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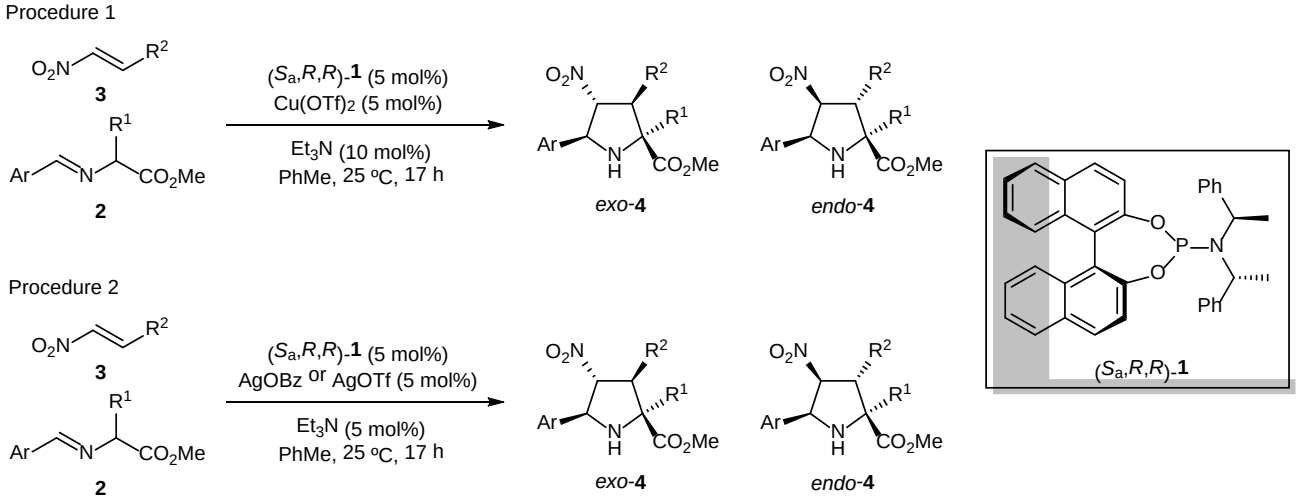
Abstract: Chiral complexes formed by privileged phosphoramidites, from chiral binol and optically pure Davies' amines, and copper(II) triflate, silver(I) triflate or silver(I) benzoate are excellent catalysts for the general 1,3-dipolar cycloaddition between azomethine ylides generated from α-amino acids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



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

Introduction

The straightforward synthesis of enantiomerically enriched polysubstituted *exo*-4-nitroprolinates can be achieved through a 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 treatments of other diseases.[4] More simple *exo*-nitroprolinates such as **4** have shown a high efficiency as organocatalysts in asymmetric aldol reactions.[5]

For the construction of these *exo*-prolinates with 2,5-*cis*-4,5-*trans* arrangement, *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.[6] The major contributions using α-

imino esters to get *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.2The only exception reported in all these examples is the employment of a copper(II) triflate·pyridyl bis(imidazolidine) as chiral complex,[8] andvery interesting switchable chiral P,N-ferrocene ligands,[9]which afforded the *endo*-adducts.

Taking in account that silver(I) is traditionally the most suitable cation to stabilize a metallodipole derived from iminoesters **3**,[10] any efficient 1,3-DC with β–nitroalkenes has been reported.[11] Only Fukuzawa's group published a highly effective asymmetric cycloaddition using benzophenone-derived iminoglycinates and nitroalkenes catalyzed by silver(I)·thioclickferrophos complexes.[12]

Very recently, we have shown that phosphoramidites,[13,14] derived from chiral binol-chiral Davies' amines, represented 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 in the literature concerning asymmetric 1,3-CD of imino esters and different dipolarophiles catalyzed by chiral phosphoramidite **1**·silver(I)complexes supported this idea,[18]obtaining, enantiomerically enriched polysubstituted *endo*-proline derivatives in good chemical yields and excellent both diastereo- and enantioselections.

Herein, we wish to report a practical procedure for the synthesis of*exo*-4-nitroprolinates **4** in which nitroalkenes underwent copper(II) and the 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); b)the catalyst originated by (S_a,*R*,*R*)-**1** and AgOTf (Scheme 1, Procedure 2, Table 1), and; c) the combination of phosphoramidite (S_a,*R*,*R*)-**1** with AgOBz (Scheme 1, Procedure 2, Table 1). Initially, the influence of the ester moiety of imines **2** was surveyed. Compound **4a** was obtained as very clear crude reaction product and with the highest *er* 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 *er* for the reactions catalyzed by the two chiral silver complexes with a slightly better *exo*-diastereoselection for the isopropyl ester was obtained. The copper(II) catalyzed process gave better *exo*/*endo* and similar enantiomeric ratios. However, the lower yields(up to 70%) of the *exo*-product **4b** mixtures obtained in all of the reactions using the isopropyl ester obeyed to the appearance of a proportion of other unidentified diastereoisomers (*ca.* 20-28% from crude product determined by ^{1}H NMR), (Table 1, entry 2). In consequence, the study of the scope of the reaction was next done with methyl α-imino esters as metallo-azomethine ylide precursors.

