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Enantioselective Synthesis of *exo*-4-Nitroprolinates from Nitroalkenes and Azomethine Ylides Catalyzed by Chiral Phosphoramidite·Silver(I) or Copper(II) Complexes

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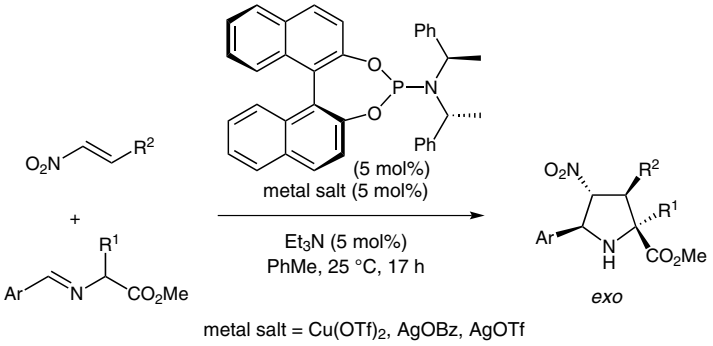

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Abstract Chiral complexes formed by privileged phosphoramidites derived from chiral binol and optically pure Davies' amines, and copper(II) triflate, silver(I) triflate or silver(I) benzoate are excellent catalysts for the general 1,3-dipolar cycloaddition between nitroalkenes and azomethine ylides generated from α-amino acid derived imino esters. These three methods can be conducted at room temperature to afford the *exo*-cycloadducts (4,5-*trans*-2,5-*cis*-4-nitroprolinates) with high diastereoselectivity and high enantioselectivity. In general, the three procedures are complementary but silver catalysts are more versatile and less sensitive to sterically congested starting materials.

Key words dipolar cycloaddition, asymmetric catalysis, azomethine ylides, phosphoramidite, copper, silver

Introduction

The straightforward synthesis of enantiomerically enriched polysubstituted *exo*-4-nitroprolinates can be achieved through 1,3-dipolar cycloaddition (1,3-DC)[1] between imino esters and nitroalkenes.[2] The introduction of the versatile nitro group at the 4-position of the pyrrolidine skeleton enhances the interest of these chiral molecules. Particularly, *exo*-4-nitroprolinates with a specific 2,5-*cis*-4,5-*trans*-configuration have been used as leukocyte function associated antigen-1 antagonists during a cancer evolution,[3] with important activity as inhibitors of $\alpha_4\beta_1$-integrin-mediated hepatic melanoma metastasis and even for the treatment of other diseases.[4] Simpler *exo*-nitroprolinates such as **4** have shown high efficiency as organocatalysts in asymmetric aldol reactions.[5]

N-Arylideneamino esters have been employed as azomethine ylide precursors in the enantioselective 1,3-DC with nitroalkenes employing both organocatalysts and metal complexes as chiral catalysts for the construction of *exo*-prolinates with 2,5-*cis*-4,5-*trans* arrangement.[6] The majority of contributions using α-imino esters to obtain *exo*-adducts were achieved under the control of chiral metal complexes.[7] Chiral Lewis acids formed by copper(I), copper(II), gold(I), and nickel(II) complexes were the most effective.[2] The only exception reported in all these examples is the employment of a copper(II) triflate·pyridyl bis(imidazolidine) as chiral complex,[8] and very interesting switchable chiral P,N-ferrocene ligands,[9] which afforded the *endo*-adducts.

Although silver(I) is traditionally the most suitable cation to stabilize a metallodipole derived from iminoesters **3**,[10] no efficient 1,3-DC between metallo-azomethine ylides and β-nitroalkanes has been reported.[11] Only Fukuzawa's group has published a highly effective asymmetric cycloaddition using benzophenone-derived iminoglycinates and nitroalkenes catalyzed by silver(I)·thioclickferrophos complexes.[12]

Very recently, we showed that phosphoramidites[13,14] derived from chiral binol-chiral Davies' amines represent a matched combination for the enantioselective 1,3-dipolar cycloaddition (1,3-DC)[15] between nitroalkenes and azomethine ylides derived from imino esters. $Cu(OTf)_2$[16] and silver(I) salts[17] afforded *exo*-4-nitroprolinates in high diastereomeric ratios and enantioselectivities. Seminal works published on the asymmetric 1,3-CD of imino esters and different dipolarophiles catalyzed by chiral phosphoramidite **1**·silver(I) complexes supported this idea,[18] with

enantiomerically enriched polysubstituted *endo*-proline derivatives being obtained in good chemical yields and excellent diastereo- and enantioselectivities.

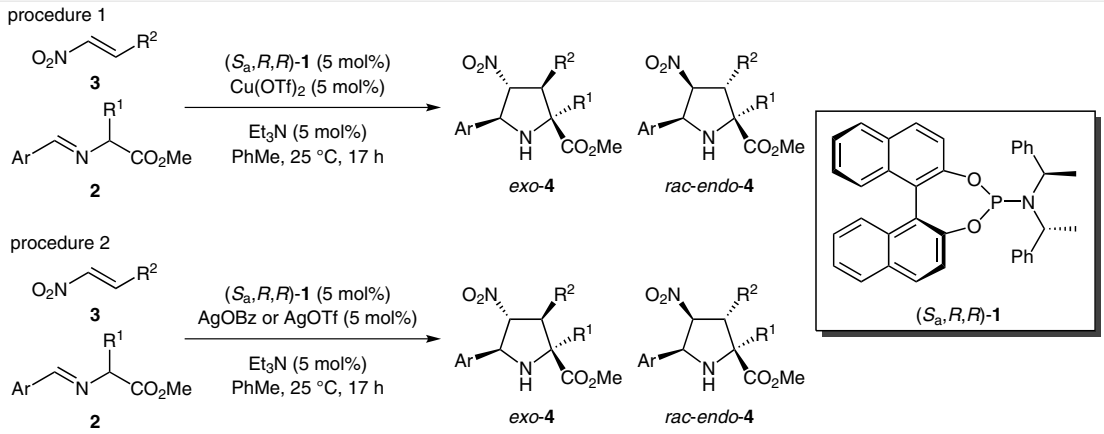
Herein, we wish to report a practical procedure for the synthesis of *exo*-4-nitroprolinates **4** in which nitroalkenes undergo copper(II)- and less known silver(I)-catalyzed 1,3-dipolar cycloaddition with azomethine ylides obtained from α-imino esters.

Scope and Limitations

The scope of the reaction was studied with different nitroalkenes **3**, employing various arylideneimino esters **2** under the control of: (a) the catalyst formed by phosphoramidite (S_a,*R*,*R*)-**1** and $Cu(OTf)_2$ (Scheme 1, Procedure 1, Table 1);[16] (b) the catalyst generated from (S_a,*R*,*R*)-**1** and AgOTf (Scheme 1, Procedure 2, Table 1),[17] and (c) the combination of phosphoramidite (S_a,*R*,*R*)-**1** with AgOBz (Scheme 1, Procedure 2, Table 1).[17] Initially, the influence of the ester moiety of imines **2** was surveyed. Compound **4a** was obtained as a very clear crude reaction product and with the highest enantiomeric ratio in the presence of (S_a,*R*,*R*)-**1**·AgOBz complex (Table 1, entry 1). When the isopropyl ester of the corresponding dipole precursor was used instead of the methyl ester, almost identical enantiomeric ratios for the reactions catalyzed by the two chiral silver complexes were obtained, with a slightly better *exo*-diastereoselection for the isopropyl ester. The copper(II)-catalyzed process gave better *exo*/*endo* ratios and similar enantiomeric ratios. However, the lower yields (up to 70%) of the *exo*-product **4b** mixtures obtained in all of the reactions by using the isopropyl ester was consistent with the appearance of a proportion of other unidentified diastereoisomers (ca. 20–28% based on ^{1}H NMR spectroscopic analysis of the crude product; Table 1, entry 2). As a consequence, subsequent studies on the scope of the reaction was undertaken with methyl α-imino esters as metallo-azomethine ylide precursors.

