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This is an **author produced version** of a paper published in:

Tetrahedron 74.29 (2018): 3947-3954

**DOI:** <https://doi.org/10.1016/j.tet.2018.05.076>

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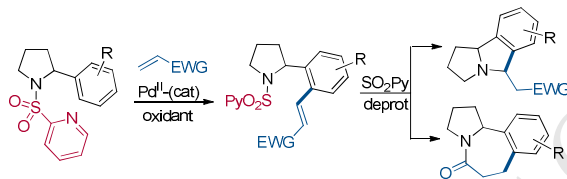
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## Graphical Abstract

**Palladium-catalyzed *ortho*-olefination of 2-arylpyrrolidines: a tool for increasing structural complexity in nitrogen heterocycles**

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Pablo D. Legarda, Alfonso García-Rubia, Ramón Gómez Arrayás\* and Juan C. Carretero\*  
Departamento de Química Orgánica, Facultad de Ciencias, UAM, Cantoblanco, 28049 Madrid, Spain





# Palladium-catalyzed *ortho*-olefination of 2-arylpiperidines: a tool for increasing structural complexity in nitrogen heterocycles<sup>†</sup>

Pablo D. Legarda<sup>a</sup>, Alfonso García-Rubia<sup>b</sup>, Ramón Gómez Arrayás<sup>a,c\*</sup> and Juan C. Carretero<sup>a,c\*</sup>

<sup>†</sup> In honor of Prof. Leon Ghosez for his deep and lifelong commitment with Tetrahedron.

<sup>a</sup> Departamento de Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Madrid (UAM), Cantoblanco, 28049 Madrid, Spain.

<sup>b</sup> Current address: Centro de Investigaciones Biológicas, Consejo Superior de Investigaciones Científicas (CSIC), Ramiro de Maeztu 9, 28040, Madrid, Spain.

<sup>c</sup> Institute for Advanced Research in Chemical Sciences (IAdChem) UAM, Madrid, Spain. E-mail: [ramon.gomez@uam.es](mailto:ramon.gomez@uam.es); [juancarlos.carretero@uam.es](mailto:juancarlos.carretero@uam.es)

## ARTICLE INFO

### Article history:

Received

Received in revised form

Accepted

Available online

### Keywords:

2-Phenylpiperidine

Palladium

Direct C–H alkenylation

2-Pyridylsulfonyl directing group

Benzopyrrolizidine

Benzazepine

## ABSTRACT

The dual role of the (2-pyridyl)sulfonyl unit as directing functionality and readily removable *N*-protecting group has enabled an efficient and practical transformation of 2-arylpiperidine derivatives into more complex tricyclic frameworks via palladium-catalyzed *ortho*-olefination with electron deficient alkenes and subsequent cyclization upon *N*-deprotection under mild conditions. The key cross coupling step in the presence of *N*-fluoro-2,4,6-trimethylpyridinium triflate ([F+]) as the terminal oxidant is both highly efficient and tolerant to a variety of steric and electronic changes at both coupling partners. By adequate choice of reductive conditions, the *N*-sulfonyl deprotection can be directed to the selective formation of benzo-fused pyrrolizidine or fused pyrrolidino-benzazepine frameworks.

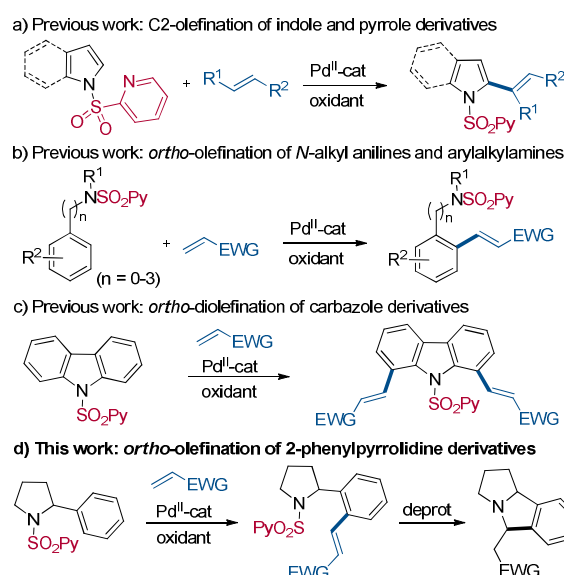
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## 1. Introduction

Nitrogen-containing heterocyclic compounds are privileged structures in terms of biological activity and continues to inspire the development of new methods for their synthesis and functionalization.<sup>1</sup> Introducing complexity and diversity on a core molecule is crucial for facilitating lead discovery and optimization in medicinal chemistry. Toward that goal, the metal catalyzed C–H alkenylation of nitrogen heterocycles has attracted much current interest as a unique tactic for rapidly increasing structural complexity due to the synthetic versatility of the newly incorporated alkenyl group.<sup>2,3</sup> Introducing a directing group on a N atom has become a commonly used strategy to ensure site-selectivity, thereby leading to great progress in this area.<sup>4</sup> However, to take full advantage of the synthetic potential of this strategy, directing groups must have the ability to be readily removed under conditions that are compatible with the presence of sensitive alkenyl groups. This is not always achievable and often removal of the *ortho*-directing group from the product requires prior derivatization of the newly incorporated alkene, which is a feat that often limits the transformation's synthetic utility. Additionally, controlling mono- vs. disubstitution selectivity is a continuing challenge in this type of processes.<sup>5</sup>

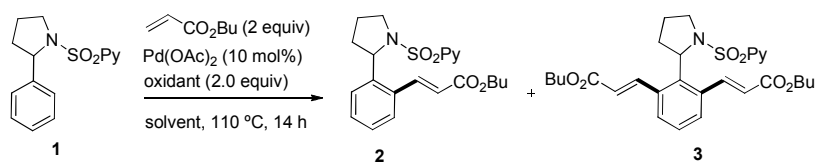
Our research group has pioneered the use of the (2-pyridyl)sulfonyl unit (SO<sub>2</sub>Py) as a weakly coordinating and readily removable directing group in metal-catalyzed C–H functionalization reactions.<sup>6</sup> The dual protecting and directing role of SO<sub>2</sub>Py in C–H functionalization was first demonstrated by

achieving an efficient and general Pd-catalyzed C2-alkenylation of indoles and pyrroles with both electron-poor and non-activated alkenes (Scheme 1a).<sup>6a,b</sup> This strategy has also been applied to the Pd-catalyzed *ortho*-C–H alkenylation of *N*-alkylated aniline, benzylamine, phenethylamine and  $\gamma$ -arylpropylamine derivatives with electron-poor alkenes (Scheme 1b).<sup>6c,j</sup> More recently, this concept was extended to the regiocontrolled direct Pd-catalyzed C1/C8-diolefination of carbazoles (Scheme 1c).<sup>6d</sup>



**Scheme 1.** *N*-SO<sub>2</sub>Py directing group in Pd-catalyzed direct C–H olefination of nitrogen heterocycles

**Table 1.** Optimization studies in the model olefination of substrate **1**<sup>a</sup>



Entry	Oxidant	Solvent	Conversion % <sup>b</sup>	2 / 3 <sup>b</sup>
1	[F <sup>+</sup> ] <sup>c</sup>	DCE	>97	92:8
2	PhI(OAc) <sub>2</sub>	DCE	67	>95:<5
3	K <sub>2</sub> S <sub>2</sub> O <sub>8</sub>	DCE	24	>95:<5
4	Oxone	DCE	11	>95:<5
5	Ce(SO <sub>4</sub> ) <sub>2</sub>	DCE	9	>95:<5
6	Cu(OAc) <sub>2</sub>	DCE	<3	–
7	[F <sup>+</sup> ] <sup>c</sup>	Toluene	45	>95:<5
8	[F <sup>+</sup> ] <sup>c</sup>	1,4-Dioxane	35	>95:<5
9	[F <sup>+</sup> ] <sup>c</sup>	DMSO	25	>95:<5
10	[F <sup>+</sup> ] <sup>c</sup>	DMF	76	>95:<5
11	[F <sup>+</sup> ] <sup>c</sup>	AcOH	90	90:10
12 <sup>d</sup>	[F <sup>+</sup> ] <sup>c</sup>	DCE	>97 (85) <sup>e</sup>	>95:<5
13 <sup>d,f</sup>	[F <sup>+</sup> ] <sup>c</sup>	DCE	70	>95:<5
14 <sup>d,g</sup>	[F <sup>+</sup> ] <sup>c</sup>	DCE	40	>95:<5

<sup>a</sup>Reaction conditions: **1** (0.15 mmol), butyl acrylate (0.30 mmol), Pd(OAc)<sub>2</sub> (0.015 mmol), oxidant (0.30 mmol), solvent (1.5 mL), 110 °C, 14 h under N<sub>2</sub>.

<sup>b</sup>Determined by <sup>1</sup>HNMR.

<sup>c</sup>[F<sup>+</sup>] = *N*-fluoro-2,4,6-trimethylpyridinium triflate.