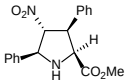
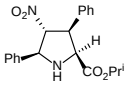
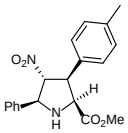
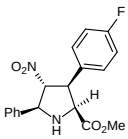
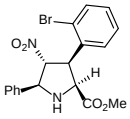
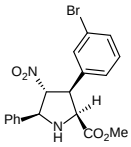
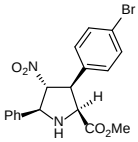
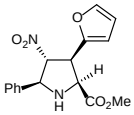
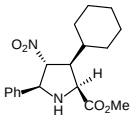
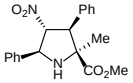
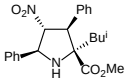
The study of the influence of the aryl substituent of the nitroalkene **3** for the 1,3-DC with methyl benzylidene glycinate revealed that, in general, higher chemical yields, *exo*-diastereoselectivities and enantioselections in products **4c-g** were observed when the reactions occurred in the presence of (S_a,*R*,*R*)-**1**·AgOBz rather than with the silver(I) or copper(II) triflates(Table 1, entries 3-7). Only one exception was recorded when *m*-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*). In the case of the heteroaromatic moiety bonded to the nitro component (2-furyl) was more appropriate with the chiral silver benzoate complex achieving 77% of chemical yield and 98% *ee* of the *exo*-**4h** (Table 2, entry 8). When the nitroalkene **3** beared an aliphatic cyclohexyl group a reversal diastereoselectivity was observed in the **1**·AgOTf catalyzed 1,3-DC. The exclusive *endo* isomer was isolated 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, whilst the *exo*-isomer **4i** was obtained in low 32% yield but with a 96% *ee* (Table 2, entry 9). On the other hand, the 1,3-DC with this nitroalkene**3** (R^2 = Cy) failed with the $Cu(OTf)_2$ complex.

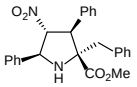
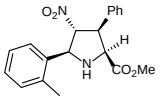
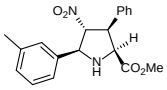
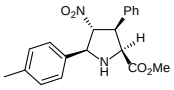
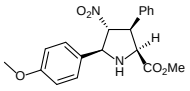
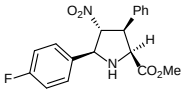
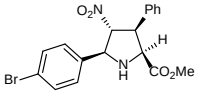
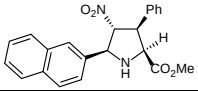
When alanine, leucine, and phenylalanine derived imino esters **2** were used as azomethine ylide precursors, an increment of the *endo*-diastereoisomers **4j-l** was observed. This diastereoisomer was always obtained as a racemic mixture (Table 1, entries 10-12). Alanine dipole precursor**2** furnished 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).

With respect to the reaction of different methyl arylideneimino glycinates **2**with nitrostyrene, the more sterically hindered *o*-tolyl imino group also favoured the generation of the *endo*-isomer **4m** but in less proportion in the case of AgOBz (Table 1, entry 13). For the *m*-tolyl imino group derivative the benzoate counteranion gave the highest

enantioselections of compound *exo*-**4n** (Table 1, entry 14). It seems that the lower steric repulsion the higher proportion of *exo*-adduct and enantioselection. This general assumption can be supported by the transformations involving *p*-substituted arylidene imino esters**2** (Table 2, 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 2, entries 15-18). Noticeably, compound *exo*-**4p** could not be prepared through the copper(II)-catalyzed method (Table 2, 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 better than $Cu(OTf)_2$ and AgOBz (Table 2, entry 19).

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.

			(S_a,*R*,*R*)-**1**·$Cu(OTf)_2$			(S_a,*R*,*R*)-**1**·AgOTf			(S_a,*R*,*R*)-**1**·AgOBz		
Entry	**4**	Structure	*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**
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
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] From the crude product, determined by ^{1}H NMR.
[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 de *endo*-isomer.
[f] The *endo*-isomer was obtained as a racemic mixture.

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 itself is able to block one of the two prochiral faces of the 1,3-dipole. Such as it can be deduced from DFT calculations,[16,17] triflate anion is closer to the copper(II)centre than the corresponding silver(I) cation, whereas the distance silver(I) cation-dipole is shorter. These reasons justify the use of (S_a,*R*,*R*)-**1**·Cu(OTf)$_2$ complex in the reactions involving α-substituted imino esters**2**.

The influence of the benzoate anion *vs.* triflate anion can be explained by the assumption that benzoate (bulkier group 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 so, we think that a variation of this aromatic group implies that triflate anion is much less sensitive than the benzoate one.[19] In this sense, the reaction regarding only **4** (R = H, Ar = Ph) and nitrostyrenes is optimally catalyzed by (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 a copper(II)- or silver(I) catalyzed 1,3-DC between imino esters and nitroalkenes. This method allows the preparation of these pyrrolidines in larger scale (0.5-0.8 g) at room temperature.(S_a,*R*,*R*)-**1**·AgOBz is the best catalyst to perform cycloadditions starting from methyl benzylideneglycinate. (S_a,*R*,*R*)-**1**·Cu(OTf)$_2$ complex is more suitable in the reactions involving α-substituted imino esters **2**. Finally, (S_a,*R*,*R*)-**1**·AgOTf catalyst is highly recommended when imines derived from aromatic aldehydes (different of benzaldehyde) are used.

