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Pd-catalyzed one-pot coupling of allylamines, activated alkenes, and unsaturated halides (or triflate): an atom efficient synthesis of highly functionalized pyrrolidines

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Abstract

A Pd-catalyzed three-component assembling of highly functionalized 4-benzyl-(and allyl-)pyrrolidines was achieved based on a combination of allyl amines, *gem*-diactivated alkenes, and unsaturated halides (or triflate).

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1. Introduction

Multicomponent assembling processes are drawing increasing attention in the search for atom efficient, environmentally friendly new synthetic methodologies. They have found widespread applications in the preparation of compound libraries and, to a lesser extent, in target directed synthesis [1]. Pd-catalyzed cascade processes are now well-established as powerful tools for the development of new multicomponent reactions [2]. In this area, we have recently reported the three-component assembling of various oxygen [3,4] and nitrogen [5] heterocycles by hetero-Michael conjugate addition/cyclization sequences involving propargylic alcohols and amines, *gem*-diactivated alkenes, and unsaturated halides (and triflates). The key step in this one-pot transformation is the Pd-mediated cyclofunctionalization of the alkyne moiety via carbopalladation/reductive elimination (Scheme 1).

Interestingly, this reaction may also be applied to the cyclofunctionalization of alkenes but these are generally much less reactive [6]. In fact, when propargylic alcohols are substituted for their allylic analogs, the above-mentionned three-component reaction becomes rather sluggish and low yielding. Besides, non-negligeable amounts of side products are formed [3,7]. We now wish to report that reactions involving allylic amines do not suffer from such drawbacks and allow the clean and selective assembling of 4-benzylpyrrolidines in moderate to good yields [8].

2. Results and discussion

In order to probe the participation of allylamines as nucleophilic partners in the three-component reaction, preliminary assays were conducted using equimolar

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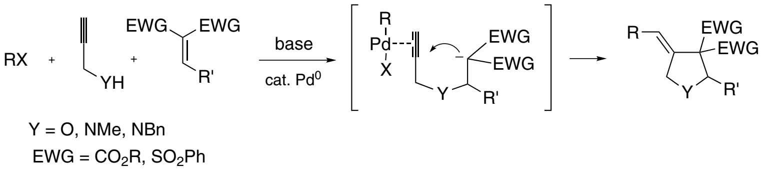


Scheme 1.

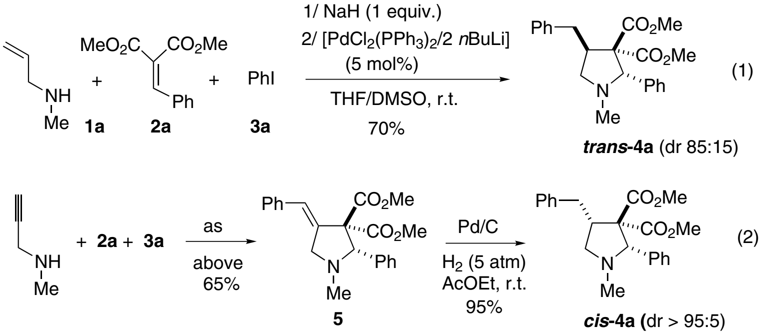
amounts of the commercially available *N*-methylallylamine (**1a**), dimethyl benzylidene malonate (**2a**) and iodobenzene (**3a**) using reaction conditions similar to those previously used for the synthesis of 4-benzylidenepyrrolidine (**5**) from *N*-methylpropargylamine (1.1 equiv. NaH, 5 mol% Pd(0) generated by reduction of $PdCl_2(PPh_3)_2$ with *n*-BuLi, THF-DMSO, room temperature). Following this procedure, we were pleased to obtain the expected 4-benzylpyrrolidine (**4a**) in 70% isolated yield with a diastereomeric ratio of 85:15 in favor of the *trans* isomer as determined by NMR experiments (NOESY) (Scheme 2, Eq. (1)). It deserves mention that the corresponding *cis* isomer can be selectively prepared in two steps upon hydrogenation of 4-benzylidenepyrrolidine (**5**) using Pd/C in ethyl acetate (the *trans* isomer was not detected in the ^1H NMR (300 MHz) spectra of the crude product) (Scheme 2, Eq. (2)). This observation demonstrates how by simply varying the nature of one of the building blocks (i.e., the amine) our multicomponent reaction may open access not only to different compounds but also, through hydrogenation, to different stereoisomers of a same compound.

