d, *J* = 10.7 Hz, 1H), 4.56 (ddd, *J* = 9.0, 4.0, 2.2 Hz, 1H), 4.46 – 4.35 (m, 2H), 3.91 (dd, *J* = 10.6, 9.0 Hz, 1H), 3.70 (s, 3H), 3.65 (d, *J* =

10.5 Hz, 1H), 1.40 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.1, 173.8, 170.3, 167.6, 159.3, 144.3, 140.8, 135.2, 133.2, 132.2, 129.3, 128.9, 128.9, 128.5, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 126.6, 122.6, 113.9, 109.9, 82.8, 67.0, 64.3, 62.6, 55.3, 50.9, 50.8, 49.3, 47.8, 14.3. **IR** (film) ν_{max} 3467, 3061, 1954, 1713, 1252, 742, 700 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{43}H_{39}N_4O_6$ 707.2864; Found 707.2868.

Ethyl (3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-2-methyl-1,3-dioxo-6,8-diphenyl-7-(1*H*-pyrazole-1-carbonyl)-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (10): White solid, 73 mg, 59% yield. R_f = 0.44 (20% EtOAc in hexanes). **MP**: 200−203 °C. dr = 83:17 $[\alpha]_D^{27}$ = +87.77 (CH_2Cl_2, c = 0.74 for 90% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 50/50, 1.0 mL/min, 254 nm): t_R = 7.72 min (minor), 10.43 min (major). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 1.4 Hz, 1H), 7.63 (d, *J* = 2.8 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 2H), 7.28 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.25 – 7.20 (m, 1H), 7.19 – 7.12 (m, 3H), 7.12 – 7.07 (m, 2H), 7.05 (dd, *J* = 5.1, 2.0 Hz, 3H), 6.94 (dt, *J* = 6.4, 2.0 Hz, 2H), 6.82 (dd, *J* = 16.3, 2.2 Hz, 1H), 6.23 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.05 (ddd, *J* = 16.2, 3.9, 1.6 Hz, 1H), 5.36 (d, *J* = 12.6 Hz, 1H), 5.08 (ddd, *J* = 12.6, 10.6, 1.8 Hz, 1H), 4.89 (dd, *J* = 10.6, 1.8 Hz, 1H), 4.45 (ddd, *J* = 9.2, 4.0, 2.2 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.78 (dd, *J* = 10.4, 9.0 Hz, 1H), 3.55 – 3.48 (m, 1H), 2.83 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 176.0, 170.2, 167.5, 144.3, 140.8, 136.5, 135.3, 133.6, 128.8, 128.5, 128.5, 128.1, 128.0, 127.9, 127.8, 127.6, 127.5, 126.5, 124.9, 109.9, 82.1, 66.8, 64.4, 62.4, 50.9, 50.8, 49.2, 47.8, 24.9, 14.2. **IR** (film) ν_{max} 3450, 2117, 1648, 1265, 1028, 749 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{37}H_{35}N_4O_5$ 615.2602; Found 615.2616.

Dimethyl (2*R*,3*S*,4*R*,5*S*)-3,5-diphenylpyrrolidine-2,4-dicarboxylate (11).

To a solution of **6aa** (77.9 mg, 0.2mol) in MeOH (2 mL) was added NaOMe (21.68 mg, 0.4 mol) at °C. After stirred for 8 hours at room temperature, the reaction was quenched with saturated aqueous NH_4Cl and extracted three times with EtOAc. Combined organic layers were washed with brine and dried over Na_2SO_4. After filtration and evaporation, the residue was purified through a small pad of silica gel by column chromatography (35% EtOAc in hexanes) to afford **11**as a colorless viscous gel (61.9 mg, 91%)