<sup>d</sup>Reaction performed in the presence of 1.2 equiv (0.18 mmol) of butyl acrylate.

<sup>e</sup>Isolated yield of the mono-olefination product after chromatographic purification.

<sup>f</sup>In the presence of 5 mol% of Pd(OAc)<sub>2</sub>.

<sup>g</sup>In the presence of 2 mol% of Pd(OAc)<sub>2</sub>.

Driven by our continued interest in the development of practical methods based on catalytic C–H functionalization for the assembly of nitrogen-containing heterocyclic architectures from simple precursors, we envisioned that the 2-arylpyrrolidine unit<sup>7</sup> could provide an ideal platform for iterative *ortho*-selective C–H alkenylation and subsequent cyclization leading to more complex polycyclic ring systems such as benzo-fused pyrrolizidines (Scheme 1d). It is important to note that the benzopyrrolizidine motif forms the core of many natural products with pharmacological relevance.<sup>8,9</sup> In this pursuit, we describe herein an efficient method for the *ortho*-olefination of 2-aryl-*N*-(2-pyridyl)sulfonylpyrrolidines with electron-deficient alkenes and their derivatization into heterocyclic systems of increased complexity such as benzo-fused pyrrolizidines or pyrrolidino-benzazepines by appropriate choice of *N*-deprotection conditions.

## 2. Results and discussion

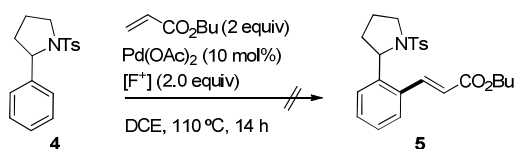
At the outset of our study, we studied the alkenylation of the *N*-SO<sub>2</sub>Py-protected parent 2-phenylpyrrolidine **1** with butyl acrylate, taking as the basis for reaction optimization the conditions previously established for the *ortho*-olefination of benzylamine derivatives.<sup>6c</sup> The results of this study are presented in Table 1. The reaction of **1** with butyl acrylate (2 equiv) in the presence of Pd(OAc)<sub>2</sub> (10 mol%) and *N*-fluoro-2,4,6-trimethylpyridinium triflate ([F<sup>+</sup>], 2 equiv) as oxidant in DCE at 110 °C for 14 hours led to the clean formation of the expected olefination product **2** with complete conversion and very good mono-/disubstitution selectivity (2/3 = 92:8, entry 1). The

superiority of [F<sup>+</sup>] as oxidant was demonstrated upon evaluation of a handful of oxidants of different oxidizing ability. PhI(OAc)<sub>2</sub> proved also to be an effective stoichiometric oxidant for this reaction, although incomplete conversion was observed (67%, entry 2). Other oxidants used in Pd-catalyzed C–H activation processes such as K<sub>2</sub>S<sub>2</sub>O<sub>8</sub>, Oxone or Ce(SO<sub>4</sub>)<sub>2</sub> provided unpractical conversions (9–24%, entries 3–5). No product was detected when the reaction was performed in the presence of Cu(OAc)<sub>2</sub>, a weaker oxidant widely used in Pd-catalyzed C–H olefinations that have been proposed to occur through catalytic cycles based on Pd<sup>II</sup>/Pd<sup>0</sup> redox shuttles (entry 6).<sup>3</sup> In contrast, the powerful oxidant [F<sup>+</sup>] has been used in Pd-catalyzed C–H transformations such as fluorination, trifluoromethylation, and aminations, for which a key stage of the proposed cycle is the oxidation of a Pd<sup>II</sup> intermediate into high-valent Pd<sup>III</sup> or Pd<sup>IV</sup> intermediates.<sup>10</sup>

A solvent screening revealed DCE as the most effective reaction media. Other aprotic solvents of varied polarity such as toluene, 1,4-dioxane or DMSO failed to provide a conversion beyond 45% (entries 7–9), whereas the use of DMF resulted in a boost in conversion up to 76% (entry 10). In accordance with the suggested important role of polar acidic solvents in the acceleration of cyclopalladation processes,<sup>11</sup> the model reaction of **1** with butyl acrylate in AcOH resulted in 90% conversion, albeit a slightly diminished mono-/di-substitution selectivity was observed (2/3 = 90:10, entry 11). The higher efficiency observed in the chlorinated solvent DCE can be plausibly ascribed to the presence of small amounts of HCl upon partial decomposition. Finally, we were glad to find that the di-*ortho*-olefination process

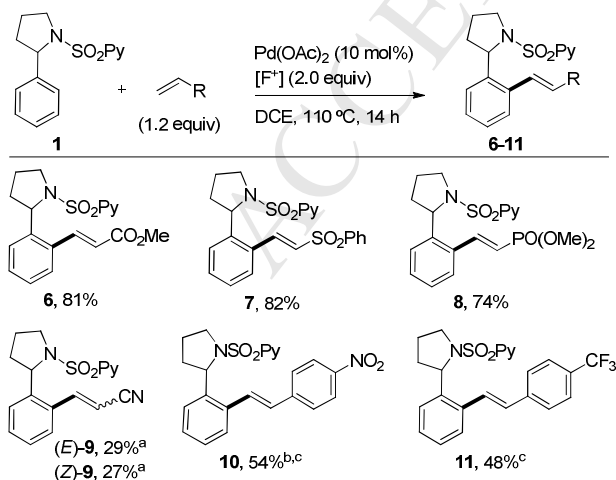
was almost completely suppressed by reducing the amount of alkene to 1.2 equiv without any appreciable impact in reactivity, thereby providing the desired monoalkenylation product **2** in 85% isolated yield (entry 12). In contrast, decreasing the palladium catalyst loading to 5 mol% and 2 mol% resulted in incomplete conversions (entries 13 and 14, respectively).

The unique directing role of the *N*-SO<sub>2</sub>Py unit was illustrated through a control experiment showing that no reaction was produced when the analogue *N*-tosylated 2-phenylpyrrolidine **4** was submitted to the reaction with butyl acrylate under otherwise identical reaction conditions, resulting in the exclusive recovery of starting material (Scheme 2).



**Scheme 2.** Control experiment with *N*-Ts substrate **4**. [F<sup>+</sup>] = *N*-fluoro-2,4,6-trimethylpyridinium triflate.

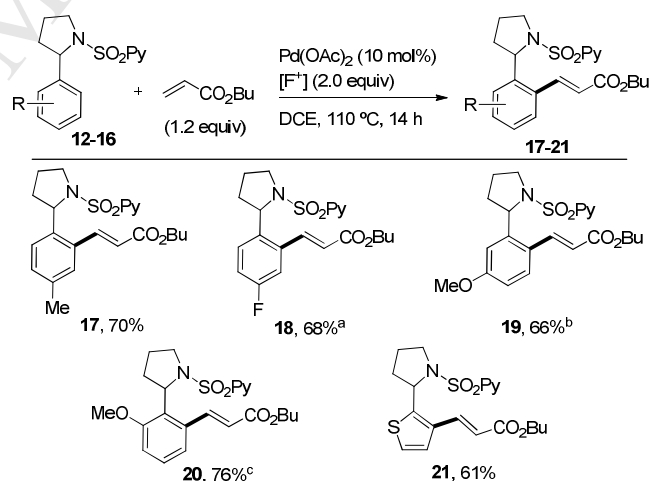
With an efficient and selective *ortho*-alkenylation protocol in hand, we next set out to investigate the scope of alkenylation of substrate **1** with various electron-deficient alkenes (Scheme 3). Not only acrylates, but also phenyl vinyl sulfone and dimethyl vinyl phosphonate, coupled efficiently with **1** to give the corresponding *ortho*-alkenylation products with excellent monosubstitution selectivity, and *E*-stereocontrol in synthetically useful yields (products **6–8**, 74–81%). Even acrylonitrile, having a potentially metal-coordinating nitrogen was also compatible with this catalytic system, providing the alkenylation product **9** as a 62:38 mixture of *E* and *Z* stereoisomers, respectively. Upon standard chromatographic separation, *E*-**9** and *Z*-**9** were isolated in 29% and 27% yield, respectively.<sup>12</sup> Unfortunately, no reaction was observed with 1,1- or 1,2-disubstituted alkenes such as  $\alpha$ -ethylacrolein or (*E*)-methyl crotonate, showing the sensitivity of the alkenylation reaction to steric effects. Styrene derivatives bearing electron-withdrawing substituents such as *p*-NO<sub>2</sub> or *p*-CF<sub>3</sub> were also suitable substrates in this olefination reaction, although an excess of 2 equivalents of the alkene was required to afford the desired products **10** and **11** (54% and 48%, respectively). The increased reactivity produced by the excess of alkene came at the cost of lower mono-/disubstitution selectivity in the case of product **10** (mono-/di- = 90:10).



**Scheme 3.** Scope with regard to the olefin coupling partner. Isolated yields of the mono-olefination product after chromatographic purification. <sup>a</sup>*E/Z* = 62:38. <sup>b</sup>Mono-/di- = 90:10.