The generality of the cyclization process was explored with various allylamines, alkenes, and organic halides (Table 1). The nicotine derivative **4b** was produced in 65% yield from the corresponding 2-pyridyl alkene (**2b**) with a diastereomeric ratio identical to that obtained for **4a** (Table 1, entry 2). In the other hand, reaction of triester **2d** led to the formation of proline ester derivative **4d** as a single *trans* diastereomer, as indicated by the ^1H NMR (300 MHz) spectra of the crude reaction product, albeit in a moderate 40% yield (Table 1, entry 4).

The participation of alkenes bearing activating groups other than esters was also investigated. For instance, α-sulfonyl ester (**2c**) led to the isolation of a mixture of three diastereomeric 3-sulfonylpyrrolines (**4c**) in 60% yield. The *trans* relationship at C-2 and C-3 in the two major isomers (phenyl group *anti* to the sulfonyl group) was deduced from NMR experiments and are consistent with our previous work on similar structures [8]. Again, 1,3-diastereoselectivity was in favor of the *trans* isomer (Table 1, entry 3). Unfortunately, the stereochemistry of the minor third isomer could not be assigned. We also found that a vinyl bromide or triflate could be used in place of the aryl iodides which opens access to 4-allylpyrrolidines (entries 5, 6). For instance, reaction of cyclohexenyl triflate (**3c**) with *N*-methylallylamine (**1a**), and dimethyl benzylidene malonate (**2a**) furnished 4-cyclohexenylpyrrolidine (**4f**), which was obtained as a single *trans* diastereomer (one diastereomer detected by 300 MHz ^1H NMR), in 90% isolated yield (Table 1, entry 6).

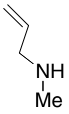
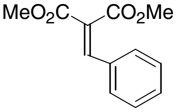
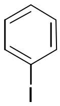
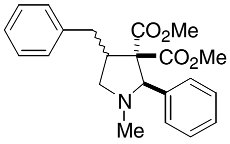
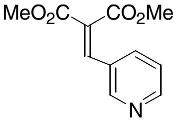
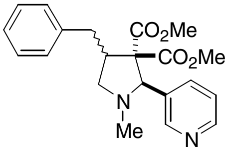
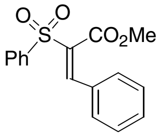
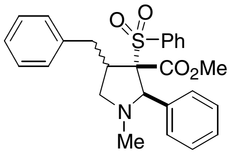
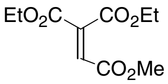
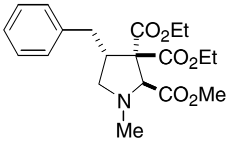
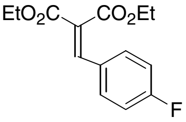
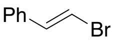
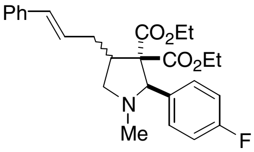
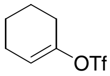
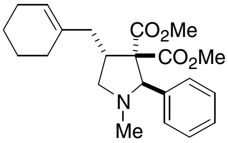
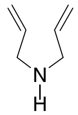
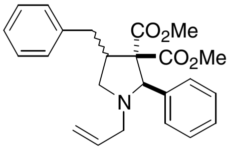
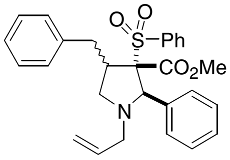
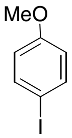
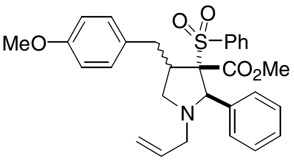
We next examined the use of commercially available diallylamine (**1b**) as nucleophilic partner as we anticipated that the corresponding *N*-allylpyrrolidines could then be deprotected to allowing further manipulations. We were pleased to find that, indeed, **1b** participated in the cyclization process with different conjugate acceptors and aryl iodides to yield the desired pyrrolidines with 1,3-diastereomeric ratios slightly in favor of the *trans* isomer (*trans*:*cis* = 55:45) (Table 1, entries 7–9).