Procedures

Anhydrous solvents were freshly distilled under an argon atmosphere and degasified by Freeze-Pump-Thaw methodology. Aldehydes were also distilled prior to use for the elaboration of the imino esters and nitroalquenes. They are very known molecules and are easily prepared. Copper salts were dried in a Kugel-Rorh apparatus and stored under an argon atmosphere. Melting points were determined with a Reichert Thermowar hot plate apparatus and are uncorrected. HPLC analyses were performed with a JASCO-2000 series equipped with a chiral column by using mixtures of *n*-hexane/isopropyl alcohol as the mobile phase at 25 ºC. Yields refer to isolated

compounds estimated to be >95% pure as determined by ^{1}H NMR spectroscopy and HPLC analyses. All silver-mediated reactions were run avoiding light exposure.

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

To a solution of the chiral phosphoramidite (0.05 mmol) and $Cu(OTf)_2$(0.05 mmol) in dry toluene (3 mL) under argon atmosphere was added a solution of imino ester (1mmol) and nitroalkene (1 mmol) in toluene (5 mL). To the resulting suspension triethylamine (0.05 mmol, 7µL) was added and the mixture stirred at room temperature (25 °C) for 16-24 h. The crude reaction mixture was filtered through a small celite path. The residue was purified by flash chromatography yielding pure exo-cycloadducts. Solid products were recrystallized inmixtures of n-hexane/ether. **4a** and **4f** were also prepared in 3 mmol scale obtaining identical results to the reported for the model reaction.

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

To a solution of the chiral phosphoramidite **1** (0.05 mmol) and AgX (0.05 mmol, triflate or benzoate) in dry toluene (3 mL) under argon atmosphere was added a solution of imino ester (1mmol) and nitroalkene (1 mmol) in toluene (5 mL). To the resulting suspension triethylamine (0.05 mmol, 7µL) was added and the mixture stirred at room temperature (25 °C). The crude reaction mixture was filtered through a small Celite path. The residue was purified by flash chromatography yielding pure *exo*-cycloadducts. Solid products were recrystallized in mixtures of *n*-hexane/ether. Compounds **4a** and **4f** were also prepared in 3 mmol scale obtaining identical results to the reported for the model reaction.

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

According to P2-AgOBz, colorless needles, *n*-hexane/Et_2O 4:1.
mp: 104–105 ºC.
$[\alpha]_D^{20}$ = 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, t_R: 25.2 min (major) and 27 min (minor), 220 nm;
IR (solid) ν_{max}: 1265, 1551, 1731 cm^{-1}.
^{1}H NMR: 2.71 (br s, 1H, NH) 3.26 (s, 3H, Me), 4.35 (t, *J* = 7.8 Hz, 1H, C*H*CO), 4.48 (d, *J* = 9.1 Hz, 1H, C*H*Ph), 4.73 (d, J = 7.8 Hz, 1H, C*H*Ph), 5.19 (t, *J* = 8.0 Hz, 1H, CHNO), 7.45–7.18 (m, 8H, Ar*H*), 7.56–7.52 (m, 2H, Ar*H*).
^{13}C-NMR δ: 51.8 (*C*H$_3$), 53.7 (*C*HPh), 64.2 (*C*HCO), 67.5 (Ph*C*HNH), 95.0 (*C*HNO$_2$), 126.8, 127.8, 128.1, 128.7, 128.9, 129.0, 135.8, 137.6 (Ar*C*), 171.8 (*C*O).
MS *m/z*: 326 (M$^+$, 0.1%), 279 (16), 220 (73), 193 (100), 178 (12), 115 (42).
EA required 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%.

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

According to P1, colorless needles, *n*-hexane/Et_2O 4:1.
mp: 130-132 ºC.
$[\alpha]_D^{20}$ = 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 min (major), 20.4 min (minor).
IR (solid) ν_{max}: 1265, 1551, 1731 cm^{-1}.
^{1}H NMR δ: 0.58 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 1.06 (d, *J* = 6.3 Hz, 3H, C*H*$_3$), 2.75 (br. s, 1H, N*H*), 4.37 (dd, *J* = 8.9, 8.0 Hz, 1H, C*H*Ph), 4.46 (d, *J* = 9.1 Hz, 1H, C*H*CO), 4.65 [dt, *J* = 12.6, 6.3 Hz, 1H, C*H*(CH$_3$)$_2$], 4.75 (d, *J* = 8.3 Hz, 1H, PhC*H*N), 5.20 (dd, *J* = 8.3, 8.3 Hz, 1H, C*H*NO$_2$), 7.19-7.30 (m, 5H, Ar*H*), 7.36-7.45 (m, 3H, Ar*H*), 7.54-7.57 (m, 2H, Ar*H*).
^{13}C-NMR δ: 20.7 (*C*H$_3$), 21.6 (*C*H$_3$), 53.5 (*C*HPh), 64.1 (*C*HCO), 67.4 [*C*H(CH$_3$)$_2$], 69.1 (Ph*C*HNH), 95.4 (*C*HNO$_2$), 126.9, 128.1, 128.8, 128.9, 129.0, 129.4, 136.3, 137.6 (Ar*C*), 170.8 (*C*O).
MS *m/z*: 356 (M$^+$, 0.01%), 307 (10), 220 (100), 193 (80), 115 (28).
HRMS required for ($C_{20}H_{22}N_2O_4$-NO$_2$): 309.4021; found 309.4028.
EA required 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%.

