Supporting Materials

Highly Enantioselective Ag(I)-Catalyzed [3 + 2] Cycloaddition of Azomethine Ylides

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General Methods: Solvents were dried with standard procedures and degassed with N₂. Column chromatography was performed using 200~400 mesh silica gel supplied by Natland International Corporation. Thin layer chromatography (TLC) was performed on EM reagents 0.25 mm silica 60-F plates. Visualilization of the developed chromatogram was performed by fluorescence quenching and KMnO₄ stain. ¹H, ¹³C and ³¹P NMR were recorded on Bruker AM-300, and AMX-360 spectrometers. Chemical shifts were reported in ppm down field from tetramethylsilane with the solvent resonance as the internal standard. Data for ¹H NMR are reported as chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and integration. Data for ¹³C NMR are reported as chemical shift. All melting points were determined in open capillary tubes and were uncorrected. Optical rotation was obtained on a Perkin-Elmer 241 polarimeter. MS spetra were recorded on a KRATOS mass spectrometer MS 9/50. GLC was performed on Helwett-Packard 6890 Series gas chromatographs equipped with a split-mode capillary injection system and flame ionization detectors using a chiral select 1000 (30 m x 0.25 mm) supplied by Supelco Inc. HPLC analysis was performed on a Waters 600 Series HPLC, UV detection monitored at 205 nm, using a Chiralcel OD column (25 cm) and chiralcel OD guard (5 cm), Chiralpak AS column (25 cm) and Chiralcel OJ column (25 cm).

The screening conditions are summarized in Table 3 and the model of transition state of [3 + 2] reaction is provided below.

Table 3. Comparison of various chiral bisphosphine ligands for the AgOAc catalyzed cycloaddition of **7a** with dimethyl maleate.

Entry ^a	Ligand	Solvent	endo- 8a		exo- 8a	
			%Yield ^b	%ee ^{c,d}	%Yield ^b	%ee ^c
1	1	Toluene	61	13	20	10
2 ^e	3	Toluene	57	23	-	-
3 ^e	4	Toluene	68	27	-	-
4 ^e	5	Toluene	73	13	-	-
5 ^e	2	Toluene	70	59	-	-
6	6a	Toluene	94	76	- ^f	-
7	6a	CH ₂ Cl ₂	73	74	19	45
8	6a	THF	89	69	7	56
9	6b	Toluene	88	86	-	-

^a Conditions: **7a** (1.0 eq), dimethyl maleate (1.2 eq), AgOAc (3 mol%), ligand (3.3 mol%), ⁱPr₂NEt (10.0 mol%), solvent (3 mL). ^b isolated yield by silica gel chromatography. ^c Enantiomeric excess determined by HPLC. ^d The major enantiomer of endo- **8a** (2 *S*, 3 *R*, 4 *R*, 5 *R*) formed was the same with all ligands. The absolute configuration was determined by correlation to a known compound, see supporting information. ^eLow yield is the result of unreacted **7a** after 24 h at rt. ^f The exo product was not detected by ¹H NMR of the crude reaction mixture.

Progress of the Ag-catalyzed [3+2] cycloaddition reaction was typically monitored by TLC analysis. Absolute configurations were determined by correlation to literature optical rotation values where indicated. Other absolute configurations were assigned by analogy.

Synthesis of (S, S)-FAP and (S, S)-xylyl-FAP:

Synthesis of 2a: To a THF (150 ml) solution of **1a** (6.75 g, 14.0 mmol) under N₂ was added H₂O (13.4 mL) and anhydrous Na₂SO₄ (104 g). After cooling to 0 °C, CF₃COOH (5.8 mL, 65.5mmol) was added and the reaction stirred overnight at rt. An additional Na₂SO₄(28 g) was added and the reaction mixture was filtered under N₂. The Na₂SO₄ was washed with THF until no color remained and the filtrate was concentrated under reduced pressure affording a yellow solid. This solid was dissolved in CH₂Cl₂ (250 mL), cooled to 0 °C and Ac₂O (25 mL, 0.26 mol) was added followed by pyridine (50 ml, 0.62 mol). The reaction mixture was stirred overnight at rt. The resulting red solution was quenched with 3 M HCl (100 mL) and the organic layers were separated. The organic phase was washed with 3 M HCl (2 X 100 mL), sat. NaHCO₃ (1 X 100 mL) and dried over Na₂SO₄. The deep red solution was concentrated under reduced pressure and the