In conclusion, we have shown that the sequential hetero-Michael conjugate addition/carbopalladation/reductive elimination process recently developed in our laboratories may also involve allylamines as nucleophilic partners which opens a new and straightforward



Scheme 2.

Table 1
Three-component synthesis of 4-benzyl pyrrolidines[a]

Entry	Allyl amine	Activated olefin	Halide (or triflate)	Product	Yield	d.r.[b] *trans/cis*
1	 **1a**	 **2a**	 **3a**	 **4a**	70%	85/15
2	**1a**	 **2b**	**3a**	 **4b**	65%	85/15
3	**1a**	 **2c**	**3a**	 **4c**	60%[c]	70/30
4	**1a**	 **2d**	**3a**	 **4d**	40%	>95/5
5	**1a**	 **2e**	 **3b**	 **4e**	66%	75/25
6	**1a**	**2a**	 **3c**	 **4f**	90%	>95/5
7	 **1b**	**2a**	**3a**	 **4g**	51%	55/45
8	**1b**	**2c**	**3a**	 **4h**	65%	55/45
9	**1b**	**2c**	 **3d**	 **4i**	40%	55/45

[a] All reactions were performed on a 1.05 mmol scale.
[b] 1,3-Diastereoselectivity.
[c] Contains approximately 10% of an uncharacterized third diastereomer.

acces to diversely functionalized 4-benzyl (and 4-allyl) pyrrolidines. In addition, this versatile and atom-economical method may allow to access different isomers of the latter compounds depending on the nature of the starting amine (allylic or propargylic). Further studies are in progress in our laboratories to explore the potential of these highly functionalized pyrrolidines as synthetic scaffolds for derivatization chemistry.

3. Experimental

3.1. General

Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere using standard syringe, cannula, and septa techniques. Commercially available reagents were used as purchased. THF and DMSO were distilled over calcium hydride. TLC was carried out on Merck silica 60/F-254 aluminium-backed plates. Flash chromatography was performed using Merck silica gel 60 (40–63 μm). Melting points were determined on a Büchi and are uncorrected. NMR spectra were recorded on a Brucker ALS 300 spectrometer in the solvent indicated. Chemical shifts δ are reported in ppm relative to the internal reference.

*3.2. General procedure for the preparation of the pyrrolidines **4***

3.2.1. Preparation of the Pd(0) catalyst

n-BuLi (2.0 M in hexanes, approx. 50 μl, 0.1 mmol) was added dropwise to a well stirred suspension of $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol) in DMSO (2.5 ml) until a dark red homogeneous solution was obtained.

3.2.2. Three-component reaction

The allylamine (1.05 mmol) was slowly added to a well stirred suspension of NaH (60% in mineral oil, 44 mg, 1.05 mmol) in THF (3 ml) and stirring was continued for 5 min. The activated alkene (1.05 mmol) was then added and the resulting enolate solution was stirred at room temperature for an additional 5 min. Meanwhile, the unsaturated iodide or triflate (1.07 mmol) was added to the freshly prepared palladium complex solution and this was subsequently transferred via cannula to the enolate solution. The resulting reaction mixture was stirred overnight at room temperature and then washed with $NaHCO_3$ (2 × 5 ml), brine (3 ml) and water (3 ml). The aqueous phases were extracted with CH_2Cl_2 (3 × 15 ml) and the combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was subjected to silica gel chromatography (ethyl acetate: petroleum ether) to afford the desired pyrrolidines.