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

According to P2-AgOBz, colorless needles, *n*-hexane/Et_2O 5:1.
mp 108-110 ºC.
$[\alpha]_D^{20}$ = 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 min (major), 24.2 min (minor).
IR (neat) ν_{max}: 1212, 1547, 1736, 2917 cm^{-1}.
^{1}H NMR δ: 2.31 (s, 3H, CH$_3$C), 2.75 (br. s, 1H, N*H*), 3.32 (s, 3H, OC*H*$_3$), 4.35 (dd, *J* = 8.5 Hz, 1H, C*H*Tol), 4.48 (d, *J* = 9 Hz, 1H, C*H*CO$_2$Me), 4.76 (d, *J* = 8.3 Hz, 1H, C*H*Ph), 5.21 (dd, *J* = 8.2, 8.2 Hz, 1H, C*H*NO$_2$), 7.13 (m, 2H, Ar*H*), 7.40-7.45 (m, 4H, Ar*H*), 7.55-7.57 (m, 3H, Ar*H*).
^{13}C-NMR δ: 21.0 (*C*H$_3$C) 51.9 (*C*HC$_6$H$_4$Me), 53.5 (*C*H$_3$), 64.2 (*C*HCO$_2$Me), 67.5 (*C*HPh), 95.1 (*C*HNO$_2$), 126.9 (*C*HCHCHC), 127.7, 129.0, 129.1, 129.4 (Ar*C*), 132.53 (CH$_3$*C*), 137.52 (*C*CHNH), 137.92 (*C*CHCHNH), 171.86 (CO).
MS *m/z* 294 (M$^+$-NO$_2$, 9%), 234 (36), 207 (100), 129 (15).
HRMS required for ($C_{19}H_{20}N_2O_4$-NO$_2$): 294.1400; found: 294.1399.
EA required 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%.

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

According to P2-AgOBz, colorless prisms, *n*-hexane/Et_2O 5:1.
mp 96.2-97 ºC.
$[\alpha]_D^{20}$ = 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 min (minor), 28.2 min (major).
IR (solid) ν_{max}: 1265, 1511, 1553, 1746 cm^{-1}.
^{1}H NMR δ 2.58 (br. s, 1H, NH), 3.34 (s, 3H, OC*H*$_3$), 4.34-4.44 (m, 1H, C*H*CHCO), 4.51 (d, *J* = 9.0 Hz, 1H, C*H*CO$_2$Me), 4.78 (d, *J* = 8.2 Hz, 1H, C*H*Ph), 5.16 (dd, *J* = 8.0, 8.0 Hz, 1H, C*H*NO$_2$), 6.99-7.11 (m, 2H, Ar*H*), 7.23-7.32 (m, 2H, Ar*H*), 7.36-7.49 (m, 3H, Ar*H*), 7.58 (d, *J* = 7.5 Hz, 2H, Ar*H*).
^{13}C NMR δ: 51.9 (*C*HCHCO), 52.8 (CH$_3$), 64.0 (*C*HCO), 67.3 (*C*HPh), 95.2 (*C*HNO$_2$), 126.8, 128.9, 129.5, 129.6, 131.8, 137.6, 161.2, 163.4 (ArC), 171.6 (*C*O).
MS *m/z*: 298 (M$^+$-NO$_2$, 10%), 238 (55), 211 (100), 133 (19), 117 (18).