<sup>c</sup>Reaction performed with 2 equivalents of alkene. [F<sup>+</sup>] = *N*-fluoro-2,4,6-trimethylpyridinium triflate.

The versatility with regard to the substitution at the 2-arylpyrrolidine component was also examined using butyl acrylate as the model alkene (Scheme 4). This scope study revealed that although both electron-withdrawing and electron-donating substituents are tolerated at the aromatic ring of the 2-arylpyrrolidine unit, both electronic and steric effects influenced the reactivity. For example, although similar good yields could be attained in the alkenylation of substrates holding either a *p*-Me (product **17**, 70%) or an electron-withdrawing *p*-F group (**18**, 68%), the need for an excess of 2.0 equivalents of alkene evidenced the lower reactivity of the latter. When a *meta*-methoxy substituent is present, a strong preference for alkenylation at the more sterically accessible *ortho* C–H bond was observed (**19**, 66%), although traces of the di-olefination product were also detected in the reaction mixture (mono-/di- = 95:5). Importantly, this alkenylation method seems to be not very sensitive to steric hindrance imposed by aryl *ortho*-substitution, as illustrated in smooth reaction observed in the case of the *ortho*-methoxy derivative, yet 2.0 equivalents of butyl acrylate were needed for achieving complete conversion (**20**, 76%). Also, the reactions did occur at the C–H bond of a heteroaryl substituent such as the 2-thienyl group (**21**, 61%), thus showing the compatibility with potentially coordinating heteroatoms that could bind the palladium species preventing successive turnovers. It is also noteworthy the capacity of the *N*-SO<sub>2</sub>Py directing group to promote the C–H alkenylation with complete site-selectivity control at C3,<sup>13</sup> thus overriding the intrinsic preference of the thiophene ring system for metalation and subsequent C–H functionalization at the C5 position.<sup>14</sup>

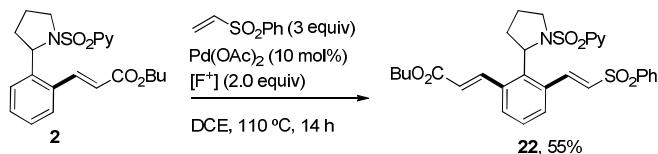


**Scheme 4.** Scope with regard to the substitution at the 2-arylpyrrolidine component. Yields are isolated yields of the mono-olefination product after chromatographic purification. <sup>a</sup>Reaction performed with 1.5 equiv of alkene. <sup>b</sup>Mono-/di- = 95:5. <sup>c</sup>Reaction performed with 2.0 equivalents of alkene. [F<sup>+</sup>] = *N*-fluoro-2,4,6-trimethylpyridinium triflate.

Encouraged by the high reactivity and the good tolerance of this catalyst system toward the steric demand of *ortho*-substituents, we wondered whether it might enable the installation of two different alkenes at the two *ortho* positions of the arene by sequential double C–H alkenylation reactions. It is important to note that few protocols have demonstrated capability for efficient twofold C–H activation of this type.<sup>15</sup> To test this hypothesis, we submitted the monoolefination product **2** to the reaction with phenyl vinyl sulfone under the standard conditions

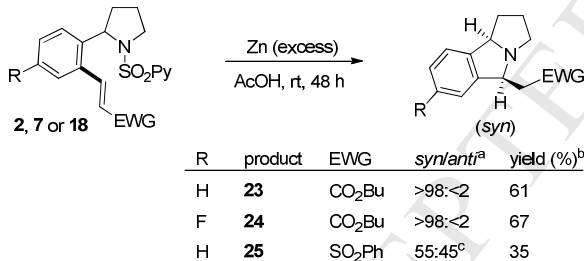


for the present method. Although the reaction required 3 equivalents of the alkene to reach full conversion,<sup>16</sup> the desired unsymmetrical diolefinated product **22** could be isolated in useful yield (55%, Scheme 5). However, while feasible, this sequential bis-olefination approach was not generally applicable as the reaction of **2** with dimethyl vinyl phosphonate failed (not shown).



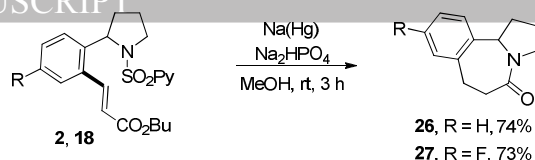
**Scheme 5.** Synthesis of the unsymmetrical bis-alkenylated product **22**.

To fully realize the synthetic potential of this C–H olefination method, we took advantage of the easy reductive removal of the *N*-SO<sub>2</sub>Py protecting/directing group under smooth conditions (Zn powder, AcOH, rt) without affecting the alkene moiety.<sup>6</sup> These conditions enabled the direct access to valuable benzopyrrolizidine derivatives, as illustrated in Scheme 6. For example, *N*-sulfonyl cleavage in compounds **2** and **18**, both with an embedded butyl acrylate moiety, triggered in situ the cyclization of the resulting free amine via intramolecular aza-Michael reaction to afford **23** and **24** in 61% and 67% yield, respectively, and complete diastereocontrol (*syn/anti* = >98:<2).<sup>17</sup> In contrast, when compound **7**, holding a vinyl sulfone as the Michael acceptor, was used as the starting material, the formation of a second isomer could be detected (*syn/anti* = 55:45). Despite the minor isomer was tentatively assigned to *anti*-**25** on the basis of the close similarity of its <sup>1</sup>H NMR spectrum with that of *syn*-**25**, all attempts at isolating this product were not successful. Indeed, conventional chromatographic purification allowed the isolation of only *syn*-**25** in a 35% isolated yield.



**Scheme 6.** *N*-Deprotection/cyclization to afford benzopyrrolizidines. <sup>a</sup>Diastereomeric ratio measured by <sup>1</sup>H NMR. <sup>b</sup>Isolated yields of *syn*-diastereomer after conventional chromatography. <sup>c</sup>Only *syn*-**25** could be isolated upon chromatographic purification.

Interestingly, when a stronger reducing agent such as sodium amalgam [Na(Hg)] was used for the *N*-desulfonylation reaction, the desired deprotection was accompanied by concomitant conjugate reduction of the acrylate moiety, which in turn triggered a spontaneous intramolecular amidation with formation of a seven-membered lactam. As shown in Scheme 7, the corresponding fused pyrrolidino-benzazepinone frameworks were obtained in good yields (products **26** and **27**, 74% and 73%, yield, respectively).



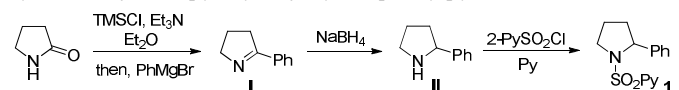
**Scheme 7.** *N*-Deprotection/cyclization to afford pyrrolidino-benzazepinones.

In conclusion, we have demonstrated the ability of the *N*-SO<sub>2</sub>Py group to serve as an efficient directing and readily removable protecting group for the Pd<sup>II</sup>-catalyzed regiocontrolled *ortho*-olefination of 2-arylpyrrolidine derivatives with activated alkenes. This method features high mono-substitution selectivity and good structural versatility in both alkene and pyrrolidine components, providing the olefination products in synthetically useful yields. Two complementary *N*-deprotection protocols enables the access to nitrogen heterocyclic systems of increased structural complexity that are relevant to medicinal chemistry such as benzopyrrolizidines or fused pyrrolidino-benzazepinone motifs.

### 3. Experimental section

**3.1. General Methods.** All general reagents were obtained from usual commercial sources and were used, except when noted, without further purification. All reactions were carried out in anhydrous solvents and under inert atmosphere, unless otherwise noted. Column chromatographies were performed on silica gel (230–400 mesh ASTM). TLC analysis was performed on 0.2 mm aluminium based plates (60 230–400 mesh). <sup>1</sup>H, <sup>13</sup>C{<sup>1</sup>H}NMR and bidimensional spectra were recorded in CDCl<sub>3</sub> solutions at 25 °C on AV-300, AVII-300 y AVIII-HD-300 (300 and 75 MHz, respectively) or DRX-500 (500 y 125 MHz, respectively) spectrometers (δ, ppm; *J*, Hz), and referenced using the solvent signal as internal standard. HRMS electron ionization (EI<sup>+</sup>) and electrospray ionization (ESI<sup>+</sup>) mass spectra were recorded using a MicroToF Q, API-QToF ESI with a mass range from 20 to 3000 *m/z* and mass resolution 15000 (FWHM). Melting points were determined in open-end capillary tubes.