The influence of the aryl substituent of nitroalkene **3** on the 1,3-DC with methyl benzylidene glycinate was investigated and the results revealed that, in general, higher chemical yields, *exo*-diastereoselectivities, and enantioselections were obtained for products **4c**–**g** when the reactions were performed in the presence of (S_a,*R*,*R*)-**1**·AgOBz rather than with the silver(I) or copper(II) triflates (Table 1, entries 3–7). An exception was noted when *meta*-brominated nitrostyrene was employed as dipolarophile (Table 1, entry 6). In this example, (S_a,*R*,*R*)-**1**·$Cu(OTf)_2$ complex was the most effective catalyst, giving the cleanest crude compound **4f** (90:10 dr, and 96:4 er). When the heteroaromatic moiety was bonded to the nitro component (2-furyl) the use of the chiral silver benzoate complex was more appropriate, achieving 77% yield and 98% ee of *exo*-**4h** (Table 1, entry 8). When nitroalkene **3**, bearing an aliphatic cyclohexyl group, was used, a reversal in diastereoselectivity was observed in the 1,3-DC catalyzed by **1**·AgOTf . The *endo* isomer was isolated exclusively in 71% yield but as a racemic mixture. However, an equimolar mixture of *endo*/*exo* diastereoisomers, in 75% overall yield, was isolated in the analogous reaction performed with AgOBz. Again, the adduct *endo*-**4i** was separated as a racemate, whereas the *exo*-isomer **4i** was obtained in low 32% yield but with 96% ee (Table 1, entry 9). On the other hand, the 1,3-DC with nitroalkene **3** (R^2 = Cy) failed with the $Cu(OTf)_2$ complex.

When alanine, leucine, or phenylalanine derived imino esters **2** were used as azomethine ylide precursors, an increase in the proportion of *endo*-diastereoisomers **4j**–**l** was observed. This diastereoisomer was always obtained as a racemic mixture (Table 1, entries 10–12). Alanine dipole precursor **2** furnished very low proportions of *exo*-**4j**, which was isolated with high optical purity in silver-catalyzed processes (Table 1, entry 10). The other two quaternized pyrrolidines, *exo*-**4k** and *exo*-**4l**, were satisfactorily isolated (>99:1 er) by employing (S_a,*R*,*R*)-**1**·$Cu(OTf)_2$ catalysis (Table 1, entries 11 and 12).



Scheme 1 General procedures for the synthesis of polysubstituted *exo*-nitroprolinates **4**

Table 1 Scope of the Diastereo- and Enantioselective 1,3-DC between Imino Esters **2** and Nitroalkenes **3** Catalyzed by (S_a,*R*,*R*)-**1**·Cu(OTf)$_2$, (S_a,*R*,*R*)-**1**·AgOTf, and (S_a,*R*,*R*)-**1**·AgOBz

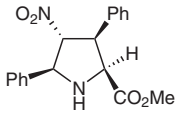
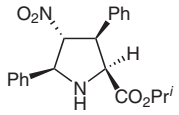
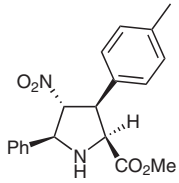
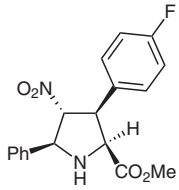
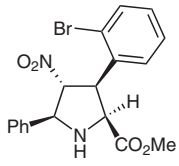
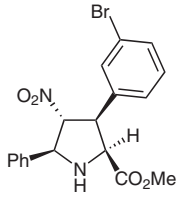
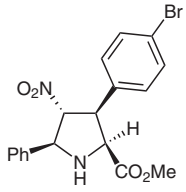
Entry	**4**	Structure	(S_a,*R*,*R*)-**1**·Cu(OTf)$_2$			(S_a,*R*,*R*)-**1**·AgOTf			(S_a,*R*,*R*)-**1**·AgOBz		
			exo/*endo*[a,b]	Yield (%)[c]	er[d]	*exo*/*endo*[a,b]	Yield (%)[c]	er[d]	*exo*/*endo*[a]	Yield (%)[c]	er[d]
1	**4a**		89:11	80	>99:1	90:10	80	98:2	**91:9**	**88**	**>99:1**
2	**4b**		99:1	69	>99:1	98:2	69	98:2	93:7[b]	70	98:2
3	**4c**		82:18	48	99:1	70:30	52	95:5	**93:7**	**92**	**99:1**
4	**4d**		82:12	73	96:4	89:11	74	98:2	**92:8**	**88**	**>99:1**
5	**4e**		73:27	56	96:4	76:24	64	97:3	**91:9**[b]	**76**	**96:4**
6	**4f**		**90:10**	**61**	**94:6**	81:19	61	93:7	**82:18**[b]	**61**	**94:6**
7	**4g**		84:16	70	95:5	85:15	56	99:1	**82:18**	**77**	**99:1**

Table 1 (continued)

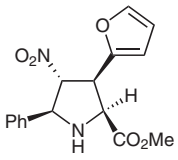
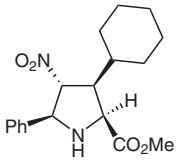
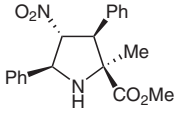
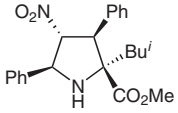
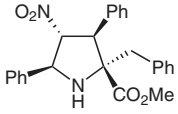
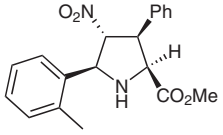
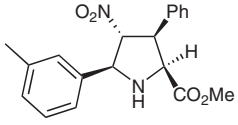
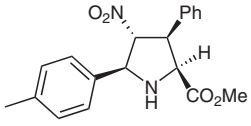
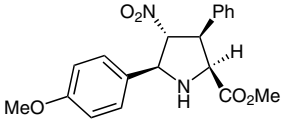
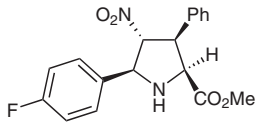
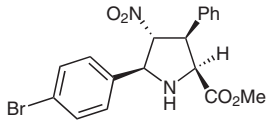
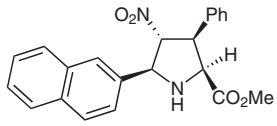
Entry	4	Structure	(S_a,*R*,*R*)-**1**·Cu(OTf)$_2$ *exo*/*endo*[a,b]	Yield (%)[c]	er[d]	(S_a,*R*,*R*)-**1**·AgOTf *exo*/*endo*[a,b]	Yield (%)[c]	er[d]	(S_a,*R*,*R*)-**1**·AgOBz *exo*/*endo*[a]	Yield (%)[c]	er[d]
8	**4h**		77:23	41	91:9	68:32	50	97:3	**84:16**	**77**	**99:1**
9	**4i**		–	–	–	1:99	71[e]	*rac*	**50:50**	**33[d] 42[e]**	**98:2[f]**
10	**4j**		26:74	18	*rac*[f]	21:79	14[d] 63[e]	93:7[f]	27:73	21[d] 69[e]	96:4[f]
11	**4k**		**92:8**	**60**	**>99:1[f]**	92:8	46	98:2	35:65	21[d] 53[e]	99:1[f]
12	**4l**		**75:25**	**65**	**>99:1[f]**	54:46	42[d] 40[e]	99:1[f]	50:50[b]	33[d] 33[e]	>99:1[f]
13	**4m**		59:41	51	75:25	56:44	33	91:9	**75:25[b]**	**56**	**95:5**
14	**4n**		79:21	61	90:10	76:24	65	94:6	**87:13**	**79**	**91:9**
15	**4o**		79:21	59	94:6	**94:6**	**79**	**97:3**	88:12[b]	60	97:3
16	**4p**		–	–	–	**93:7**	**81**	**98:2**	90:10	75	96:4