HRMS required for ($C_{18}H_{17}FN_2O_4$-NO_2): 298.1181; found: 298.1175.
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 3-(2-bromophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4e)**.
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 min (major), 23.9 min (minor).
IR (neat) ν_{max}: 1549, 1736, 2926 cm^{-1}.
^{1}H NMR δ 2.53 (br. s, 1H, N*H*), 3.29 (s, 3H, C*H*$_3$), 4.70 (d, *J* = 9.1 Hz,1H, C*H*Ph), 4.83 (d, *J* = 8.6 Hz, 1H, C*H*CO_2Me), 4.98 (dd, *J* = 9.3, 9.3 Hz, 1H, C*H*C_6H_4Br), 5.30 (dd, *J* = 9.0, 9.0 Hz, 1H, C*H*NO_2), 7.17 (dd, *J* = 7.7, 1.4 Hz,1H, Ar*H*), 7.36-7.45 (m, 6H, Ar*H*), 7.55-7.63 (m, 2H, Ar*H*).
^{13}C NMR δ: 51.9 (*C*HAr), 52.2 (*C*H$_3$), 61.9 (*C*HCO_2Me), 67.2 (*C*HPh), 92.9 (*C*HNO_2), 127.1 (*C*Br), 127.2, 127.8, 128.6, 128.7, 129.1, 129.2, 133.3, 134.6, 137.3 (Ar*C*), 172.2 (CO).
MS *m/z* 360 (M^+-NO_2, 28%), 358 (28), 347 (11), 345 (11), 300 (96), 298 (100), 273 (94), 271 (96), 219 (36), 192 (92).
HRMS required for ($C_{18}H_{17}BrN_2O_4$ –NO_2): 359.0338; found: 359.0343.
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 3-(3-bromophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4f)**.
According to P1, pale yellow prisms, *n*-hexane/Et_2O 5:1.
mp 72-74 ºC.
$[\alpha]_D^{20}$ = 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 min (minor), 44.3 min (major).
IR (solid) ν_{max}: 1547, 1735, 2928 cm^{-1}.
^{1}H NMR δ: 2.73 (br. s, 1H, N*H*), 3.38 (s, 3H, C*H*$_3$), 4.33 (dd, 1H, *J* = 8.8, 7.8 Hz, C*H*C_6H_4Br), 4.50 (d, *J* = 8.9 Hz, 1H, C*H*CO_2Me), 4.75 (d, *J* = 8.1 Hz, 1H, C*H*Ph), 5.13 (dd, *J* = 7.9, 7.9 Hz, 1H, C*H*NO_2), 7.20-7.22 (m, 2H, Ar*H*), 7.41-7.55 (m, 5H, Ar*H*), 7.55-7.57 (m, 2H, Ar*H*).
^{13}C NMR δ: 52.0 (*C*HC_6H_4Br), 53.0 (*C*H$_3$), 64.1 (*C*HCO_2Me), 67.4 (*C*HPh), 94.9 (*C*HNO_2), 122.8 (*C*Br), 126.3, 126.9, 129.1, 129.1, 130.3, 131.2, 131.4, 137.5, 138.4 (Ar*C*), 171.5 (CO).
MS *m/z*: 360 (M^+-NO_2, 17%), 358 (17), 298 (86), 270 (77), 192 (100), 117 (76).
HRMS required for ($C_{18}H_{17}BrN_2O_4$-NO_2): 359.0338; found 359.0334.
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 3-(4-bromophenyl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4g)**.
According to P2-AgOBz, colorless prisms, *n*-hexane/Et_2O 4:1.
mp 89-91ºC.
$[\alpha]_D^{20}$ = 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 min (major), 26.8 min (minor).
IR (solid) ν_{max}: 1544, 1737, 2925 cm^{-1}.
^{1}H NMR δ: 2.75 (br. s, 1H, N*H*), 3.34 (s, 3H, C*H*$_3$), 4.21-4.33 (m, 1H, C*H*C_6H_4Br), 4.48 (d, *J* = 8.9 Hz, 1H, C*H*CO_2Me), 4.73 (d, *J* = 8.1 Hz, 1H, C*H*Ph), 5.08 (dd, *J* = 7.8, 7.8 Hz, 1H, C*H*NO_2), 7.12-7.14 (m, 2H, Ar*H*), 7.37-7.44 (m, 5H, Ar*H*), 7.50-7.51 (m, 2H, Ar*H*).
^{13}C NMR δ: 52.0 (*C*HC_6H_4Br), 52.9 (*C*H$_3$), 64.0 (*C*HCO_2Me), 67.3 (*C*HPh), 95.1 (*C*HNO_2), 122.3 (*C*Br), 126.8, 129.0, 129.1, 129.6, 132.0, 135.3, 137.6 (Ar*C*), 171.5 (CO).
MS *m/z*: 360 (M^+- NO_2, 15%), 359 (15), 300 (52), 298 (51), 273 (99), 271 (100), 219 (26), 192 (89), 117 (43), 115 (26).
HRMS required for ($C_{18}H_{17}BrN_2O_4$-NO_2): 359.0338, found 359.0330.
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 3-(furan-2-yl)-4-nitro-5-phenylpyrrolidine-2-carboxylate (4h)**.
According to P2-AgOBz, yellow prisms *n*-hexane/Et_2O 3:1.
mp 60-62 ºC.
$[\alpha]_D^{20}$ = 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 min (major), 18.8 min (minor).
IR (neat) ν_{max}: 1209, 1549, 1740, 2341, 2359 cm^{-1}. ^{1}H NMR δ: 2.77 (br. s, 1H, NH), 3.51 (s, 3H, OCH_3), 4.40 (d, *J* = 8.5 Hz, 1H, C*H*CO), 4.50 (dd, *J* = 8.4, 7.2 Hz, 1H, C*H*furyl), 4.65 (d, *J* = 8.0 Hz, 1H, C*H*Ph), 5.23 (dd, *J* = 7.9, 7.0 Hz, 1H, C*H*NO_2), 6.20 (d, *J* = 3.1 Hz, 1H, CC*H*), 6.29 (dd, *J* = 3.2, 1.8 Hz, 1H, CCHC*H*CHO), 7.25–7.61 (m, 6H, Ar*H* and OC*H*).
^{13}C NMR δ: 47.9 (*C*Hfuryl), 52.2 (*C*H$_3$), 63.2(*C*HCO), 68.2(*C*HPh), 93.6 (*C*HNO_2), 108.4 (C*C*H), 110.5 (CCH*C*HCHO), 126.8, 128.6, 128.9, 137.2 (ArC), 142.8 (O*C*H), 148.9 (O*C*), 171.1 (*C*O).
MS *m/z* 270 (M^+-NO_2, 12%), 183(100), 155(10), 117 (12).
HRMS required for ($C_{16}H_{16}N_2O_5$): 316.1059; found: 316.1049.

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

According to P2-AgOBz, white needles. *n*-hexane/Et_2O 4:1.

mp 125-127 ºC.

$[\alpha]_D^{20}$ = 0.2 (*c* 1,0 $CHCl_3$) 52:48 *er*. HPLC (Chiralpak AD-H, 2-propanol 10% in hexane, flow 1.0 mL min, 14.5 min (minor), 16.2 min (major).*Exo*-**4i** (Chiralpak AD-H, 2-propanol 10% in hexane, flow 1.0 mL min, 17.1 min (major), 19.0 min (minor).