*Dimethyl (±)-(2RS,4RS)-4-benzyl-1-methyl-2-phenylpyrrolidine-3,3-dicarboxylate (trans-**4a**)*: Colorless solid (m.p.: 73–74 °C). ^{1}H NMR (300 MHz, C_6D_6): δ 2.20 (s, 3H), 2.32 (t, $J = 12.8$ Hz, 1H), 2.45 (dd, $J = 8.8$, 10.7 Hz, 1H), 3.00 (s, 3H), 3.15 (dd, $J = 6.2$, 8.8 Hz, 1H), 3.36 (dd, $J = 3.8$, 12.8 Hz, 1H), 3.45 (s, 3H), 3.95 (m, 1H), 4.74 (s, 1H), 7.13–7.63 (m, 10H). ^{13}C NMR (75 MHz, C_6D_6): δ 37.1, 40.3, 46.4, 51.7, 51.9, 60.5, 69.7, 76.6, 126.7, 127.6, 128.0, 128.2, 128.3, 128.5, 129.0, 129.2, 129.4, 140.9, 170.0, 171.3. Anal. Calc. for $C_{18}H_{25}NO_4$ (319.40): C, 71.42; H, 6.87. Found: C, 71.71; H, 6.77%.

*Dimethyl (±)-(2RS,4SR)-4-benzyl-1-methyl-2-phenylpyrrolidine-3,3-dicarboxylate (cis-**4a**)*: Selected data deduced from a mixture of diastereomers: ^{1}H NMR (300 MHz, C_6D_6): δ 2.13 (s, 3H), 2.52 (t, $J = 9.3$ Hz, 1H), 2.84 (m, 1H), 3.13 (s, 3H), 3.46 (s, 3H), 3.47 (t, $J = 7.3$ Hz, 2H), 3.66 (dd, $J = 7.7$, 9.3 Hz, 1H), 4.50 (s, 1H), 7.13–7.94 (m, 10H). ^{13}C NMR (75 MHz, C_6D_6): δ 37.0, 40.8, 47.6, 51.3, 52.0, 59.2, 69.0, 76.0, 126.6, 126.7, 127.6, 127.9, 128.2, 128.5, 129.0, 129.2, 129.3, 129.5, 141.6, 167.9, 171.3.

*Dimethyl (±)-(2RS,4RS)-4-benzyl-1-methyl-2-pyridinepyrrolidine-3,3-dicarboxylate (trans-**4b**)*: Pale yellow solid (m.p.: 70–71 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.13 (t, $J = 12.6$ Hz, 1H), 2.20 (s, 3H), 2.33 (dd, $J = 9.2$, 10.8 Hz, 1H), 3.04–3.10 (m, 2H), 3.16 (s, 3H), 3.48–3.52 (m, 1H), 3.82 (s, 3H), 4.39 (s, 1H), 7.23–7.35 (m, 7H), 7.68 (d, $J = 7.9$ Hz, 1H), 8.53 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.5, 40.6, 45.9, 52.3, 52.8, 60.2, 69.3, 73.6, 126.8, 128.9, 129.0, 136.3, 140.1, 149.5, 150.9, 169.8, 171.0. CIMS: 369 (MH^+).

*Dimethyl (±)-(2RS,4SR)-4-benzyl-1-methyl-2-pyridinepyrrolidine-3,3-dicarboxylate (cis-**4b**)*: Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.16 (s, 3H), 2.60 (t, $J = 9.5$ Hz, 1H), 2.85–2.92 (m, 1H), 3.04 (t, $J = 12.5$ Hz, 1H), 3.13 (dd, $J = 3.8$, 12.5 Hz, 1H), 3.37 (s, 3H), 3.41 (dd, $J = 2.5$, 9.5 Hz, 1H), 3.80 (s, 3H), 4.22 (s, 1H), 7.18–7.85 (m, 6H), 7.86 (d, $J = 7.5$ Hz, 1H), 8.52 (s, 1H), 8.71 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.7, 41.2, 46.9, 52.1, 53.0, 59.2, 68.8, 74.0, 126.7, 129.0, 129.1, 137.0, 140.9, 149.3, 150.8, 168.0, 171.2.