#### 3.2. Typical procedure for the synthesis of starting materials: Synthesis of *N*-(2-pyridylsulfonyl)-2-phenylpyrrolidine<sup>18</sup> (**I**)



A flask equipped with a frit with Schlenk valves and sealed with a two-necked dummy flask on the other end was charged with pyrrolidin-2-one (2.0 g, 24 mmol), diethyl ether (50 ml) and triethylamine (3.5 mL, 25 mmol, 1.05 equiv). The mixture was cooled to 0 °C before chlorotrimethylsilane (3.2 mL, 25 mmol, 1.05 equiv) was added slowly. Once the addition was completed, the mixture was stirred under reflux for 30 min, then cooled to room temperature and the resulting Et<sub>3</sub>NHCl filtered off under argon through the glass frit into the round-bottomed flask. To the filtrate was slowly added under argon a 3 M solution of phenylmagnesium bromide in THF (8 mL, 24 mmol, 1.0 equiv) and the resulting mixture was stirred under reflux for further 3 h. The mixture was allowed to cool to room temperature before it was quenched with 1 M HCl aq. solution (10 mL). The aqueous phase was separated, basified to pH 10 with 2 M NaOH solution and extracted with EtOAc (3 x 20 mL). The combined organic phase was washed with brine (10 mL), then dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated in vacuo to give **I** as a colorless oil, which was used without further purification.

To a solution of the crude **I** in MeOH/H<sub>2</sub>O (4:1, 25 mL) was added NaBH<sub>4</sub> (980 mg, 26 mmol, 1.1 equiv). The mixture was stirred at room temperature overnight before it was acidified to pH 1-3 with a 2 M HCl aq. solution and maintained at this pH for 30 min. Then, the mixture was basified to pH 13-14 with 2 M NaOH solution and it was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 30 mL). The combined organic phase was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in vacuo to give **II** as a colorless oil, which was used without further purification.

To a solution of the crude 2-phenylpyrrolidine and pyridine (2.9 mL, 36 mmol, 1.5 equiv) in THF (50 mL), cooled to 0 °C and under Ar, was added slowly 2-pyridylsulfonyl chloride (6.4 g, 36 mmol, 1.5 equiv).<sup>19</sup> The resulting solution was allowed to reach room temperature and stirred at room temperature overnight. The mixture was quenched with a sat aq. NH<sub>4</sub>Cl solution (40 mL) and extracted with EtOAc (3 x 50 mL). The combined organic phase was dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane-EtOAc 4:1) to afford *N*-(2-pyridylsulfonyl)-2-phenylpyrrolidine **1** as a white solid; yield: 1.44 g (21%); mp: 101-103 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.69 (d, *J* = 4.6 Hz, 1H), 7.85 – 7.74 (m, 2H), 7.48 – 7.41 (m, 1H), 7.30 – 7.13 (m, 5H), 5.14 (dd, *J* = 7.8, 3.3 Hz, 1H), 3.83 – 3.64 (m, 2H), 2.31 – 2.15 (m, 1H), 2.00 – 1.74 (m, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 149.9, 143.0, 137.6, 128.2, 126.9, 126.4, 126.3, 126.1, 122.9, 63.9, 50.0, 35.8, 24.2. ESI<sup>+</sup> calcd. for C<sub>15</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 289.1005. Found: 289.1011.

*2-[[2-(*p*-Tolyl)pyrrolidin-1-yl]sulfonyl]pyridine (12)* Following the typical procedure, the *N*-silylation of 2-pyrrolidinone (2.0 g, 24 mmol), with Et<sub>3</sub>N (3.5 mL, 25 mmol, 1.05 equiv) and TMSCl (3.2 mL, 25 mmol, 1.05 equiv), followed by addition of *p*-tolylmagnesium bromide (24 mL, 24 mmol, 1.0 equiv) and reduction with NaBH<sub>4</sub> (980 mg, 26 mmol, 1.1 equiv), afforded 2-(*p*-tolyl)pyrrolidine as a yellow oil. Subsequent *N*-sulfonylation with pyridine (2.9 mL, 36 mmol, 1.5 equiv) and 2-pyridylsulfonyl chloride (6.4 g, 36 mmol, 1.5 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the product **12** (1.6 g, 22%) as a white solid; mp: 96-99 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.70 (d, *J* = 4.6 Hz, 1H), 7.88 – 7.76 (m, 2H), 7.51 – 7.39 (m, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 7.9 Hz, 2H), 5.10 (dd, *J* = 7.6, 3.2 Hz, 1H), 3.85 – 3.64 (m, 2H), 2.30 (s, 3H), 2.26 – 2.10 (m, 1H), 1.97 – 1.71 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.6, 149.9, 140.0, 137.5, 136.5, 128.9, 126.3, 126.1, 123.0, 63.8, 50.0, 35.8, 24.2, 21.0. ESI<sup>+</sup> calcd. for C<sub>16</sub>H<sub>19</sub>N<sub>2</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 303.1162. Found: 303.1168.

*2-[[2-(4-Fluorophenyl)pyrrolidin-1-yl]sulfonyl]pyridine (13)* Following the typical procedure, the *N*-silylation of 2-pyrrolidinone (2.0 g, 24 mmol) with Et<sub>3</sub>N (3.5 mL, 25 mmol, 1.05 equiv) and TMSCl (3.2 mL, 25 mmol, 1.05 equiv), followed by addition of 4-fluorophenylmagnesium bromide (24 mL, 24 mmol, 1.0 equiv) and reduction with NaBH<sub>4</sub> (980 mg, 26 mmol, 1.1 equiv), afforded 2-(4-fluorophenyl)pyrrolidine as a yellow oil. Subsequent *N*-sulfonylation with pyridine (2.9 mL, 36 mmol, 1.5 equiv) and 2-pyridylsulfonyl chloride (6.4 g, 36 mmol, 1.5 equiv) afforded after column chromatography (cyclohexane-EtOAc 4:1) the product **13** (1.3 g, 18%) as a light pink solid; mp: 91-92 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.70 (d, *J* = 4.6 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.47 (dd, *J* = 8.6, 4.8 Hz, 1H), 7.26 (t, *J* = 6.9 Hz, 2H), 6.95 (t, *J* = 8.7 Hz, 2H), 5.15 (dd, *J* = 7.9, 3.3 Hz, 1H), 3.80 – 3.62 (m, 2H), 2.30 – 2.16 (m, 1H), 1.98 – 1.78 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 161.7 (d, *J*<sub>C-F</sub> = 244.9 Hz), 157.2, 149.9, 138.8 (d, *J*<sub>C-F</sub> = 2.9 Hz), 137.6, 127.6 (d, *J*<sub>C-F</sub> = 8.1 Hz), 126.4, 122.9, 114.9 (d, *J*<sub>C-F</sub> = 21.5 Hz), 63.3, 49.9, 35.7, 24.0. ESI<sup>+</sup> calcd. for C<sub>15</sub>H<sub>16</sub>FN<sub>2</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 307.0911. Found: 307.0917.

#### *2-[[2-(3-Methoxyphenyl)pyrrolidin-1-yl]sulfonyl]pyridine (14)*

Following the typical procedure, the *N*-silylation of 2-pyrrolidinone (2.0 g, 24 mmol) with Et<sub>3</sub>N (3.5 mL, 25 mmol, 1.05 equiv) and TMSCl (3.2 mL, 25 mmol, 1.05 equiv), followed by addition of 3-methoxyphenylmagnesium bromide (24 mL, 24 mmol, 1.0 equiv) and reduction with NaBH<sub>4</sub> (980 mg, 26 mmol, 1.1 equiv), afforded 2-(3-methoxyphenyl)pyrrolidine as an orange oil. Subsequent *N*-sulfonylation with pyridine (2.9 mL, 36 mmol, 1.5 equiv) and 2-pyridylsulfonyl chloride (6.4 g, 36 mmol, 1.5 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the product **14** (1.45 g, 19%); as a white solid; mp: 107-110 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.73 (d, *J* = 4.5 Hz, 1H), 7.95 – 7.79 (m, 2H), 7.53 – 7.44 (m, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.24 – 7.16 (m, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 5.34 (dd, *J* = 7.9, 2.2 Hz, 1H), 3.78 (s, 3H), 3.86 – 3.62 (m, 2H), 2.26 – 2.06 (m, 1H), 1.93 – 1.73 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.5, 155.7, 149.9, 137.5, 131.2, 127.9, 127.2, 126.3, 123.0, 120.2, 110.1, 59.7, 55.1, 50.0, 33.9, 24.0. ESI<sup>+</sup> calcd. for C<sub>16</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub>S (M+H)<sup>+</sup>: 319.1111. Found: 319.1116.