Table 1 (continued)

Entry	4	Structure	(S_a,*R*,*R*)-**1**·Cu(OTf)$_2$ *exo*/*endo*[a,b]	Yield (%)[c]	er[d]	(S_a,*R*,*R*)-**1**·AgOTf *exo*/*endo*[a,b]	Yield (%)[c]	er[d]	(S_a,*R*,*R*)-**1**·AgOBz *exo*/*endo*[a]	Yield (%)[c]	er[d]
17	**4q**		87:13	70	99:1	**88:12**	**72**	**>99:1**	88:12	83	92
18	**4r**		89:11	76	95:5	**91:9**	**77**	**>99:1**	94:6[b]	83	99:1
19	**4s**		86:14	70	85:15	**86:14**	**70**	**92:8**	80:20[b]	66	88:12

[a] Based on NMR spectroscopic analysis of the crude product.
[b] Other stereoisomers were detected in noticeable proportions.
[c] Isolated yield (for the *exo*-adduct) after purification by flash chromatography.
[d] For the *exo*-stereoisomer (HPLC).
[e] For the *endo*-isomer.
[f] The *endo*-isomer was obtained as a racemic mixture.

With respect to the reaction of different methyl arylidene glycinates **2** with nitrostyrene, the more sterically hindered *o*-tolyl imino group also favored the generation of the *endo*-isomer **4m**, but to a lesser extent in the case of AgOBz (Table 1, entry 13). For the *m*-tolyl imino group derivative, the benzoate counteranion gave the highest enantioselectivities for compound *exo*-**4n** (Table 1, entry 14). It seems that the lower the steric repulsion the higher the proportion of *exo*-adduct and enantioselection. This general assumption can be supported by the transformations involving *para*-substituted arylidene imino esters **2** (Table 1, entries 15–18). Thus, better results for compounds **4o**–**r** were observed when (S_a,*R*,*R*)-**1**·AgOTf was the selected catalyst, rather than the processes mediated by the silver benzoate (Table 1, entries 15–18). Notably, compound *exo*-**4p** could not be prepared through the copper(II)-catalyzed method (Table 1, entry 16). Finally, in the reaction using substrate **2** with a 2-naphthyl substituent, product *exo*-**4s** was obtained with up to 72% de and 85% ee when AgOTf was used, which was better than the results obtained with Cu(OTf)$_2$ and AgOBz (Table 1, entry 19).

In these efficient copper(II) or silver(I)-catalyzed cycloadditions of nitroalkenes, the influence of the position of the anion in the transition state is crucial to explain the diastereo- and enantioselectivity of the whole process because the anion blocks one of the two prochiral faces of the 1,3-dipole. DFT calculations[16,17] indicate that the triflate anion is closer to the copper(II) center than to the corresponding silver(I) cation, whereas the silver(I) cation–dipole distance is shorter. These results justify the use of the (S_a,*R*,*R*)-**1**·Cu(OTf)$_2$ complex in the reactions involving α-substituted imino esters **2**.

The influence of the benzoate anion versus the triflate anion in the silver-catalyzed cycloaddition can be explained by the assumption that benzoate, which has more steric bulk than triflate, is oriented along the arylidene moiety of the dipole. Thus, a small π-stacking interaction is observed when **4** (R = H, Ar = Ph) is computed with the benzoate anion, so we think that a variation of the aromatic moiety of the imino group would increase the steric repulsion with the bulkier benzoate anion rather than with triflate.[19] In this sense, the reaction of nitrostyrenes with **2** when R^1 = H and Ar = Ph, is optimally catalyzed by the (S_a,*R*,*R*)-**1**·AgOBz complex. In contrast, when different aryl substituents are bonded to the 1,3-dipole precursor, the employment of (S_a,*R*,*R*)-**1**·AgOTf complex is desirable.

In conclusion, an efficient preparation of enantiomerically enriched polysubstituted *exo*-4-nitroprolinates has been achieved through copper(II)- or silver(I)-catalyzed 1,3-DC between imino esters and nitroalkenes. These methods allows the preparation of pyrrolidines in larger scale (0.5–0.8 g) at room temperature. (S_a,*R*,*R*)-**1**·AgOBz is the best catalyst for cycloadditions starting from methyl benzylideneglycinate, whereas (S_a,*R*,*R*)-**1**·Cu(OTf)$_2$ complex is more suitable for reactions involving α-substituted imino esters **2**. Finally, (S_a,*R*,*R*)-**1**·AgOTf catalyst is recommended when imines derived from aromatic aldehydes other than benzaldehyde are used.

Anhydrous solvents were freshly distilled under an argon atmosphere and degassed by freeze–pump–thaw methodology. Aldehydes were also distilled prior to use for the elaboration of the imino esters and nitroalkenes. The substrates are known molecules and are easily prepared.[16,17] Copper salts were dried in a Kugelrohr apparatus and stored under an argon atmosphere. All silver-mediated reactions were run in the dark. Melting points were determined with a Reichert Thermovar hot plate apparatus and are uncorrected. HPLC analyses were performed with a JASCO-2000 series instrument equipped with the indicated chiral column by using mixtures of *n*-hexane–isopropyl alcohol as the mobile phase at 25 °C. Yields refer to isolated compounds (after flash chromatography) estimated to be >95% pure as determined by ^{1}H NMR spectroscopic and HPLC analyses. Only the structurally most important peaks of the IR spectra (recorded on a Nicolet 510 P-FT and on a Jasco FTIR 4100) are listed. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were obtained on a Bruker AC-300 using $CDCl_3$ as solvent and Me_4Si as internal standard, unless otherwise stated. Low-resolution electron impact (EI) mass spectra were obtained at 70eV on a Shimadzu QP-5000 and high-resolution mass spectra were obtained on a Finnigan VG Platform. HRMS (EI) were recorded on a Finnigan MAT 95S. Microanalyses were performed on a Perkin Elmer 2400 and a Carlo Erba EA1108.