*Methyl (±)-(2RS,3SR,4SR)3-benzenesulfonyl-4-benzyl-1-methyl-2-phenylpyrrolidine-3-carboxylate (trans-**4c**)*: Orange solid (m.p.: 144–145 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.23 (s, 3H), 3.01–3.09 (m, 1H), 3.12–3.16 (m, 1H), 3.14 (s, 3H), 3.35–3.52 (m, 2H), 3.73–3.81 (m, 1H), 4.17 (s, 1H), 7.06–8.15 (m, 10 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 34.4, 40.6, 50.1, 52.3, 58.8, 75.9, 86.9, 126.6, 128.4, 128.7, 129.4, 132.8, 134.5, 139.4, 139.7, 142.0, 167.0.

*Diethyl (±)-(2SR,4RS)-4-benzyl-2-methoxycarbonyl-1-methylpyrrolidine-3,3-dicarboxylate (trans-**4d**)*: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.22–1.32 (m, 6H), 2.15 (t, J = 12.7 Hz, 1H), 2.40 (dd, J = 8.9, 10.9 Hz, 1H), 2.44 (s, 3H), 2.94 (dd, J = 6.4, 8.9 Hz, 1H), 3.26 (dd, J = 3.4, 12.7 Hz, 1 H), 3.68 (s, 3H), 3.91 (s, 1H), 3.31–3.45 (m, 1H), 4.07–4.30 (m, 4H), 7.18–7.29 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.3, 14.6, 36.2, 41.6, 46.8, 52.5, 59.9, 62.0, 62.4, 65.8, 73.7, 126.7, 128,8, 129.0, 140.4, 169.2, 170.0. Anal. Calc. for $C_{20}H_{27}NO_6$ (377.43): C, 63.65; H, 7.21. Found: C, 63.70; H, 7.39%.

*Dimethyl (±)-(2RS,4RS)-2-(4-fluoro-phenyl)-1-methyl-4-(1-phenylpropen-1-yl)pyrrolidine-3,3-dicarboxylate (cis- and trans-**4e**)*: Inseparable mixture of diastereomers: Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74 (t, J = 7.2 Hz, 2.25H), 0.79 (t, J = 7.1 Hz, 0.75 H), 1.27 (t, J = 7.0 Hz, 3H), 2.15 (s, 3H), 2.53–2.60 (m, 1H), 2.70 (d, J = 9.2 Hz, 1H), 3.20–3.34 (m, 2H), 3.69–3.78 (m, 0.75 H), 3.80–3.86 (m, 0.25 H), 4.08–4.27 (m, 4H), 4.15 (s, 0.25 H), 4.21 (s, 0.75 H), 6.08–6.18 (m, 1H), 6.37 (d, J = 15.8 Hz, 0.75 H), 6.41 (d, J = 16.0 Hz, 0.25 H), 6.91 (t, J = 8.7 Hz, 2H), 7.16 (t, J = 7.0 Hz, 1H), 7.21–7.30 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 13.5, 14.1, 33.7, 34.1, 40.2, 40.8, 43.2, 44.6, 59.1, 60.4, 60.6, 61.0, 61.2, 61.3, 67.8, 68.6, 114.4 (2 CH, d, $^{2}J_{(C,F)} = 21$ Hz), 114.6 (2 CH, d, $^{2}J_{(C,F)} = 21$ Hz), 126.0–129.0, 130.2 (2 CH, d, $^{3}J_{(C,F)} = 8$ Hz), 130.4 (2 CH, d, $^{3}J_{(C,F)} = 8$ Hz), 131.3, 131.5, 133.7 (C, d, $^{4}J_{(C,F)} = 3$ Hz), 135.5 (C, d, $^{4}J_{(C,F)} = 3$ Hz), 137.3, 137.5, 162.3 (C, d, $^{1}J_{(C,F)} = 245$ Hz), 162.4 (C, d, $^{1}J_{(C,F)} = 245$ Hz), 167.3, 169.8, 170.2, 170.7.