crude product purified by passing through a short column of silica gel eluting with EtOAc. Product **2a** was obtained as a yellow solid (5.7 g, 75% yield). mp = 146-147 °C; $[\alpha]_D = -147.6$ (c = 0.55, CH₂Cl₂); ¹H NMR (360 MHz, CD₂Cl₂) δ 0.96 (d, J = 6.8 Hz, 3H, CH₃), 1.05 (d, J = 6.7 Hz, 3H, CH₃), 1.71 (s, 3H, CH₃), 2.08 (m, 1H, CH); 3.71 (s, 1H), 3.72-3.87 (m, 2H), 4.19 (s, 5H), 4.49-4.52 (m, 2H), 5.15 (s, 1H), 5.32 (br, 1H, NH), 7.16-7.18 (m, 2H), 7.28-7.30 (m, 3H), 7.41-7.51 (m, 5H), ¹³C NMR (90 MHz, CD₂Cl₂) δ 19.5, 19.8, 23.4, 29.7 (d, J=4.5 Hz), 53.9, 65.1, 71.4, 72.8, 75.3 (d, J_{p-c} = 1.5 Hz), 75.9-76.1 (m), 78.1 (d, J_{p-c} = 15 Hz), 128.5-128.7 (m, 3 different aromatic C's), 129.8, 132.2 (d, J_{p-c} = 17.9 Hz), 135.7 (d, J_{p-c} = 21.8 Hz), 138.1 (d, J_{p-c} = 11.7 Hz), 140.4 (d, J_{p-c} = 13.3 Hz), 169.5, 171.6 (d, J_{p-c} = 2.6 Hz); ³¹P NMR (145 MHz, CD₂Cl₂) δ -15.42; HRMS (MALDI) for C₃₀H₃₂NO₃PFeH (MH⁺) calculated: 542.1548, found: 542.1580

Synthesis of 2b: Product **2b** was obtained in 74% yield as a yellow solid following the procedure described for **2a**. mp = 176-178 °C; $[\alpha]_D = -135.9$ (c = 0.78, CH₂Cl₂); ¹H NMR (360 MHz, CD₂Cl₂) δ 0.96 (d, J = 6.7 Hz, 3H, CH₃), 1.06 (d, J = 6.7 Hz, 3H, CH₃), 1.69 (s, 3H, CH₃), 2.16-2.22 (m, 1H, CH), 2.21 (s, 3H, CH₃), 2.32 (s, 3H, CH₃), 1.69 (s, 3H, CH₃), 2.16-2.22 (m, 1H, CH), 2.21 (s, 3H, CH₃), 2.32 (s, 3H, CH₃), 3.74 (m, 1H), 3.79-3.87 (m, 2H, CH₂), 4.18 (s, 5H), 4.46-4.51 (m, 2H), 5.14 (m, 1H), 5.43 (br s, 1H, NH), 6.75 (m, 2H), 6.92 (s, 1H), 7.06-7.11 (m, 3H); ¹³C NMR (90 MHz, CD₂Cl₂) δ 19.6, 19.8, 21.4, 21.4, 23.1, 29.6 (d, J_{p-c} = 5.7 Hz), 53.9, 65.2, 71.3, 72.6, 75.3, 75.9 (d, J_{p-c} = 17.0 Hz), 76.2 (d, J_{p-c} = 4.4 Hz), 78.4 (d, J_{p-c} = 15.6 Hz), 130.0 (d, J_{p-c} = 18.5 Hz), 130.4, 131.4, 133.3 (d, J_{p-c} = 21.9 Hz), 137.8-138.1 (m, 3 different aromatic C's), 139.9 (d, J_{p-c} = 12.4 Hz), 169.5, 171.8 (d, J_{p-c} = 2.7 Hz); ³¹P NMR (145 MHz, CD₂Cl₂) -15.56; HRMS (APCI) for C₃₄H₄₀NO₃PFeH (MH⁺) Calculated: 598.2174, found: 598.2179.

Synthesis of 3a: To a slurry of t-BuOK (4.13 g, 36.9 mmol) in Et₂O (100 ml) at 0 °C was added H₂O (0.17 ml). The slurry was stirred at 0 °C for 5 min before adding **2a** (1.08 g, 2.0 mmol). The reaction was warmed to rt and stirred for 24 h then was quenched with ice H₂O, the layers separated and the aqueous layer washed once with Et₂O. The aqueous phase was acidified with 3M HCl and extracted with CH₂Cl₂. The organic phase was dried over Na₂SO₄ and concentrated under reduced pressure. The crude product residue was purified by passing through a short pad of silica gel eluting with EtOAc. The desired product was obtained as an orange powder (0.79 g, 96% yield). mp = 146-148 °C; $[\alpha]_D = -249.5$ (c = 1.07, CH₂Cl₂); ¹H NMR (360 MHz, CD₂Cl₂) δ 3.82 (s, 1H), 4.26 (s, 5H), 4.54 (t, J = 2.5 Hz, 1H), 5.12 (s, 1H), 7.18-7.22 (m, 2H), 7.28-7.30 (m, 3H), 7.40-7.41 (m, 3H), 7.49-7.54 (m, 2H); ¹³C NMR (90 MHz, CD₂Cl₂) δ 71.7, 73.1, 74.3 (d, J_{p-c} = 15.3 Hz), 75.3, 76.4 (d, J_{p-c} = 4.7 Hz), 80.0 (d, J_{p-c} = 17.5 Hz), 128.4-128.6 (m, 3 different aromatic