Copper-Catalyzed Synthesis of *exo*-Cycloadducts 4; General Procedure 1 (P1)

To a solution of the chiral phosphoramidite (0.05 mmol) and $Cu(OTf)_2$ (0.05 mmol) in anhydrous toluene (3 mL) under an argon atmosphere was added a solution of imino ester (1 mmol) and nitroalkene (1 mmol) in toluene (5 mL). To the resulting suspension, Et_3N (0.05 mmol, 7 µL) was added and the mixture was stirred at r.t. (25 °C) for 16–24 h. The crude reaction mixture was filtered through a small Celite pad and the residue was purified by flash chromatography to give the pure *exo*-cycloadducts. Solid products were recrystallized from *n*-hexane–Et_2O. Compounds **4a** and **4f** were also prepared on a 3 mmol scale, and the results were identical to those reported for the model reaction.

Silver-Catalyzed Synthesis of *exo*-Cycloadducts 4; General Procedure 2 (P2-AgOTf) or (P2-AgOBz)

To a solution of chiral phosphoramidite **1** (0.05 mmol) and AgX (0.05 mmol, triflate or benzoate) in anhydrous toluene (3 mL) under an argon atmosphere was added a solution of imino ester (1 mmol) and nitroalkene (1 mmol) in toluene (5 mL). To the resulting suspension, Et_3N (0.05 mmol, 7 µL) was added and the mixture was stirred at r.t. (25 °C). The crude reaction mixture was filtered through a small Celite pad and the residue was purified by flash chromatography to give the pure *exo*-cycloadducts. Solid products were recrystallized from *n*-hexane–Et_2O. Compounds **4a** and **4f** were also prepared on a 3 mmol scale, and the results were identical to those reported for the model reaction.

(2*S*,3*S*,4*R*,5*S*)-Methyl 4-Nitro-3,5-diphenylpyrrolidine-2-carboxylate (4a)

Obtained ccording to P2-AgOBz.

Colorless needles (*n*-hexane–Et_2O, 4:1); mp 104–105 °C; $[\alpha]_D^{20}$ 128 (*c* 1.1, $CHCl_3$); >99:1 er; HPLC (Daicel Chiralpak AS-H; 2-propanol–hexane, 20:80; flow rate 0.4 mL/min; 220 nm): t_R = 25.2 (major), 27 (minor) min.

IR (solid): 1265, 1551, 1731 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.71 (br s, 1 H, NH), 3.26 (s, 3 H, CH_3), 4.35 (t, *J* = 7.8 Hz, 1 H, CHCO), 4.48 (d, *J* = 9.1 Hz, 1 H, CHPh), 4.73 (d, *J* = 7.8 Hz, 1 H, CHPh), 5.19 (t, *J* = 8.0 Hz, 1 H, CHNO), 7.45–7.18 (m, 8 H, ArH), 7.56–7.52 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.8 (CH_3), 53.7 (CHPh), 64.2 (*C*HCO), 67.5 (PhCHNH), 95.0 ($CHNO_2$), 126.8, 127.8, 128.1, 128.7, 128.9, 129.0, 135.8, 137.6 (ArC), 171.8 (CO).

MS (EI): *m*/*z* (%) = 326 (0.1) [M]$^+$, 279 (16), 220 (73), 193 (100), 178 (12), 115 (42).

Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.3; H, 5.6; N, 8.6. Found: C, 66.4; H, 5.3; N, 8.6.

(2*S*,3*R*,4*R*,5*S*)-Isopropyl 4-Nitro-3,5-diphenylpyrrolidine-2-carboxylate (4b)

Obtained according to P1.

Colorless needles (*n*-hexane–Et_2O, 4:1); mp 130–132 °C; $[\alpha]_D^{20}$ 82.3 (*c* 1.02 $CHCl_3$); >99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–hexane, 10:90; flow rate 1.0 mL/min): t_R = 15.5 (major), 20.4 (minor) min.

IR (solid): 1265, 1551, 1731 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.58 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.06 (d, *J* = 6.3 Hz, 3 H, CH_3), 2.75 (br s, 1 H, NH), 4.37 (dd, *J* = 8.9, 8.0 Hz, 1 H, CHPh), 4.46 (d, *J* = 9.1 Hz, 1 H, CHCO), 4.65 [dt, *J* = 12.6, 6.3 Hz, 1 H, C*H*(CH_3)$_2$], 4.75 (d, *J* = 8.3 Hz, 1 H, PhCHN), 5.20 (dd, *J* = 8.3, 8.3 Hz, 1 H, $CHNO_2$), 7.19–7.30 (m, 5 H, ArH), 7.36–7.45 (m, 3 H, ArH), 7.54–7.57 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (CH_3), 21.6 (CH_3), 53.5 (CHPh), 64.1 (*C*HCO), 67.4 [*C*H(CH_3)$_2$], 69.1 (PhCHNH), 95.4 ($CHNO_2$), 126.9, 128.1, 128.8, 128.9, 129.0, 129.4, 136.3, 137.6 (ArC), 170.8 (CO).

MS (EI): *m*/*z* (%) = 356 (0.01) [M]$^+$, 307 (10), 220 (100), 193 (80), 115 (28).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{22}N_2O_4$ – NO_2: 309.4021; found: 309.4028.

Anal. Calcd for $C_{20}H_{22}N_2O_4$: C, 67.8; H, 6.3; N, 7.9. Found: C, 67.4; H, 6.3; N, 8.3.

(2*S*,3*S*,4*R*,5*S*)-Methyl 4-Nitro-5-phenyl-3-(*p*-tolyl)-pyrrolidine-2-carboxylate (4c)

Obtained according to P2-AgOBz.

Colorless needles (*n*-hexane–Et_2O, 5:1); mp 108–110 °C; $[\alpha]_D^{20}$ 144.8 (*c* 1.0, $CHCl_3$); 99:1 er; HPLC (Daicel Chiralpak AS-H; 2-propanol–*n*-hexane, 5:95; flow rate 1.1 mL/min): t_R = 23.2 (major), 24.2 (minor) min.

IR (neat): 1212, 1547, 1736, 2917 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, CH_3C), 2.75 (br s, 1 H, NH), 3.32 (s, 3 H, OCH_3), 4.35 (dd, *J* = 8.5 Hz, 1 H, CHTol), 4.48 (d, *J* = 9 Hz, 1 H, $CHCO_2$Me), 4.76 (d, *J* = 8.3 Hz, 1 H, CHPh), 5.21 (dd, *J* = 8.2, 8.2 Hz, 1 H, $CHNO_2$), 7.13 (m, 2 H, ArH), 7.40–7.45 (m, 4 H, ArH), 7.55–7.57 (m, 3 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0 (*C*H_3C), 51.9 (*C*HC_6H_4Me), 53.5 (CH_3), 64.2 (*C*HCO_2Me), 67.5 (CHPh), 95.1 ($CHNO_2$), 126.9 (*C*HCHCHC), 127.7, 129.0, 129.1, 129.4 (ArC), 132.53 (CH_3*C*), 137.52 (*C*CHNH), 137.92 (*C*CHCHNH), 171.86 (CO).

MS (EI): *m*/*z* (%) = 294 (9) [M$^+$ – NO_2], 234 (36), 207 (100), 129 (15).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}N_2O_4$ – NO_2: 294.1400; found: 294.1399.

Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.0; H, 5.9; N, 8.2. Found: C, 67.3; H, 6.2; N, 7.9.

(2*S*,3*S*,4*R*,5*S*)-Methyl 3-(4-Fluorophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4d)

Obtained according to P2-AgOBz.

Colorless prisms (*n*-hexane–Et_2O, 5:1); mp 96.2–97 °C; $[\alpha]_D^{20}$ 108.1 (*c* 1, $CHCl_3$); >99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 21.0 (minor), 28.2 (major) min.

IR (solid): 1265, 1511, 1553, 1746 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.58 (br s, 1 H, NH), 3.34 (s, 3 H, OCH_3), 4.34–4.44 (m, 1 H, C*H*CHCO), 4.51 (d, *J* = 9.0 Hz, 1 H, C*H*CO_2Me), 4.78 (d, *J* = 8.2 Hz, 1 H, CHPh), 5.16 (dd, *J* = 8.0, 8.0 Hz, 1 H, $CHNO_2$), 6.99–7.11 (m, 2 H, ArH), 7.23–7.32 (m, 2 H, ArH), 7.36–7.49 (m, 3 H, ArH), 7.58 (d, *J* = 7.5 Hz, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.9 (*C*HCHCO), 52.8 (CH_3), 64.0 (*C*HCO), 67.3 (CHPh), 95.2 ($CHNO_2$), 126.8, 128.9, 129.5, 129.6, 131.8, 137.6, 161.2, 163.4 (ArC), 171.6 (CO).

MS (EI): *m*/*z* (%) = 298 (10) [M^+-NO_2], 238 (55), 211 (100), 133 (19), 117 (18).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}FN_2O_4$ – NO_2: 298.1181; found: 298.1175.

Anal. Calcd for $C_{18}H_{17}N_2O_4$: C, 62.8; H, 5.0; N, 8.1. Found: C, 62.5; H, 5.2; N, 7.9.

(2*S*,3*S*,4*R*,5*S*)-Methyl 3-(2-Bromophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4e)

Obtained according to P2-AgOBz.

Pale-yellow oil; $[\alpha]_D^{20}$ 57.7 (*c* 1.0 $CHCl_3$); 95:5 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 20.1 (major), 23.9 (minor) min.

IR (neat): 1549, 1736, 2926 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.53 (br s, 1 H, NH), 3.29 (s, 3 H, CH_3), 4.70 (d, *J* = 9.1 Hz, 1 H, CHPh), 4.83 (d, *J* = 8.6 Hz, 1 H, $CHCO_2Me$), 4.98 (dd, *J* = 9.3, 9.3 Hz, 1 H, C*H*C_6H_4Br), 5.30 (dd, *J* = 9.0, 9.0 Hz, 1 H, $CHNO_2$), 7.17 (dd, *J* = 7.7, 1.4 Hz, 1 H, ArH), 7.36–7.45 (m, 6 H, ArH), 7.55–7.63 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.9 (CHAr), 52.2 (CH_3), 61.9 (*C*CO_2Me), 67.2 (CHPh), 92.9 ($CHNO_2$), 127.1 (CBr), 127.2, 127.8, 128.6, 128.7, 129.1, 129.2, 133.3, 134.6, 137.3 (ArC), 172.2 (CO).

MS (EI): *m*/*z* (%) = 360 (28) [M^+-NO_2], 358 (28), 347 (11), 345 (11), 300 (96), 298 (100), 273 (94), 271 (96), 219 (36), 192 (92).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}BrN_2O_4$ – NO_2: 359.0338; found: 359.0343.

Anal. Calcd for $C_{18}H_{17}BrN_2O_4$: C, 53.3; H, 4.2; N, 6.9. Found: C, 53.1; H, 4.1; N, 6.5.

(2*S*,3*S*,4*R*,5*S*)-Methyl 3-(3-Bromophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4f)

Obtained according to P1.

Pale-yellow prisms (*n*-hexane–Et_2O, 5:1); mp 72–74 °C; $[\alpha]_D^{20}$ = 60.5 (*c* 0.85, $CHCl_3$); 94:6 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 5:95; flow rate 1.0 mL/min): t_R = 41.5 (minor), 44.3 (major) min.

IR (solid): 1547, 1735, 2928 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.73 (br s, 1 H, NH), 3.38 (s, 3 H, CH_3), 4.33 (dd, *J* = 8.8, 7.8 Hz, 1 H, C*H*C_6H_4Br), 4.50 (d, *J* = 8.9 Hz, 1 H, CHCO_2Me), 4.75 (d, *J* = 8.1 Hz, 1 H, CHPh), 5.13 (dd, *J* = 7.9, 7.9 Hz, 1 H, $CHNO_2$), 7.20–7.22 (m, 2 H, ArH), 7.41–7.55 (m, 5 H, ArH), 7.55–7.57 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.0 (*C*HC_6H_4Br), 53.0 (CH_3), 64.1 (*C*HCO_2Me), 67.4 (CHPh), 94.9 ($CHNO_2$), 122.8 (CBr), 126.3, 126.9, 129.1, 129.1, 130.3, 131.2, 131.4, 137.5, 138.4 (ArC), 171.5 (CO).

MS (EI): *m*/*z* (%) = 360 (17) [M^+-NO_2], 358 (17), 298 (86), 270 (77), 192 (100), 117 (76).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}BrN_2O_4$ – NO_2: 359.0338; found: 359.0334.

Anal. Calcd for $C_{18}H_{17}BrN_2O_4$: C, 53.3; H, 4.2; N, 6.9. Found: C, 52.9; H, 4.1; N, 6.6.

(2*S*,3*S*,4*R*,5*S*)-Methyl 3-(4-Bromophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4g)

Obtained according to P2-AgOBz.

Colorless prisms (*n*-hexane–Et_2O, 4:1); mp 89–91 °C; $[\alpha]_D^{20}$ 96.0 (*c* 0.7, $CHCl_3$); 99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 19.4 (major), 26.8 (minor) min.

IR (solid): 1544, 1737, 2925 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.75 (br s, 1 H, NH), 3.34 (s, 3 H, CH_3), 4.21–4.33 (m, 1 H, C*H*C_6H_4Br), 4.48 (d, *J* = 8.9 Hz, 1 H, $CHCO_2Me$), 4.73 (d, *J* = 8.1 Hz, 1 H, CHPh), 5.08 (dd, *J* = 7.8, 7.8 Hz, 1 H, $CHNO_2$), 7.12–7.14 (m, 2 H, ArH), 7.37–7.44 (m, 5 H, ArH), 7.50–7.51 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.0 (*C*HC_6H_4Br), 52.9 (CH_3), 64.0 (*C*HCO_2Me), 67.3 (CHPh), 95.1 ($CHNO_2$), 122.3 (CBr), 126.8, 129.0, 129.1, 129.6, 132.0, 135.3, 137.6 (ArC), 171.5 (CO).

MS (EI): *m*/*z* (%) = 360 (15) [M^+ – NO_2], 359 (15), 300 (52), 298 (51), 273 (99), 271 (100), 219 (26), 192 (89), 117 (43), 115 (26).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}BrN_2O_4$ – NO_2: 359.0338; found: 359.0330.