Viscous gel, 62 mg, 91% yield. R_f = 0.35 (30% EtOAc in hexanes). $[\alpha]_D^{26}$ = +16.66 (CH_2Cl_2, c = 0.52 for 99% ee). **HPLC** (Chiralpak IC , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.04 min (major), 13.05 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.44 – 7.40 (m, 2H), 7.40 – 7.33 (m, 6H), 7.32 – 7.26 (m, 2H), 4.88 (d, *J* = 8.7 Hz, 1H), 4.09 (d, *J* = 8.9 Hz, 1H), 3.92 (dd, *J* = 8.9, 7.9 Hz, 1H), 3.75 (s, 3H), 3.56 (dd, *J* = 8.8, 7.9 Hz, 1H), 3.18 (s, 3H), 3.03 (s, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 173.1, 171.9, 140.2, 139.5, 128.8, 128.5, 127.8, 127.7, 127.2, 127.1, 67.8, 65.4, 58.9, 52.4, 52.3, 51.4. **IR** (film) ν_{max} 3380, 3036, 30323, 2925, 2102, 1959, 1736, 1439, 1265, 1169, 751, 701 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{22}NO_4$ 340.1543; Found 340.1556.

[**Note:** The optical rotation of compound **11** $[\alpha]_D^{26}$ = +16.7 (c = 0.52, $CHCl_3$) was compared with previous report in literature $[\alpha]_D^{23}$ = +19.2 (c = 1.0, $CHCl_3$)].[27]

Ethyl (2*R*,3*S*,4*R*,5*S*)-4-(hydroxymethyl)-3,5-diphenylpyrrolidine-2-carboxylate (12).

A solution of ester **6aa** (77.9 mg, 0.2 mmol) in MeOH/CH_2Cl_2 (1.5 mL 9:1, v/v) was cooled to 0 °C using an ice-water mixture. The reaction mixture was charged with portion wise addition of $NaBH_4$ (30.26 mg, 0.8 mmol) at the same temperature. The reaction mixture was then stirred for 3 hours at

room temperature. Upon completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated aqueous NH_4Cl solution and the solvent was removed in vacuo. The resulting aqueous solution was extracted five times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified through a small pad of silica gel by column chromatography using 45% EtOAc in hexanes as eluent to afford compound **12** as a colorless viscous gel (60 mg, 92% yield)

Viscous gel, 60 mg, 92% yield. $\boldsymbol{R_f}$ = 0.20 (40% EtOAc in hexanes). $[\alpha]_D^{24}$ = -3.108 (CH_2Cl_2, c = 1.673 for 99% ee). **HPLC** (Chiralcel OD-H , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 6.22 min (minor), 9.02 min (major).**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 6.1 Hz, 4H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.29 (dt, *J* = 8.8, 2.8 Hz, 1H), 4.80 (d, *J* = 7.7 Hz, 1H), 4.23 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.15 (dq, *J* = 10.9, 7.1 Hz, 1H), 4.06 (d, *J* = 8.9 Hz, 1H), 3.43 (t, *J* = 8.4 Hz, 1H), 3.36 (dd, *J* = 11.4, 4.3 Hz, 1H), 3.31 (dd, *J* = 11.4, 6.4 Hz, 1H), 2.75 (qd, *J* = 7.6, 5.4 Hz, 1H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 173.3, 141.5, 140.7, 128.7, 128.6, 127.9, 127.5, 127.2, 126.9, 67.2, 64.4, 62.1, 61.0, 53.9, 50.8, 14.1. **IR** (film) ν_{max} 3423, 2925, 2100, 1729, 1642, 1207, 1030, 751, 701 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{20}H_{24}NO_3$ 326.1751; Found 326.1776.

((2*R*,3*S*,4*R*,5*S*)-3,5-diphenylpyrrolidine-2,4-diyl)dimethanol (13):

A solution of ester **6aa** (97.3 mg, 0.25 mmol) in anhydrous THF (3 mL) was cooled to -20 °C. The reaction mixture was charged with portion wise addition of $LiBH_4$ (27.22 mg, 1.25 mmol) at the same temperature. The reaction mixture was gradually allowed to stir at 10 °C temperature for 16 hours. Upon completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated aqueous NH_4Cl solution and the solvent was removed in *vacuo*. The resulting aqueous solution was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified through a short pad of silica gel by column chromatography using 45% EtOAc in hexanes as eluent to afford compound **13** as a white solid (61.8 mg, 81% yield)

