Visible-Light-Mediated Annulation of Electron-Rich Alkenes and Nitrogen-Centered Radicals from *N*-Sulfonylallylamines: Construction of Chloromethylated Pyrrolidine Derivatives

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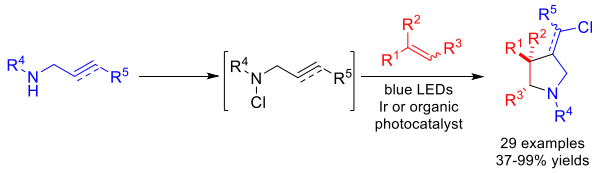
Supporting Information Placeholder

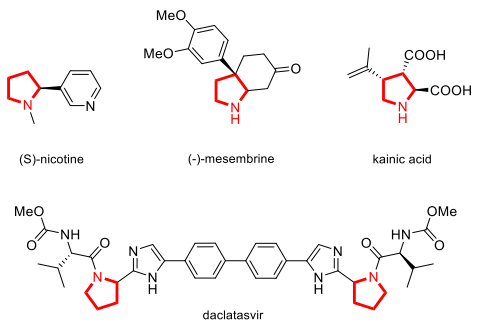


ABSTRACT: A visible-light-mediated annulation of *N*-sulfonylallylamines and olefins is reported. Rapid access to highly functionalized chloromethylated pyrrolidines can be achieved using mild conditions for the generation of nitrogen-centered radicals. Both a transition metal based catalyst and an organic dye can be used as photosensitizers, with 0.5 mol% loading. The reaction was found to be applicable to a large variety of electron-rich/electron-neutral olefins.

INTRODUCTION

In recent years, there has been increasing interest in the medicinal chemistry community in moving away from flat motifs towards 3D scaffolds, typically aliphatic heterocycles.[1] Pyrrolidines are prevalent in many biologically active natural products and pharmaceutical drug candidates[2] and are of significant interest as scaffolds in drug discovery. Additionally, they are widely used in organic synthesis as organocatalysts and ligands[3] (Scheme 1).

Scheme 1. Natural products and drugs containing pyrrolidine rings

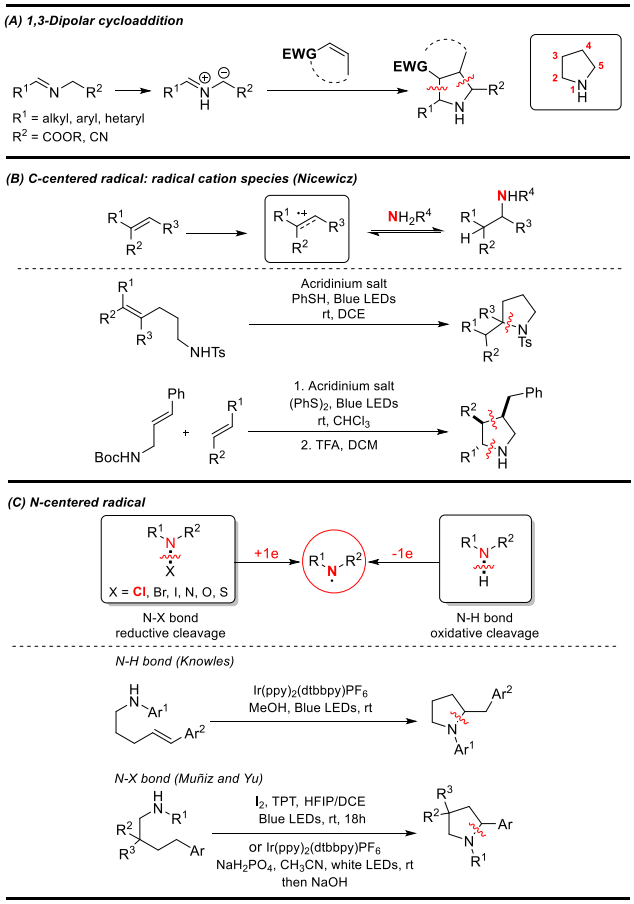


Due to the ubiquity and importance of these structures, the pyrrolidine scaffold has been the target of numerous synthetic efforts. The [3+2] cycloaddition with azomethine ylides and electron-deficient olefins is one of the most widely used methods for the construction of functionalized pyrrolidines[4] (Scheme 2 (A)) while methods using radical species were until recently largely neglected.[5] Indeed, the use of radical initiators, high reaction temperature or high-energy ultraviolet (UV) photolysis presented limitations such as low functional group compatibility, substrate scope or practicability. However, due to renewed interest in photochemistry using visible-light mediated electron/energy transfer chemistry,[6] the use of radical species has increased dramatically and led to the development of methods for pyrrolidine preparation utilizing different bond disconnections.[7] These approaches are of significant interest as they bring more diversity to the substitution pattern of pyrrolidines by using electron-rich olefins as coupling partners. Indeed, they represent a complementary method to the classical [3+2] cycloaddition, which almost exclusively utilizes electron-poor olefins.[4f]

A recent example of the use of radical cation species *via* photoredox catalysis to form C-N bonds through intra- or intermolecular hydroamination of alkenes has been described by the group of Nicewicz; however the scope for the intermolecular approach was limited to four examples (Scheme 2 (B)).[8] A promising, yet less studied strategy, is the use of nitrogen-centered radicals which have the potential to be powerful tools for the construction of C-N bonds (Scheme 2 (C)).[9] These nitrogen-centered radicals can be accessed by the reductive cleavage of the relatively weak N-X bond (X = Cl, Br, I, N, O, S) or by the oxidative cleavage of N-H bonds. Traditionally prepared using harsh conditions such as radical initiators or UV-irradiation, recent developments in the field of visible-light photocatalysis have enabled their generation to be carried

out in a milder and selective way. The pathway using the oxidative scission of N-H bonds has been applied by Knowles in a photoredox protocol for intramolecular olefin hydroamination, giving access to diverse pyrrolidines with moderate diastereoselectivity.[10] In parallel, the generation of nitrogen-centered radicals using *N*-halo compounds was carried out by the groups of Muñiz and Yu through the use of halogen-photoredox-catalysis for an intramolecular C-H amination Hofmann-Löffler-type reaction.[11]

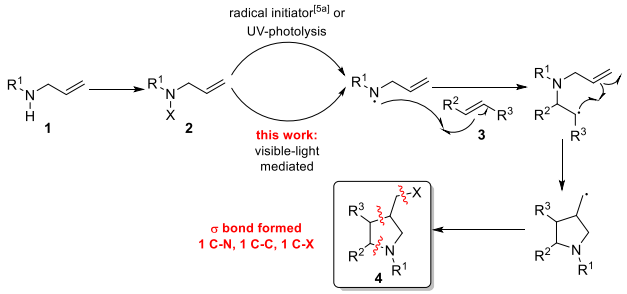
Scheme 2. Current approaches for the preparation of pyrrolidines



N-halo substrates have also found applications for the construction of *N*-aryl bonds using visible light.[12] Likewise, if the preparation of pyrrolidines (and piperidines) was described recently via aminohalogenation of olefins with aminyl radical using copper-catalyzed N-X activation or NIS-promoted aminocyclization,[13] although no reactions using visible-light-mediated have been reported so far. More particularly, the intermolecular version of the radical amination remains a significant challenge due to the propensity of nitrogen-centered radicals to undergo competitive hydrogen abstraction. The intermolecular version was only studied using a radical initiator by the group of Oshima[5a] (Scheme 3) while one isolated example reported by Yu showed that it was possible to perform chloramination of olefins with *N*-chlorosulfonamide under visible-light-promoted conditions.[14]

With the aim of using conditions involving visible-light for the preparation of pyrrolidines, we decided to investigate the annulation of olefins with *N*-haloallylamines (Scheme 3). We believed this approach would offer the advantage of milder reaction conditions and better functional group tolerance, allowing broader variations on the substitution pattern of the pyrrolidine scaffold. The challenging intermolecular strategy would allow access to complex pyrrolidines from simple and readily available starting materials. The *N*-halo partner **2** could be prepared *via in situ* halogenation of the corresponding free amine **1** and would serve as both nitrogen and chlorine sources. Electron-neutral and electron-rich alkenes (which are typically unreactive toward the classical [3+2] cycloaddition) would be suitable partners as nitrogen-centered radicals are electron deficient species. Transfer of the halogen atom from the nitrogen to the carbon of the 4-position would also allow the possibility of further functionalization of the heterocycle.

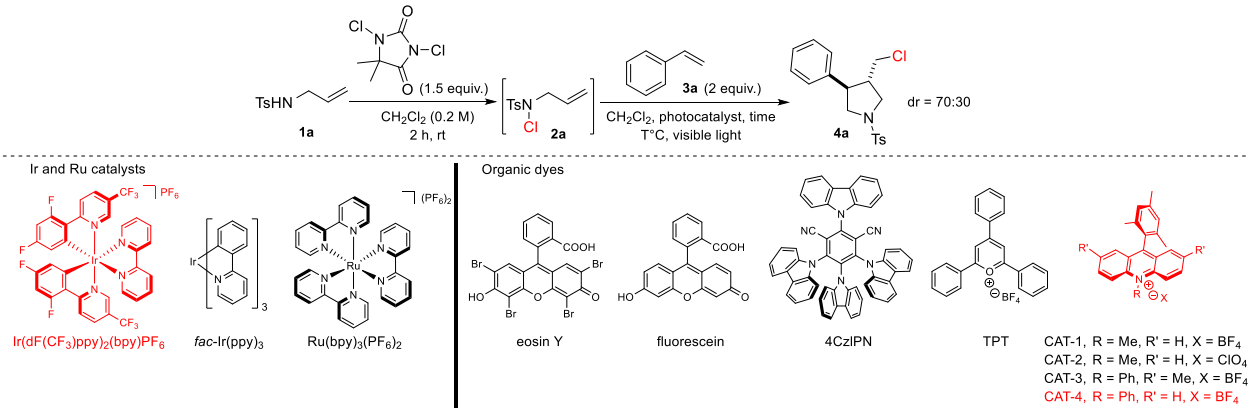
Scheme 3. Proposed visible-light-promoted annulation of *N*-haloallylamines with olefins



RESULTS AND DISCUSSION

As a starting point, our investigation focused on the formation of *N*-chloroallylamine from the corresponding NH-allylamine. N-Cl species have been preferentially used to generate related *N*-radicals owing to their ease of preparation and their high stability compared to the N-Br or N-I analogues. In order to avoid the isolation of the *N*-chloro-intermediates, an *in situ* protocol was envisaged, allowing the formation of the pyrrolidines **4** in a one-pot procedure starting directly from the readily available allylamine **1**. The *N*-tosylallylamine **1a** was chosen for the optimization as it had previously demonstrated the best results using radical initiators for the generation of the radical species.[5a] The optimal conditions for the *N*-chlorination of **1a** to form the intermediate **2a** were established to be using 1,3-dichoro-5,5′-dimethylhydantoin as the chlorinating reagent in CH_2Cl_2 (0.2 M) at rt for 2 h, with 99% yield. A one-pot procedure was then investigated, where only two equivalents of the alkene partner were required to observe complete conversion (Table 1). Visible-light irradiation (blue LEDs – 450 nm) was found to be crucial for the reaction to proceed (Table 1, entry 1) while the use of a photocatalyst was not mandatory in the first instance (Table 1, entry 2).

Table 1. Optimization of the annulation of NH-tosylallylamine 1a and styrene



entry	photocatalyst (mol%)	visible-light	$[CH_2Cl_2]$ (mol/L)	temperature (°C)	reaction time (h)	yield[a] (%)
1	-	-	0.2	35	48	0[b]
2	-	blue LEDs	0.2	35	24	58
3	-	blue LEDs	0.2	55	24	80[c]
4	-	blue LEDs	0.2	55	1	12[d]
5	$Ir(dF(CF_3)ppy)_2(bpy)PF_6$ (0.5)	blue LEDs	0.2	35	1	70
6	**$Ir(dF(CF_3)ppy)_2(bpy)PF_6$ (0.5)**	**blue LEDs**	**0.05**	**35**	**1**	**91**
7	*fac*-$Ir(ppy)_3$ (0.5)	blue LEDs	0.05	35	1	/[e]
8	$Ru(bpy)_3(PF_6)_2$ (0.5)	blue LEDs	0.05	35	1	39
9	eosin Y (0.5)	green LEDs	0.05	35	1	<5[d]
10	fluorescein (0.5)	blue LEDs	0.05	35	1	<5[d]
11	4CzlPN (0.5)	blue LEDs	0.05	35	1	79
12	TPT (0.5)	blue LEDs	0.05	35	1	28[d]
13	CAT-1 (0.5)	blue LEDs	0.05	35	1	71
14	CAT-2 (0.5)	blue LEDs	0.05	35	1	68
15	CAT-3 (0.5)	blue LEDs	0.05	35	1	61
16	**CAT-4 (0.5)**	**blue LEDs**	**0.05**	**35**	**1**	**86**

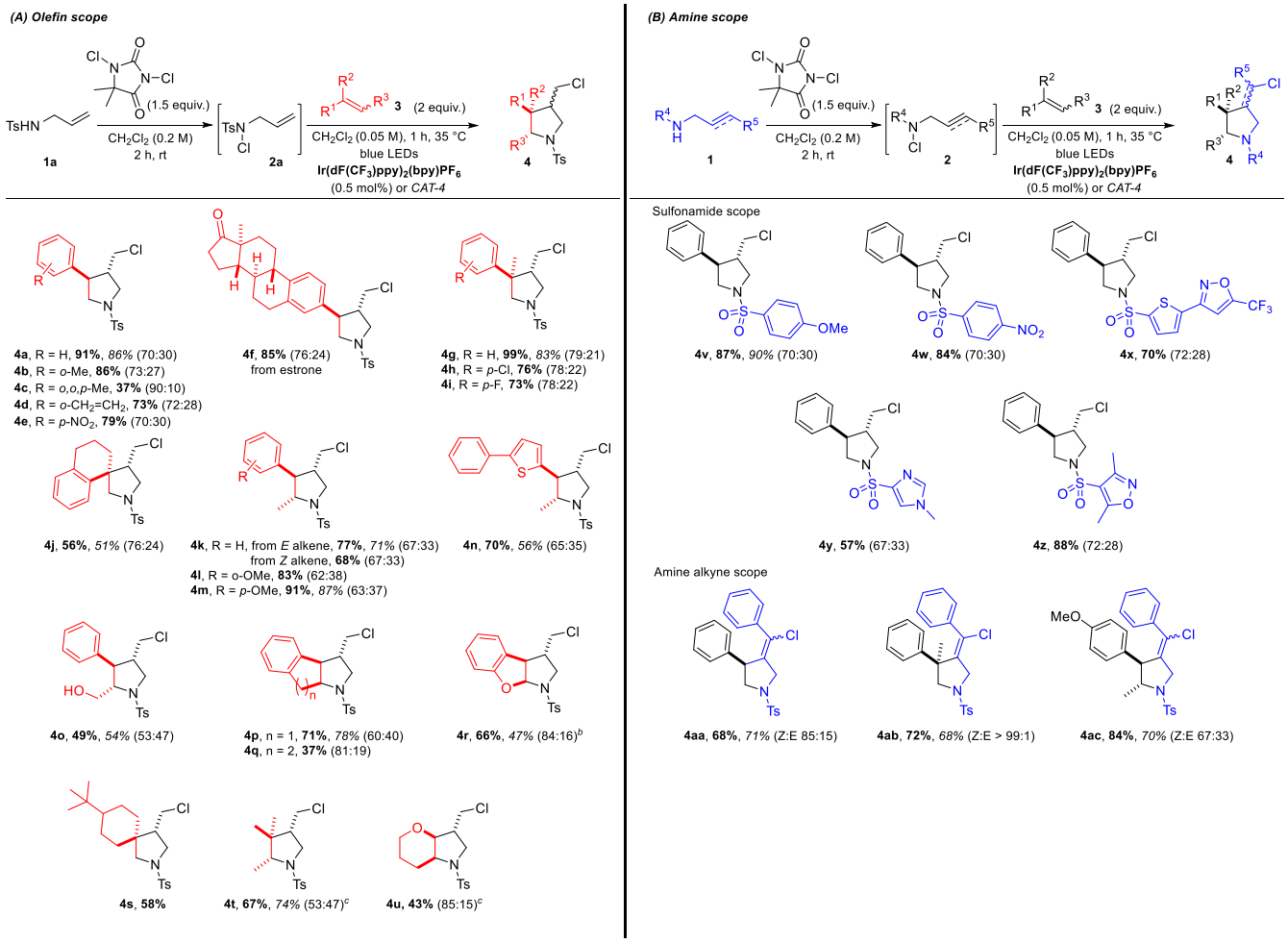
[a]Isolated yields reported unless stated otherwise. [b]No reaction. [c]Partial decomposition observed. [d]Percentage conversion of starting material observed by ^1H NMR. [e]Starting material consumed, unknown products observed by ^1H NMR.