Anal. Calcd for $C_{18}H_{17}BrN_2O_4$: C, 53.3; H, 4.2; N, 6.9. Found: C, 52.9; H, 4.2; N, 6.6.

(2*S*,3*S*,4*R*,5*S*)-Methyl 3-(Furan-2-yl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4h).

Obtained according to P2-AgOBz.

Yellow prisms (*n*-hexane–Et_2O, 3:1); mp 60–62 °C; $[\alpha]_D^{20}$ 89.0 (*c* 1, $CHCl_3$); 99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 15.4 (major), 18.8 (minor) min.

IR (neat): 1209, 1549, 1740, 2341, 2359 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.77 (br s, 1 H, NH), 3.51 (s, 3 H, OCH_3), 4.40 (d, *J* = 8.5 Hz, 1 H, CHCO), 4.50 (dd, *J* = 8.4, 7.2 Hz, 1 H, CHfuryl), 4.65 (d, *J* = 8.0 Hz, 1 H, CHPh), 5.23 (dd, *J* = 7.9, 7.0 Hz, 1 H, $CHNO_2$), 6.20 (d, *J* = 3.1 Hz, 1 H, CCH), 6.29 (dd, *J* = 3.2, 1.8 Hz, 1 H, CCHC*H*CHO), 7.25–7.61 (m, 6 H, ArH and OCH).

^{13}C NMR (75 MHz, $CDCl_3$): 47.9 (CHfuryl), 52.2 (CH_3), 63.2 (*C*HCO), 68.2 (CHPh), 93.6 ($CHNO_2$), 108.4 (*C*CH), 110.5 (CCH*C*HCHO), 126.8, 128.6, 128.9, 137.2 (ArC), 142.8 (OCH), 148.9 (OC), 171.1 (CO).

MS (EI): *m*/*z* (%) = 270 (12) [M^+ – NO_2], 183 (100), 155 (10), 117 (12).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}N_2O_5$: 316.1059; found: 316.1049.

(2*S*,3*R*,4*S*,5*S*)-Methyl 3-Cyclohexyl-4-nitro-5-phenylpyrrolidine-2-carboxylate (4i)

Obtained according to P2-AgOBz.

White needles (*n*-hexane–Et_2O, 4:1); mp 125–127 °C; $[\alpha]_D^{20}$ 0.2 (*c* 1.0, $CHCl_3$); 52:48 er; HPLC (Chiralpak AD-H; 2-propanol–hexane, 10%; flow rate 1.0 mL/min): t_R = 14.5 (minor), 16.2 (major) min. *exo*-**4i** (Chiralpak AD-H; 2-propanol–hexane, 10:90; flow rate 1.0 mL/min): t_R = 17.1 (major), 19.0 (minor) min.

IR (neat): 1202, 1544, 1737, 2927 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.32 (m, 5 H, CH_2), 1.58–1.67 [m, 1 H, $CH(CH_2)_2$], 1.72–1.86 (m, 5 H, CH_2), 2.87 [td, *J* = 7, 2.4 Hz, 1 H, $CHCH(CH_2)_2$], 3.28 (dd, *J* = 11.5, 10.7 Hz, 1 H, NH), 3.83 (m, 1 H, CH-CO_2Me), 3.86 (s, 3 H, Me), 4.47 (dd, *J* = 12.3, 5.9 Hz, 1 H, CHPh), 5.11 (dd, *J* = 5.9, 2.4 Hz, 1 H, $CHNO_2$), 7.26–7.35 (m, 5 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.13 ($CH_2CH_2CH_2CH$), 29.94 (2 × $CH_2CH_2CH_2CH$), 31.51 (2 × $CH_2CH_2CH_2CH$), 39.73 ($CH_2CH_2CH_2CH$), 52.65 (CHCy), 57.09 (CH_3), 63.10 ($CHCO_2Me$), 67.73 (CHPh), 93.33 ($CHNO_2$), 126.17, 128.46, 128.65, 134.26 (ArC), 172.38 (CO).

MS (EI): *m*/*z* (%) = 285 (13) [M^+ – NO_2], 273 (16), 226 (82), 144 (100), 117 (28).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{24}N_2O_4$: 332.3934; found: 332.3927.

(2*S*,3*S*,4*S*,5*S*)-Methyl 2-Methyl-4-nitro-3,5-diphenylpirrolidine-2-carboxylate (4j)

Obtained according to P2-AgOTf.

Yellow oil; $[\alpha]_D^{20}$ –10.7 (*c* 1, $CHCl_3$); 55:45 er; HPLC (Chiralpak AD-H; 2-propanol–hexane, 10:90; flow rate 1.0 mL/min): t_R = 9.3 (minor), 15.6 (major) min. *exo*-**4j** (Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow 1.0 mL/min): t_R = 9.1 (minor), 17.4 (major) min.

IR (neat): 1257, 1549, 1731 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (s, 3 H, CCH_3), 3.25 (br, 1 H, NH), 3.86 (s, 3 H, CO_2CH_3), 4.52 (d, *J* = 6.1 Hz, 1 H, CHC), 5.08 (d, *J* = 7.4 Hz, 1 H, CHN), 5.65 (dd, *J* = 7.4, 6.1 Hz, 1 H, $CHNO_2$), 7.23–7.49 (m, 10 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.0 (CCH_3), 52.9 (*C*HC), 56.9 (OCH_3), 64.9 (CHN), 68.8 (CCH_3), 95.6 ($CHNO_2$), 126.8 (ArC), 128.0 (ArC), 128.5 (ArC), 128.6 (ArC), 128.7 (ArC), 128.8 (ArC), 135.3 (ArC), 135.5 (ArC), 174.7 (CO).

MS (EI): *m*/*z* (%) = 281 (45) [M^+ – NO_2], 234 (100), 219 (17), 193 (37), 115 (21).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}N_2O_4$: 340.1422, found: 281.1428.

(2*S*,3*R*,4*R*,5*S*)-Methyl 2-Isobutyl-4-nitro-3,5-diphenylpyrrolidine-2-carboxylate (4k)

Obtained according to P1.

Colorless prisms (*n*-hexane–Et_2O, 4:1); mp 105–107 °C; $[\alpha]_D^{20}$ 59.0 (*c* 1, $CHCl_3$); 99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 9.9 (major), 14.5 (minor) min.

IR (solid): 1230, 1545, 1730 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.81 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.04 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.57 (br s, 1 H, NH), 1.79 (td, *J* = 13.3, 6.7 Hz, 1 H, CH), 1.96 (dd, *J* = 13.9, 5.7, Hz, 1 H, CH_2), 2.15 (dd, *J* = 13.9, 6.9 Hz, 1 H, CH_2), 3.19 (s, 3 H, CH_3), 4.00 (d, *J* = 9.9 Hz, 1 H, CHC), 4.75 (d, *J* = 9.2 Hz, 1 H, *CH*NH), 5.23 (dd, *J* = 9.2, 9.2 Hz, 1 H, $CHNO_2$), 7.14–7.22 (m, 2 H, ArH), 7.25–7.47 (m, 6 H, ArH), 7.54–7.61 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.8, 24.3 (2 × CH_3), 25.6 (CH_2), 46.2 (*C*HCH$_2$), 51.8, 62.7 (2 × CHPh), 66.1 (CCO_2), 73.2, 94.9 ($CHNO_2$), 126.9, 127.7, 128.2, 128.6, 128.9, 129.1, 135.6, 137.2 (ArC), 174.5 (CO).