IR (neat): 1202, 1544, 1737, 2927 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.25-1.32 (m, 5H, C*H*$_2$), 1.58-1.67 [m, 1H, C*H*$(CH_2)_2$], 1.72-1.86 (m, 5H, CH_2), 2.87 (td, *J* = 7, 2.4 Hz, 1H, C*H*CH$(CH_2)_2$), 3.28 (dd, *J* = 11.5, 10.7 Hz, 1H, N*H*), 3.83 (m, 1H, C*H*CO_2Me), 4.47 (dd, *J* =12.3, 5.9 Hz, 1H, C*H*Ph), 5.11(dd, *J* = 5.9, 2.4 Hz, 1H, C*H*NO_2), 7.26-7.35 (m, 5H, Ar*H*).
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 26.13 (*C*$H_2CH_2CH_2$CH), 2 x 29.94(CH_2*C*H_2CH_2CH), 2 x 31.51 (CH_2CH_2*C*H_2CH), 39.73 ($CH_2CH_2CH_2$*C*H), 52.65 (*C*HCy), 57.09 (*C*H$_3$), 63.10 (*C*HCO_2Me), 67.73 (*C*HPh), 93.33(*C*HNO_2), 126.17, 128.46, 128.65, 134.26 (Ar*C*), 172.38 (*C*O). MS *m/z* (M^+-NO_2) 285 (13), 273 (16), 226 (82), 144 (100),117 (28). HRMS required for ($C_{18}H_{24}N_2O_4$): 332.3934; found: 332.3927.

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

According to P2-AgOTf , yellow oil.

$[\alpha]_D^{20}$ = -10.7 (*c* 1, $CHCl_3$) 55:45 *er*. HPLC (Chiralpak AD-H, 2-propanol 10% in hexane, flow 1.0 mL min, 9.3 min (minor), 15.6 min (major). *Exo*-**4j**(Chiralpak AD-H, 2-propanol 10% in hexane, flow 1.0 mL min, 9.1 min (minor), 17.4 min (major).

IR (neat): 1257, 1549, 1731 cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.19 (s, 3H, CC*H*$_3$), 3.25 (br, 1H, NH), 3.86 (s, 3H, CO_2CH_3), 4.52 (d, *J* = 6.1 Hz, 1H, C*H*C), 5.08 (d, *J* = 7.4 Hz, 1H, C*H*N), 5.65 (dd, *J* = 7.4, 6.1 Hz, 1H, C*H*NO_2), 7.23-7.49 (m, 10H, Ar*H*). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 22.0 (C*C*H$_3$), 52.9 (*C*HC), 56.9 (*OC*H$_3$), 64.9 (*C*HN), 68.8 (*C*CH$_3$), 95.6 (*C*HNO_2), 126.8 (Ar*C*), 128.0 (Ar*C*), 128.5 (Ar*C*), 128.6 (Ar*C*), 128.7 (Ar*C*), 128.8(Ar*C*), 135.3(Ar*C*), 135.5(Ar*C*), 174.7(*C*O). MS *m/z* (M^+ - NO_2) 281(45), 234(100), 219(17), 193(37), 115(21). HRMS required for ($C_{19}H_{20}N_2O_4$): 340.1422, found: 281.1428.

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

According to P1, colorless prisms, *n*-hexane/Et_2O 4:1.

mp 105-107 ºC.

$[\alpha]_D^{20}$ = 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 min (major), 14.5 min (minor). IR (solid) ν_{max}: 1230, 1545, 1730 cm^{-1}.

^{1}H NMR δ: 0.81 (d, *J* = 6.7 Hz, 3H, C*H*$_3$), 1.04 (d, *J* = 6.7 Hz, 3H, C*H*$_3$), 1.57 (br. s, 1H, N*H*), 1.79 (td, *J* = 13.3, 6.7 Hz, 1H, C*H*), 1.96 (dd, *J* = 13.9, 5.7, Hz, 1H, C*H*$_2$), 2.15 (dd, *J* = 13.9, 6.9 Hz, 1H, C*H*$_2$), 3.19 (s, 3H, C*H*$_3$), 4.00 (d, *J* = 9.9 Hz, 1H, C*H*C), 4.75 (d, *J* = 9.2 Hz, 1H, C*H*NH), 5.23 (dd, *J* = 9.2, 9.2 Hz, 1H, C*H*NO_2), 7.14-7.22 (m, 2H, Ar*H*), 7.25-7.47 (m, 6H, Ar*H*), 7.54-7.61 (m, 2H, Ar*H*).

^{13}C NMR δ: 22.8, 24.3 (2xMe), 25.6 (CH_2), 46.2 (*C*HCH_2), 51.8, 62.7 (2x*C*HPh), 66.1 (*C*CO_2), 73.2, 94.9 (*C*HNO_2), 126.9, 127.7, 128.2, 128.6, 128.9, 129.1, 135.6, 137.2 (Ar*C*), 174.5 (*C*O).

MS *m/z*: 337 (M^+-NO_2, 25%), 193(100), 115(20).

HRMS required for ($C_{22}H_{26}N_2O_4$-NO_2): 321.1729; found: 321.1750. EA required 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%.

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

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 min (minor), 30.1 min (major).