This suggests the reaction may not take place through a photoredox process but *via* a direct visible-light photolysis of the N-Cl bond. However, long reaction times and heat were necessary (24 h at 55 °C) to obtain the product **4a** in 80% yield (Table 1, entry 3).

The limited scope with these conditions led us to explore the addition of a photocatalyst/sensitizer in order to speed up the reaction. The use of $Ir(dF(CF_3)ppy)_2(bpy)PF_6$ ($dF(CF_3)ppy$ = 2-(2,4-difluorophenyl)-5-(trifluoromethyl) pyridine; bpy = 2,2′-bipyridine) reduced the reaction time to 1 h at 35 °C[15] and gave the desired product in 70% yield (*versus* only 12% conversion without the catalyst at 55 °C – Table 1, entries 4 and 5). More dilute conditions in the visible-light-mediated step from 0.2 M to 0.05 M led to an increase of the yield to 91% (Table 1, entry 6). A transition metal based photocatalyst screen showed that $Ir(dF(CF_3)ppy)_2(bpy)PF_6$ was the preferred catalyst and could be used with a low loading of 0.5 mol% (Table 1, entries 6-8). In order to study a cheaper and transition metal-free process, a survey of organic photocatalysts was then attempted (Table 1, entries 9-16): CAT-4 (9-mesityl-10-phenylacridinium tetrafluoroborate) was found to give the best results, with a yield on the same range as the iridium catalyst (86% *versus* 91%). Both of these catalysts were chosen to explore the scope of the reaction.

We began by exploring the scope of the visible-light-mediated annulation using the iridium catalyst by changing the alkene partner **3** (Scheme 4 (A)). A mixture of two diastereoisomers was observed in the majority of the examples. Monosubstituted olefins led to pyrrolidines **4** in good yield (**4a**-**4e**), even in the presence of a more complex alkene bearing the estrone core (**4f**). Increasing of the hindrance on the alkene with 2,4,6-trimethylstyrene caused a decrease in yield (37%) with a corresponding rise in diastereoselectivity of up to 90:10. *Gem*-disubstituted olefins were suitable partners (**4g**-**4i**), even giving access to spiro-pyrrolidines (**4j**). The use of *Z* or *E* 1,2-disubstituted alkenes had no impact on the selectivity and gave a similar mixture of diastereoisomers (**4k**), demonstrating that the alkene geometry was lost during the course of the reaction. The major diastereoisomer was found to have a *trans-trans* configuration, as confirmed by X-ray structural analysis of **4l** (Scheme 5).[16] Internal 1,2-disubstituted alkenes were also tolerated: pyrrolidine **4p** derived from indane was prepared with 71% yield. The low yield of 37% observed in the case of **4q** was due to a hydrogen-abstraction side reaction: this process can sometimes be problematic with nitrogen-centered radicals when the olefin partner is a good hydrogen donor for radical species.[5a]

Scheme 4. Preparation of pyrrolidines: olefin and amine scope[a]



[a]Conditions: 1) **1** (0.2 mmol), 1,3-dichoro-5,5′-dimethylhydantoin (0.3 mmol), CH_2Cl_2 (0.2 M), 2 h, rt. 2) **3** (0.4 mmol), photocatalyst (0.5 mol%), CH_2Cl_2 (0.05 M in total), blue LEDs (450 nm, 14.4 W), 1 h, 35 °C. The yield corresponding to the use of $Ir(dF(CF_3)ppy)_2(bpy)PF_6$ is indicated in bold, the one using the CAT-4 is following in italics. The diastereoselectivity ratio is given in parenthesis with the major diastereoisomer shown. [b]The intermediate **2** was isolated by purification before using it in the photolysis step. The indicated yield corresponds to the overall of the 2 steps. [c]10 equiv. of the olefin was used.

Internal and external aliphatic alkenes also reacted to form the corresponding pyrrolidines in moderate yields although they required a large excess of the olefin (**4s**-**4u**).

Finally, the reaction showed good functional group tolerance, with electron withdrawing and donating groups on the aromatic ring being tolerated. A ketone (**4f**), a free alcohol (**4o**), heteroaromatics (**4n**-**4r**) and a second alkene (**4d**) in the molecule were tolerated as well as addition to enol ethers (**4u**).

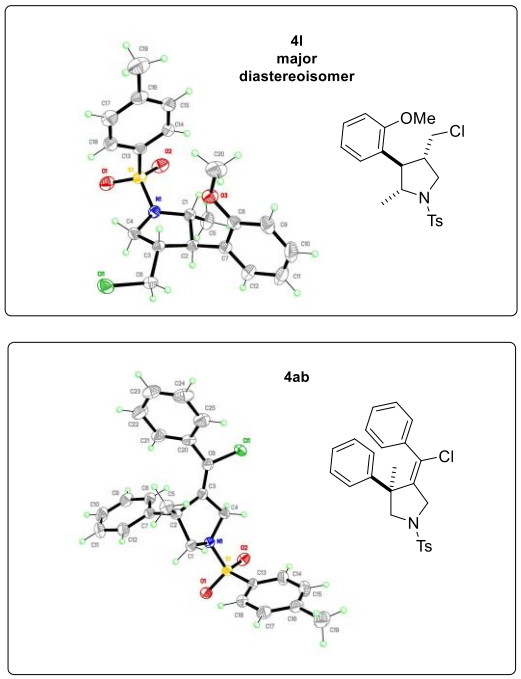
Next, a variety of amines **1** were examined (Scheme 4 (B)). As the *N*-chlorination step was performed under acidic conditions, protecting groups such as acetyl, formyl and Boc were unsuitable for the reaction. However, a wide range of aromatic and heteroaromatic sulfonamides were found to react smoothly with styrene, leading to pyrrolidines in excellent yields (**4v**-**4z**), giving the possibility of varying the nitrogen substituent. The fact that the nosyl group is tolerated also offers the possibility of deprotection and further elaboration on the nitrogen atom (**4w**).

Aryl-substituted alkyne amines were also efficient partners for the visible-light-mediated annulation reaction. If the free alkyne only performed the first addition to the styrene without the cyclization to form the pyrrolidine core, the phenyl-substituted alkyne amine reacted smoothly to lead to pyrrolidines bearing an exocyclic double bond as a *Z*/*E* mixture (**4aa**-**4ac**). In the case of the addition to the α-methylstyrene, only the *Z* product **4ab** was observed, as confirmed by X-ray structural analysis (Scheme 5).[17] This result suggests that in the case of the *Z*/*E* mixtures observed for **4aa** and **4ac**, the major product would have a *Z* configuration.

Lastly, as proof of concept, a selection of examples were also carried out using the organic dye CAT-4. Pleasingly, the majority of these worked in comparable yields to the iridium reactions, demonstrating the possibility of having a cheaper and transition metal free process (Scheme 4). The

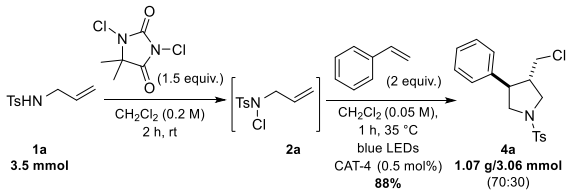
visible-light-mediated annulation was then carried out on 3.5 mmol scale, using the organic dye CAT-4, with 1.07 g (88%) of pyrrolidine **4a** prepared (Scheme 6).

Scheme 5. X-rays analyses of compounds 4l (major diastereoisomer) and 4ab[a]



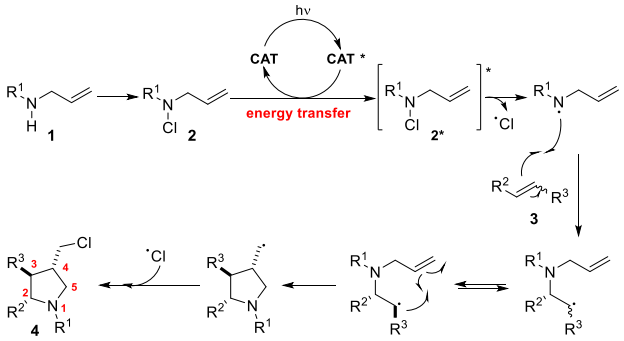
[a]Displacement ellipsoids are shown at 50% probability for compounds **4l** and **4ab**.

Scheme 6. Larger scale preparation of pyrrolidine 4a



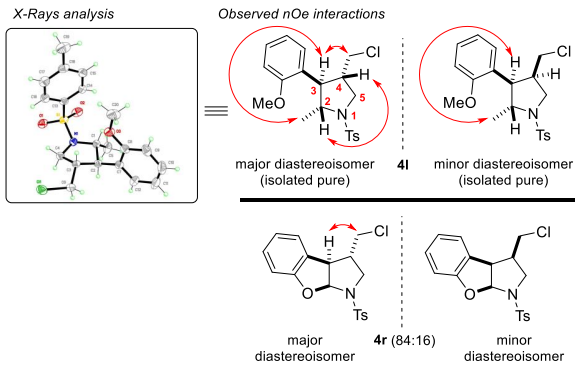
To gain insight into the course of the reaction, a control experiment was performed in the presence of the radical scavenger 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO): wherby the reaction was completey inhibited and no product was observed. From a mechanistic perspective, it was determined that the intramolecular radical cyclization occurred *via* a 5-exo-trig mode as no 6-membered ring was observed by ^{1}H NMR analysis during the investigation. Scheme 7 shows a plausible mechanism for the annulation. While a photoredox initiated process cannot be completely ruled out,[18] the method of initiation of the radical seems to be more likely photosensitization, a physical process of energy transfer,[19] as the reaction was found to proceed without a catalyst. Indeed, if light itself can slowly excite the intermediate **2** (in 24 h at 55 °C), the presence of a catalyst promotes a faster and milder activation of **2** (35 °C, 1 h). A plausible mechanism would be that the photocatalyst **CAT** absorbs a photon to generate a long lived, excited triplet state **CAT***,[6,20] which would then transfer its energy to the intermediate **2** while the catalyst returns to its ground state. It is envisaged that the excited molecule **2*** undergoes a homolytic cleavage of the nitrogen-chloride bond to form a nitrogen-centered radical which would then initiate the radical reaction. The nitrogen-centered radical would first attack in an intermolecular fashion the alkene **3** to form a carbon-centered radical which then would induce the formation of the pyrrolidine core *via* an intramolecular reaction with the allyl group. The remaining radical would finally trap the chlorine radical to lead to the product **4**. A typical propagation step would also result in C-Cl bond formation.

Scheme 7. Proposed mechanism



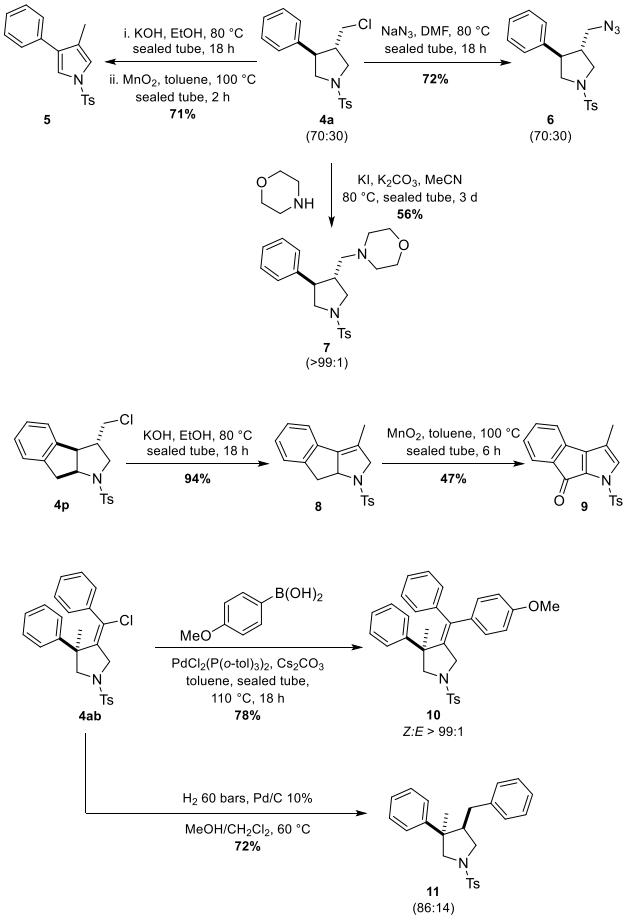
Analyses by ^{1}H NMR and NOESY experiments of pyrrolidine **4l** (where both diastereoisomers were isolated pure) and **4r (**mixture of both diastereoisomers), as well as X-ray structural analysis of the major diastereoisomer of **4l** allowed us to define the stereochemistry of the different stereogenic centers (Scheme 8). The reaction pathway seems to favor the thermodynamic product, providing a *trans-trans* configuration. Control of the relative stereochemistry at the C2 and C3 positions was found to be high, with only one configuration observed: the use of *Z* or *E* 1,2-disubstituted alkenes gave an identical mixture of diastereoisomers, indicating that the alkene geometry was lost during the course of the reaction.[7,21] The analyses indicate that the major diastereoisomer has a *trans* configuration between the C2/C3 group to minimize steric hindrance. The only exception is when using an internal alkene where the C2/C3 configuration is forced to remain *cis* by ring strain. The selectivity between the carbons C3 and C4 proceeds with lower diastereoselectivity during the radical cyclization (dr from 53:47 to 90:10), still in favor of the thermodynamic product, providing a *trans* configuration between the C3 and C4 groups (Scheme 8).[22]

Scheme 8. Regioselectivity observed by ^{1}H, NOESY NMR and X-ray structural analyses



Finally, we studied further manipulation of the cycloadducts to demonstrate the potential for further elaboration (Scheme 9). Pyrrole **5** was prepared *via* an HCl elimination/oxidation process from **4a**. The chlorine functionality could be exchanged by morpholine or an azide group through nucleophilic substitution (**6**, **7**). The small nucleophile azide reacted with **4a** with no discrimination between the two diastereoisomers. On the other hand, the product **7** was isolated with 56% yield as one diastereoisomer: only the major diastereoisomer of **4a** was found to react with morpholine, due to the more hindered nature of the nucleophile.[23] Previously unknown fused pyrrole **9** could also be prepared by the two steps HCl elimination/oxidation procedure. Pyrrolidine **4ab** could be used in a palladium-catalyzed Suzuki-Miyaura coupling to form tetra-substituted alkene **10**. Finally, hydrogenation of **4ab** was seen to lead to compound **11** in 72% yield with good diastereoselectivity (dr = 86:14), with hydrogenation preferentially occurring on the least hindered face.