C's), 129.5, 132.4 (d, $J_{\text{P-C}} = 19.1$ Hz), 135.5 (d, $J_{\text{P-C}} = 21.6$ Hz), 138.5 (d, $J_{\text{P-C}} = 13.1$ Hz), 140.1 (d, $J_{\text{P-C}} = 13.3$ Hz), 178.3 (d, $J_{\text{P-C}} = 2.4$ Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ -17.29; HRMS (MALDI) for $\text{C}_{23}\text{H}_9\text{O}_2\text{PFeH} (\text{MH}^+)$ calculated: 415.0551, found: 415.0534

Synthesis of 3b: Acid **3b** was obtained in 98% yield as a yellow solid following the procedure described for **3a**. mp = 78-80 °C; $[\alpha]_{\text{D}} = -194.2$ ($c = 0.72$, CH_2Cl_2); ^1H NMR (360 MHz, CD_2Cl_2) δ 2.22 (s, 6H, CH_3), 2.31 (s, 6H, CH_3), 3.86 (s, 1H, CH), 4.21 (s, 5H, CH), 4.53 (s, 1H, CH), 5.09 (m, 1H, CH), 6.76 (d, $J_{\text{P-H}} = 7.8$ Hz, 2H), 6.92 (s, 1H), 7.05 (s, 1H), 7.12 (d, $J_{\text{P-H}} = 8.0$ Hz, 2H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 21.4, 71.6, 72.9, 74.4 (d, $J_{\text{P-C}} = 16.0$ Hz), 75.1, 76.5 (d, $J_{\text{P-C}} = 4.5$ Hz), 80.2 (d, $J_{\text{P-C}} = 16.4$ Hz), 130.0, 130.2 (d, $J_{\text{P-C}} = 3.1$ Hz), 131.2, 133.1 (d, $J_{\text{P-C}} = 21.5$ Hz), 137.8-138.1 (m, 3 different aromatic C's), 139.4 (d, $J_{\text{P-C}} = 11.3$ Hz), 176.7; ^{31}P NMR (145 MHz, CD_2Cl_2) δ -18.16; HRMS (APCI) for $\text{C}_{27}\text{H}_{27}\text{O}_2\text{PFeH} (\text{MH}^+)$ calculated: 471.1177, found: 471.1187.

Synthesis of (S, S)-FAP: In a Schlenk flask under N_2 was combined acid **3a** (798 mg, 1.93 mmol), (1S, 2S)-diaminocyclohexane (100 mg, 0.88 mmol), 4-dimethylaminopyridine (11 mg, 0.09 mmol) and CH_2Cl_2 (11 ml). To the resulting orange solution was added EDCI (403 mg, 2.10 mmol) in one portion. The reaction was stirred overnight at rt. The reaction solution was washed with H_2O and the aqueous phase extracted twice with CH_2Cl_2 . The combined organic layers were washed with brine and dried over Na_2SO_4 . Removal of Na_2SO_4 by filtration and concentration by rotary evaporation afforded an orange solid, which was purified by silica gel chromatography (Hexanes/EtOAc = 3/1 to 2/1). The product was obtained as an orange powder (670 mg, 84% yield). mp = 155-160 °C (dec.); $[\alpha]_{\text{D}} = -198.2$ ($c = 1.1$, CH_2Cl_2); ^1H NMR (360 MHz, CD_2Cl_2) δ 1.12 (m, 4H), 1.70 (br, 2H), 1.99 (br, 2H), 3.66 (m, 4H), 4.05 (s, 10H), 4.41 (t, $J = 2.6$ Hz, 2H), 5.07 (m, 2H), 7.05-7.16 (m, 10H), 7.34-7.45 (m, 10H), 7.57 (m, 2H, NH); ^{13}C NMR (90 MHz, CD_2Cl_2) 25.5, 33.0, 55.5, 71.3, 71.6, 72.7, 74.9 (d, $J_{\text{P-C}} = 4.3$ Hz), 77.4 (d, $J_{\text{P-C}} = 11.7$ Hz), 80.0 (d, $J_{\text{P-C}} = 15.3$ Hz), 128.3-128.6 (3 different aromatic C's), 129.6, 132.5 (d, $J_{\text{P-C}} = 18.0$ Hz), 135.4 (d, $J_{\text{P-C}} = 21.2$ Hz), 137.7 (d, $J_{\text{P-C}} = 10.4$ Hz), 139.5 (d, $J_{\text{P-C}} = 9.5$ Hz), 171.5 (d, $J_{\text{P-C}} = 2.7$ Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ -18.90; HRMS (APCI) for $\text{C}_{52}\text{H}_{48}\text{N}_2\text{O}_2\text{P}_2\text{Fe}_2\text{H} (\text{MH}^+)$ calculated: 907.1971, found: 907.1954.