#### *2-[[2-(2-Methoxyphenyl)pyrrolidin-1-yl]sulfonyl]pyridine (15)*

Following the typical procedure, the *N*-silylation of 2-pyrrolidinone (2.0 g, 24 mmol) with Et<sub>3</sub>N (3.5 mL, 25 mmol, 1.05 equiv) and TMSCl (3.2 mL, 25 mmol, 1.05 equiv), followed by addition of 2-methoxyphenylmagnesium bromide (24 mL, 24 mmol, 1.0 equiv) and reduction with NaBH<sub>4</sub> (980 mg, 26 mmol, 1.1 equiv), afforded 2-(2-methoxyphenyl)pyrrolidine as a yellow oil. Subsequent *N*-sulfonylation with pyridine (2.9 mL, 36 mmol, 1.5 equiv) and 2-pyridylsulfonyl chloride (6.4 g, 36 mmol, 1.5 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the product **15** (1.3 g, 17%) as a white solid; mp: 112-115 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.69 (d, *J* = 4.4 Hz, 1H), 7.86 – 7.74 (m, 2H), 7.49 – 7.41 (m, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.84 (dd, *J* = 10.5, 4.8 Hz, 2H), 6.73 (dd, *J* = 8.1, 2.3 Hz, 1H), 5.13 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.76 (s, 3H), 3.84 – 3.60 (m, 2H), 2.29 – 2.11 (m, 1H), 1.97 – 1.73 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 159.5, 157.4, 149.8, 144.7, 137.5, 129.2, 126.3, 122.9, 118.4, 112.2, 111.8, 63.8, 55.1, 49.9, 35.6, 24.1. ESI<sup>+</sup> calcd. for C<sub>16</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub>S (M+H)<sup>+</sup>: 319.1111. Found: 319.1116.

#### *2-[[2-(Thiophen-2-yl)pyrrolidin-1-yl]sulfonyl]pyridine (16)*

Following the typical procedure, the *N*-silylation of 2-pyrrolidinone (2.0 g, 24 mmol) with Et<sub>3</sub>N (3.5 mL, 25 mmol, 1.05 equiv) and TMSCl (3.2 mL, 25 mmol, 1.05 equiv), followed by addition of 2-thienylmagnesium bromide (24 mL, 24 mmol, 1.0 equiv) and reduction with NaBH<sub>4</sub> (980 mg, 26 mmol, 1.1 equiv), afforded 2-(2-thiophenyl)pyrrolidine as a yellow oil. Subsequent *N*-sulfonylation with pyridine (2.9 mL, 36 mmol, 1.5 equiv) and 2-pyridylsulfonyl chloride (6.4 g, 36 mmol, 1.5 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the product **16** (1.68 g 17%) as a white solid; mp: 83-85 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.68 (d, *J* = 4.5 Hz, 1H), 7.91 – 7.76 (m, 2H), 7.49 – 7.40 (m, 1H), 7.12 (d, *J* = 4.9 Hz, 1H), 6.97 (d, *J* = 3.1 Hz, 1H), 6.88 (dd, *J* = 4.9, 3.8 Hz, 1H), 5.47 (dd, *J* = 7.4, 1.9 Hz, 1H), 3.81 – 3.67 (m, 1H), 3.66 – 3.51 (m, 1H), 2.29 – 2.12 (m, 1H), 2.12 – 1.97 (m, 2H), 1.97 – 1.83 (m, 1H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.2, 149.8, 146.9, 137.6, 126.5, 126.4, 124.4, 124.2, 122.8, 59.9, 49.1, 35.3, 24.3. ESI<sup>+</sup> calcd. for C<sub>13</sub>H<sub>15</sub>N<sub>2</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 295.0569. Found: 295.0575.

**3.3. Typical procedure for the C–H alkenylation reaction: Synthesis of (*E*)-butyl 3-[[2-[[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]phenyl]acrylate (2)** A screw-capped test tube was charged with 2-arylpyrrolidine **1** (0.15 mmol), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv). The mixture was placed under nitrogen atmosphere before DCE (1.5 mL) and the corresponding

alkene (0.15 to 0.45 mmol, 1.0 to 3.0 equiv) were successively added. The mixture was heated to 110 °C for 16 h, and then it was allowed to reach room temperature, diluted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL) and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (cyclohexane-EtOAc 6:1) to afford **2** (53 mg, 85%) as a yellow oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.75 (d, *J* = 4.6 Hz, 1H), 8.00 (d, *J* = 15.7 Hz, 1H), 7.94 – 7.82 (m, 2H), 7.61 – 7.46 (m, 3H), 7.35 (t, *J* = 7.1 Hz), 7.29 – 7.16 (m, 2H), 6.34 (d, *J* = 15.7 Hz, 1H), 5.48 (dd, *J* = 8.0, 3.7 Hz, 1H), 4.21 (t, *J* = 6.6 Hz, 2H), 3.89 – 3.67 (m, 2H), 2.35 – 2.19 (m, 1H), 1.95 – 1.63 (m, 6H), 1.53 – 1.37 (m, 3H), 0.97 (t, *J* = 7.3 Hz, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.9, 157.2, 150.1, 142.2, 141.5, 137.7, 131.5, 130.0, 127.3, 126.8, 126.7, 126.6, 123.0, 120.3, 64.4, 61.3, 50.2, 35.7, 30.7, 24.0, 19.2, 13.7. ESI<sup>+</sup> calcd. for C<sub>22</sub>H<sub>27</sub>N<sub>2</sub>O<sub>4</sub>S (M+H)<sup>+</sup>: 415.1686. Found: 415.1689.

(*E*)-Methyl-3-*[(1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl)phenyl]acrylate* (**6**) Following the typical procedure, the reaction of **1** (43 mg, 0.15 mmol) with methyl acrylate (16 μL, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **6** (45 mg, 81 %) as a white solid; mp: 129–131 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.70 – 8.65 (m, 1H), 7.94 (d, *J* = 15.7 Hz, 1H), 7.86 – 7.74 (m, 2H), 7.50 – 7.37 (m, 3H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.21 – 7.11 (m, 1H), 6.26 (d, *J* = 15.7 Hz, 1H), 5.39 (dd, *J* = 7.9, 3.9 Hz, 1H), 3.73 (s, 3H), 3.80 – 3.58 (m, 2H), 2.29 – 2.13 (m, 1H), 1.89 – 1.40 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 167.2, 157.2, 150.1, 142.3, 141.8, 137.74, 131.5, 130.0, 127.3, 126.8, 126.7, 126.6, 123.0, 119.9, 61.2, 51.7, 50.2, 35.7, 24.1. ESI<sup>+</sup> calcd. for C<sub>19</sub>H<sub>21</sub>N<sub>2</sub>O<sub>4</sub>S (M+H)<sup>+</sup>: 373.1217. Found: 373.1223.

(*E*)-2-*[[2-(2-(4-(Phenylsulfonyl)vinyl)phenyl)pyrrolidin-1-yl]sulfonyl]pyridine* (**7**) Following the typical procedure, the reaction of **1** (43 mg, 0.15 mmol) with phenyl vinyl sulfone (30 mg, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 2:1), the compound **7** (56 mg, 82 %); as a white solid; mp: 149–151 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.82 (d, *J* = 4.3 Hz, 1H), 8.10 (d, *J* = 15.1 Hz, 1H), 8.05 – 7.87 (m, 4H), 7.67 – 7.50 (m, 5H), 7.43 – 7.35 (m, 2H), 7.31 – 7.20 (m, 1H), 6.77 (d, *J* = 15.1 Hz, 1H), 5.50 (dd, *J* = 7.9, 4.2 Hz, 1H), 3.85 – 3.65 (m, 2H), 2.43 – 2.26 (m, 1H), 1.96 – 1.75 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 156.9, 150.3, 142.9, 140.5, 139.7, 137.9, 133.4, 130.9, 129.6, 129.3, 129.1, 127.6, 127.5, 127.2, 127.1, 126.7, 123.1, 61.3, 50.2, 35.9, 24.2. ESI<sup>+</sup> calcd. for C<sub>23</sub>H<sub>23</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub> (M+H)<sup>+</sup>: 455.1094. Found: 455.1099.

(*E*)-Dimethyl-*[(1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl)styryl]phosphonate* (**8**) Following the typical procedure, the reaction of **1** (43 mg, 0.15 mmol) with dimethyl vinylphosphonate (22 μL, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (CH<sub>2</sub>Cl<sub>2</sub>-EtOAc 2:1), the compound **8** (47 mg, 74 %) as a light yellow solid; mp: 149–151 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.75 (d, *J* = 4.7 Hz, 1H), 8.02 – 7.72 (m, 3H), 7.60 – 7.44 (m, 3H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.19 (m, 1H), 6.14 (dd, *J*<sub>H-P</sub> = 18.8 Hz, *J* = 17.3 Hz, 1H), 5.47 (dd, *J* = 8.1, 4.1 Hz, 1H), 3.77 (d, *J*<sub>H-P</sub> = 11.1 Hz, 3H), 3.76 (d, *J*<sub>H-P</sub> = 11.1 Hz, 3H), 3.81 – 3.65 (m, 2H), 2.37 – 2.22 (m, 1H), 1.94 – 1.68 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.0, 150.1, 146.8 (d, *J*<sub>C-P</sub> = 7.2 Hz), 141.9, 137.8, 132.3, 132.0, 132.1 (d, *J*<sub>C-P</sub> = 22.9 Hz), 130.1, 127.3, 126.7

(d, *J*<sub>C-P</sub> = 1.1 Hz), 126.6, 126.6 (d, *J*<sub>C-P</sub> = 1.6 Hz), 123.0, 114.9 (d, *J*<sub>C-P</sub> = 190.7 Hz), 61.1, 52.5 (d, *J*<sub>C-P</sub> = 8.3 Hz), 52.4 (d, *J*<sub>C-P</sub> = 8.4 Hz), 35.6, 24.1. ESI<sup>+</sup> calcd. for C<sub>19</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub>PS (M+H)<sup>+</sup>: 407.1189. Found: 407.1194.