Scheme 9. Synthetic transformations of chloromethylated pyrrolidines 4



CONCLUSIONS

In conclusion, we have reported a simple, mild and regioselective approach to access chloromethylated pyrrolidine derivatives in good to excellent yields with moderate to good diastereoselectivity through a visible-light-mediated annulation of *N*-sulfonylallylamines with alkenes. This method allows the formation of three new bonds starting from simple and readily available starting materials, giving access to 29 different pyrrolidine products, of which 24 were previously unknown. This method demonstrates a wide range of functional group compatibility and is complementary to the classical [3+2] cycloaddition, bringing more diversity to the substitution pattern of pyrrolidines by enabling the use of electron-neutral and electron-rich olefins.

EXPERIMENTAL SECTION

General Experimental Methods. Unless otherwise stated, reagents were obtained from commercial sources and used without further purification. Alkenes **3** were commercialy available except for **3f**, **3j**, **3l**, **3n** and **3s** (numbering for the starting materials **3** can be found in SI). Solvents were freshly distilled over calcium hydride and lithium aluminium hydride (tetrahydrofuran and diethyl ether) or calcium hydride (dichloromethane, methanol, n-hexanes, toluene, and ethyl acetate). Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel glass plates (Merck 60 F254), visualised using ultraviolet light (254 nm) or an alkaline solution of potassium permanganate. Flash column chromatography (FCC) was performed whether using high-purity grade silica gel Merck with 60-120 mesh particle size under air pressure or using Florisil® with 100-200 mesh particle under air pressure (as Florisil® was giving better yields than silica gel for the pyrrolidine purification- increase of the yield up to 5-10%). All solvents used for chromatographic purification were distilled prior to use. ^{1}H-NMR spectra were recorded on a DRX-600 spectrometer at 600 MHz and are reported as follows: chemical shift δ in ppm (multiplicity, coupling constants *J* in Hz, number of protons). The multiplicity and shape of the ^{1}H signals are designated by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, or combinations of thereof. All chemical shifts δ are reported to the nearest 0.01 (1H) / 0.1(13C) ppm, relative to the residual protic solvent as the internal reference ($CDCl_3$ = 7.26 (^{1}H) / 77.16 (^{13}C) ppm). ^{19}F-NMR spectra were recorded on a Bruker DPX-400 spectrometer at 376 MHz with ^{1}H decoupling. All chemical shifts δ are reported to the nearest 0.1 ppm with $CFCl_3$ as the external standard ($CFCl_3$ = 0.0 ppm). Spectra were assigned using ^{1}H-COSY, DEPT-135, HSQC and HMBC where appropriate to facilitate structural determination. Assignement was made for ^{1}H and ^{13}C NMR of pyrrolidines. Infrared spectra were recorded neat as thin films on a Perkin-Elmer Spectrum One FTIR spectrometer. Absorbances were recored in the range 4000-650 cm^{-1}. High resolution mass spectrometry (HRMS) was performed using whether a Waters Micromass LCT Premier™ spectrometer using time of flight mass detection and positive electrospray ionization method (+ESI), a Waters Vion IMS Qtof spectrometer using positive electrospray ionization method (+ESI) or a Waters Xevo G25 Qtof spectrometer using Atmospheric Solids Analysis Probe ionization method (ASAP+). All reported values are within 5 ppm of the calculated value. Melting points were recorded on a Stuart Scientific SMP3 melting point apparatus. The lamps utilized for the visible-light-mediated reaction were blue LEDs (450 nm, 14.4 W).

Preparation of catalysts. $Ir(dF(CF_3)ppy)_2(bpy)PF_6$ was kindly furnished by Merck Rahway USA. fac-$Ir(ppy)_3$, $Ru(bpy)_3(PF6)_2$, eosin Y, fluorescein, TPT (2,4,6-triphenylpyrylium tetrafluoroborate), CAT-1 (9-mesityl-10-methylacridinium tetrafluoroborate), CAT-2 (9-mesityl-10-methylacridinium perchlorate), CAT-3 (9-mesityl-2,7-dimethyl-10-phenylacridinium tetrafluoroborate) and CAT-4 (9-mesityl-10-phenylacridinium tetrafluoroborate) were commercially available. 4CzlPN was prepared according to published literature

procedures. Spectral data were in agreement with literature values.[24]

General Procedure A: Preparation of sulfonylamines 1a-1f.[25] In an oven-dried flask under argon was placed the amine (1.1 equiv.) in CH_2Cl_2 (0.25 M). The reaction mixture was cooled to 0 °C and triethylamine (1.1 equiv.) was added. The corresponding sulfonylchloride (1.0 equiv.) was then added in small portions and the reaction mixture was stirred at 0 °C for 1 h, then 18 h at room temperature. The crude was added to a satured solution of $NaHCO_3$ and the aqueous layer was extracted with CH_2Cl_2 (3x). The organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to yield the desired product.

N-allyl-4-methylbenzenesulfonamide (1a). According to general procedure A and starting from 1.95 g of tosylchloride (10 mmol), isolated as a white solid (1.96 g, 9.3 mmol, 93%). Spectral data were in agreement with literature values.[25]

***N*-allyl-4-methoxybenzenesulfonamide (1b).** According to general procedure A and starting from 1.88 g of 4-methoxybenzenesulfonyl chloride (9.1 mmol), isolated as an off-white solid (2.10 g, 9.1 mmol, quant.). Spectral data were in agreement with literature values.[26]

***N*-allyl-4-nitrobenzenesulfonamide (1c).** According to general procedure A and starting from 1.99 g of 4-nitrobenzenesulfonyl chloride (9.0 mmol), isolated as an off-white solid (1.48 g, 6.1 mmol, 68%). Spectral data were in agreement with literature values.[26]

***N*-allyl-5-(5-(trifluoromethyl)isoxazol-3-yl)thiophene-2-sulfona-mide (1d).** According to general procedure A and starting from 635 mg of 5-(5-(trifluoromethyl)isoxazol-3-yl)thiophene-2-sulfonyl chloride (2.0 mmol), isolated as a white solid (500 mg, 1.48 mmol, 74%). R_f 0.18 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.63 (d, *J* = 3.9 Hz), 7.47 (d, *J* = 3.9 Hz, 1H), 6.98 (d, *J* = 1.0 Hz, 1H), 5.79 (ddt, *J* = 17.1, 10.2, 5.6 Hz, 1H), 5.25 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.18 (dq, *J* = 10.2, 1.5 Hz, 1H), 4.67 (t, *J* = 6.2 Hz, 1H), 3.76 (tt, *J* = 6.2, 1.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 156.7, 144.1, 134.5, 132.3, 132.2, 128.1, 118.4, 103.4, 46.0; ^{19}F NMR ($CDCl_3$) δ -65.1; FTIR (ν_{max} cm^{-1}) 3270 (NH), 1552 (C=C), 1322 (sulfone), 1154 (sulfone); HRMS (ESI+) calculated for $C_{11}H_{10}O_3N_2S_2F_3$ $[M+H]^+$ 339.0085, found 339.0076; M.p.: 124-127 °C.

***N*-allyl-1-methyl-1H-imidazole-4-sulfonamide (1e).** According to general procedure A and starting from 361 mg of 1-methyl-1H-imidazole-4-sulfonyl chloride (2.0 mmol), isolated as a white solid (146 mg, 0.73 mmol, 36%). R_f 0.22 (10% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 7.51 (d, *J* = 1.4 Hz, 1H), 7.47 (d, *J* = 1.4 Hz, 1H), 5.84-5.77 (m, 1H), 5.23 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.15 (br s, 1H), 5.12 (dd, *J* = 10.2, 1.6 Hz, 1H), 3.76 (s, 3H), 3.65 (t, *J* = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 140.2, 139.0, 133.3, 124.0, 117.4, 45.9, 34.0; FTIR (ν_{max} cm^{-1}) 3168 (NH), 1534 (C=C), 2857 (sp^3 C-H), 1358 (sulfone), 1158 (sulfone); HRMS (ESI+) calculated for $C_7H_{12}O_2N_3S$ $[M+H]^+$ 202.0650, found 202.0654; M.p.: 136-138 °C.

***N*-allyl-3,5-dimethylisoxazole-4-sulfonamide (1f).** According to general procedure A and starting from 391 mg of 3,5-dimethylisoxazole-4-sulfonyl chloride (2.0 mmol), isolated as a colorless oil (273 mg, 1.26 mmol, 63%). R_f 0.21 (50% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 5.75 (ddt, *J* = 17.1, 10.2, 5.9 Hz, 1H), 5.21 (dd, *J* = 17.1, 1.2 Hz, 1H), 5.16 (dd, *J* = 10.2, 1.2 Hz, 1H), 4.75 (t, *J* = 6.3 Hz, 1H), 3.63 (tt, *J* = 6.3, 1.2 Hz, 2H), 2.63 (s, 3H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.1, 157.5, 132.6, 118.3, 118.2, 116.2, 45.3, 12.7, 10.8; FTIR (ν_{max} cm^{-1}) 3294 (NH), 2929 ((sp^3 C-H), 1596 (C=C), 1326 (sulfone), 1175 (sulfone); HRMS (ESI+) calculated for $C_8H_{13}O_3N_2S$ $[M+H]^+$ 217.0647, found 217.0656.

4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide (1g). To a solution of 4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (628 mg, 3 mmol, 1.0 equiv.), $PdCl_2(PPh_3)_2$ (42 mg, 0.06 mmol, 0.02 equiv.) and CuI (22 mg, 0.12 mmol, 0.04 equiv.) in THF (0.2 M) were added phenyl iodide (0.4 mL, 3.6 mmol, 1.2 equiv.) and Et_3N (1.25 mL, 9 mmol, 3 equiv.) successively under an argon atmosphere. The resulting mixture was stirred at room temperature for 18 h. The crude was filtered through a small pad of celite and the filtrate was concentrated under reduced pressure. The crude was purified by silica flash column chromatography (85/15 to 7/3 hexane/EtOAc) to yield the desired amine **1g** as an off-white solid (613 mg, 2.15 mmol, 72%).[27] Spectral data were in agreement with literature values.[28]

***N*-allyl-*N*-chloro-4-methylbenzenesulfonamide (2a).** In an oven-dried flask under argon were placed the amine **1a** (500 mg, 2.37 mmol, 1 equiv.) and 1,3-dichloro-5,5′-dimethylhydantoin (699 mg, 3.55 mmol, 1.5 equiv.) in CH_2Cl_2 (12 mL, 0.2 M). The reaction mixture was stirred at room temperature for 2 h. The crude was concentrated *in vacuo* and then purified by silica flash column chromatography to afford the desired product **2a** as a clear yellow oil (580 mg, 2.36 mmol, 99%). R_f 0.55 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 2H), 5.86-5.77 (m, 1H), 5.33-5.26 (m, 2H), 3.86 (dd, *J* = 6.5, 1.3 Hz, 2H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 145.5, 130.6, 129.9, 129.7, 129.6, 121.1, 59.3, 21.7; FTIR (ν_{max} cm^{-1}) 2977 (sp^3 C-H), 2911 (sp^3 C-H), 1596 (C=C), 1356 (sulfone), 1157 (sulfone); HRMS (ESI+) calculated for $C_{10}H_{13}O_2NSCl$ $[M+H]^+$ 246.0350, found 246.0344.

(8*R*,9*S*,13*S*,14*S*)-13-methyl-3-vinyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (3f). Prepared according to published literature procedure. Spectral data were in agreement with literature values.[29]

General Procedure B: Preparation of alkenes 3j, 3l, 3n and 3s. Following a typical Wittig reaction procedure, the alkyl phosphonium bromide (2.0 equiv.) was suspended in THF (0.2 M) under an argon atmosphere and the reaction mixture was cooled to 0 °C. *t*BuOK (2.0 equiv.) was added in one portion and the mixture was sitrred for 15 min. Then, a solution of the aldehyde/ketone (1.0 equiv.) in THF (1 mL/mmol) was added dropwise. After 1 h, the reaction mixture was warmed to room temperature and stirred for 18 h. Satured NH_4Cl was then added, the two phases separated and the aqueous phase was extracted with diethyl ether (x3). The organic phase was dried over $MgSO_4$, filtered and solvent was removed *in vacuo*. The crude was purified by silica flash column chromatography (95/5 hexane/EtOAc) to yield the desired alkene precursor.

1-methylene-1,2,3,4-tetrahydronaphthalene (3j). According to general procedure B and starting from 0.67 mL of 3,4-dihydronaphthalen-1(2H)-one (5.0 mmol), isolated as clear yellow oil (649 mg, 4.5 mmol, 90%). Spectral data were in agreement with literature values.[30]

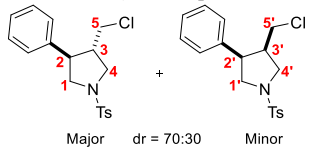
1-methoxy-4-(prop-1-en-1-yl)benzene (3l). According to general procedure B and starting from 817 mg of 2-methoxybenzaldehyde (6.0 mmol), isolated as a clear yellow oil (646 mg, 4.4 mmol, 73%) of a Z/E 1/1 non separable mixture. Spectral data were in agreement with literature values.[31]

2-phenyl-5-(prop-1-en-1-yl)thiophene (3n). According to general procedure B and starting from 377 mf of 5-phenylthiophene-2-carbaldehyde (2.0 mmol), isolated as an orange solid (346 mg, 1.7 mmol, 87%) of a Z/E 75/25 non separable mixture. R_f 0.68 (20% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *alkene Z* 7.64-7.60 (m, 2H), 7.40-7.25 (m, 3H), 7.24 (d, *J* = 3.7 Hz, 1H), 6.96 (d, *J* = 3.7 Hz, 1H), 6.58-6.53 (m, 1H), 5.72 (dq, *J* = 11.4, 7.3 Hz, 1H), 2.04 (dd, *J* = 7.3, 1.8 Hz, 3H) *alkene E* 7.60-7.56 (m, 2H), 7.40-7.25 (m, 3H), 7.15 (d, *J* = 3.7 Hz, 1H), 6.82 (d, *J* = 3.7 Hz, 1H), 6.53-6.47 (m, 1H), 6.10 (dq, *J* = 15.6, 6.8 Hz, 1H), 1.88 (dd, *J* = 6.8, 1.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ *alkene E/Z* 143.7, 142.6, 141.6, 140.4, 134.4, 134.3, 128.9, 128.8, 128.1, 127.3, 127.2, 125.9, 125.6, 125.5, 125.1, 124.9, 124.4, 123.2, 123.1, 122.7, 18.4, 15.2; FTIR (ν_{max} cm^{-1}) 2906 (sp^3 C-H),

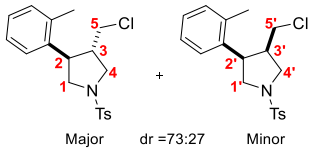
2846 (sp^3 C-H), 1597 (C=C); HRMS (ASAP+) calculated for $C_{13}H_{12}S$ $[M]^+$ 200.0660, found 200.0653; M.p.: 42-44 °C (lit. 43 °C).[32]

1-(*tert*-butyl)-4-methylenecyclohexane (3s). According to general procedure B and starting from 0.93 g of 4-*tert*butylcyclohexanone (6.0 mmol), isolated as a colorless oil (630 mg, 4.1 mmol, 69%). Spectral data were in agreement with literature values.[33]

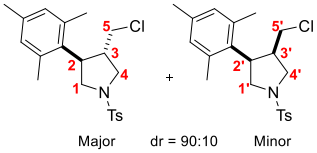
General Procedure C: Preparation of pyrrolidines 4a-4ac. Conditions C1: A 10 mL microwave vial was charged with the amine **1** (0.2 mmol, 1.0 equiv.), 1,3-dichloro-5,5′-dimethylhydantoin (0.3 mmol, 1.5 equiv.) and CH_2Cl_2 (1 mL, 0.2 M). The tube was flushed with argon and the reaction mixture was stirred for 2 h at room temperature. Then, the corresponding alkene **3** (0.4 mmol, 2 equiv.), $Ir(dF(CF_3)ppy)_2(bpy)PF_6$ (0.001 mol, 0.5 mol%) and CH_2Cl_2 (3 mL, 0.05 M in total) were successively added and the reaction mixture was stirred at 35 °C under blue LEDs irradation (450 nm, 14.4 W) for 1 h. The crude was concentrated *in vacuo* and purified by Florisil® flash column chromatography to yield the desired pyrrolidine **4** as a mixture of two diastereoisomers. **Conditions C2:** Same conditions using CAT-4 (0.001 mol, 0.5 mol%) as the photosensitizer.