White solid, 62 mg, 81% yield. $\boldsymbol{R_f}$ = 0.25 (40% EtOAc in hexanes). **MP**: 68−71 °C. $[\alpha]_D^{28}$ = +32.20 (CH_2Cl_2, c = 0.41 for 93% ee). **HPLC** (Chiralpak IC , *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 7.26 min (major), 8.07 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.50 – 7.44 (m, 2H), 7.44 – 7.36 (m, 5H), 7.34 – 7.29 (m, 3H), 4.93 (d, *J* = 9.3 Hz, 1H), 4.65 (dd, *J* = 9.2, 7.4 Hz, 1H), 4.20 (dd, *J* = 11.4, 2.8 Hz, 1H), 3.61 (dd, *J* = 11.4, 1.5 Hz, 1H), 3.51 (t, *J* = 10.6 Hz, 1H), 3.37 – 3.22 (m, 3H), 2.89 (tdd, *J* = 10.2, 6.8, 4.1 Hz, 1H), 2.06 (s, 2H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 138.9, 136.2, 129.2, 128.9, 128.6, 128.0, 127.8, 127.7, 73.3, 72.6, 61.49, 57.0, 51.25, 47.4. **IR** (film) ν_{max} 3041, 2927, 2364, 1726, 1644, 1408, 1170, 1037, 744, 401 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{18}H_{22}NO_2$ 284.1645; Found 284.1662.

(2*R*,3*S*,4*R*,5*S*)-2-carboxy-4-(hydroxymethyl)-3,5-diphenylpyrrolidi*n*-1-ium chloride (14):

A solution of ester **6aa** (77.9 mg, 0.2 mmol) in MeOH/CH_2Cl_2 (1.5 mL 2:1, v/v) was cooled to 0 °C using an ice-water mixture. The reaction mixture was charged with portion wise addition of $NaBH_4$ (30.26 mg, 0.8 mmol) at the same temperature. The reaction mixture was then stirred for 3 hours at room temperature. Upon completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated aqueous NH_4Cl solution and the solvent was removed in vacuo. The resulting aqueous solution was extracted five times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was

purified through a small pad of silica gel by column chromatography using 45% EtOAc in hexanes as eluent to afford compound **12** as a colorless viscous gel which was dissolved in MeOH/H_2O (1.5 mL, 2:1, v/v), and LiOH·H_2O (38.6 mg, 0.92 mmol) was added. The reaction mixture was stirred at room temperature for 3 hours. Upon completion of the reaction (monitored by TLC), the reaction mixture was neutralized with 1 N HCl (pH 1-3) and extracted with EtOAc/MeOH mixture (3 × 15 mL).The solvent was removed in vacuo. The residue was purified through a short pad of silica gel by column chromatography using 10% MeOH in CH_2Cl_2 as eluent to afford compound **14** as a white solid (67.9 mg, 70% yield)

White solid, 68 mg, 70% yield. $\boldsymbol{R_f}$ = 0.08 (40% EtOAc in hexanes). **MP**: 87−90 °C. $[\alpha]_D^{29}$ = +13.33 (MeOH, c = 0.3). The compound was crystalized from MeOH/ CH_2Cl_2 mixture at room temperature. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.56 – 7.48 (m, 4H), 7.45 (dd, *J* = 8.2, 6.4 Hz, 2H), 7.39 (q, *J* = 7.3 Hz, 3H), 7.33 – 7.27 (m, 1H), 5.17 (d, *J* = 7.9 Hz, 1H), 4.54 (dd, *J* = 9.8, 1.5 Hz, 1H), 3.60 (dd, *J* = 9.8, 8.0 Hz, 1H), 3.20 – 3.11 (m, 2H), 2.99 (dd, *J* = 10.7, 6.9 Hz, 1H), 2.87 – 2.77 (m, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 169.83, 140.8, 133.8, 129.1, 128.8, 128.7, 128.4, 128.3, 127.7, 95.9, 65.2, 64.6, 59.7, 52.6, 48.9. **IR** (film) ν_{max} 3247, 2949, 2836, 2526, 2042, 1652, 1452, 1111, 1023, 695 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M-Cl]^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1438; Found 298.1448.