(*E*)- and (*Z*)-3-*[(1-(Pyridin-2-ylsulfonyl)pyrrolidin-2-yl)phenyl]acrylonitrile* [(*E*)-**9** and (*Z*)-**9**]

Following the typical procedure, the reaction of **1** (43 mg, 0.15 mmol) with acrylonitrile (15 μL, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded a mixture of compounds (*E*)-**9** and (*Z*)-**9**. The column chromatography purification (cyclohexane-EtOAc 6:1) afforded (*E*)-**9** (29%) followed by (*Z*)-**9** (27%). Compound (*E*)-**9**: white solid; mp: 131–132 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.84 – 8.74 (m, 1H), 7.97 – 7.86 (m, 2H), 7.80 (d, *J* = 16.4 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.53 (ddd, *J* = 6.1, 4.7, 2.9 Hz, 1H), 7.48 – 7.37 (m, 2H), 7.31 – 7.23 (m, 1H), 5.80 (d, *J* = 16.4 Hz, 1H), 5.48 (dd, *J* = 8.0, 4.1 Hz, 1H), 3.87 – 3.70 (m, 1H), 3.63 (dt, *J* = 10.0, 7.3 Hz, 1H), 2.38 – 2.23 (m, 1H), 1.98 – 1.66 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.1, 150.1, 148.0, 142.2, 137.8, 131.0, 130.7, 127.6, 126.9, 126.8, 126.0, 123.1, 118.2, 98.3, 61.1, 50.1, 35.7, 24.1. ESI<sup>+</sup> calcd. for C<sub>18</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 340.1114. Found: 340.1104. Compound (*Z*)-**9**: white solid; mp: 123–124 °C. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.71 (d, *J* = 4.7 Hz, 1H), 7.83 (d, *J* = 3.7 Hz, 2H), 7.75 (dd, *J* = 7.2, 1.4 Hz, 1H), 7.64 (d, *J* = 11.8 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.46 – 7.41 (m, 1H), 7.36 – 7.28 (m, 2H), 5.58 (d, *J* = 11.7 Hz, 1H), 5.40 (dd, *J* = 8.0, 4.5 Hz, 1H), 3.81 – 3.72 (m, 1H), 3.65 (dt, *J* = 10.1, 7.1 Hz, 1H), 2.35 – 2.22 (m, 1H), 2.00 – 1.87 (m, 1H), 1.87 – 1.79 (m, 1H), 1.80 – 1.71 (m, 1H). <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 157.3, 150.0, 147.9, 141.9, 137.7, 131.1, 130.4, 128.3, 127.5, 126.6, 126.6, 123.0, 116.8, 98.5, 61.3, 50.0, 35.6, 24.3. ESI<sup>+</sup> calcd. for C<sub>18</sub>H<sub>18</sub>N<sub>3</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 340.1114. Found: 340.1108.

(*E*)-2-*[[2-(2-(4-Nitrostyryl)phenyl)pyrrolidin-1-yl]sulfonyl]pyridine* (**10**) Following the typical procedure, the reaction of **1** (43 mg, 0.15 mmol) with 4-nitrostyrene (45 mg, 0.3 mmol, 2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **10** (35 mg, 54 %); as a yellow solid; mp: 158–161 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.73 (d, *J* = 4.5 Hz, 1H), 8.24 (d, *J* = 8.7 Hz, 2H), 7.94 – 7.79 (m, 2H), 7.71 – 7.59 (m, 3H), 7.59 – 7.41 (m, 3H), 7.33 – 7.19 (m, 3H), 6.99 (d, *J* = 16.0 Hz, 1H), 5.61 (dd, *J* = 7.9, 3.7 Hz, 1H), 3.88 – 3.76 (m, 1H), 3.76 – 3.59 (m, 1H), 2.43 – 2.22 (m, 1H), 2.00 – 1.72 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.4, 150.0, 146.8, 143.9, 141.1, 137.7, 133.8, 130.7, 128.7, 127.3, 127.0, 126.6, 126.5, 126.5, 124.1, 123.0, 61.4, 50.0, 35.4, 24.2. ESI<sup>+</sup> calcd. for C<sub>23</sub>H<sub>22</sub>N<sub>3</sub>O<sub>4</sub>S (M+H)<sup>+</sup>: 436.1325. Found: 436.1315.

(*E*)-2-*[[2-(2-(4-(Trifluoromethyl)styryl)phenyl)pyrrolidin-1-yl]sulfonyl]pyridine* (**11**) Following the typical procedure, the reaction of **1** (43 mg, 0.15 mmol) with 4-(trifluoromethyl)styrene (44 μL, 0.3 mmol, 2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv), afforded, after column chromatography (cyclohexane-EtOAc 6:1) the compound **11** (33 mg, 48 %); as a white solid; mp: 153–154 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.73 (d, *J* = 3.8 Hz, 1H), 7.82 – 7.69 (m, 2H), 7.67 – 7.55 (m, 3H), 7.57 – 7.39 (m, 4H), 7.31 – 7.16 (m, 3H), 6.96 (d, *J* = 16.0 Hz, 1H), 5.64 – 5.52 (m, 1H), 3.90 – 3.77 (m, 1H), 3.77 – 3.63 (m, 1H), 2.38 – 2.18 (m, 1H), 2.00 – 1.77 (m, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 157.4, 150.0, 140.9, 140.8, 137.6, 134.2, 129.5, 128.9 (q, *J*<sub>C-F</sub> = 34.9 Hz), 127.3, 126.7, 126.5, 126.4, 126.0,



125.9, 125.6 (q,  $J_{C-F} = 3.8$  Hz), 124.2 (q,  $J_{C-F} = 271.8$  Hz), 123.0, 118.7, 61.5, 50.1, 35.3, 24.2. ESI<sup>+</sup>: calcd. for C<sub>24</sub>H<sub>22</sub>F<sub>3</sub>N<sub>2</sub>O<sub>2</sub>S (M+H)<sup>+</sup>: 459.1348. Found: 459.1331.

(*E*)-Butyl 3-{5-methyl-2-[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]phenyl}acrylate (**17**) Following the typical procedure, the reaction of **12** (46 mg, 0.15 mmol) with butyl acrylate (26 μL, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **17** (65 mg, 70 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.75 (d,  $J = 4.4$  Hz, 1H), 7.98 (d,  $J = 15.7$  Hz, 1H), 7.95 – 7.82 (m, 2H), 7.54 – 7.47 (m, 1H), 7.44 (d,  $J = 7.9$  Hz, 1H), 7.34 (s, 1H), 7.17 (d,  $J = 8.0$  Hz, 1H), 6.33 (d,  $J = 15.7$  Hz, 1H), 5.42 (dd,  $J = 7.8, 3.7$  Hz, 1H), 4.20 (t,  $J = 6.6$  Hz, 2H), 3.86 – 3.66 (m, 2H), 2.33 (s, 3H), 2.40 – 2.20 (m, 1H), 1.94 – 1.62 (m, 5H), 1.51 – 1.36 (m, 2H), 0.97 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 167.0, 157.3, 150.1, 141.7, 139.5, 137.7, 136.9, 131.4, 130.9, 127.4, 126.8, 126.5, 123.1, 120.0, 64.4, 61.2, 50.3, 35.8, 30.8, 24.1, 20.9, 19.2, 13.7. ESI<sup>+</sup> calcd. for C<sub>23</sub>H<sub>29</sub>N<sub>2</sub>O<sub>4</sub>S (M+H)<sup>+</sup>: 429.1843. Found: 429.1848.

(*E*)-Butyl 3-{5-fluoro-2-[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]phenyl}acrylate (**18**) Following the typical procedure, the reaction of **13** (46 mg, 0.15 mmol) with butyl acrylate (32 μL, 0.225 mmol, 1.5 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **18** (44 mg, 68 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.75 (d,  $J = 4.3$  Hz, 1H), 8.02 – 7.81 (m, 3H), 7.62 – 7.45 (m, 2H), 7.20 (dd,  $J = 9.6, 2.5$  Hz, 1H), 7.09 – 6.90 (m, 1H), 6.32 (d,  $J = 15.7$  Hz, 1H), 5.44 (dd,  $J = 7.8, 3.9$  Hz, 1H), 4.21 (t,  $J = 6.6$  Hz, 2H), 3.85 – 3.60 (m, 2H), 2.35 – 2.17 (m, 1H), 1.95 – 1.63 (m, 5H), 1.51 – 1.33 (m, 2H), 0.97 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 166.5, 161.8 (d,  $J_{C-F} = 246.1$  Hz), 157.1, 150.1, 140.2 (d,  $J_{C-F} = 2.1$  Hz), 138.2, 137.8, 133.4 (d,  $J_{C-F} = 7.4$  Hz), 128.7 (d,  $J_{C-F} = 8.1$  Hz), 126.66, 123.07, 121.46, 116.8 (d,  $J_{C-F} = 21.3$  Hz), 113.2 (d,  $J_{C-F} = 22.6$  Hz), 64.6, 60.9, 50.2, 35.8, 30.7, 24.0, 19.2, 13.7. ESI<sup>+</sup> calcd. for C<sub>22</sub>H<sub>26</sub>FN<sub>2</sub>O<sub>4</sub>S (M+H)<sup>+</sup>: 433.1592. Found: 433.1597.