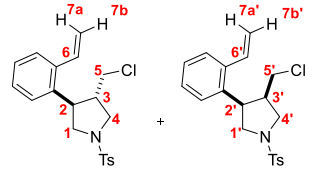
3-(chloromethyl)-4-phenyl-1-tosylpyrrolidine (4a). According to general procedure C1, isolated as a clear yellow oil (64 mg, 0.183 mmol, 91%) of a mixture of non separable diastereoisomers (dr = 70:30). With general procedure C2 (60 mg, 0.171 mmol, 86%). A larger scale reaction was performed using conditions C1, starting with 3.5 mmol of amine **1a**, to prepare the product **4a** (1.07 g, 3.07 mmol, 88%). R_f 0.41 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.77 (d, *J* = 7.9 Hz, 2H), 7.41-7.37 (m, 2H), 7.32-7.24 (m, 3H), 7.11 (d, *J* = 7.4 Hz, 2H), 3.77-3.66 (m, 2H, H^1, H^4), 3.46 (dd, *J* = 11.3, 4.0 Hz, 1H, H^5), 3.37-3.27 (m, 3H, H^1, H^4, H^5), 3.06-3.00 (m, 1H, H^2), 2.56-2.50 (m, 1H, H^3), 2.48 (s, 3H); *minor diastereoisomer* 7.81 (d, *J* = 7.9 Hz, 2H), 7.41-7.37 (m, 2H), 7.32-7.24 (m, 3H), 7.06 (d, *J* = 7.4 Hz, 2H), 3.77-3.66 (m, 1H, $H^{1'}$), 3.64-3.60 (m, 2H, $H^{1'}$, $H^{4'}$), 3.52-3.48 (m, 1H, $H^{2'}$), 3.37-3.27 (m, 1H, $H^{4'}$), 3.06-3.00 (m, 1H, $H^{5'}$), 2.82 (dd, *J* = 11.3, 9.2 Hz, 1H, $H^{5'}$), 2.66-2.61 (m, 1H, $H^{3'}$), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.8, 138.4, 133.5, 129.8, 129.0, 127.6, 127.4, 127.3, 54.6 (C^1), 51.3 (C^4), 48.0 (C^3), 47.3 (C^2), 44.2 (C^5), 21.6; *minor diastereoisomer* 143.8, 137.5, 133.8, 129.9, 128.8, 127.8, 127.5, 127.3, 52.5 ($C^{1'}$), 50.3 ($C^{4'}$), 45.8 ($C^{2'}$), 45.6 ($C^{3'}$), 43.1 ($C^{5'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2959 (sp^3 C-H), 2878 (sp^3 C-H), 1346 (sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{18}H_{20}ClNO_2S$ $[M+H]^+$ 350.0976, found 350.0977.



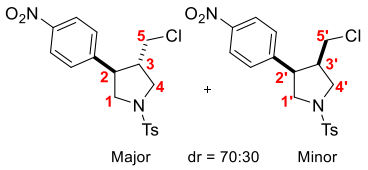
3-(chloromethyl)-4-(o-tolyl)-1-tosylpyrrolidine (4b). According to general procedure C1, isolated as a colorless oil (62.8 mg, 0.173 mmol, 86%) of a mixture of non separable diastereoisomers (dr = 73:27). R_f 0.42 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.77 (d, *J* = 8.2 Hz, 2H), 7.40-7.35 (m, 2H), 7.16-7.11 (m, 3H), 7.03-6.99 (m, 1H), 3.74 (dd, *J* = 10.0, 7.7 Hz, 1H, H^1), 3.72-3.63 (m, 1H, H^4), 3.44 (dd, *J* = 11.3, 4.2 Hz, 1H, H^5), 3.34 (dd, *J* = 10.5, 8.1 Hz, 1H, H^4), 3.30-3.25 (m, 2H, H^2, H^5), 3.20 (dd, *J* = 10.0, 8.9 Hz, 1H, H^1), 2.64-2.56 (m, 1H, H^3), 2.47 (s, 3H), 2.26 (s, 3H); *minor diastereoisomer* 7.80 (d, *J* = 8.2 Hz, 2H), 7.40-7.35 (m, 2H), 7.16-7.11 (m, 2H), 7.10-7.06 (m, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 3.72-3.63 (m, 3H, $H^{1'}$, $H^{2'}$, $H^{4'}$), 3.59-3.56 (m, 1H, $H^{1'}$), 3.48 (dd, *J* = 10.8, 4.9 Hz, 1H, $H^{4'}$), 2.99-2.96 (m, 1H, $H^{5'}$), 2.77-2.70 (m, 2H, $H^{3'}$, $H^{5'}$), 2.47 (s, 3H), 2.27 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.8, 136.6, 136.5, 133.6, 130.8, 129.8, 127.6, 127.2, 126.7, 125.5, 54.3 (C^1), 50.1 (C^4), 47.4 (C^3), 44.3 (C^2), 42.5 (C^5), 21.6, 19.7; *minor diastereoisomer* 143.8, 136.2, 135.2, 133.4, 130.9, 129.8, 127.6, 127.3, 126.4, 126.3, 51.9, 51.2, 43.8, 43.7, 42.1, 21.6, 19.9; FTIR (ν_{max} cm^{-1}) 2957 (sp^3 C-H), 2861 (sp^3 C-H), 1343 (sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{23}ClNO_2S$ $[M+H]^+$ 364.1133, found 364.1126.



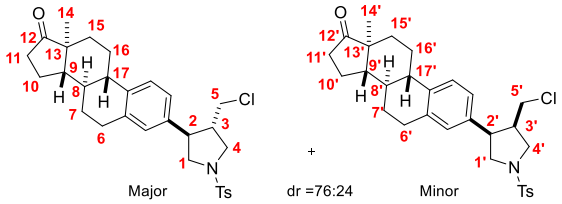
3-(chloromethyl)-4-mesityl-1-tosylpyrrolidine (4c). According to general procedure C1, isolated as a colorless oil (28.7 mg, 0.073 mmol, 37%) of a mixture of non separable diastereoisomers (dr = 90:10). R_f 0.48 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.75 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 6.80 (s, 2H), 3.79 (dd, *J* = 10.0, 7.5 Hz, 1H, H^4), 3.51-3.44 (m, 4H, $2H^1$, H^2, H^5), 3.32 (dd, *J* = 11.2, 7.1 Hz, 1H, H^5), 3.14 (dd, *J* = 11.2, 7.5 Hz, 1H, H^4), 3.01-2.94 (m, 1H, H^3), 2.47 (s, 3H), 2.22 (s, 9H); *minor diastereoisomer* when seen 7.84 (d, *J* = 8.0 Hz, 2H), 7.39-7.34 (m, 2H), 6.89 (s, 2H), 2.47 (s, 3H), 2.20 (s, 9H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.7, 136.7, 132.8, 131.2, 129.7, 127.9, 127.8, 51.8 (C^1 or C^4), 51.7 (C^1 or C^4), 45.2 (C^2 or C^3), 45.1 (C^2 or C^3), 41.9 (C^5), 21.6, 20.6; *minor diastereoisomer* signals for carbons were not observed; FTIR (ν_{max} cm^{-1}) 2926 (sp^3 C-H), 2856 (sp^3 C-H), 1346 (sulfone), 1161 (sulfone); HRMS (ESI+) calculated for $C_{21}H_{27}ClNO_2S$ $[M+H]^+$ 392.1446, found 392.1434.



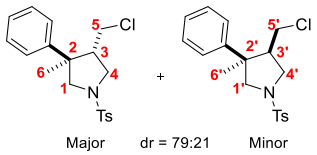
3-(chloromethyl)-1-tosyl-4-(2-vinylphenyl)pyrrolidine (4d). According to general procedure C1, isolated as a colorless oil (55.1 mg, 0.147 mmol, 73%) of a mixture of non separable diastereoisomers (dr = 72:28). R_f 0.45 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.78 (d, *J* = 7.6 Hz, 2H), 7.41-7.36 (m, 2H), 7.35-7.20 (m, 2H), 7.14-7.00 (m, 2H), 6.71-6.56 (m, 1H, H^6), 5.75-5.68 (m, 1H, H^{7a}), 5.29-5.24 (m, 1H, H^{7b}), 3.76-3.68 (m, 2H, H^1, H^4), 3.52-3.45 (m, 1H, H^5), 3.37-3.27 (m, 3H, H^1, H^4, H^5), 3.06-2.98 (m, 1H, H^2), 2.56-2.50 (m, 1H, H^3), 2.48 (s, 3H); *minor diastereoisomer* 7.81 (d, *J* = 7.6 Hz, 2H), 7.41-7.36 (m, 2H), 7.35-7.20 (m, 2H), 7.14-7.00 (m, 2H), 6.71-6.56 (m, 1H, $H^{6'}$), 5.75-5.68 (m, 1H, $H^{7a'}$), 5.29-5.24 (m, 1H, $H^{7b'}$), 3.76-3.68 (m, 1H, $H^{1'}$), 3.65-3.60 (m, 2H, $H^{1'}$, $H^{4'}$), 3.52-3.45 (m, 1H, $H^{2'}$), 3.37-3.27 (m, 1H, $H^{4'}$), 3.06-2.98 (m, 1H, $H^{5'}$), 2.86-2.81 (m, 1H, $H^{5'}$), 2.67-2.59 (m, 1H, $H^{3'}$), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.8, 138.8, 138.3, 136.3 (C^6), 133.6, 129.8, 129.2, 127.6, 126.7, 125.4, 125.3, 114.6 (C^7), 54.5 (C^1), 51.3 (C^4), 47.9 (C^3), 47.3 (C^2), 44.1 (C^5), 21.6; *minor diastereoisomer* 143.7, 138.1, 137.8, 136.4 ($C^{6'}$), 133.9, 129.9, 129.0, 127.5, 125.8, 125.1, 124.6, 114.2 ($C^{7'}$), 52.5 ($C^{1'}$), 50.3 ($C^{4'}$), 45.7 ($C^{2'}$ or $C^{3'}$), 45.6 ($C^{2'}$ or $C^{3'}$), 43.0 ($C^{5'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2957 (sp^3 C-H), 2871 (sp^3 C-H), 1596 (C=C), 1340 (sulfone), 1154 (sulfone); HRMS (ESI+) calculated for $C_{20}H_{23}ClNO_2S$ $[M+H]^+$ 376.1133, found 376.1117.



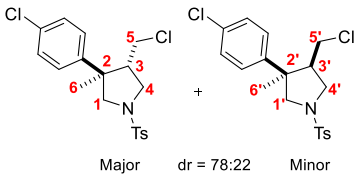
3-(chloromethyl)-4-(4-nitrophenyl)-1-tosylpyrrolidine (4e). According to general procedure C1, isolated as a colorless oil (62.1 mg, 0.157 mmol, 79%) of a mixture of non separable diastereoisomers (dr = 70:30). R_f 0.27 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 8.17 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.41-7.38 (m, 2H), 7.32-7.30 (m, 2H), 3.72 (dd, *J* = 10.3, 7.9 Hz, 2H, H^1, H^4), 3.44 (dd, *J* = 11.5, 4.7 Hz, 1H, H^5), 3.38 (dd, *J* = 10.3, 8.3 Hz, 1H, H^1), 3.32 (dd, *J* = 11.5, 6.6 Hz, 1H, H^5), 3.29-3.22 (m, 2H, H^2, H^4), 2.60-2.54 (m, 1H, H^3), 2.48 (s, 3H); *minor diastereoisomer* 8.13 (d, *J* = 8.8 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.41-7.38 (m, 2H), 7.32-7.30 (m, 2H), 3.68-3.65 (m, 1H, $H^{1'}$), 3.63-3.60 (m, 2H, $H^{2'}$, $H^{4'}$), 3.29-3.22 (m, 1H, $H^{1'}$), 3.21-3.15 (m, 1H, $H^{4'}$), 2.95 (dd, *J* = 11.2, 7.8 Hz, 1H, $H^{5'}$), 2.88 (dd, *J* = 11.2, 7.3 Hz, 1H, $H^{5'}$), 2.73-2.69 (m, 1H, $H^{3'}$), 2.49 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 146.7, 144.1, 133.1, 129.9, 128.9, 128.3, 127.7, 124.2, 54.0 (C^1), 50.9 (C^4), 48.1 (C^3), 46.9 (C^2), 43.8 (C^5), 21.6; *minor diastereoisomer* 147.4, 145.3, 133.1, 130.0, 128.9, 128.3, 127.5, 123.9, 52.7 ($C^{1'}$), 49.7 ($C^{4'}$), 45.6 ($C^{3'}$), 45.4 ($C^{2'}$), 42.2 ($C^{5'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2954 (sp^3 C-H), 2925 (sp^3 C-H), 1516 (NO_2), 1343 (NO_2 and sulfone), 1155 (sulfone); HRMS (ESI+) calculated for $C_{18}H_{20}ClN_2O_4S$ $[M+H]^+$ 395.0832, found 395.0824.