Synthesis of (S, S)-xylyl-FAP: Ligand xylyl-FAP was obtained 84% yield as an orange powder following the procedure described for the synthesis of (S, S)-FAP. mp = 160-162 °C; $[\alpha]_{\text{D}} = -169.9$ ($c = 1.04$, CH_2Cl_2); ^1H NMR (360 MHz, CD_2Cl_2) δ 1.26-1.35 (m, 6H), 1.75 (br s, 2H), 2.06 (s, 12H, CH_3), 2.30 (s, 12H, CH_3), 3.70 (br s, 2H), 3.77

(s, 2H), 4.05 (s, 10H), 4.44 (m, 2H), 5.13 (m, 2H), 6.72 (d, $J_{\text{P-H}}$, 4H), 6.84 (s, 2H), 7.03 (s, 2H), 7.09 (d, $J_{\text{P-H}}$ = 8.2 Hz, 4H), 7.72 (br m, 2H, NH); ^{13}C NMR (90 MHz, CD_2Cl_2) 21.3, 21.4, 25.2, 32.6, 55.3, 71.3, 72.7, 75.1 (m), 77.7 (d, $J_{\text{P-C}}$ = 12.5 Hz), 80.1 (d, $J_{\text{P-C}}$ = 16.0 Hz), 130.2 (d, $J_{\text{P-C}}$ = 4.5 Hz), 130.4, 131.2, 133.0 (d, $J_{\text{P-C}}$ = 20.8 Hz), 137.4 (d, $J_{\text{P-C}}$ = 9.6 Hz), 137.8-138.0 (2 different aromatic C's), 139.2 (d, $J_{\text{P-C}}$ = 8.4 Hz), 171.3 (d, $J_{\text{P-C}}$ = 2.6 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ -19.45; HRMS (APCI) for $\text{C}_{52}\text{H}_{48}\text{N}_2\text{O}_2\text{P}_2\text{Fe}_2\text{H}$ (MH^+) calculated: 1019.3224, found: 1019.3254.

General Procedure for the Synthesis of α -iminoesters. A suspension of glycine methyl ester hydrochloride (1.1 eq), excess MgSO_4 and NEt_3 (1.1 eq) in CH_2Cl_2 was stirred at rt for 1h. The aldehyde (1.0 eq) was added and the reaction stirred at rt overnight. The MgSO_4 was removed by filtration and the filtrate was washed once with H_2O . The aqueous phase was extracted once with CH_2Cl_2 and the combined organic layers were washed with brine. The organic phase was dried over Na_2SO_4 , filtered and concentrated. Most products were sufficiently pure but if necessary could be purified by either bulb-to-bulb distillation or trituration.

General Procedure for the Ag-Catalyzed [3+2] Cycloaddition Reaction. The following procedure is representative for all substrates: The catalyst was prepared by stirring AgOAc (2.3 mg, 0.014 mmol) and xyl-FAP (15.3 mg, 0.015 mmol) in toluene (2 mL) for 1h. After it was cooled to 0 °C, imine substrate (0.45 mmol) was added as a solution in toluene (1 ml) followed by dimethylmaleate (84 μL , 0.68 mmol) and *i*-Pr $_2\text{NEt}$ (8 μL , 0.045 mmol). Upon consumption of the limiting reagent, the toluene was removed and the product isolated by silica gel chromatography.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-phenylpyrrolidine (Table 1, entry 1): Prepared according to the general procedure with *N*-benzyliden-glycinmethylester (80 mg, 0.45 mmol) and dimethyl maleate (84 μL , 0.68 mmol) to afford the title compound as a colorless solid in 86.8% yield (126 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et $_3\text{N}$); 87% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r = 13.1 and 22.6 min. mp = 91-93 °C. $[\alpha]_D = 64.7$ (c = 1.07, CH_2Cl_2). Literature $[\alpha]_D = 18.2$ (c = 0.6, CH_2Cl_2). ^1H NMR and ^{13}C NMR data were consistent with previously reported value.²

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5- (4-chlorophenyl) pyrrolidine (Table 1, entry 4): Prepared according to the general procedure with *N*-(4-chlorobenzyliden)-glycinmethylester (95.2 mg, 0.45 mmol) and dimethyl maleate (84 μL ,