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

^{1}H NMR δ: 2.49 (br. s, 1H, N*H*), 3.22 (s, 3H, OC*H*$_3$), 3.32 (d, *J* = 13.6 Hz, 1H, C*H*$_2$), 3.42 (d, *J* = 13.5 Hz, 1H, C*H*$_2$), 4.15 (d, *J* = 9.7 Hz, 1H, C*H*CCC), 4.67 (d, *J* = 9.0 Hz, 1H, C*H*Ph), 5.23 (dd, *J* = 9.4, 9.4 Hz, 1H, C*H*NO_2), 7.15-7.56 (m, 15 H, Ar*H*).

^{13}C NMR δ: 42.8 (*C*H$_2$), 51.9 (*C*HPh), 60.3 (*C*H$_3$), 65.8 (N*C*HPh), 73.6 (q*C*), 95.1 (*C*HNO_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 (Ar*C*), 173.42 (*C*O).

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

HRMS required for ($C_{25}H_{24}N_2O_4$-CO_2Me): 357.1608; found 357.1604.

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

According to P2-AgOBz, pale yellow needles, *n*-hexane/Et_2O 5:1.

mp 71-72 ºC.

$[\alpha]_D^{20}$ = 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 min (minor), 25.3 min (major).

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

^{1}H NMR δ: 2.38 (s, 3H, CC*H*$_3$), 2.55 (br. s, 1H, NH), 3.28 (s, 3H, OC*H*$_3$), 4.43 (dd, *J* = 10.1, 7.1 Hz, 1H, C*H*Ph), 4.50 (d, *J* = 9.4 Hz, 1H, C*H*CO), 5.10 (d, *J* = 8.8 Hz, 1H, C*H*Tol), 5.34 (dd, *J* = 8.7, 8.7 Hz, 1H, C*H*NO_2), 7.20-7.37 (m, 9H, Ar*H*).

^{13}C NMR δ: 19.2 (C*C*H$_3$), 51.8 (*C*HPh), 54.0 (O*C*H$_3$), 63.3 (*C*HCO), 64.0 (*C*HTol), 93.8 (*C*HNO_2), 125.6, 126.8, 127.7, 128.2, 128.6, 128.7, 130.9, 135.9, 135.6, 137.1 (Ar*C*), 172.1 (*C*O).

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

EA required 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%.

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

According to P2-AgOBz, pale yellow prisms, *n*-hexane/Et_2O 5:1.

mp 56-58 ºC.

$[\alpha]_D^{20}$ = 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 min (minor), 19.9 min (major).

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

^{1}H NMR δ: 2.22 (br. s, 1H, NH), 2.39 (s, 3H, C*H*$_3$C), 3.30 (s, 3H, OC*H*$_3$), 4.40 (dd, *J* = 8.7, 8.7 Hz, 1H, C*H*Ph), 4.53 (d, *J* = 9.2 Hz, 1H, C*H*CO), 4.77 (d, *J* = 8.5 Hz, 1H, C*H*Tol), 5.26 (dd, *J* = 8.4, 8.4 Hz, 1H, C*H*NO_2), 7.19-7.38 (m, 9H, Ar*H*).

^{13}C NMR δ: 21.5 (C*C*H$_3$), 52.0 (*C*HPh), 53.7 (O*C*H$_3$), 64.0 (*C*HCO), 67.4 (*C*HTol), 94.5 (*C*HNO_2), 123.9, 127.6, 127.8, 128.2, 128.4, 128.8, 129.0, 129.4, 129.9, 138.9 (Ar*C*), 171.6 (*C*O).

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

HRMS required for ($C_{19}H_{20}N_2O_4$-NO_2): 294.1572, found: 294.1565.

EA required 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%.

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

According to P2-AgOTf, pale yellow prisms, *n*-hexane/Et_2O 8:1.

mp 90-92 ºC.