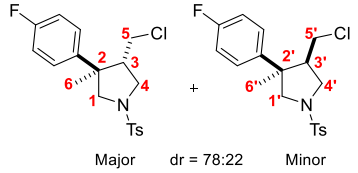
3-(4-(chloromethyl)-1-tosylpyrrolidin-3-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (4f). According to general procedure C1, isolated as a colorless oil (89.5 mg, 0.170 mmol, 85%) of a mixture of non separable diastereoisomers (dr = 76:24). R_f 0.24 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.75 (d, *J* = 8.2 Hz, 2H), 7.39-7.35 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.83-6.79 (m, 1H), 3.72-3.68 (m, 2H, H^1, H^4), 3.46 (dd, *J* = 11.3, 3.9 Hz, 1H, H^5), 3.35-3.23 (m, 3H, H^1, H^4, H^5), 2.96 (d, *J* = 9.6 Hz, 1H, H^2), 2.87-2.83 (m, 2H, $2H^6$), 2.53-2.48 (m, 2H, H^3, H^{10}), 2.47 (s, 3H), 2.40-2.35 (m, 1H, H^{16}), 2.29-2.21 (m, 1H, H^{17}), 2.17-2.10 (m, 1H, H^{10}), 2.09-1.98 (m, 2H, H^7, H^{11}), 1.97-1.93 (m, 1H, H^{15}), 1.67-1.38 (m, 5H, H^7, H^8, H^9, H^{11}, H^{15}, H^{16}), 0.90 (s, 3H, H^{14}); *minor diastereoisomer* 7.79 (d, *J* = 8.2 Hz, 2H), 7.39-7.35 (m, 2H), 7.16 (d, *J* = 8.2 Hz, 1H), 6.83-6.79 (m, 1H), 6.72 (d, *J* = 18.3 Hz, 1H), 3.67-3.64 (m, 1H, $H^{1'}$), 3.63-3.59 (m, 1H, $H^{4'}$), 3.57 (dd, *J* = 10.1, 4.8 Hz, 1H, $H^{1'}$), 3.43-3.40 (m, 1H, $H^{2'}$), 3.35-3.23 (m, 1H, $H^{4'}$), 3.08-3.03 (m, 1H, $H^{5'}$), 2.82-2.75 (m, 3H, $H^{5'}$, $2H^{6'}$), 2.63-2.56 (m, 1H, $H^{3'}$), 2.53-2.48 (m, 1H, $H^{10'}$), 2.47 (s, 3H), 2.40-2.35 (m, 1H, $H^{16'}$), 2.29-2.21 (m, 1H, $H^{17'}$), 2.17-2.10 (m, 1H, $H^{10'}$), 2.09-1.98 (m, 2H, $H^{7'}$, $H^{11'}$), 1.97-1.93 (m, 1H, $H^{15'}$), 1.67-1.38 (m, 6H, $H^{7'}$, $H^{8'}$, $H^{9'}$, $H^{11'}$, $H^{15'}$, $H^{16'}$), 0.90 (s, 3H, $H^{14'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 220.6 (C^{11}), 143.7, 139.2, 137.2, 135.8, 136.6, 129.8, 128.0, 127.6, 125.9, 124.8, 54.6 (C^1), 51.4 (C^{13}), 50.4 (C^4), 47.9 (C^3), 46.9 (C^2), 44.3 (C^5 and C^{17}), 38.0 (C^{11}), 35.8 (C^{10}), 31.5 (C^{15}), 29.4 (C^6), 26.4 (C^7), 25.6 (C^{16}), 21.6, 13.8 (C^{14}); *minor diastereoisomer* 220.6 ($C^{11'}$), 143.7, 139.0, 137.0, 134.8, 133.8, 129.9, 128.2, 127.5, 125.7, 125.3, 52.5 ($C^{1'}$), 51.4 ($C^{13'}$), 50.3 ($C^{4'}$), 45.6 ($C^{3'}$), 46.9 ($C^{2'}$), 44.3 ($C^{5'}$ or $C^{17'}$), 43.2 ($C^{5'}$ or $C^{17'}$), 38.0 ($C^{11'}$), 35.8 ($C^{10'}$), 31.5 ($C^{15'}$), 29.6 ($C^{6'}$), 26.4 ($C^{7'}$), 25.6 ($C^{16'}$), 21.6, 13.8 ($C^{14'}$); FTIR (ν_{max} cm^{-1}) 2924 (sp^3 C-H), 2863 (sp^3 C-H), 1734 (C=O), 1338 (sulfone), 1161 (sulfone); HRMS (ESI+) calculated for $C_{30}H_{36}ClNO_3SNa$ $[M+Na]^+$ 548.1996, found 548.1991.



4-(chloromethyl)-3-methyl-3-phenyl-1-tosylpyrrolidine (4g). According to general procedure C1, isolated as a colorless oil (72.9 mg, 0.2 mmol, 99%) of a mixture of non separable diastereoisomers (dr = 79:21). With general procedure C2 (60.1 mg, 0.153 mmol, 83%). R_f 0.47 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.76 (d, *J* = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.34-7.21 (m, 5H), 3.77 (dd, *J* = 10.4, 8.0 Hz, 1H, H^4), 3.49-3.43 (m, 3H, $2H^1$, H^5), 3.32 (dd, *J* = 10.4, 9.0 Hz, 1H, H^4), 3.24 (t, *J* = 11.0 Hz, 1H, H^5), 2.78-2.70 (m, 1H, H^3), 2.46 (s, 3H), 1.21 (s, 3H, H^6); *minor diastereoisomer* 7.81 (d, *J* = 8.0 Hz, 2H), 7.34-7.21 (m, 3H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.74-3.70 (m, 1H, $H^{4'}$), 3.69 (d, *J* = 9.7 Hz, 1H, $H^{1'}$), 3.49-3.43 (m, 3H, $H^{1'}$, $H^{4'}$, $H^{5'}$), 3.17-3.13 (m, 1H, $H^{5'}$), 2.45 (s, 3H), 2.41-2.38 (m, 1H, $H^{3'}$), 1.35 (s, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.7, 142.9, 133.8, 129.8, 128.8, 127.5, 127.1, 125.6, 61.7 (C^1), 51.1 (C^4), 50.3 (C^3), 47.4 (C^2), 42.9 (C^5), 21.6, 19.7 (C^6); *minor diastereoisomer* 143.7, 141.8, 133.8, 129.8, 128.8, 127.4, 127.0, 126.1, 57.7 ($C^{1'}$), 50.8 ($C^{3'}$), 50.3 ($C^{4'}$), 48.5 ($C^{2'}$), 43.9 ($C^{5'}$), 28.1 ($C^{6'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2921 (sp^3 C-H), 2858 (sp^3 C-H), 1343 (sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{22}ClNO_2SNa$ $[M+Na]^+$ 386.0942, found 386.0948.

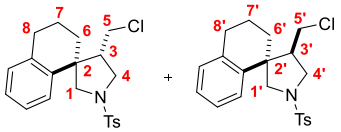


4-(chloromethyl)-3-(4-chlorophenyl)-3-methyl-1-tosyl pyrrolidine (4h). According to general procedure C1, isolated as a colorless oil (60.2 mg, 0.151 mmol, 76%) of a mixture of non separable diastereoisomers (dr = 78:22). R_f 0.51 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.73 (d, *J* = 8.2 Hz, 2H), 7.37-7.33 (m, 2H), 7.28-7.24 (m, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 3.73 (dd, *J* = 10.5, 7.9 Hz, 1H, H^4), 3.45-3.37 (m, 3H, $2H^1$, H^5), 3.29 (dd, *J* = 10.5, 8.7 Hz, 1H, H^4), 3.20 (t, *J* = 11.0 Hz, 1H, H^5), 2.70-2.63 (m, 1H, H^3), 2.45 (s, 3H), 1.17 (s, 3H, H^6); *minor diastereoisomer* 7.78 (d, *J* = 8.2 Hz, 2H), 7.37-7.33 (m, 2H), 7.28-7.24 (m, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 3.71-3.67 (m, 1H, $H^{4'}$), 3.65 (d, *J* = 9.7 Hz, 1H, $H^{1'}$), 3.45-3.37 (m, 3H, $H^{1'}$, $H^{4'}$, $H^{5'}$), 3.12-3.08 (m, 1H, $H^{5'}$), 2.44 (s, 3H), 2.37-2.32 (m, 1H, $H^{3'}$), 1.32 (s, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.8, 141.5, 133.7, 133.0, 129.8, 128.8, 127.4, 127.1, 61.5 (C^1), 51.0 (C^4), 50.4 (C^3), 47.1 (C^2), 42.6 (C^5), 21.6, 19.6 (C^6); *minor diastereoisomer* 143.9, 140.3, 133.7, 133.0, 129.9, 128.9, 127.7, 127.4, 58.0 ($C^{1'}$), 50.7 ($C^{3'}$), 50.4 ($C^{4'}$), 48.1 ($C^{2'}$), 43.5 ($C^{5'}$), 27.7 ($C^{6'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2972 (sp^3 C-H), 2926 (sp^3 C-H), 2881 (sp^3 C-H), 1343 (sulfone), 1154 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{21}Cl_2NO_2SNa$ $[M+Na]^+$ 420.0562, found 420.0553.

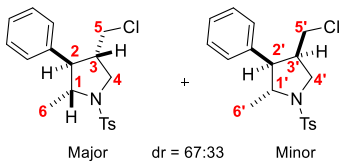


4-(chloromethyl)-3-(4-fluorophenyl)-3-methyl-1-tosyl pyrrolidine (4i). According to general procedure C1, isolated as a

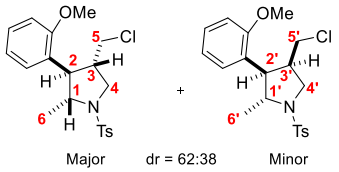
colorless oil (56.0 mg, 0.147 mmol, 73%) of a mixture of non separable diastereoisomers (dr = 78:22). R_f 0.40 (25% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.74 (d, *J* = 8.3 Hz, 2H), 7.37-7.35 (m, 2H), 7.21-7.19 (m, 2H), 7.01-6.97 (m, 2H), 3.75 (dd, *J* = 10.4, 7.8 Hz, 1H, H^4), 3.45-3.40 (m, 3H, $2H^1$, H^5), 3.31 (dd, *J* = 10.4, 8.8 Hz, 1H, H^4), 3.22 (t, *J* = 11.0 Hz, 1H, H^5), 2.68 (dtd, *J* = 11.0, 8.4, 4.0 Hz, 1H, H^3), 2.46 (s, 3H), 1.19 (s, 3H, H^6); *minor diastereoisomer* 7.79 (d, *J* = 8.3 Hz, 2H), 7.37-7.35 (m, 2H), 7.12-7.09 (m, 2H), 7.01-6.97 (m, 2H), 3.71 (dd, *J* = 10.4, 7.8 Hz, 1H, $H^{4'}$), 3.67 (d, *J* = 10.0 Hz, 1H, $H^{1'}$), 3.45-3.40 (m, 3H, $H^{1'}$, $H^{4'}$, $H^{5'}$), 3.12 (dd, *J* = 11.0, 4.0 Hz, 1H, $H^{5'}$), 2.45 (s, 3H), 2.38-2.32 (m, 1H, $H^{3'}$), 1.34 (s, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 161.6 (d, *J* = 247 Hz), 143.8, 138.7 (d, *J* = 3 Hz), 133.7, 129.8, 127.4, 127.3 (d, *J* = 8 Hz), 115.5 (d, *J* = 21 Hz), 61.6 (C^1), 51.0 (C^4), 42.7 (C^5), 21.6, 19.7 (C^6); *minor diastereoisomer* 143.7, 137.5 (d, *J* = 3 Hz), 133.7, 129.9, 127.8 (d, *J* = 8 Hz), 127.4, 115.7 (d, *J* = 21 Hz), 58.2 ($C^{1'}$), 50.8 ($C^{4'}$), 43.6 ($C^{5'}$), 27.8 ($C^{6'}$), 21.6; ^{19}F NMR ($CDCl_3$) δ -116.2, -116.4; FTIR (ν_{max} cm^{-1}) 2968 (sp^3 C-H), 2880 (sp^3 C-H), 1341 (sulfone), 1153 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{22}ClNO_2SF$ $[M+H]^+$ 382.1038, found 382.1026.



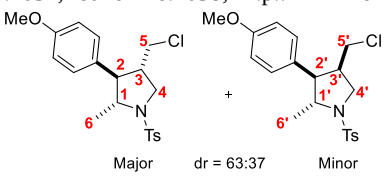
4'-(chloromethyl)-1'-tosyl-3,4-dihydro-2H-spiro[naphthalene-1,3'-pyrrolidine] (4j). According to general procedure C1, isolated as an off-white solid (44 mg, 0.113 mmol, 56%) of a mixture of non separable diastereoisomers (dr = 76:24). With general procedure C2 (39.5 mg, 0.101 mmol, 51%). R_f 0.51 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.78-7.74 (m, 2H), 7.40-7.35 (m, 2H), 7.15-7.03 (m, 4H), 3.87 (dd, *J* = 10.3, 7.9 Hz, 1H, H^4), 3.62 (d, *J* = 10.3 Hz, 1H, H^1), 3.33-3.24 (m, 3H, H^4, $2H^5$), 3.23 (d, *J* = 10.3 Hz, 1H, H^1), 2.91-2.85 (m, 1H, H^3), 2.73-2.66 (m, 2H, $2H^8$), 2.47 (s, 3H), 1.76-1.69 (m, 1H, H^7), 1.67-1.56 (m, 1H, H^7), 1.47-1.37 (m, 2H, $2H^6$); *minor diastereoisomer* 7.78-7.74 (m, 2H), 7.40-7.35 (m, 2H), 7.15-7.03 (m, 4H), 3.71 (d, *J* = 10.1 Hz, 1H, $H^{1'}$), 3.64-3.60 (m, 1H, $H^{4'}$), 3.41 (dd, *J* = 10.5, 6.7 Hz, 1H, $H^{4'}$), 3.17 (d, *J* = 10.1 Hz, 1H, $H^{1'}$), 3.06 (dd, *J* = 11.0, 3.8 Hz, 1H, $H^{5'}$), 2.90-2.82 (m, 1H, $H^{5'}$), 2.77 (t, *J* = 6.3 Hz, 2H, $2H^{8'}$), 2.48 (s, 3H), 2.45-2.41 (m, 1H, $H^{3'}$), 1.81-1.76 (m, 3H, $H^{6'}$, $2H^{7'}$), 1.76-1.69 (m, 1H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.6, 138.6, 136.0, 134.1, 129.8, 127.4, 126.9, 126.6, 125.6, 61.7 (C^1), 51.0 (C^3), 50.6 (C^4), 47.2 (C^2), 42.6 (C^5), 30.1 (C^8), 27.0 (C^6), 21.6, 19.7 (C^7); *minor diastereoisomer* 143.8, 137.0, 136.9, 132.6, 129.6, 127.9, 127.2, 126.9, 126.1, 62.6 ($C^{1'}$), 52.6 ($C^{4'}$), 52.1 ($C^{3'}$), 46.1 ($C^{5'}$), 37.5 ($C^{2'}$), 29.7 ($C^{8'}$), 29.3 ($C^{6'}$), 21.6, 20.0 ($C^{7'}$); FTIR (ν_{max} cm^{-1}) 2914 (sp^3 C-H), 2853 (sp^3 C-H), 1340 (sulfone), 1161 (sulfone); HRMS (ESI+) calculated for $C_{21}H_{24}ClNO_2SNa$ $[M+Na]^+$ 412.1109, found 412.1095.