(*E*)-Butyl 3-{4-methoxy-2-[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]phenyl}acrylate (**19**) Following the typical procedure, the reaction of **14** (48 mg, 0.15 mmol) with butyl acrylate (26 μL, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **19** (44 mg, 66 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.71 (d,  $J = 3.9$  Hz, 1H), 8.30 (d,  $J = 15.8$  Hz, 1H), 7.75 (t,  $J = 7.7$  Hz, 1H), 7.65 (d,  $J = 7.6$  Hz, 1H), 7.46 – 7.37 (m, 1H), 7.19 (t,  $J = 8.0$  Hz, 1H), 7.03 (d,  $J = 7.7$  Hz, 1H), 6.78 (d,  $J = 8.2$  Hz, 1H), 6.19 (d,  $J = 15.7$  Hz, 1H), 5.34 (t,  $J = 8.3$  Hz, 1H), 4.21 (t,  $J = 6.7$  Hz, 2H), 4.09 (t,  $J = 9.1$  Hz, 1H), 3.82 – 3.65 (m, 1H), 3.72 (s, 3H), 2.24 – 2.05 (m, 2H), 2.04 – 1.87 (m, 1H), 1.82 – 1.65 (m, 3H), 1.52 – 1.36 (m, 2H), 0.97 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 166.8, 157.5, 157.5, 149.8, 143.6, 137.3, 128.6, 128.4, 126.0, 122.7, 120.1, 112.4, 64.4, 57.5, 55.7, 50.4, 44.0, 30.8, 26.1, 19.2, 13.7. ESI<sup>+</sup> calcd. for C<sub>23</sub>H<sub>29</sub>N<sub>2</sub>O<sub>5</sub>S (M+H)<sup>+</sup>: 445.1792. Found: 445.1795.

(*E*)-Butyl 3-{3-methoxy-2-[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]phenyl}acrylate (**20**) Following the typical procedure, the reaction of **15** (48 mg, 0.15 mmol) with butyl acrylate (44 μL, 0.3 mmol, 2.0 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3

mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **20** (51 mg, 76 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.75 (d,  $J = 4.6$  Hz, 1H), 8.04 – 7.80 (m, 3H), 7.64 – 7.41 (m, 2H), 7.10 (d,  $J = 2.4$  Hz, 1H), 6.78 (dd,  $J = 8.4, 2.5$  Hz, 1H), 6.25 (d,  $J = 15.6$  Hz, 1H), 5.48 (dd,  $J = 8.0, 3.5$  Hz, 1H), 4.19 (t,  $J = 6.6$  Hz, 2H), 3.83 (s, 3H), 3.84 – 3.68 (m, 2H), 2.37 – 2.22 (m, 1H), 1.97 – 1.62 (m, 5H), 1.51 – 1.31 (m, 2H), 0.96 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 167.27, 161.2, 157.2, 150.1, 144.4, 140.9, 137.8, 128.5, 126.6, 124.0, 123.1, 117.6, 112.8, 112.3, 64.3, 61.3, 55.3, 50.3, 35.7, 30.8, 24.0, 19.2, 13.7. ESI<sup>+</sup> calcd. for C<sub>23</sub>H<sub>29</sub>N<sub>2</sub>O<sub>5</sub>S (M+H)<sup>+</sup>: 445.1792. Found: 445.1797.

(*E*)-Butyl 3-{2-[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]thiophen-3-yl}acrylate (**21**) Following the typical procedure, the reaction of **16** (44 mg, 0.15 mmol) with butyl acrylate (26 μL, 0.18 mmol, 1.2 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (87 mg, 0.3 mmol, 2.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 4:1), the compound **21** (38 mg, 61 %) as a colorless oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.73 (d,  $J = 4.5$  Hz, 1H), 7.95 – 7.80 (m, 2H), 7.71 (d,  $J = 15.7$  Hz, 1H), 7.50 (ddd,  $J = 6.8, 4.7, 2.0$  Hz, 1H), 7.17 (d,  $J = 5.4$  Hz, 1H), 7.12 (d,  $J = 5.4$  Hz, 1H), 6.21 (d,  $J = 15.7$  Hz, 1H), 5.66 (dd,  $J = 7.9, 3.2$  Hz, 1H), 4.19 (t,  $J = 6.7$  Hz, 2H), 3.84 – 3.71 (m, 1H), 3.67 – 3.48 (m, 1H), 2.42 – 2.22 (m, 1H), 2.14 – 1.98 (m, 1H), 1.98 – 1.79 (m, 2H), 1.77 – 1.63 (m, 2H), 1.51 – 1.32 (m, 2H), 0.96 (t,  $J = 7.3$  Hz, 3H). <sup>13</sup>C NMR (76 MHz, CDCl<sub>3</sub>) δ 167.5, 157.1, 150.9, 150.0, 137.8, 135.8, 131.5, 126.7, 125.6, 124.1, 123.1, 117.9, 64.4, 58.8, 49.7, 36.3, 30.8, 24.3, 19.2, 13.7. ESI<sup>+</sup> calcd. for C<sub>20</sub>H<sub>25</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub> (M+H)<sup>+</sup>: 421.1250. Found: 421.1254.

(*E*)-Methyl 3-{3-[(*E*)-2-(phenylsulfonyl)vinyl]-2-[1-(pyridin-2-ylsulfonyl)pyrrolidin-2-yl]phenyl}acrylate (**22**) Following the typical procedure, the reaction of the olefinated product **2** (56 mg, 0.15 mmol) with phenyl vinyl sulfone (76 mg, 0.45 mmol, 3.0 equiv), Pd(OAc)<sub>2</sub> (3.32 mg, 0.015 mmol, 10 mol%) and 1-fluoro-2,4,6-trimethylpyridinium triflate (130 mg, 0.45 mmol, 3.0 equiv) afforded, after column chromatography (cyclohexane-EtOAc 3:1), the compound **22** (44 mg, 55 %) as a yellow solid; mp: 141–144 °C. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 9.02 – 8.83 (m, 1H), 8.51 (d,  $J = 15.1$  Hz, 1H), 8.41 (d,  $J = 15.8$  Hz, 1H), 8.03 – 7.86 (m, 4H), 7.66 – 7.51 (m, 5H), 7.47 (d,  $J = 7.7$  Hz, 1H), 7.42 – 7.33 (m, 1H), 7.33 – 7.15 (m, 2H), 6.69 (d,  $J = 15.1$  Hz, 1H), 6.23 (d,  $J = 15.7$  Hz, 1H), 5.62 – 5.44 (m, 1H), 4.08 – 3.85 (m, 2H), 3.82 (s, 3H), 2.29 – 2.14 (m, 1H), 2.12 – 1.94 (m, 2H), 1.75 – 1.55 (m, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 166.9, 156.4, 150.6, 143.7, 141.8, 140.4, 139.5, 137.9, 133.4, 130.2, 129.4(2C), 128.0, 127.8, 126.8, 123.3, 60.9, 51.7, 50.2, 35.1, 25.4. ESI<sup>+</sup>: calcd. for C<sub>27</sub>H<sub>27</sub>N<sub>2</sub>O<sub>6</sub>S<sub>2</sub> (M+H)<sup>+</sup>: 539.1305. Found: 539.1290.