$[\alpha]_D^{20}$ = 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 min (minor), 28.0 min (major).
IR (solid) ν_{max}: 1220, 1545, 1725 cm^{-1}.
^{1}H NMR δ: 2.30 (s, 3H, CH_3C), 2.65 (br. s, 1H, NH), 3.21 (s, 3H, OCH_3), 4.29 (dd, *J* = 9.0, 9.0 Hz, 1H, C*H*Ph), 4.41 (d, *J* = 9.1 Hz, 1H, C*H*CO), 4.64 (d, *J* = 8.4 Hz, 1H, C*H*Tol), 5.12 (dd, *J* = 8.1, 8.1 Hz, 1H, C*H*NO_2), 7.14-7.38 (m, 9H, Ar*H*).
^{13}C NMR δ: 21.2 (CCH_3), 51.8 (*C*HPh), 53.8 (OCH_3), 64.2 (*C*HCO), 67.5 (*C*HTol), 95.1 (*C*HNO_2), 126.9, 127.8, 128.1, 128.8, 129.2, 129.7, 134.5, 135.9 (Ar*C*), 171.9 (*C*O). MS *m/z*: 294 (M^+-NO_2, 10%), 293 (25), 234 (85), 207 (100), 191 (16), 131 (26), 115 (26).
HRMS required for ($C_{19}H_{20}N_2O_4$-NO_2): 294.1572; found: 294.1562.
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 5-(4-methoxyphenyl)-4-nitro-3-phenylpyrrolidine-2carboxylate (4p)**.
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 30% in hexane, flow 1.0 mL min, 19.9 min (minor), 25.2 min (major).
IR(neat): 1177, 1213, 1248, 1513, 1547, 1735 cm^{-1}.
^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.29 (s, 3H, PhOCH_3), 3.83 (s, 3H, CO_2CH_3), 4.41 (dd, *J* = 8.4, 8.4 Hz, 1H, C*H*Ph), 4.50 (d, *J* = 9.2 Hz, 1H, C*H*CO), 4.74 (d, *J* = 8.5 Hz, 1H, C*H*N), 5.22 (dd, *J* = 8.4, 8.4 Hz, 1H, C*H*NO_2), 6.95 (d, *J* = 8.7 Hz, 2H, ArH), 7.19-7.36 (m, 5H, ArH), 7.50 (d, *J* = 8.7 Hz, 2H).
^{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 *m/z* (M^+ - NO_2) 309(35), 250(100), 223(88).207(39), 147(47), 115(28).
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 5-(4-fluorophenyl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4q)**.
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 min (minor), 19.4 min (major).
IR (neat) ν_{max}: 1221, 1509, 1548, 1736 cm^{-1}.
^{1}H NMR δ: 2.62 (br. s, 1H, NH), 3.30 (s, 3H, OCH_3), 4.41 (dd, *J* = 8.2, 8.2 Hz, 1H C*H*Ph), 4.50 (d, *J* = 9.1 Hz, 1H, C*H*CO), 4.77 (d, *J* = 8.3 Hz, 1H, C*H*N), 5.21 (dd, *J* = 8.2, 8.2 Hz, 1H, C*H*NO_2), 7.07-7.16 (m, 2H, Ar*H*), 7.24-7.38 (m, 5H, Ar*H*), 7.56-7.62 (m, 2H, Ar*H*).
^{13}C NMR δ: 51.8 (*C*HPh), 53.4 (OCH_3), 64.0 (*C*HCO), 66.8 (*C*HN), 94.9 (*C*HNO_2), 115.9, 127.8, 128.2, 128.7, 128.8, 133.7, 135.7, 161.7, 164.2 (Ar*C*), 171.9 (*C*O).
MS *m/z*: 297 (M^+-NO_2, 14), 238 (74), 211 (100), 135 (23), 133 (20), 115 (21).
HRMS required for ($C_{18}H_{17}FN_2O_4$-NO_2) 297.1181; found: 297.1175.

***(2S,3S,4R,5S)*-Methyl 5-(4-bromophenyl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4r)**.
According to P2-AgOTf, colorless prisms, *n*-hexane/Et_2O 3:1. mp 149-151 ºC.
$[\alpha]_D^{20}$ = 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 min (minor), 25.5 min (major).
IR (solid) ν_{max}: 1213, 1547, 1738 cm^{-1}.
^{1}H NMR δ 2.73 (br. s, 1H, NH), 3.31 (s, 3H, OCH_3), 4.40 (dd, *J* = 8.7 Hz, 1H, C*H*Ph), 4.53 (d, *J* = 9.1, 1Hz, C*H*CO), 4.80 (d, *J* = 8.4 Hz, 1H, C*H*N), 5.23 (dd, *J* = 8.4, 8.4 Hz, 1H, C*H*NO_2), 7.17-7.29 (m, 2H, Ar*H*), 7.31-7.33 (m, 3H, Ar*H*), 7.44-7.51 (m, 2H, Ar*H*), 7.55-7.61 (m, 2H, Ar*H*).
^{13}C NMR δ: 52.0 (*C*HPh), 53.2 (OCH_3), 63.8 (*C*HCO), 66.4 (*C*HN), 94.1 (*C*HNO_2), 123.3, 127.7, 127.8, 128.9, 129.4, 132.3, 132.4, 134.9 (Ar*C*), 171.4 (*C*O).
MS *m/z*:359 (M^+-NO_2, 21%), 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 required for ($C_{18}H_{17}BrN_2O_4$-NO_2): 359.0343; found: 359.0334.
EA required 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%.

***(2S,3S,4R,5S)*-Methyl 5-(naphth-2-yl)-4-nitro-3-phenylpyrrolidine-2-carboxylate (4s)**.
According to P2-AgOTf, colorless prisms, *n*-hexane/Et_2O 5:1. mp 76-78 ºC.
$[\alpha]_D^{20}$ = 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 min (minor), 23.0 min (major).
IR (solid) ν_{max}: 1550, 1743 cm^{-1}.
^{1}H NMR δ: 2.83 (br. s, 1H, NH), 3.33 (s, 3H, OCH_3), 4.46 (dd, *J* = 8.7, 8.7 Hz, 1H C*H*Ph), 4.60 (d, *J* = 9.1 Hz, 1H, C*H*CO), 5.02 (d, *J* = 8.5 Hz, 1H, C*H*Naph), 5.41 (dd, *J* = 8.4, 8.4 Hz, 1H, C*H*NO_2), 7.26-7.36 (m, 5H, Ar*H*), 7.51-7.53 (m, 2H, Ar*H*), 7.73 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 7.72-7.9 (m, 4H, Ar*H*).
^{13}C NMR δ: 52.0 (*C*HPh), 53.5 (OCH_3), 64.0 (*C*HCO), 67.4(*C*HNf), 94.1 (*C*HNO_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 (Ar*C*), 171.8 (*C*O).
MS *m/z*: 329 (M^+-NO_2, 38%), 271 (19), 270 (88), 244 (20), 243 (100), 227 (14), 167 (34), 165 (27), 115(26).
HRMS required for ($C_{22}H_{20}N_2O_4$) 376.1442, found: 376.1432.
EA required 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%.

References and Notes

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