MS (EI): *m*/*z* (%) = 337 (25) [M^+ – NO_2], 193 (100), 115 (20).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{26}N_2O_4$ – NO_2: 321.1729; found: 321.1750.

Anal. Calcd for $C_{22}H_{26}N_2O_4$: C, 69.1; H, 6.9; N, 7.3. Found: C, 69.5; H, 6.8; N, 7.4.

(2*S*,3*R*,4*R*,5*S*)-Methyl 2-Benzyl-4-nitro-3,5-diphenylpyrrolidine-2-carboxylate (4l)

Obtained according to P1.

Colorless oil; $[\alpha]_D^{20}$ = 25.2 (*c* 1.0, $CHCl_3$); >99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 20.8 (minor), 30.1 (major) min.

IR (neat): 1208, 1547, 1723, 2946 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.49 (br s, 1 H, NH), 3.22 (s, 3 H, OCH_3), 3.32 (d, *J* = 13.6 Hz, 1 H, CH_2), 3.42 (d, *J* = 13.5 Hz, 1 H, CH_2), 4.15 (d, *J* = 9.7 Hz, 1 H, CHCCC), 4.67 (d, *J* = 9.0 Hz, 1 H, CHPh), 5.23 (dd, *J* = 9.4, 9.4 Hz, 1 H, $CHNO_2$), 7.15–7.56 (m, 15 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.8 (CH_2), 51.9 (CHPh), 60.3 (CH_3), 65.8 (NCHPh), 73.6 (qC), 95.1 ($CHNO_2$), 127.0, 127.1, 127.9, 128.3, 128.3, 128.4, 129.0, 129.1, 130.5, 135.8, 136.0, 137.5 (ArC), 173.42 (CO).

MS (EI): *m*/*z* (%) = 326 (19) [M^+ – Bn], 325 (97), 279 (20), 278 (100), 246 (76), 219 (41), 193 (20), 115 (29).

HRMS (EI): *m*/*z* calcd for $C_{25}H_{24}N_2O_4$ – CO_2Me: 357.1608; found: 357.1604.

(2*S*,3*S*,4*R*,5*S*)-Methyl 4-Nitro-3-phenyl-5-(2-tolyl)pyrrolidine-2-carboxylate (4m)

Obtained according to P2-AgOBz.

Pale-yellow needles (*n*-hexane–Et_2O, 5:1); mp 71–72 °C; $[\alpha]_D^{20}$ 108.2 (*c* 0.3, $CHCl_3$); 95:5 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 20.4 (minor), 25.3 (major) min.

IR (solid): 1213, 1548, 1736 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CCH_3), 2.55 (br s, 1 H, NH), 3.28 (s, 3 H, OCH_3), 4.43 (dd, *J* = 10.1, 7.1 Hz, 1 H, CHPh), 4.50 (d, *J* = 9.4 Hz, 1 H, CHCO), 5.10 (d, *J* = 8.8 Hz, 1 H, CHTol), 5.34 (dd, *J* = 8.7, 8.7 Hz, 1 H, $CHNO_2$), 7.20–7.37 (m, 9 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2 (CCH_3), 51.8 (CHPh), 54.0 (OCH_3), 63.3 (*C*HCO), 64.0 (CHTol), 93.8 ($CHNO_2$), 125.6, 126.8, 127.7, 128.2, 128.6, 128.7, 130.9, 135.9, 135.6, 137.1 (ArC), 172.1 (CO).

MS (EI): *m*/*z* (%) = 359 (21) [M^+ – NO_2], 340 (2), 293 (12), 234 (61), 207 (100), 191 (12), 131 (20), 115 (25).

Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.0; H, 5.9; N, 8.2. Found: C, 66.9; H, 5.5; N, 8.4.

(2*S*,3*S*,4*R*,5*S*)-Methyl 4-Nitro-3-phenyl-5-(3-tolyl)pyrrolidine-2-carboxylate (4n)

Obtained according to P2-AgOBz.

Pale-yellow prisms (*n*-hexane–Et_2O, 5:1); mp 56–58 °C; $[\alpha]_D^{20}$ 99.8 (*c* 0.74, $CHCl_3$); 95:5 er (after recrystallization). HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 15.1 (minor), 19.9 (major) min.

IR (solid): 1213, 1265, 1549, 1737 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.22 (br s, 1 H, NH), 2.39 (s, 3 H, CH_3C), 3.30 (s, 3 H, OCH_3), 4.40 (dd, *J* = 8.7, 8.7 Hz, 1 H, CHPh), 4.53 (d, *J* = 9.2 Hz, 1 H, CHCO), 4.77 (d, *J* = 8.5 Hz, 1 H, CHTol), 5.26 (dd, *J* = 8.4, 8.4 Hz, 1 H, $CHNO_2$), 7.19–7.38 (m, 9 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (CCH_3), 52.0 (CHPh), 53.7 (OCH_3), 64.0 (*C*HCO), 67.4 (*C*HTol), 94.5 ($CHNO_2$), 123.9, 127.6, 127.8, 128.2, 128.4, 128.8, 129.0, 129.4, 129.9, 138.9 (ArC), 171.6 (CO).

MS (EI): *m*/*z* (%) = 294 (21) [$M^+ - NO_2$], 234 (75), 207 (100), 131 (20), 115 (29).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}N_2O_4 - NO_2$: 294.1572; found: 294.1565.

Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.0; H, 5.9; N, 8.2. Found: C, 67.2; H, 6.0; N, 8.2.

(2*S*,3*S*,4*R*,5*S*)-Methyl 4-Nitro-3-phenyl-5-(4-tolyl)pyrrolidine-2-carboxylate (4o)

Obtained according to P2-AgOTf.

Pale-yellow prisms (*n*-hexane–Et_2O, 8:1); mp 90–92 °C; $[\alpha]_D^{20}$ 81.9 (*c* 0.72, $CHCl_3$); 97:3 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 22.3 (minor), 28.0 (major) min.

IR (solid): 1220, 1545, 1725 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, CH_3C), 2.65 (br s, 1 H, NH), 3.21 (s, 3 H, OCH_3), 4.29 (dd, *J* = 9.0, 9.0 Hz, 1 H, CHPh), 4.41 (d, *J* = 9.1 Hz, 1 H, CHCO), 4.64 (d, *J* = 8.4 Hz, 1 H, CHTol), 5.12 (dd, *J* = 8.1, 8.1 Hz, 1 H, $CHNO_2$), 7.14–7.38 (m, 9 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CCH_3), 51.8 (CHPh), 53.8 (OCH_3), 64.2 (*C*HCO), 67.5 (*C*HTol), 95.1 ($CHNO_2$), 126.9, 127.8, 128.1, 128.8, 129.2, 129.7, 134.5, 135.9 (ArC), 171.9 (CO).

MS (EI): *m*/*z* (%) = 294 (10) [$M^+ - NO_2$], 293 (25), 234 (85), 207 (100), 191 (16), 131 (26), 115 (26).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{20}N_2O_4 - NO_2$: 294.1572; found: 294.1562.

Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.0; H, 5.9; N, 8.2. Found: C, 66.8; H, 5.8; N, 7.9.

(2*S*,3*S*,4*R*,5*S*)-Methyl 5-(4-Methoxyphenyl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4p)

Obtained according to P2-AgOTf.

Yellow oil; $[\alpha]_D^{20}$ 95.2 (*c* 1.9, $CHCl_3$); 98:2 er; HPLC (Chiralpak AD-H; 2-propanol–*n*-hexane, 30:70; flow rate 1.0 mL/min): t_R = 19.9 (minor), 25.2 (major) min.

IR (neat): 1177, 1213, 1248, 1513, 1547, 1735 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.29 (s, 3 H, $PhOCH_3$), 3.83 (s, 3 H, CO_2CH_3), 4.41 (dd, *J* = 8.4, 8.4 Hz, 1 H, CHPh), 4.50 (d, *J* = 9.2 Hz, 1 H, CHCO), 4.74 (d, *J* = 8.5 Hz, 1 H, CHN), 5.22 (dd, *J* = 8.4, 8.4 Hz, 1 H, $CHNO_2$), 6.95 (d, *J* = 8.7 Hz, 2 H, ArH), 7.19–7.36 (m, 5 H, ArH), 7.50 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.01, 160.07, 135.88, 129.53, 128.77, 128.14, 127.82, 127.70, 114.46, 113.86, 95.07, 77.34, 77.02, 76.70, 67.36, 64.18, 55.33, 53.67, 51.81.

MS (EI): *m*/*z* (%) = 309 (35) [$M^+ - NO_2$], 250 (100), 223 (88), 207 (39), 147 (47), 115 (28).

Anal. Calcd for $C_{19}H_{20}N_2O_5$: C, 64.0; H, 5.7; N, 7.9. Found: C, 63.8; H, 5.8; N, 7.9.

(2*S*,3*S*,4*R*,5*S*)-Methyl 5-(4-Fluorophenyl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4q)

Obtained according to P2-AgOTf.

Pale-yellow oil; $[\alpha]_D^{20}$ 65.2 (*c* 1.2, $CHCl_3$); 99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 16.9 (minor), 19.4 (major) min.

IR (neat): 1221, 1509, 1548, 1736 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.62 (br s, 1 H, NH), 3.30 (s, 3 H, OCH_3), 4.41 (dd, *J* = 8.2, 8.2 Hz, 1 H CHPh), 4.50 (d, *J* = 9.1 Hz, 1 H, CHCO), 4.77 (d, *J* = 8.3 Hz, 1 H, CHN), 5.21 (dd, *J* = 8.2, 8.2 Hz, 1 H, $CHNO_2$), 7.07–7.16 (m, 2 H, ArH), 7.24–7.38 (m, 5 H, ArH), 7.56–7.62 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.8 (CHPh), 53.4 (OCH_3), 64.0 (*C*HCO), 66.8 (CHN), 94.9 ($CHNO_2$), 115.9, 127.8, 128.2, 128.7, 128.8, 133.7, 135.7, 161.7, 164.2 (ArC), 171.9 (CO).

MS (EI): *m*/*z* (%) = 297 (14) [$M^+ - NO_2$], 238 (74), 211 (100), 135 (23), 133 (20), 115 (21).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}FN_2O_4 - NO_2$: 297.1181; found: 297.1175.

(2*S*,3*S*,4*R*,5*S*)-Methyl 5-(4-Bromophenyl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4r)

Obtained according to P2-AgOTf.

Colorless prisms (*n*-hexane–Et_2O, 3:1); mp 149–151 °C; $[\alpha]_D^{20}$ 66.4 (*c* 1, $CHCl_3$); 99:1 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 23.6 (minor), 25.5 (major) min.

IR (solid): 1213, 1547, 1738 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.73 (br s, 1 H, NH), 3.31 (s, 3 H, OCH_3), 4.40 (dd, *J* = 8.7 Hz, 1 H, CHPh), 4.53 (d, *J* = 9.1 Hz, 1 H, CHCO), 4.80 (d, *J* = 8.4 Hz, 1 H, CHN), 5.23 (dd, *J* = 8.4, 8.4 Hz, 1 H, $CHNO_2$), 7.17–7.29 (m, 2 H, ArH), 7.31–7.33 (m, 3 H, ArH), 7.44–7.51 (m, 2 H, ArH), 7.55–7.61 (m, 2 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.0 (CHPh), 53.2 (OCH_3), 63.8 (*C*HCO), 66.4 (CHN), 94.1 ($CHNO_2$), 123.3, 127.7, 127.8, 128.9, 129.4, 132.3, 132.4, 134.9 (ArC), 171.4 (CO).

MS (EI): *m*/*z* (%) = 359 (21) [$M^+ - NO_2$], 357 (22), 300 (65), 298 (68), 273 (97), 271 (100), 219 (30), 218 (14), 197 (15), 195 (21), 192 (96), 191 (35), 115 (17), 114 (32).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{17}BrN_2O_4 - NO_2$: 359.0343; found: 359.0334.

Anal. Calcd for $C_{18}H_{17}BrN_2O_4$: C, 53.3; H, 4.2; N, 6.9. Found: C, 52.9; H, 4.0; N, 6.8.

(2*S*,3*S*,4*R*,5*S*)-Methyl 5-(Naphth-2-yl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4s)

Obtained according to P2-AgOTf.

Colorless prisms (*n*-hexane–Et_2O, 5:1); mp 76–78 °C; $[\alpha]_D^{20}$ 46.0 (*c* 0.6, $CHCl_3$); 92:8 er; HPLC (Daicel Chiralpak AD-H; 2-propanol–*n*-hexane, 10:90; flow rate 1.0 mL/min): t_R = 19.9 (minor), 23.0 (major) min.

IR (solid): 1550, 1743 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.83 (br s, 1 H, NH), 3.33 (s, 3 H, OCH_3), 4.46 (dd, *J* = 8.7, 8.7 Hz, 1 H CHPh), 4.60 (d, *J* = 9.1 Hz, 1 H, CHCO), 5.02 (d, *J* = 8.5 Hz, 1 H, CHNaph), 5.41 (dd, *J* = 8.4, 8.4 Hz, 1 H, $CHNO_2$), 7.26–7.36 (m, 5 H, ArH), 7.51–7.53 (m, 2 H, ArH), 7.73 (dd, *J* = 8.5, 1.8 Hz, 1 H, ArH), 7.72–7.9 (m, 4 H, ArH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.0 (CHPh), 53.5 (OCH_3), 64.0 (*C*HCO), 67.4 (CHNf), 94.1 ($CHNO_2$), 123.9, 126.7, 127.8, 128.2, 128.4, 128.5, 128.6, 128.9, 129.3, 129.4, 133.2, 133.6, 134.9, 135.9 (ArC), 171.8 (CO).

MS (EI): *m*/*z* (%) = 329 (38) [$M^+ - NO_2$], 271 (19), 270 (88), 244 (20), 243 (100), 227 (14), 167 (34), 165 (27), 115 (26).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{20}N_2O_4$: 376.1442; found: 376.1432.

Anal. Calcd for $C_{22}H_{20}N_2O_4$: C, 70.2; H, 5.4; N, 7.4. Found: C, 69.8; H, 5.5; N, 7.4.

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