0.68 mmol) to afford the title compound as a colorless solid in 96.0% yield (154 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 92% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r = 16.3 and 26.6 min. mp = 128-130 °C. [α]_D = 55.6 (c = 1.09, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 7.22 (s, 4H), 4.38 (d, *J* = 6.9 Hz, 1H), 4.08 (d, *J* = 8.8 Hz, 1H), 3.73 (s, 3H), 3.62-3.67 (m, 1H), 3.61 (s, 3H), 3.48-3.52 (m, 1H), 3.20 (s, 3H), 3.18 (bs, 1H); ¹³C NMR (90 MHz, CDCl₃) δ = 170.9, 170.62, 170.60, 135.8, 133.4, 128.4, 128.1, 64.5, 62.0, 52.3, 52.2, 52.0, 51.3, 50.8.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(2-chlorophenyl)pyrrolidine (Table 1, entry 7): Prepared according to the general procedure with *N*-(2-chlorobenzyliden)-glycinmethylester (95.2 mg, 0.45 mmol) and dimethyl maleate (84 μL, 0.68 mmol) to afford the title compound as a colorless oil in 96.1% yield (154 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 86% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r = 15.1 and 33.7 min. [α]_D = 116.2 (c = 1.04, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 7.48 (d, *J* = 1.5 Hz, 1H), 7.31-7.46 (m, 1H), 7.18-7.26 (m, 2H), 4.73 (m, 1H), 4.09 (t, *J* = 8.9 Hz, 1H), 3.72-3.87 (m, 2H), 3.83 (s, 3H), 3.63 (s, 3H), 3.28 (m, 1H), 3.15 (s, 3H); ¹³C NMR (90 MHz, CDCl₃) δ = 171.2, 170.7, 170.5, 134.6, 133.2, 129.2, 128.8, 127.4, 126.7, 61.8, 61.2, 52.4, 52.1, 51.3, 50.8, 50.1.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(2-methylphenyl)pyrrolidine (Table 1, entry 8): Prepared according to the general procedure with *N*-(2-methylbenzyliden)-glycinmethylester (86 mg, 0.45 mmol) and dimethyl maleate (84 μL, 0.68 mmol) to afford the title compound as a colorless oil in 97.0% yield (146 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 90% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r = 12.5 and 33.9 min. [α]_D = 100.1 (c = 1.12, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 7.33-7.36 (m, 1H), 7.08-7.18 (m, 3H), 4.58 (bs, 1H), 4.08 (bs, 1H), 3.80 (s, 3H), 3.63-3.73 (m, 2H), 3.64 (s, 3H), 3.61 (bs, 1H), 3.09 (s, 3H), 2.32 (s, 3H); ¹³C NMR (90 MHz, CDCl₃) δ = 171.2, 170.7, 170.6, 135.5, 134.8, 130.1, 127.5, 125.9, 125.2, 61.9, 61.7, 52.3, 52.0, 51.2, 50.8, 50.7, 19.6.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(4-methoxyphenyl)pyrrolidine (Table 1, entry 3): Prepared according to the general procedure with *N*-(4-methoxybenzyliden)-glycinmethylester (93.2 mg, 0.45 mmol) and dimethyl maleate (84

μL , 0.68 mmol) to afford the title compound as a colorless solid in 97.8% yield (155 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 92% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r =17.3 and 35.8 min. mp=108-109 °C. $[\alpha]_D^{25}$ =60.6 (c =1.03, CH₂Cl₂). Literature $[\alpha]_D^{25}$ =71.4 (c =2.25, CH₂Cl₂).¹ ¹H NMR and ¹³C NMR data were consistent with previously reported value.¹

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(4-methylphenyl)pyrrolidine (Table 1, entry 2): Prepared according to the general procedure with *N*-(4-methylbenzyliden)-glycinmethylester (86 mg, 0.45 mmol) and dimethyl maleate (84 μL , 0.68 mmol) to afford the title compound as a colorless solid in 93.2% yield (141 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 88% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r = 12.2 and 29.2 min. mp = 114-115 °C. $[\alpha]_D^{25}$ = 61.9 (c = 1.10, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ =7.21 (d, J = 7.7 Hz, 2H), 7.08 (d, J = 7.7 Hz, 2H), 4.23-4.38 (bs, 1H), 4.18 (bs, 1H), 3.77 (s, 3H), 3.67-3.69 (m, 1H), 3.65 (s, 3H), 3.49-3.53 (m, 1H), 3.33 (bs, 1H), 3.22 (s, 3H), 2.28 (s, 3H); ¹³C NMR (90 MHz, CDCl₃) δ =171.0, 170.9, 170.8, 137.2, 133.9, 128.9, 126.5, 65.2, 62.1, 52.4, 52.3, 52.0, 51.3, 51.0, 21.0.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(1-naphthyl)pyrrolidine (Table 1, entry 9): Prepared according to the general procedure with *N*-[(naphthalen-1-yl methylene)-amino]-acetic acid methyl ester (102.2 mg, 0.45 mmol) and dimethyl maleate (84 μL , 0.68 mmol) to afford the title compound as a colorless solid in 72.8% yield (122 mg) after silica chromatography (50% EtOAc/Hex containing 1% Et₃N); 85% ee. Product ratio were determined by HPLC (Chiralpak AS column, 70% IPA/Hex, 1.0 ml/min, t_r = 18.3 and 39.4 min. mp=128-129 °C. $[\alpha]_D^{25}$ = 199.8 (c =1.12, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 7.92 (d, J = 8.1 Hz, 1H), 7.82-7.84 (m, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 7.0 Hz, 1H), 7.40-7.51 (m, 3H), 5.16 (d, J = 4.8 Hz, 1H), 4.19-4.24 (m, 1H), 3.81-3.87 (m, 5H), 3.63 (s, 3H), 3.42 (bs, 1H), 3.92 (s, 3H); ¹³C NMR (90 MHz, CDCl₃) δ =171.2, 170.6, 170.5, 133.4, 132.3, 131.0, 128.9, 128.2, 126.2, 125.5, 125.1, 123.1, 122.5, 61.2, 52.3, 52.0, 51.9, 51.1, 51.0.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(2-naphthyl)pyrrolidine (Table 1, entry 10): Prepared according to the general procedure with *N*-[(naphthalen-2-yl methylene)-amino]-acetic acid methyl ester (102.2 mg, 0.45 mmol) and dimethyl maleate (84 μL , 0.68 mmol) to afford the title compound as a colorless solid in 98.1% yield (164