7a-ethyl 2-methyl (2*S*,3*R*,5*S*,6*R*,7*S*,7a*R*)-5,7-diphenyl-6-(1*H*-pyrazole-1-carbonyl)-3-((*E*)-styryl)tetrahydro-1*H*-pyrrolizine-2,7a(5*H*)-dicarboxylate (15): White solid, 77 mg, 66% yield. $\boldsymbol{R_f}$ = 0.30 (20% EtOAc in hexanes). **MP**: 46−49 °C. dr = 80:20 $[\alpha]_D^{22}$ = +3.13 (CH_2Cl_2, c = 0.51 for 99% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 5.62 min (major), 6.54 min (minor). **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 2.8 Hz, 1H), 7.56 (s, 1H), 7.33 (dd, *J* = 10.8, 7.6 Hz, 4H), 7.25 (dt, *J* = 15.0, 7.6 Hz, 4H), 7.18 (t, *J* = 8.1 Hz, 2H), 7.01 (s, 5H), 6.42 (d, *J* = 15.6 Hz, 1H), 6.24 (q, *J* = 6.2 Hz, 2H), 5.32 – 5.17 (m, 2H), 4.76 (d, *J* = 11.0 Hz, 1H), 4.32 (t, *J* = 7.7 Hz, 3H), 3.57 (dd, *J* = 13.4, 5.7 Hz, 1H), 3.52 (s, 3H), 2.18 (dd, *J* = 13.5, 11.1 Hz, 1H), 1.91 (dd, *J* = 13.5, 6.8 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 175.3, 173.1, 168.5, 144.0, 141.1, 137.1, 136.6, 135.9, 128.6, 128.5, 128.3, 128.2, 127.9, 127.9, 127.4, 127.3, 127.1, 126.8, 124.8, 109.7, 80.2, 67.2, 65.1, 61.7, 52.2, 51.9, 49.2, 48.7, 34.1, 14.4. **IR** (film) ν_{max} 3433, 3059, 2925, 2855, 1731, 1641, 1387, 1264, 1031, 741, 701 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+Na]^+$ Calcd for $C_{36}H_{35}N_3O_5Na$ 612.2469; Found 612.2455.

Ethyl (3*R*,3a*S*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*R*)-3-hydroxy-7-(hydroxymethyl)-1-oxo-2,6,8-triphenyl-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-8a(6*H*)-carboxylate (16): A solution of ester **9aa** (135.35 mg, 0.2 mmol) in MeOH/CH_2Cl_2 (3 mL 2:1, v/v) was cooled to 0 °C using an ice-water mixture. The reaction mixture was charged with portion wise addition of $NaBH_4$ (60.52 mg, 1.6 mmol) at the same temperature. The reaction mixture was then stirred for 3 h at room temperature. Upon completion of the reaction (monitored by TLC), the reaction mixture was quenched with saturated aqueous NH_4Cl solution and the solvent was removed in vacuo. The resulting aqueous solution was extracted five times with EtOAc. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified through a small pad of silica gel by column chromatography using 55% EtOAc in hexanes as eluent to afford compound **16** as a colorless viscous gel (96 mg, 78% yield)

White solid, 96 mg, 78% yield. $\boldsymbol{R_f}$ = 0.10 (40% EtOAc in hexanes). **MP**: 100−103 °C. dr = 20:1 $[\alpha]_D^{25}$ = +128.15 (CH_2Cl_2, c = 0.47 for 99% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 11.68 min (minor), 23.71 min (major). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.25 (m, 13H), 7.19 (d, *J* = 7.4 Hz, 3H), 6.64 (d, *J* = 16.2 Hz, 1H), 6.21 (dd, *J* = 16.3, 5.1 Hz, 1H), 5.39 (s, 1H), 4.71 (d, *J* = 8.8 Hz, 1H), 4.50 (d, *J*