4-(chloromethyl)-2-methyl-3-phenyl-1-tosylpyrrolidine (4k). According to general procedure C1, from the *E*-β-methylstyrene, isolated as a colorless oil (56.3 mg, 0.155 mmol, 77%) of a mixture of non separable diastereoisomers (dr = 67:33). With *Z*-β-methylstyrene (49.8 mg, 0.137 mmol, 68%). R_f 0.49 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.81 (d, *J* = 8.0 Hz, 2H), 7.43-7.39 (m, 2H), 7.29-7.23 (m, 2H), 7.11 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 7.2 Hz, 2H), 3.95-3.89 (m, 1H, H^4), 3.63 (dq, *J* = 9.2, 6.1 Hz, 1H, H^1), 3.40 (dd, *J* = 11.8, 10.5 Hz, 1H, H^4), 3.35 (dd, *J* = 11.4, 3.5 Hz, 1H, H^5), 3.20 (dd, *J* = 11.4, 7.6 Hz, 1H, H^5), 2.66 (dd, *J* = 9.2, 1.3 Hz, 1H, H^2), 2.50 (s, 3H), 2.12-2.02 (m, 1H, H^3), 1.37 (d, *J* = 6.2 Hz, 3H, H^6); *minor diastereoisomer* 7.84 (d, *J* = 8.0 Hz, 2H), 7.43-7.39 (m, 2H), 7.29-7.23 (m, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 7.2 Hz, 2H), 3.95-3.89 (m, 1H, $H^{1'}$), 3.76 (dd, *J* = 10.2, 6.6 Hz, 1H, $H^{4'}$), 3.30 (dd, *J* = 10.2, 8.0 Hz, 1H, $H^{4'}$), 3.16 (dd, *J* = 7.1, 4.4 Hz, 1H, $H^{2'}$), 2.92 (dd, *J* = 10.8, 5.9 Hz, 1H, $H^{5'}$), 2.88-2.79 (m, 1H, $H^{3'}$), 2.60 (dd, *J* = 10.8, 9.3 Hz, 1H, $H^{5'}$), 2.51 (s, 3H), 1.49 (d, *J* = 6.2 Hz, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.7, 137.7, 135.1, 129.8, 129.0, 128.6, 127.7, 127.5, 63.9 (C^1), 57.0 (C^2), 52.3 (C^4), 46.7 (C^3), 43.7 (C^5), 21.6, 20.6 (C^6); *minor diastereoisomer* 143.6, 137.8, 135.1, 129.9, 127.9, 127.7, 127.5, 127.3, 61.2 ($C^{1'}$), 54.7 ($C^{2'}$), 51.1 ($C^{4'}$), 44.1 ($C^{3'}$), 43.0 ($C^{5'}$), 23.1 ($C^{6'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2967 (sp^3 C-H), 2924 (sp^3 C-H), 1343 (sulfone), 1161 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{22}ClNO_2SNa$ $[M+Na]^+$ 386.0951, found 386.0944.

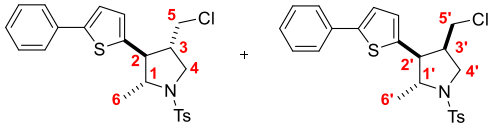


4-(chloromethyl)-3-(2-methoxyphenyl)-2-methyl-1-tosylpyrrolidine (4l). According to general procedure C1, isolated as a white solid (65.3 mg, 0.166 mmol, 83%) of a mixture of separable diastereoisomers (dr = 62:38). *Analyses for major diastereoisomer* (white solid). R_f 0.55 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.79 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.20 (ddd, *J* = 8.8, 7.5, 1.7 Hz, 1H), 6.86-6.80 (m, 2H), 6.77 (dd, *J* = 7.5, 1.7 Hz, 1H), 3.86 (dd, J = 11.5, 7.5 Hz, 1H, H^4), 3.73 (dq, *J* = 9.3, 6.2 Hz, 1H, H^1), 3.64 (s, 3H, OMe), 3.38 (dd, *J* = 11.5, 9.8 Hz, 1H, H^4), 3.33 (dd, *J* = 11.2, 3.9 Hz, 1H, H^5), 3.24 (dd, *J* = 11.2, 8.6 Hz, 1H, H^5), 3.06 (dd, *J* = 10.9, 9.3 Hz, 1H, H^2), 2.48 (s, 3H), 2.36-2.28 (m, 1H, H^3), 1.34 (d, *J* = 6.2 Hz, 3H, H^6); ^{13}C NMR ($CDCl_3$) δ 157.6, 143.4, 135.1, 129.7, 128.8, 128.6, 127.7, 125.6, 120.9, 110.9, 62.1 (C^1), 55.1 (OMe), 52.8 (C^4), 51.6 (C^2), 45.1 (C^3), 44.8 (C^5), 21.6, 21.0 (C^6); FTIR (ν_{max} cm^{-1}) 2964 (sp^3 C-H), 2921 (sp^3 C-H), 2848 (sp^3 C-H), 1333 (sulfone), 1245 (ether C-O), 1164 (sulfone); HRMS (ESI+) calculated for $C_{20}H_{24}ClNO_3SNa$ $[M+Na]^+$ 416.1054, found 416.1050; M.p.: 105-107 °C. *Analyses for minor diastereoisomer* (white solid). R_f 0.60 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.17 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 6.81 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.66 (td, *J* = 7.4, 1.2 Hz, 1H), 6.42 (d, *J* = 7.4 Hz, 1H), 3.91 (p, J = 6.7 Hz, 1H, $H^{1'}$), 3.81-3.88 (m 1H, $H^{4'}$), 3.76 (s, 3H, OMe), 3.59 (t, *J* = 6.7 Hz, 1H, $H^{2'}$), 3.42 (dd, *J* = 10.6, 6.1 Hz, 1H, $H^{4'}$), 3.06 (dd, *J* = 11.2, 4.1 Hz, 1H, $H^{5'}$), 2.89-2.78 (m, 1H, $H^{3'}$), 2.35 (t, *J* = 11.2 Hz, 1H, $H^{5'}$), 2.48 (s, 3H), 1.46 (d, *J* = 6.2 Hz, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) 157.1, 143.5, 135.1, 129.8, 128.2, 127.5, 125.4, 120.5, 110.3, 59.5 ($C^{1'}$), 55.2 (OMe), 51.6 ($C^{4'}$), 43.6 ($C^{5'}$), 42.9 ($C^{3'}$), 22.6 ($C^{6'}$), 21.6. $C^{2'}$ was not observed; FTIR (ν_{max} cm^{-1}) 2970 (sp^3 C-H), 2924 (sp^3 C-H), 2851 (sp^3 C-H), 1346 (sulfone), 1245 (ether C-O), 1162 (sulfone); HRMS (ESI+) calculated for $C_{20}H_{24}ClNO_3SNa$ $[M+Na]^+$ 416.1054, found 416.1058; M.p.: 114-116 °C.

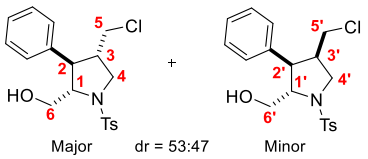


4-(chloromethyl)-3-(4-methoxyphenyl)-2-methyl-1-tosyl pyrrolidine (4m). According to general procedure C1, isolated as a clear yellow oil (71.5 mg, 0.182 mmol, 91%) of a mixture of non separable diastereoisomers (dr = 63:37). With general procedure C2 (68.8 mg, 0.175 mmol, 87%). R_f 0.35 (30%

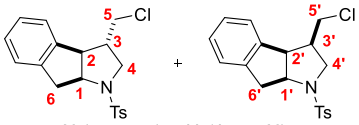
EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.79 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.83-6.77 (m, 4H), 3.91-3.85 (m, 1H, H^4), 3.77 (s, 3H, OMe), 3.54 (dq, *J* = 9.2, 6.2 Hz, 1H, H^1), 3.40-3.31 (m, 2H, H^4, H^5), 3.18 (dd, *J* = 11.4, 7.6 Hz, 1H, H^5), 2.60 (dd, *J* = 11.7, 9.2 Hz, 1H, H^2), 2.48 (s, 3H), 2.03-1.95 (m, 1H, H^3), 1.35 (d, *J* = 6.2 Hz, 3H, H^6); *minor diastereoisomer* 7.82 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.63 (d, *J* = 8.9 Hz, 2H), 6.57 (d, *J* = 8.9 Hz, 2H), 3.91-3.85 (m, 1H, $H^{1'}$), 3.74-3.70 (m, 1H, $H^{4'}$), 3.74 (s, 3H, OMe), 3.27 (dd, *J* = 10.2, 8.0 Hz, 1H, $H^{4'}$), 3.10 (dd, *J* = 7.1, 4.4 Hz, 1H, $H^{2'}$), 2.92 (dd, *J* = 10.8, 5.9 Hz, 1H, $H^{5'}$), 2.85-2.74 (m, 1H, $H^{3'}$), 2.60 (dd, *J* = 11.7, 9.6 Hz, 1H, $H^{5'}$), 2.49 (s, 3H), 1.46 (d, *J* = 6.2 Hz, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 159.1, 143.7, 135.1, 129.8, 129.4, 128.7, 127.5, 114.4, 63.9 (C^1), 56.3 (C^2), 55.3 (OMe), 52.2 (C^4), 46.6 (C^3), 43.7 (C^5), 21.6, 20.5 (C^6); *minor diastereoisomer* 158.6, 143.6, 135.1, 129.9, 129.6, 128.9, 127.5, 113.9, 61.4 ($C^{1'}$), 55.2 (OMe), 53.9 ($C^{2'}$), 51.1 ($C^{4'}$), 44.1 ($C^{3'}$), 43.1 ($C^{5'}$), 23.0 ($C^{6'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2964 (sp^3 C-H), 2929 (sp^3 C-H), 1343 (sulfone), 1247 (ether C-O), 1141 (sulfone); HRMS (ESI+) calculated for $C_{20}H_{24}ClNO_3SNa$ $[M+Na]^+$ 416.1058, found 416.1049.



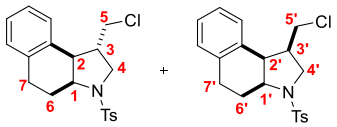
4-(chloromethyl)-2-methyl-3-(5-phenylthiophen-2-yl)-1-tosylpyrrolidine (4n). According to general procedure C1, isolated as an orange oil (62.1 mg, 0.139 mmol, 70%) of a mixture of non separable diastereoisomers (dr = 65:35). With general procedure C2 (50.1 mg, 0.112 mmol, 56%). R_f 0.43 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.80 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 2H), 7.42-7.33 (m, 3H), 7.30-7.25 (m, 2H), 7.10 (d, *J* = 3.6 Hz, 1H), 6.71 (d, *J* = 3.6 Hz, 1H), 3.89-3.8 (m, 1H, H^4), 3.65 (dq, *J* = 9.0, 6.2 Hz, 1H, H^1), 3.51 (dd, *J* = 11.5, 3.5 Hz, 1H, H^5), 3.46-3.39 (m, 1H, H^4), 3.34 (dd, *J* = 11.5, 7.2 Hz, 1H, H^5), 3.01 (dd, *J* = 11.1, 9.0 Hz, 1H, H^2), 2.48 (s, 3H), 2.07-1.99 (m, 1H, H^3), 1.48 (d, *J* = 6.2 Hz, 3H, H^6); *minor diastereoisomer* 7.83 (d, *J* = 8.0 Hz, 2H), 7.42-7.33 (m, 6H), 7.30-7.25 (m, 1H), 7.01 (d, *J* = 3.6 Hz, 1H), 6.50 (d, *J* = 3.6 Hz, 1H), 3.89-3.82 (m, 1H, $H^{1'}$), 3.80 (dd, *J* = 9.9, 5.8 Hz, 1H, $H^{4'}$), 3.32-3.28 (m, 1H, $H^{4'}$), 3.46-3.39 (m, 1H, $H^{2'}$),3.14-3.09 (m, 1H, $H^{5'}$), 2.90-2.85 (m, 2H, $H^{3'}$, $H^{5'}$), 2.45 (s, 3H), 1.54 (d, *J* = 6.2 Hz, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.8, 143.6, 140.5, 134.8, 133.9, 129.9, 128.9, 127.8, 127.6, 126.8, 125.6, 122.9, 64.2 (C^1), 52.0 (C^2), 51.9 (C^4), 47.4 (C^3), 43.5 (C^5), 21.6, 20.8 (C^6); *minor diastereoisomer* 143.7, 143.6, 139.7, 134.8, 133.8, 129.8, 128.9, 127.7, 127.1, 126.4, 125.5, 122.5, 62.7 ($C^{1'}$), 50.5 ($C^{2'}$ or $C^{4'}$), 50.4 ($C^{2'}$ or $C^{4'}$), 43.8 ($C^{3'}$), 42.6 ($C^{5'}$), 23.2 ($C^{6'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2962 (sp^3 C-H), 2924 (sp^3 C-H), 2851 (sp^3 C-H), 1341 (sulfone), 1161 (sulfone); HRMS (ESI+) calculated for $C_{23}H_{25}ClNO_2S_2$ $[M+H]^+$ 446.1010, found 446.0999.



4-(chloromethyl)-3-phenyl-1-tosylpyrrolidin-2-yl)methanol (4o). According to general procedure C1, isolated as an colorless oil (37.2 mg, 0.098 mmol, 49%) of a mixture of non separable diastereoisomers (dr = 53:47). With general procedure C2 (41 mg, 0.108 mmol, 54%). R_f 0.27 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.83 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 6.9 Hz, 2H), 7.25-7.21 (m, 3H), 6.80 (dd, J = 6.0, 2.7 Hz, 2H), 4.04-3.98 (m, 1H, H^4), 3.63-3.55 (m, 2H, H^1, H^6), 3.87 (d, *J* = 11.4 Hz, 1H, H^6), 3.40 (t, *J* = 11.5 Hz, 1H, H^4), 3.36-3.31 (m, 1H, H^5), 3.20 (dd, *J* = 11.4, 8.1 Hz, 1H, H^5), 2.79 (br s, 1H, OH), 2.98 (dd, *J* = 11.4, 9.0 Hz, 1H, H^2), 2.52 (s, 3H), 2.03-1.96 (m, 1H, H^3); *minor diastereoisomer* 7.85 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 6.9 Hz, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 2H), 6.58 (d, *J* = 7.6 Hz, 2H), 3.94 (d, *J* = 9.8 Hz, 1H, $H^{6'}$), 3.84-3.75 (m, 3H, $H^{1'}$, $H^{4'}$, $H^{6'}$), 3.50 (dd, *J* = 7.2, 5.1 Hz, 1H, $H^{2'}$), 3.36-3.31 (m, 1H, $H^{4'}$), 2.90 (dd, *J* = 10.6, 5.6 Hz, 1H, $H^{5'}$), 2.70 (br s, 1H, OH), 2.87-2.81 (m, 1H, $H^{3'}$), 2.52 (s, 3H), 2.44 (t, *J* = 10.6 Hz, 1H, $H^{5'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 144.3, 135.5, 134.2, 130.1, 129.1, 127.8, 127.8, 127.7, 69.7 (C^1), 63.1 (C^6), 53.6 (C^4), 50.7 (C^2), 46.9 (C^3), 43.4 (C^5), 21.6; *minor diastereoisomer* 144.4, 135.4, 133.8, 130.1, 128.7, 127.9, 127.8, 127.4, 66.9 ($C^{1'}$), 65.4 ($C^{6'}$), 52.3 ($C^{4'}$), 50.0 ($C^{2'}$), 44.4 ($C^{3'}$), 42.9 ($C^{5'}$), 21.6; FTIR (ν_{max} cm^{-1}) 3487 (OH), 2926 (sp^3 C-H), 2871 (sp^3 C-H), 1335 (sulfone), 1154 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{23}ClNO_3S$ $[M+H]^+$ 380.1082, found 380.1074.