mg) after silica chromatography (50% EtOAc/Hex containing 1% Et₃N); 97% ee. Product ratio were determined by HPLC (Chiralpak AS column, 70% IPA/Hex, 1.0 ml/min, t_r = 15.9 and 38.4 min. mp=129-130 °C. [α]_D = 46.4 (c = 1.12, CH₂Cl₂). ¹H NMR and ¹³C NMR data were consistent with previously reported value.³

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(4-cynaophenyl)pyrrolidine (Table 1, entry 6): Prepared according to the general procedure with *N*-(4-cycanobenzyliden)-glycinmethylester (91 mg, 0.45 mmol) and dimethyl maleate (84 μL, 0.68 mmol) to afford the title compound as a colorless solid in 90.2% yield (141 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 96% ee. Product ratio were determined by HPLC (Chiralpak AS column, 20% IPA/Hex, 1.0 ml/min, t_r = 135.9 and 153.1 min. mp = 175-176 °C. [α]_D = 59.1 (c = 1.13, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 7.59 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 4.49 (d, *J* = 6.8 Hz, 1H), 4.13 (d, *J* = 8.7 Hz, 1H), 3.76 (s, 3H), 3.68-3.73 (m, 1H), 3.65 (s, 3H), 3.57-3.61 (m, 1H), 3.22 (s, 3H), 2.94 (bs, 1H); ¹³C NMR (90 MHz, CDCl₃) δ = 170.8, 170.5, 170.3, 143.0, 132.0, 127.7, 118.5, 111.5, 64.6, 62.0, 52.5, 52.2, 52.0, 51.5, 50.8.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(4-florophenyl)pyrrolidine (Table 1, entry 5): Prepared according to the general procedure with *N*-(4-florobenzyliden)-glycinmethylester (87.8 mg, 0.45 mmol) and dimethyl maleate (84 μL, 0.68 mmol) to afford the title compound as a colorless solid in 96.1% yield (147 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 90% ee. Product ratio were determined by HPLC (Chiralpak AS column, 50% IPA/Hex, 1.0 ml/min, t_r = 13.4 and 21.7 min. mp = 103-105 °C. [α]_D = 62.4 (c = 1.22, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 7.28-7.32 (m, 2H), 6.96-7.00 (m, 2H), 4.44 (d, *J* = 7.0 Hz, 1H), 4.12 (d, *J* = 8.7 Hz, 1H), 3.77 (s, 3H), 3.66-3.70 (m, 1H), 3.66 (s, 3H), 3.51-3.53 (m, 1H), 3.23 (s, 3H), 2.89 (bs, 1H); ¹³C NMR (90 MHz, CDCl₃) δ = 170.9, 170.71, 170.68, 162.1 (d), 133.0 (d, *J*_{C-F} = 2.9 Hz), 128.4 (d, *J*_{C-F} = 8.1 Hz), 115.1 (d), 64.5, 62.0, 52.3, 52.0, 51.3, 50.7.

(2S, 3R, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-(3-pyridinyl)pyrrolidine (Table 1, entry 11): Prepared according to the general procedure with *N*-[(pyridinyl-3-yl methylene)-amino]-acetic acid methyl ester (80.1 mg, 0.45 mmol) and dimethyl maleate (84 μL, 0.68 mmol) to afford the title compound as a colorless solid in 98.4% yield (143 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 84% ee. Product ratio were determined by HPLC (Chiralpak AS column, 30% IPA/Hex, 1.0 ml/min, t_r = 28.7 and 35.1 min. mp=108-110 °C. [α]_D = 61.0 (c = 1.05, CH₂Cl₂). ¹H NMR (360 MHz,

CDCl₃) δ = 8.68 (s, 1H), 8.62 (d, J = 5.4 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.35-7.40 (m, 1H), 4.62 (d, J = 7.6 Hz, 1H), 4.27 (d, J = 8.6 Hz, 1H), 3.90 (s, 3H), 3.81-3.86 (m, 1H), 3.79 (s, 3H), 3.71-3.75 (m, 1H), 3.36 (s, 3H), 2.26 (bs, 1H); ¹³C NMR (90 MHz, CDCl₃) δ = 170.7, 170.6, 170.4, 149.0, 148.8, 134.2, 133.1, 123.2, 62.7, 62.1, 52.4, 52.1, 51.4, 50.7.