**3.4. Typical procedure for acidic condition cyclization reaction: synthesis of butyl 2-(2,3,5,9b-tetrahydro-1H-pyrrolo[2,1-*a*]isoindol-5-yl)acetate (**23**)** To a solution of the olefinated product **2** (62 mg, 0.15 mmol) in acetic acid (1 mL) under N<sub>2</sub> atmosphere, Zn (294 mg, 4.5 mmol, 30 equiv) was added and the suspension was stirred 48 hours at room temperature. The mixture was diluted with EtOAc (5 mL) and filtered. Over the filtrate a solution 2M NaOH was added until slightly basic pH was reached and the mixture was stirred for 15 min. The aqueous phase was extracted with EtOAc (3 x 5 mL) and the combined organic phases were dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The residue was purified by flash chromatography (CH<sub>2</sub>Cl<sub>2</sub>-EtOAc 2:1) to afford **23** (29 mg, 61%) as a light yellow oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.33 – 7.23 (m, 2H), 7.19 (d,  $J = 6.7$  Hz, 1H), 7.13 (d,  $J = 7.0$  Hz, 1H), 4.92 (t,  $J = 7.3$  Hz, 1H), 4.74 (d,  $J = 7.4$  Hz, 1H), 4.27 – 4.13 (m, 2H),

3.10 – 2.96 (m, 1H), 2.96 – 2.88 (m, 2H), 2.58 – 2.43 (m, 1H), 2.42 – 2.21 (m, 1H), 2.09 – 1.90 (m, 2H), 1.89 – 1.75 (m, 1H), 1.73 – 1.59 (m, 2H), 1.51 – 1.30 (m, 2H), 0.95 (t,  $J = 7.3$  Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  171.2, 144.3, 140.7, 128.1, 127.5, 122.9, 122.5, 68.6, 65.0, 62.1, 46.9, 35.5, 30.6, 29.7, 25.4, 19.1, 13.7.  $\text{ESI}^+$ : calcd. para  $\text{C}_{17}\text{H}_{24}\text{NO}_2$  ( $\text{M}+\text{H}$ ) $^+$ : 274.1801. Found: 274.1797.

*Butyl 2-(7-fluoro-2,3,5,9b-tetrahydro-1H-pyrrolo[2,1-a]isoindol-5-yl)acetate (24)* Following the typical procedure, the reaction of the olefinated product **18** (65 mg, 0.15 mmol) with activated Zn (294 mg, 4.5 mmol, 30 equiv) afforded, after column chromatography ( $\text{CH}_2\text{Cl}_2$ -EtOAc 2:1), the compound **24** (33 mg, 67%) as a light yellow oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.10 (dd,  $J = 8.1, 4.8$  Hz, 1H, Ar), 6.95 (td,  $J = 8.6, 2.2$  Hz, 1H), 6.82 (dd,  $J = 8.6, 1.8$  Hz, 1H), 4.77 (t,  $J = 7.3$  Hz, 1H), 4.57 – 4.50 (m, 1H), 4.31 – 4.13 (m, 2H), 2.87 (d,  $J = 7.3$  Hz, 2H), 2.50 – 2.35 (m, 1H), 2.32 – 2.17 (m, 2H), 1.98 – 1.77 (m, 3H), 1.74 – 1.59 (m, 2H), 1.49 – 1.34 (m, 2H), 0.96 (t,  $J = 7.3$  Hz, 3H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 162.6 (d,  $J_{\text{C-F}} = 244.4$  Hz), 144.6 (d,  $J_{\text{C-F}} = 7.3$  Hz), 141.7 (d,  $J_{\text{C-F}} = 2.3$  Hz), 123.8 (d,  $J_{\text{C-F}} = 9.1$  Hz), 114.5 (d,  $J_{\text{C-F}} = 22.9$  Hz), 109.9 (d,  $J_{\text{C-F}} = 23.0$  Hz), 67.6, 64.9, 61.9 (d,  $J_{\text{C-F}} = 2.1$  Hz), 6.7, 35.6, 30.6, 29.7, 29.7, 25.6, 19.1, 13.7.  $\text{ESI}^+$ : calcd. for  $\text{C}_{17}\text{H}_{23}\text{FNO}_2$  ( $\text{M}+\text{H}$ ) $^+$ : 292.1695. Found: 292.1696.

*5-[(Phenylsulfonyl)methyl]-2,3,5,9b-tetrahydro-1H-pyrrolo[2,1-a]isoindole (25)* Following the typical procedure, the reaction of the olefinated product **7** (68 mg, 0.15 mmol) with activated Zn (294 mg, 4.5 mmol, 30 equiv) afforded a 55:45 mixture of two isomers. After column chromatography ( $\text{CH}_2\text{Cl}_2$ -EtOAc 1:1) the compound *syn*-**25** was isolated (26 mg, 35%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  8.09 (d,  $J = 7.8$  Hz, 2H), 7.73 – 7.65 (m, 1H), 7.64 – 7.56 (m, 2H), 7.35 – 7.23 (m, 3H), 7.23 – 7.14 (m, 1H), 4.88 – 4.78 (m, 1H), 4.68 – 4.53 (m, 1H), 3.70 (d,  $J = 6.0$  Hz, 2H), 2.96 – 2.80 (m, 1H), 2.51 – 2.35 (m, 1H), 2.18 – 2.07 (m, 1H), 2.02 – 1.70 (m, 3H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  144.8, 139.3, 139.1, 134.0, 129.4, 128.5(2C), 127.7, 123.0(2C), 68.4, 59.9, 57.0, 46.8, 29.5, 25.0.  $\text{EI}^+$ : calcd. for  $\text{C}_{18}\text{H}_{19}\text{NO}_2\text{S}$  ( $\text{M}$ ) $^+$ : 313.1137. Found: 313.1132.

*3.5. Typical procedure for cyclization with sodium amalgam: synthesis of 2,3,6,7-tetrahydro-1H-benzo[c]pyrrolo[1,2-a]azepin-5(11bH)-one (26)* Over a suspension of the olefinated product **2** (62 mg, 0.15 mmol) and  $\text{Na}_2\text{HPO}_4$  (64 mg, 0.45 mmol, 3.0 equiv) in MeOH (1.5 mL) under  $\text{N}_2$  atmosphere, 10% Na(Hg) was added (155 mg, 2.5 equiv, w/w). The resulting mixture was stirred until the starting material was disappeared (liquid Hg was observed, typically 3 h, TLC), was diluted in EtOAc and filtered. The filtrate was washed with water, was dried ( $\text{MgSO}_4$ ) and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane-EtOAc 2:1) to afford **26** (15 mg, 74%) as a colorless oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.18 (m, 4H, Ar), 5.07 (t,  $J = 7.2$  Hz, 1H), 3.82 (ddd,  $J = 12.0, 7.4, 4.7$  Hz, 1H), 3.51 (dt,  $J = 12.0, 7.6$  Hz, 1H), 3.32 – 3.18 (m, 1H), 3.02 – 2.90 (m, 1H), 2.88 – 2.78 (m, 1H), 2.61 – 2.45 (m, 2H), 2.43 – 2.31 (m, 1H), 2.09 – 1.84 (m, 2H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.6, 140.8, 138.2, 128.9, 128.1, 126.5, 124.4, 56.9, 48.0, 35.9, 30.6, 29.1, 22.8.  $\text{ESI}^+$ : calcd. for  $\text{C}_{13}\text{H}_{15}\text{NO}$  ( $\text{M}$ ) $^+$ : 201.1154. Found: 201.1155.

*9-Fluoro-2,3,6,7-tetrahydro-1H-benzo[c]pyrrolo[1,2-a]azepin-5(11bH)-one (27)* Following the typical procedure, the reaction of the olefinated product **18** (65 mg, 0.15 mmol) with  $\text{Na}_2\text{HPO}_4$  (64 mg, 0.45 mmol, 3.0 equiv) and Na(Hg) (155 mg, 2.5 equiv, w/w) afforded, after column chromatography (cyclohexane-EtOAc 2:1), the compound **27** (16 mg, 73%) as a colorless oil.

$^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31 – 7.19 (m, 1H), 6.98 – 6.83 (m, 2H), 5.01 (t,  $J = 7.2$  Hz, 1H), 3.88 – 3.73 (m, 1H), 3.55 – 3.44 (m, 1H), 3.30 – 3.15 (m, 1H), 3.04 – 2.88 (m, 1H), 2.87 – 2.72 (m, 1H), 2.60 – 2.29 (m, 3H), 2.06 – 1.82 (m, 2H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  170.6, 162.3 (d,  $J_{\text{C-F}} = 247.3$  Hz), 143.1 (d,  $J_{\text{C-F}} = 7.6$  Hz), 134.0 (d,  $J_{\text{C-F}} = 3.2$  Hz), 126.3 (d,  $J_{\text{C-F}} = 8.4$  Hz), 115.8 (d,  $J_{\text{C-F}} = 21.3$  Hz), 113.0 (d,  $J_{\text{C-F}} = 21.0$  Hz), 56.50, 48.12, 35.53, 30.91, 29.0 (d,  $J_{\text{C-F}} = 1.4$  Hz).  $\text{ESI}^+$ : calcd. for  $\text{C}_{13}\text{H}_{14}\text{FNO}$  ( $\text{M}$ ) $^+$ : 219.1059. Found: 219.1052.

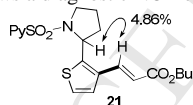
## Acknowledgments

We thank the Spanish *Ministerio de Economía y Competitividad* (MINECO, Project CTQ2012-35790), and MINECO/FEDER, UE (Project CTQ2015-66954-P) for financial support. P.D.L. thanks MECED for a FPU predoctoral fellowship.

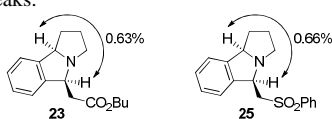
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## Supplementary Material

Experimental procedures, characterization data,  $^1H$  and  $^{13}C$  NMR spectra for new compounds (PDF).