*Dimethyl (±)-(2RS,4RS)-4-cyclohexenyl-1-methyl-2-phenylpyrrolidine-3,3-dicarboxylate (trans-**4f**)*: Colorless solid (m.p.: 75–76 °C).^{1}H NMR (300 MHz, $CDCl_3$): δ 1.56–1.65 (m, 5H), 1.86–1.93 (m, 1H), 2.00 (s, 2H), 2.15–2.29 (m, 2H), 2.22 (s, 3H), 3.03 (s, 3H), 3.25–3.30 (m, 1H), 3.35–3.48 (m, 1H), 3.74 (s, 3H), 4.26 (s, 1H), 5.47 (s, 1H), 7.19–7.32 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.2, 23.2, 25.4, 28.0, 38.8, 40.6, 41.9, 60.6, 76.2, 123.2, 127.7, 128.0, 128.6, 135.6, 139.8, 170.1, 171.1. Anal. Calc. for $C_{22}H_{29}NO_4$ (371.48): C, 71.13; H, 7.87. Found: C, 71.12; H, 7.87%.

*Dimethyl (±)-1-allyl-4-benzyl-2-phenylpyrrolidine-3,3-dicarboxylate (cis- and trans-**4g**)*: Inseparable mixture of diastereomers: colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.02 (t, J = 12.6 Hz, 0.55H), 2.20 (dd, J = 9.0, 10.9 Hz, 0.55H), 2.56 (t, J = 9.4 Hz, 0.45H), 2.60–2.68 (m, 0.90H), 2.75–2.81 (dd, J = 7.5, 13.6 Hz, 0.55H), 2.99 (s, 3H), 3.01–3.11 (m, 1H), 3.17 (s, 1.1H), 3.37–3.49 (m, 0.90H), 3.78 (s, 3H), 4.53 (s, 1H), 4.99–5.11 (m, 2H), 5.70–5.84 (m, 1H), 7.15–7.44 (m, 10 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.5, 46.1, 47.6, 52.6, 52.8, 56.6, 56.7, 68.5, 68.9, 73.4, 73.8, 117.3, 126.7, 128.0, 128.2, 128.9, 129.1, 129.3, 135.4, 136.0, 140.6, 168.2, 170.04, 171.5. Anal. Calc. for $C_{24}H_{27}NO_4$: C, 73.25; H, 6.92. Found: C, 73.43; H, 7.13%.

*Methyl (±)-(2RS,3SR,4SR)-1-Allyl-3-benzenesulfonyl-4-benzyl-2-phenylpyrrolidine-3-carboxylate (trans-**4h**)*: Brown solid (m.p.: 155–156 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.48 (dd, J = 2.3 Hz, J = 13.2 Hz, 1H), 2.68 (dd, J = 11.3, 13.2 Hz, 1H), 2.75 (dd, J = 7.9, 9.8 Hz, 1H), 3.00 (dd, J = 6.8, 14.0 Hz, 1H), 3.23 (s, 3H), 3.29–3.39 (m, 3H), 4.96 (s, 1H), 5.03–5.19 (m, 2H), 5.71–5.85 (m, 1H), 7.06 (d, J = 7.1 Hz, 1H), 7.21–7.30 (m, 7H), 7.41 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.5 Hz, 2H), 7.70 (t, J = 7.3 Hz, 1H), 8.22 (d, J = 7.3 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 36.5, 46.7, 51.6, 57.5, 66.0, 72.3, 86.9, 117.3, 126.6, 127.7, 127.8, 128.5, 128.7, 128.9, 131.7, 134.3, 135.5, 138.5, 138.8, 139.9, 166.2.