= 10.9 Hz, 1H), 4.43 (dd, *J* = 10.5, 5.1 Hz, 1H), 4.32 (dt, *J* = 14.3, 7.2 Hz, 1H), 4.22 (p, *J* = 6.9 Hz, 1H), 3.54 (d, *J* = 10.2 Hz, 1H), 3.37 (dd, *J* = 11.3, 3.4 Hz, 1H), 3.04 (t, *J* = 9.8 Hz, 1H), 2.97 (t, *J* = 10.3 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 172.2, 172.3, 142.1, 137.4, 137.2, 136.5, 132.5, 129.0, 128.9, 128.8, 128.6, 128.5, 128.0, 127.9, 127.5, 127.3, 126.5, 126.1, 125.9, 123.1, 85.8, 82.6, 69.0, 64.8, 61.8, 61.6, 52.3, 50.4, 49.0, 48.1, 14.0. **IR** (film) ν_{max} 3418, 2308, 1680, 1498, 1267, 1040, 738 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{39}H_{39}N_2O_5$ 615.2853; Found 615.2868.

((3a*R*,4*R*,6*S*,7*R*,8*S*,8a*S*,8b*S*)-2,6,8-triphenyl-4-((*E*)-styryl)octahydropyrrolo[3,4-a]pyrrolizine-7,8a(6*H*)-diyl)dimethanol (17): A solution of **9aa** (135.35 mg, 0.2mmol) in anhydrous THF (2 mL) was added to a stirred solution of $LiAlH_4$ (34.85 mg, 1.6 mmol) in anhydrous THF (1 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and refluxed for 14 h. Upon completion of the reaction (monitored by TLC), the reaction mixture was quenched with 15% aqueous NaOH. The reaction mixture was extracted three times with EtOAc and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified through a small pad of silica gel by column chromatography using 25% EtOAc in hexanes as eluent to afford compound **17** as a colorless viscous gel (68.45 mg, 60% yield)

White solid, 68 mg, 60% yield. R_f = 0.40 (30% EtOAc in hexanes). **MP**: 73−76 °C. $[\alpha]_D^{28}$ = +62.22 (CH_2Cl_2, c = 0.77 for 99% ee). **HPLC** (Chiralpak ID , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 8.41 min (major), 28.78 min (minor) **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.50 – 7.41 (m, 6H), 7.38 (q, *J* = 7.4 Hz, 3H), 7.28 (td, *J* = 13.7, 12.8, 7.2 Hz, 4H), 7.21 (dd, *J* = 8.6, 7.2 Hz, 2H), 7.13 – 7.04 (m, 2H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 2H), 6.49 (dd, *J* = 16.2, 1.6 Hz, 1H), 6.12 (dd, *J* = 16.1, 5.7 Hz, 1H), 4.64 (d, *J* = 9.8 Hz, 1H), 3.88 – 3.77 (m, 3H), 3.71 (d, *J* = 11.2 Hz, 1H), 3.42 – 3.23 (m, 6H), 3.12 (dd, *J* = 9.9, 7.7 Hz, 1H), 2.71 (dd, *J* = 10.8, 1.8 Hz, 1H), 2.51 (dd, *J* = 10.8, 8.4 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 148.5, 142.5, 137.7, 136.6, 131.5, 129.1, 128.7, 128.6, 128.6, 128.5, 128.5, 128.1, 127.6, 127.5, 127.4, 126.3, 117.9, 114.2, 78.7, 69.2, 63.6, 62.5, 58.1, 51.6, 48.6, 47.5, 47.3, 46.7, 45.5. **IR** (film) ν_{max} 3439, 3059, 2928, 1957, 1639, 1602, 1497, 1032, 747 cm^{-1}; **HRMS** (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{37}H_{39}N_2O_2$ 543.3006; Found 543.3007.

Associated Content

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Notes

The authors declare no competing financial interest.

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Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

Crystallographic data for compounds **6da**, **6d'a'**, **9da** and **14**.

^{1}H, $^{13}C\{^{1}H\}$NMR spectra for all compounds and HPLC chromatograms

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