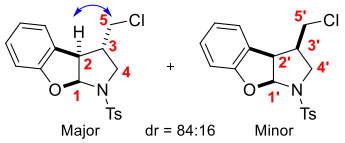


3-(chloromethyl)-1-tosyl-1,2,3,3a,8,8a-hexahydroindeno[2,1-b]pyrrole (4p). According to general procedure C1, isolated as a yellow oil (51.5 mg, 0.142 mmol, 71%) of a mixture of non separable diastereoisomers (dr = 60:40). With general procedure C2 (56.2 mg, 0.155 mmol, 78%). R_f 0.44 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.79-7.74 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.24-7.15 (m, 4H), 4.45 (dt, *J* = 8.0, 5.4 Hz, 1H, H^1), 3.89 (t, *J* = 7.7 Hz, 1H, H^2), 3.52-3.46 (m, 1H, H^4), 3.36-3.29 (m, 4H, $2H^5$, $2H^6$), 3.20 (dd, *J* = 10.9, 7.7 Hz, 1H, H^4), 2.46 (s, 3H), 2.44-2.39 (m, 1H, H^3); *minor diastereoisomer* 7.79-7.74 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.24-7.15 (m, 4H), 4.37 (dt, J = 6.9, 2.3 Hz, 1H, $H^{1'}$), 3.57 (dd, *J* = 7.2, 3.5 Hz, 1H, $H^{2'}$), 3.45-3.37 (m, 2H, $H^{4'}$, $H^{6'}$), 3.36-3.29 (m, 1H, $H^{6'}$), 3.29-3.24 (m, 2H, $H^{4'}$, $H^{5'}$), 2.97 (dd, *J* = 11.1, 8.4 Hz, H, $H^{5'}$), 2.64-2.59 (m, 1H, $H^{3'}$), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.7, 143.3, 137.9, 134.6, 129.8, 128.0, 127.5, 126.9, 125.3, 123.5, 64.0 (C^1), 52.3 (C^2), 52.2 (C^4), 44.8 (C^3), 43.2 (C^6), 40.9 (C^5), 21.6; *minor diastereoisomer* 143.7, 141.7, 141.4, 134.7, 129.8, 127.9, 127.4, 127.0, 125.3, 123.5, 63.3 ($C^{1'}$), 53.7 ($C^{2'}$), 51.8 ($C^{4'}$), 47.1 ($C^{3'}$), 45.1 ($C^{5'}$), 40.7 ($C^{6'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2912 (sp^3 C-H), 2853 (sp^3 C-H), 1338 (sulfone), 1154 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{20}ClNO_2SNa$ $[M+Na]^+$ 384.0795, found 384.0791.

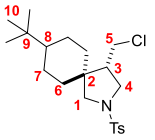


1-(chloromethyl)-3-tosyl-2,3,3a,4,5,9b-hexahydro-1H-benzo[e]indole (4q). According to general procedure C1, isolated as a clear yellow oil (27.6 mg, 0.073 mmol, 37%) of a mixture of non separable diastereoisomers (dr = 81:19). R_f 0.46 (30% EtOAc/hexane); ^{1}H ($CDCl_3$) δ for *major diastereoisomer* 7.78 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.18-7.10 (m, 3H), 6.99 (d, *J* = 6.9 Hz, 1H), 3.99 (td, *J* = 7.9, 4.5 Hz, 1H, H^1), 3.62 (dd, *J* = 10.0, 6.9 Hz, 1H, H^4), 3.57 (dd, *J* = 11.5, 3.9 Hz, 1H, H^5), 3.43 (dd, *J* = 11.5, 6.3 Hz, 1H, H^5), 3.19 (t, *J* = 9.4 Hz, 1H, H^4), 2.91 (t, *J* = 8.2 Hz, 1H, H^2), 2.89-2.83 (m, 1H, H^7), 2.76-2.70 (m, 1H, H^7), 2.50-2.46 (m, 1H, H^3), 2.45 (s, 3H), 2.21-2.14 (m, 1H, H^6), 2.06-1.99 (m, 1H, H^6); *minor diastereoisomer* 7.78 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.18-7.10 (m, 3H), 7.05 (d, *J* = 6.9 Hz, 1H), 3.86 (td, *J* = 9.7, 4.5 Hz, 1H, $H^{1'}$), 3.67-3.63 (m, 1H, $H^{4'}$), 3.35 (t, *J* = 8.3 Hz, 1H, $H^{2'}$), 3.32-3.24 (m, 2H, $H^{3'}$, $H^{4'}$), 2.83-2.77 (m, 1H, $H^{7'}$), 2.69-2.64 (m, 1H, $H^{7'}$), 2.45 (s, 3H), 2.40-2.35 (m, 1H, $H^{6'}$), 1.75-1.67 (m, 1H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.7, 137.1, 134.6, 133.9, 129.8, 128.9,

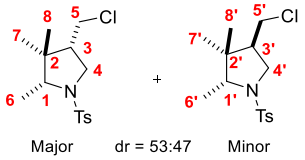
128.6, 127.6, 126.9, 126.3, 58.9 (C^1), 50.6 (C^4), 46.6 (C^3), 44.0 (C^5), 43.4 (C^2), 29.0 (C^6), 27.0 (C^7), 21.6; *minor diastereoisomer* 143.8, 137.7, 134.6, 133.9, 129.8, 129.0, 128.7, 127.7, 126.7, 126.6, 58.8 ($C^{1'}$), 51.6 ($C^{4'}$), 46.0 ($C^{3'}$), 44.3 ($C^{5'}$), 43.9 ($C^{2'}$), 30.0 ($C^{6'}$), 27.6 ($C^{7'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2931 (sp^3 C-H), 2853 (sp^3 C-H), 1335 (sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{20}H_{22}ClNO_2SNa$ $[M+Na]^+$ 398.0952, found 398.0949.



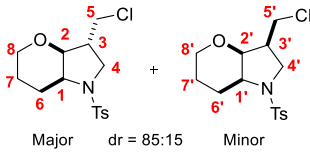
3-(chloromethyl)-1-tosyl-2,3,3a,8a-tetrahydro-1H-benzofuro[2,3-b]pyrrole (4r). A 10 mL microwave vial was charged with the amine **2a** (0.2 mmol, 1.0 equiv.), benzofuran (0.4 mmol, 2 equiv.), $Ir(dF(CF_3)_2ppy)_2(bpy)PF_6$ (0.001 mol, 0.5 mol%) and CH_2Cl_2 (4 mL, 0.05 M). The reaction mixture was stirred at 35 °C under blue LEDs irradation (450 nm, 14.4 W) for 1 h. The crude was concentrated *in vacuo* and purified by Florisil® flash column chromatography to yield the desired pyrrolidine **4r** as an off-white solid (48.1 mg, 0.132 mmol, 66%) of a mixture of two diastereoisomers (dr = 84:16). With the same conditions using CAT-4 (0.001 mol, 0.5 mol%) as the photocatalyst (34.1 mg, 0.094 mmol, 47%). R_f 0.44 (30% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ *major diastereoisomer* 7.84 (d, *J* = 8.3 Hz, 2H), 7.33-7.25 (m, 3H), 7.16-7.09 (m, 1H), 6.89-6.84 (m, 1H), 6.70-6.65 (m, 1H), 6.54 (d, *J* = 6.8 Hz, 1H, H^1), 4.26 (t, *J* = 7.5 Hz, 1H, H^2), 3.76 (dd, *J* = 9.6, 6.8 Hz, 1H, H^4), 3.61 (dd, J = 11.1, 8.2 Hz, 1H, H^5), 3.41 (dd, *J* = 11.1, 7.3 Hz, 1H, H^5), 2.98-2.89 (m, 1H, H^3), 2.62 (dd, *J* = 11.4, 9.6 Hz, 1H, H^4), 2.42 (s, 3H); *minor diastereoisomer* 7.84 (d, *J* = 8.3 Hz, 2H), 7.33-7.25 (m, 3H), 7.16-7.09 (m, 1H), 6.89-6.84 (m, 1H), 6.70-6.65 (m, 1H), 6.45 (d, *J* = 6.8 Hz, 1H, $H^{1'}$), 4.01 (d, *J* = 6.8 Hz, 1H, $H^{2'}$), 3.58-3.51 (m, 3H, $H^{3'}$, $H^{4'}$, $H^{5'}$), 3.11 (dd, *J* = 10.5, 5.7 Hz, 1H, $H^{5'}$), 2.62 (dd, *J* = 11.4, 9.6 Hz, 1H, $H^{4'}$), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 159.7, 143.8, 136.3, 129.5, 129.2, 127.8, 125.9, 121.7, 121.1, 109.7, 96.1 (C^1), 48.9 (C^4), 48.7 (C^2), 45.5 (C^3), 42.0 (C^5), 21.6; *minor diastereoisomer* 158.6, 143.8, 136.2, 129.5, 129.2, 127.8, 126.0, 124.4, 121.5, 109.6, 95.0 ($C^{1'}$), 50.6 ($C^{4'}$), 48.8 ($C^{2'}$), 45.8 ($C^{3'}$), 42.0 ($C^{5'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2926 (sp^3 C-H), 2859 (sp^3 C-H), 1346 (sulfone), 1222 (ether C-O), 1159 (sulfone); HRMS (ESI+) calculated for $C_{18}H_{18}ClNO_3SNa$ $[M+Na]^+$ 386.0588, found 386.0584.



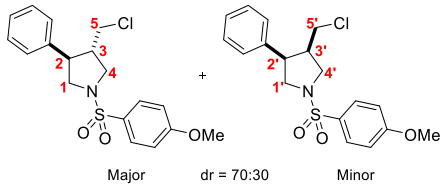
8-(*tert*-butyl)-4-(chloromethyl)-2-tosyl-2-azaspiro[4.5]decane (4s). According to general procedure C1, isolated as a white solid (46.3 mg, 0.116 mmol, 58%). R_f 0.59 (30% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 3.62 (d, *J* = 11.0 Hz, 1H, H^4), 3.48-3.43 (m, 2H, H^4, H^5), 3.01 (d, *J* = 9.8 Hz, 1H, H^1), 2.91 (d, *J* = 9.8 Hz, 1H, H^1), 2.74 (t, *J* = 11.1 Hz, 1H, H^5), 2.44 (s, 3H), 2.30-2.26 (m, 1H, H^3), 1.66-1.63 (m, 1H, H^6 or H^7), 1.60-1.57 (m, 1H, H^6 or H^7), 1.57-1.54 (m, 1H, H^6 or H^7), 1.49-1.46 (m, 1H, H^6 or H^7), 1.20 (td, *J* = 13.7, 3.6 Hz, 1H, H^6 or H^7), 1.04-1.02 (m, 2H, $2H^6$ or H^7), 0.98-0.92 (m, 1H, H^8), 0.88-0.84 (m, 1H, H^6 or H^7), 0.81 (s, 9H, H^{10}); ^{13}C NMR ($CDCl_3$) δ 143.5, 133.6, 129.6, 127.4, 59.1 (C^1), 49.8 (C^4), 47.6 (C^8), 44.6 (C^2), 44.0 (C^5), 43.9 (C^3), 36.7 (C^6 or C^7), 32.3 (C^9), 30.4 (C^6 or C^7), 27.4 (C^{10}), 24.0 (C^6 or C^7), 23.2 (C^6 or C^7), 21.6; FTIR (ν_{max} cm^{-1}) 2942 (sp^3 C-H), 2951 (sp^3 C-H), 1338 (sulfone), 1156 (sulfone); HRMS (ESI+) calculated for $C_{21}H_{33}NO_2SCl$ $[M+H]^+$ 398.1921, found 398.1922; M.p.: 140-142 °C.



4-(chloromethyl)-2,3,3-trimethyl-1-tosylpyrrolidine (4t). According to general procedure C1 and using 10 equiv. of 2-methylbut-2-ene, isolated as a colorless oil (42.3 mg, 0.134 mmol, 67%) of a mixture of non separable diastereoisomers (dr = 53:47). With general procedure C2 (46.7 mg, 0.148 mmol, 74%). R_f 0.44 (30% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ *major diastereoisomer* 7.74-7.69 (m, 2H), 7.35-7.29 (m, 2H), 3.76-3.67 (m, 1H, H^4), 3.50-3.45 (m, 1H, H^5), 3.28 (t, *J* = 10.7 Hz, 1H, H^5), 3.19 (t, *J* = 11.0 Hz, 1H, H^4), 2.99 (q, *J* = 6.4 Hz, 1H, H^1), 2.44 (s, 3H), 1.65-1.58 (m, 1H, H^3), 1.29 (d, *J* = 6.5 Hz, 3H, H^6), 0.84 (s, 3H, H^7 or H^8), 0.76 (s, 3H, H^7 or H^8); *minor diastereoisomer* 7.74-7.69 (m, 2H), 7.35-7.29 (m, 2H), 3.76-3.67 (m, 1H, $H^{4'}$), 3.50-3.45 (m, 1H, $H^{5'}$), 3.37 (q, *J* = 6.4 Hz, 1H, $H^{1'}$), 3.08 (t, J = 11.0 Hz, 1H, $H^{5'}$), 2.94 (t, *J* = 9.8 Hz, 1H, $H^{4'}$), 2.42 (s, 3H), 2.39-2.29 (m, 1H, $H^{3'}$), 1.23 (d, *J* = 6.5 Hz, 3H, $H^{6'}$) 0.94 (s, 3H, $H^{7'}$ or $H^{8'}$), 0.37 (s, 3H, $H^{7'}$ or $H^{8'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.5, 133.9, 129.7, 127.5, 66.4 (C^1), 52.0 (C^4), 49.7 (C^3), 43.6 (C^2), 42.8 (C^5), 24.8 (C^7 or C^8), 21.6, 15.7 (C^6), 15.6 (C^7 or C^8); *minor diastereoisomer* 143.3, 134.7, 129.6, 127.3, 66.6 ($C^{1'}$), 50.7 ($C^{4'}$), 48.0 ($C^{3'}$), 43.0 ($C^{2'}$), 42.9 ($C^{5'}$), 22.2 ($C^{7'}$ or $C^{8'}$), 21.5, 21.5 ($C^{7'}$ or $C^{8'}$), 18.9 ($C^{6'}$); FTIR (ν_{max} cm^{-1}) 2972 (sp^3 C-H), 2921 (sp^3 C-H), 1338 (sulfone), 1156 (sulfone); HRMS (ESI+) calculated for $C_{15}H_{22}ClNO_2SNa$ $[M+Na]^+$ 338.0952, found 338.0946.

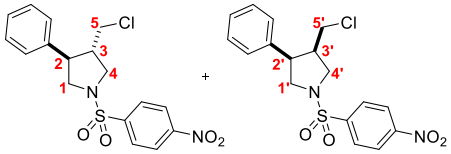


3-(chloromethyl)-1-tosyloctahydropyrano[3,2-b]pyrrole (4u). According to general procedure C1 and using 10 equiv. of 3,4-dihydro-2H-pyran, a mixture of diastereoisomers was observed (dr = 85:15) and the major diastereoisomer was isolated as a colorless oil (28.4 mg, 0.086 mmol, 43%). R_f 0.39 (30% EtOAc/hexane); ^1H NMR for *major diastereoisomer* ($CDCl_3$) δ 7.71 (d, *J* = 8.2 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 3.93-3.89 (m, 1H, H^8), 3.88 (t, *J* = 3.1 Hz, 1H, H^2), 3.70 (dd, *J* = 10.8, 8.0 Hz, 1H, H^4), 3.59 (dd, *J* = 10.8, 7.8 Hz, 1H, H^5), 3.40-3.29 (m, 4H, H^1, H^4, H^5, H^8), 2.62 (dt, *J* = 14.5, 4.9 Hz, 1H, H^6), 2.44 (s, 3H), 1.88-1.79 (m, 2H, H^3, H^7), 1.69 (tt, *J* = 13.6, 4.0 Hz, 1H, H^6), 1.37 (dd, *J* = 13.6, 2.2 Hz, 1H, H^7); ^{13}C NMR for *major diastereoisomer* ($CDCl_3$) δ 143.6, 134.2, 129.8, 127.4, 76.3 (C^2), 66.6 (C^8), 59.4 (C^1), 51.8 (C^4), 45.5 (C^3), 40.6 (C^5), 26.2 (C^6), 21.5, 20.2 (C^7); FTIR (ν_{max} cm^{-1}) 2952 (sp^3 C-H), 2922 (sp^3 C-H), 2899 (sp^3 C-H), 2853 (sp^3 C-H), 1336 (ether C-O and sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{15}H_{21}ClNO_3S$ $[M+H]^+$ 330.0931, found 330.0923.