*Methyl (±)-(2RS,3SR,4RS)-1-Allyl-3-benzenesulfonyl-4-benzyl-2-phenylpyrrolidine-3-carboxylate carboxylate (cis-**4h**)*: Brown solid (m.p.: 131–132 °C).^{1}H NMR (300 MHz, $CDCl_3$): δ 2.85 (dd, J = 8.3, 13.5 Hz, 1H), 2.97 (t, J = 8.3 Hz, 1H), 3.04 (s, 3H), 3.08–3.15 (m, 2H), 3.29 (t, J = 12.4 Hz, 1H) 3.42 (dd, J = 2.8, 13.5 Hz, 1H), 3.62–3.70 (m, 1H), 4.32 (s, 1H), 4.97 (s, 1H), 5.01 (d, J = 5.2 Hz, 1H), 5.62–5.76 (m, 1H), 6.95–7.67 (m, 13H), 8.02 (d, J = 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 29.8, 34.17, 49.30, 52.0, 55.1, 55.6, 86.2, 126.2, 127.8, 128.0, 128.4, 128.6, 128.7, 128.8, 129.0, 132.4, 134.2, 134.7, 139.3, 141.6, 166.6.

*Methyl (±)-(2RS,3SR,4SR)-1-Allyl-3-benzenesulfonyl-4-(4-methoxy-benzyl)-2-phenylpyrrolidine-3-carboxylate (trans-**4i**)*: Colorless solid (m.p.: 153–154 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.40 (dd, J = 3.0, 13.6 Hz, 1H), 2.62 (dd, J = 11.3, 13.6 Hz, 1H), 2.89 (dd, J = 7.5, 9.8 Hz, 1H), 3.00 (dd, J = 6.6, 14.3, 1H), 3.23 (s, 3H), 3.29–3.43 (m, 3H), 3.79 (s, 3H), 4.98 (s, 1H), 5.11 (ddd, J = 1.5, 9.4, 17.3 Hz, 2H), 5.72–5.85 (m, 1H), 6.82 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 7.20–29 (m, 3 H), 7.43 (d, J = 7.2 Hz, 2H), 7.59 (t, J = 7.9 Hz, 2H), 7.67 (d, 1H), 8.22 (d, J = 8.3 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 35.6, 38.7, 46.9, 51.5, 55.3, 57.5, 72.2, 86.9, 114.0, 117.3, 127.6, 127.8, 128.4, 128.8, 129.6, 131.6, 131.9, 134.3, 135.5, 138.4, 139.2, 158.2, 166.2. CIRMS: 506 (MH^+), 366. HRCIMS: Calc. for $C_{29}H_{32}NO_5S$: 506.2001. Found: 506.2010.

*Methyl (±)-(2RS,3SR,4RS)-1-Allyl-3-benzenesulfonyl-4-(4-methoxybenzyl)-2-phenylpyrrolidine-3-carboxylate (cis-**4i**)*: Brown solid (m.p.: 131–132 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.91–2.99 (m, 1H), 3.05–3.22 (m, 3H), 3.14 (s, 3H), 3.29–3.48 (m, 2H), 3.68–3.76 (m, 1H), 3.84 (s, 3H), 4.42 (s, 1H), 5.07 (s, 1H), 5.12 (d, 1H), 5.73–5.87 (m, 1H), 6.61 (s, 2H), 6.89 (d, 2H), 7.04–7.12 (m, 3H), 7.28 (t, 3H), 7.65 (t, 2H), 7.78 (t, 1H), 8.12 (d, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 33.3, 49.6, 52.0, 55.2, 55.4, 55.6, 72.5, 86.2, 114.0, 117.7, 127.9, 128.0, 128.1, 128.4, 130.0, 132.5, 133.8, 134.2, 139.4, 158.1, 166.7.

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