(2S, 3R, 4R, 5S)-2, 3, 4-tricarbomethoxy-5-isopropylpyrrolidine (Table 1, entry 12): Prepared according to the general procedure with *N*-isobutylidene-glycinmethyl ester (64.4 mg, 0.45 mmol) and dimethyl maleate (84 μ l, 0.68 mmol) to afford the title compound as a colorless solid in 82% yield (106 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 70% ee. Product ratio were determined by GLC (Chiral Select 1000, 180 °C, 1.0 ml/min) t_r = 23.4 and 25.0 min. mp = 63-64 °C. $[\alpha]_D$ = 14.8 (c = 1.17, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 4.03 (d, J = 10.1 Hz, 1H), 3.71 (s, 3H), 3.63 (s, 3H), 3.62 (s, 3H), 3.50-3.55 (m, 1H), 3.13-3.16 (m, 1H), 2.67-2.71 (m, 2H), 1.60 (m, 1H), 1.04 (d, J = 6.5 Hz, 3H), 0.92 (d, J = 6.5 Hz, 3H); ¹³C NMR (90 MHz, CDCl₃) δ = 171.6, 171.2, 170.5, 70.2, 61.5, 52.3, 52.0, 51.5, 49.1, 29.8, 21.4, 20.6.

(2S, 3R, 4R, 5S)-2, 3, 4-tricarbomethoxy-5-cyclohexylpyrrolidine (Table 1, entry 13): Prepared according to the general procedure with *N*-cyclohexylidene-glycinmethyl ester (82.4 mg, 0.45 mmol) and dimethyl maleate (84 μ L, 0.68 mmol) to afford the title compound as a colorless oil in 81.9% yield (121 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 81% ee. Product ratio were determined by GLC (Chiral Select 1000, 200 °C, 1.0 ml/min) t_r = 49.5 and 51.7 min. $[\alpha]_D$ = 7.3 (c = 1.07, CH₂Cl₂). ¹H NMR (360 MHz, CDCl₃) δ = 4.04 (d, J = 10.2 Hz, 1H), 3.72 (s, 3H), 3.65 (s, 3H), 3.63 (s, 3H), 3.51 (dd, J = 10.1 Hz and 7.4 Hz, 1H), 3.14-3.16 (m, 1H), 2.77-2.78 (m, 2H), 2.01 (m, 1H), 1.63-1.80 (m, 4H), 1.03-1.22 (m, 6H); ¹³C NMR (90 MHz, CDCl₃) δ = 172.1, 171.2, 170.6, 68.7, 61.3, 52.3, 52.0, 51.8, 51.5, 48.8, 39.1, 31.5, 30.9, 26.2, 25.8, 25.6.

Table 2. Cycloaddition of **7a** with various dipolarophile substrates

entry ^a	dipolarophile	product	yield (%) ^b	ee (%) ^c
1			87	87
2			88	52
3			85	87
4			90	60
5			85	93
6			87	71
7			87	79

^a Conditions: imine (1.0 eq), dimethyl maleate (1.2 eq), AgOAc (3 mol%), ligand **6b** (3.3 mol%), ⁱPr₂NEt (10.0 mol%), toluene (3 mL) at 0 °C. ^b isolated yield by silica gel chromatography. ^c Enantiomeric excess determined by HPLC.

(2S, 3R, 4R, 5R)-5-phenylpyrrolidine-2, 3, 4-tricarboxylic acid-3, 4-isopropyl ester-2-methyl ester (Table 2, entry 3): Prepared according to the general procedure with N-benzyliden-glycinmethyl ester (80 mg, 0.45 mmol) and di-isopropyl maleate (136 mg, 0.68 mmol) to afford the title compound as a colorless solid in 84.7% yield (144 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et₃N); 87% ee. Product

ratio were determined by HPLC (Chiralpak AS column, 20% IPA/Hex, 1.0 ml/min, t_r =12.2 and 33.9 min. mp=146-148 °C. $[\alpha]_D = 49.9$ ($c = 1.47$, CH_2Cl_2). ^1H NMR (360 MHz, CDCl_3) δ = 7.00-7.16 (m, 5H), 4.76-4.81 (m, 1H), 4.32-4.39 (m, 1H), 4.23 (d, $J = 6.7$ Hz, 1H), 3.90 (d, $J = 9.1$ Hz, 1H), 3.59 (s, 3H), 3.44-3.49 (m, 1H), 3.33-3.37 (m, 1H), 2.95 (bs, 1H), 1.03 (d, $J = 6.2$ Hz, 3H), 0.99 (d, $J = 6.3$ Hz, 3H), 0.72 (d, $J = 6.2$ Hz, 3H), 0.41 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR (90 MHz, CDCl_3) δ = 171.0, 169.8, 169.7, 137.2, 128.2, 127.5, 126.9, 68.7, 68.0, 65.3, 62.0, 52.8, 52.1, 51.6, 21.7, 21.6, 21.4, 20.8.

(2S, 3S, 4R, 5R)-2, 3, 4-tricarbomethoxy-5-phenylpyrrolidine (Table 2, entry 2):

Prepared according to the general procedure with N-benzyliden-glycinmethylester (80 mg, 0.45 mmol) and dimethyl fumarate (98 mg, 0.68 mmol) to afford the title compound as a colorless oil in 88.3% yield (128 mg) after silica chromatography (15% EtOAc/Hex containing 1% Et_3N); 52% ee. Product ratio were determined by HPLC (Chiralcel OJ column, 30% IPA/Hex, 1.0 ml/min, t_r = 36.8 and 56.6 min. $[\alpha]_D = 9.04$ ($c = 1.54$, CH_2Cl_2). ^1H NMR and ^{13}C NMR data were consistent with previously reported value.²

(2S, 4S, 5R)-5-phenyl-2, 4-dicarbomethoxy-pyrrolidene (Table 2, entry 4):

Prepared according to the general procedure with N-benzyliden-glycinmethyl ester (80 mg, 0.45 mmol) and methyl acrylate (58.5 mg, 0.68 mmol) to afford the title compound as a colorless solid in 90% yield (107 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et_3N); 60% ee. mp=68-69 °C. Product ratio were determined by HPLC (Chiralpak OD column, 50% IPA/Hex, 1.0 ml/min, t_r = 17.5 and 24.8 min. $[\alpha]_D = 33.1$ ($c = 1.11$, CH_2Cl_2). ^1H NMR and ^{13}C NMR data were consistent with previously reported value.²

(2S, 4S, 5R)-5-phenyl-pyrrolidine-2, 4-dicarboxylic-4-tert-butyl ester-2-methyl ester (Table 2, entry 5): Prepared according to the general procedure with N-benzyliden-glycinmethyl ester (80 mg, 0.45 mmol) and t-butyl acrylate (87 mg, 0.68 mmol) to afford the title compound as a colorless solid in 85.1% yield (117 mg) after silica chromatography (33% EtOAc/Hex containing 1% Et_3N); 93% ee. Product ratio were determined by HPLC (Chiralpak As column, 10% IPA/Hex, 1.0 ml/min, t_r = 13.3 and 19.2 min. mp = 68-69 °C. $[\alpha]_D = 33.1$ ($c = 1.11$, CH_2Cl_2). ^1H NMR and ^{13}C NMR data were consistent with previously reported value.²

(2S, 3R, 4R, 5R)-methyl-4, 7-diphenyl-6, 8-dioxo-3, 7-diazabicyclo [3. 3. 0] octane-2-carboxylate (Table 2, entry 6): Prepared according to the general procedure

with N-benzyliden-glycinmethyl ester (80 mg, 0.45 mmol) and *N*-phenylmaleimide (108 mg, 0.68 mmol) to afford the title compound as a colorless solid in 87.3% yield (138 mg) after silica chromatography (50% EtOAc/Hex containing 1% Et₃N); 71% ee. Product ratio were determined by HPLC (Chiralpak AS column, 70% IPA/Hex, 1.0 ml/min, t_r = 20.2 and 44.4 min. mp = 160-162 °C. [α]_D = 91.1 (c = 1.22, CH₂Cl₂). ¹H NMR and ¹³C NMR data were consistent with previously reported value.⁴

(2S, 3R, 4R, 5R)-methyl-4-phenyl-7-methyl-6, 8-dioxo-3, 7-diazabicyclo [3. 3. 0] octane-2-carboxylate (Table 2, entry 7): Prepared according to the general procedure with N-benzyliden-glycinmethyl ester (80 mg, 0.45 mmol) and *N*-methylmaleimide (66 mg, 0.68 mmol) to afford the title compound as a colorless solid in 86.6% yield (112 mg) after silica chromatography (50% EtOAc/Hex containing 1% Et₃N); 79% ee. Product ratio were determined by HPLC (Chiralpak AS column, 80% IPA/Hex, 1.0 mL/min, t_r = 16.9 and 40.1 min. mp = 176-177 °C. [α]_D = 61.0 (c = 1.18, CH₂Cl₂). ¹H NMR and ¹³C NMR data were consistent with previously reported value.⁵

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11-12-61

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11-12-82

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j1-12-81

11-12-65

Current Data Parameters

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PROCNO 1

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1D NMR plot parameters

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