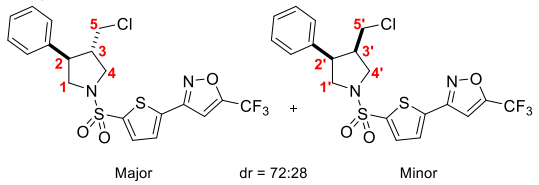


3-(chloromethyl)-1-((4-methoxyphenyl)sulfonyl)-4-phenyl pyrrolidine (4v). According to general procedure C1, isolated as a clear yellow oil (63.3 mg, 0.173 mmol, 87%) of a mixture of non separable diastereoisomers (dr = 70:30). With general procedure C2 (66.0 mg, 0.180 mmol, 90%). R_f 0.31 (30% EtOAc/hexane); ^1H NMR ($CDCl_3$) δ *major diastereoisomer* 7.81 (d, *J* = 8.9 Hz, 2H), 7.32-7.23 (m, 3H), 7.11 (d, *J* = 7.1 Hz, 2H), 7.08-7.02 (m, 2H), 3.90 (s, 3H), 3.75-3.64 (m, 2H, H^1, H^4), 3.46

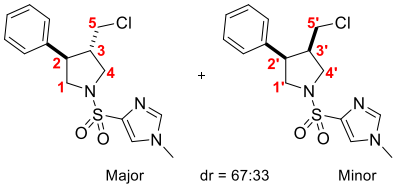
(dd, J = 11.3, 4.0 Hz, 1H, H^5), 3.36-3.24 (m, 3H, H^1, H^4, H^5), 3.05-2.98 (m, 1H, H^2), 2.56-2.48 (m, 1H, H^3); *minor diastereoisomer* 7.85 (d, J = 8.9 Hz, 2H), 7.32-7.23 (m, 4H), 7.08-7.02 (m, 3H), 3.90 (s, 3H), 3.75-3.64 (m, 1H, $H^{1'}$), 3.64-3.58 (m, 2H, $H^{1'}$, $H^{4'}$), 3.52-3.48 (m, 1H, $H^{2'}$), 3.36-3.24 (m, 1H, $H^{4'}$), 3.05-2.98 (m, 1H, $H^{5'}$), 2.81 (dd, J = 11.0, 9.2 Hz, 1H, $H^{5'}$), 2.66-2.60 (m, 1H, $H^{3'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 163.1, 138.5, 129.7, 129.0, 128.1, 127.6, 127.4, 114.4, 55.6, 54.6 (C^1), 51.3 (C^4), 48.0 (C^3), 47.3 (C^2), 44.2 (C^5); *minor diastereoisomer* 163.1, 137.5, 129.6, 128.8, 128.4, 127.8, 127.5, 114.4, 55.5, 52.5 ($C^{1'}$), 50.3 ($C^{4'}$), 45.8 ($C^{2'}$), 45.6 ($C^{3'}$), 43.1 ($C^{5'}$); FTIR (ν_{max} cm^{-1}) 2947 (sp^3 C-H), 2843 (sp^3 C-H), 1343 (sulfone), 1260 (ether C-O), 1154 (sulfone); HRMS (ESI+) calculated for $C_{18}H_{20}ClNO_3SNa$ $[M+Na]^+$ 388.0744, found 388.0743.



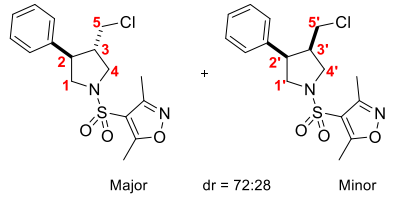
3-(chloromethyl)-1-((4-nitrophenyl)sulfonyl)-4-phenyl pyrrolidine (4w). According to general procedure C1, isolated as a yellow solid (64.3 mg, 0.169 mmol, 84%) of a mixture of non separable diastereoisomers (dr = 70:30). R_f 0.41 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 8.45-8.40 (m, 2H), 8.06 (d, J = 8.5 Hz, 2H), 7.34-7.25 (m, 3H), 7.12 (d, J = 7.4 Hz, 2H), 3.83-3.75 (m, 2H, H^1, H^4), 3.50 (dd, J = 11.5, 3.6 Hz, 1H, H^5), 3.40 (t, J = 10.0 Hz, 1H, H^1), 3.37-3.29 (m, 2H, H^4, H^5), 3.12-3.04 (m, 1H, H^2), 2.65-2.58 (m, 1H, H^3); *minor diastereoisomer* 8.45-8.40 (m, 2H), 8.10 (d, J = 8.5 Hz, 2H), 7.34-7.25 (m, 3H), 7.07 (d, J = 7.4 Hz, 2H), 3.73-3.69 (m, 2H, $2H^{1'}$), 3.66 (dd, J = 10.6, 7.3 Hz, 1H, $H^{4'}$), 3.55 (q, J = 6.5 Hz, 1H, $H^{2'}$), 3.44 (dd, J = 10.6, 6.3 Hz, 1H, $H^{4'}$), 3.12-3.04 (m, 1H, $H^{5'}$), 2.84 (dd, J = 11.1, 9.2 Hz, 1H, $H^{5'}$), 2.72-2.67 (m, 1H, $H^{3'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 150.2, 142.8, 137.4, 129.1, 128.6, 127.9, 127.3, 124.5, 54.6 (C^1), 51.1 (C^4), 47.8 (C^3), 47.2 (C^2), 43.7 (C^5); *minor diastereoisomer* 150.2, 142.9, 136.8, 129.0, 128.1, 127.7, 127.6, 124.5, 52.5 ($C^{1'}$), 50.4 ($C^{4'}$), 45.8 ($C^{2'}$), 45.6 ($C^{3'}$), 42.8 ($C^{5'}$); FTIR (ν_{max} cm^{-1}) 2959 (sp^3 C-H), 2888 (sp^3 C-H), 1530 (NO_2), 1351 (sulfone), 1310 (NO_2), 1167 (sulfone); HRMS (ESI+) calculated for $C_{17}H_{17}ClN_2O_4SNa$ $[M+Na]^+$ 403.0490, found 403.0478.



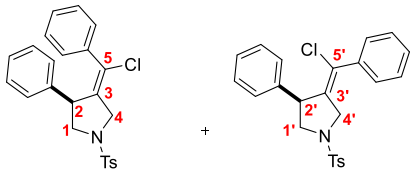
3-(5-((-3-(chloromethyl)-4-phenylpyrrolidin-1-yl)sulfonyl)thiophen-2-yl)-5-(trifluoromethyl)isoxazole (4x). According to general procedure C1, isolated as a colorless oil (67.0 mg, 0.141 mmol, 70%) of a mixture of non separable diastereoisomers (dr = 72:28). R_f 0.36 (25% EtOAc/hexane); ^{1}H ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.66-7.65 (m, 1H), 7.57-7.56 (m, 1H), 7.34-7.27 (m, 3H), 7.16-7.13 (m, 2H), 7.01-7.00 (m, 1H), 3.88-3.80 (m, 2H, H^1, H^4), 3.51-3.44 (m, 2H, H^1, H^5), 3.40-3.31 (m, 2H, H^4, H^5), 3.19-3.11 (m, 1H, H^2), 2.65-2.58 (m, 1H, H^3); *minor diastereoisomer* 7.69-7.68 (m, 1H), 7.57-7.56 (m, 1H), 7.34-7.27 (m, 3H), 7.16-7.13 (m, 2H), 7.01-7.00 (m, 1H), 3.77-3.75 (m, 2H, $2H^{1'}$), 3.71-3.68 (m, 1H, $H^{4'}$), 3.59-3.55 (m, 1H, $H^{2'}$), 3.51-3.44 (m, 1H, $H^{4'}$), 3.09-3.05 (m, 1H, $H^{5'}$), 2.93-2.86 (m, 1H, $H^{5'}$), 2.73-2.68 (m, 1H, $H^{3'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 156.7, 139.7, 137.5, 134.7, 132.4, 129.1, 128.3, 129.7, 127.4, 117.5 (q, J = 270 Hz), 103.5 (q, J = 5 Hz), 54.7 (C^1), 51.4 (C^4), 47.8 (C^3), 47.2 (C^2), 43.7 (C^5); *minor diastereoisomer* when seen 159.9, 139.8, 137.4, 136.9, 132.3, 129.0, 128.4, 127.7, 127.4, 54.9 ($C^{1'}$), 50.5 ($C^{4'}$), 45.9 ($C^{2'}$), 45.6 ($C^{3'}$), 42.8 ($C^{5'}$); ^{19}F NMR ($CDCl_3$) δ -65.1, -65.2; FTIR (ν_{max} cm^{-1}) 2954 (sp^3 C-H), 2925 (sp^3 C-H), 1343 (sulfone), 1155 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{17}ClN_2O_3S_2F_3$ $[M+H]^+$ 477.0316, found 477.0304.



3-(chloromethyl)-4-phenylpyrrolidin-1-yl)sulfonyl)-1-methyl-1H-imidazole (4y). According to general procedure C1, isolated as a bright yellow solid (39.0 mg, 0.115 mmol, 57%) of a mixture of non separable diastereoisomers (dr = 67:33). R_f 0.18 (2% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.54 (d, J = 1.4 Hz, 1H), 7.50 (d, J = 1.4 Hz, 1H), 7.33-7.30 (m, 2H), 7.27-7.22 (m, 1H), 7.19-7.17 (m, 2H), 3.96 (dd, J = 10.3, 8.0 Hz, 1H, H^1), 3.90-3.81 (m, 1H, H^4), 3.78 (s, 3H), 3.59-3.54 (m, 1H, H^1), 3.48 (dd, J = 11.3, 4.0 Hz, 1H, H^5), 3.44-3.39 (m, 1H, H^4), 3.32 (dd, J = 11.3, 7.4 Hz, 1H, H^5), 3.13 (td, J = 9.8, 8.0 Hz, 1H, H^2), 2.64-2.57 (m, 1H, H^3); *minor diastereoisomer* 7.53-7.52 (m, 2H), 7.33-7.30 (m, 2H), 7.27-7.22 (m, 3H), 3.90-3.81 (m, 2H, $2H^{1'}$), 3.79-3.76 (s, 4H, $H^{4'}$, Me), 3.59-3.54 (m, 1H, $H^{2'}$), 3.44-3.39 (m, 1H, $H^{4'}$), 3.01 (dd, J = 11.0, 6.2 Hz, 1H, $H^{5'}$), 2.93 (dd, J = 11.0, 9.1 Hz, 1H, $H^{5'}$), 2.71-2.65 (m, 1H, $H^{3'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 139.3, 138.4, 138.3, 128.9, 127.9, 127.5, 124.9, 54.9 (C^1), 51.6 (C^4), 48.0 (C^3), 47.4 (C^2), 44.2 (C^5), 34.0; *minor diastereoisomer* 139.3, 138.3, 137.4, 128.8, 127.5, 127.4, 124.9, 52.6 ($C^{1'}$), 50.4 ($C^{4'}$), 46.0 ($C^{2'}$), 45.7 ($C^{3'}$), 43.1 ($C^{5'}$), 34.0; FTIR (ν_{max} cm^{-1}) 2980 (sp^3 C-H), 1278 (sulfone), 1160 (sulfone); HRMS (ESI+) calculated for $C_{15}H_{18}ClN_3O_2S$ $[M+H]^+$ 340,0881, found 340.0887.

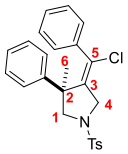


4-((-3-(chloromethyl)-4-phenylpyrrolidin-1-yl)sulfonyl)-3,5-dimethylisoxazole (4z). According to general procedure C1, isolated as a colorless oil (62.4 mg, 0.176 mmol, 88%) of a mixture of non separable diastereoisomers (dr = 72:28). R_f 0.53 (25% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.34 (q, J = 7.0 Hz, 2H), 7.30-7.28 (m, 1H), 7.20 (d, J = 7.0 Hz, 2H), 3.76 (dd, J = 9.8, 7.0 Hz, 2H, H^1, H^4), 3.55 (dd, J = 11.4, 3.7 Hz, 1H, H^5), 3.42-3.37 (m, 2H, H^1, H^5), 3.34 (dd, J = 9.8, 9.0 Hz, 1H, H^4), 3.19 (td, J = 9.8, 8.1 Hz, 1H, H^2), 2.73-2.71 (m, 1H, H^3), 2.67 (s, 3H), 2.45 (s, 3H); *minor diastereoisomer* 7.34 (q, J = 7.2 Hz, 2H), 7.30-7.28 (m, 1H), 7.16 (d, J = 7.0 Hz, 2H), 3.72-3.68 (m, 2H, $H^{1'}$, $H^{4'}$), 3.67-3.64 (m, 1H, $H^{1'}$), 3.62 (dt, J = 7.2, 3.5 Hz, 1H, $H^{2'}$), 3.42-3.37 (m, 1H, $H^{4'}$),3.14 (dd, J = 11.2, 5.7 Hz, 1H, $H^{5'}$), 2.99 (dd, J = 11.2, 9.2 Hz, 1H, $H^{5'}$), 2.84-2.81 (m, 1H, $H^{3'}$), 2.70 (s, 3H), 2.48 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 173.6, 157.9, 137.8, 129.2, 127.9, 127.4, 114.6, 54.1 (C^1), 50.6 (C^4), 47.9 (C^3), 47.4 (C^2), 43.9 (C^5), 13.0, 11.4; *minor diastereoisomer* 173.6, 157.8, 137.0, 129.0, 127.7, 127.6, 114.9, 52.0 ($C^{1'}$), 50.0 ($C^{4'}$), 45.9 ($C^{2'}$), 45.6 ($C^{3'}$), 43.1 ($C^{5'}$), 13.0, 11.4; FTIR (ν_{max} cm^{-1}) 2952 (sp^3 C-H), 2881 (sp^3 C-H), 1360 (sulfone), 1175 (sulfone); HRMS (ESI+) calculated for $C_{16}H_{20}ClN_2O_3S$ $[M+H]^+$ 355.0883, found 355.0880.

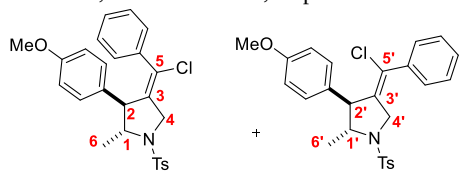


Major Z:E = 85:15 Minor

3-(chloro(phenyl)methylene)-4-phenyl-1-tosylpyrrolidine (4aa). According to general procedure C1, isolated as an off-white solid (57.2 mg, 0.135 mmol, 68%) of a mixture of non separable isomers *Z:E* (85:15). With general procedure C2 (60.2 mg, 0.142 mmol, 71%). R_f 0.50 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *Z isomer* 7.74 (d, *J* = 8.2 Hz, 2H), 7.39-7.33 (m, 2H), 7.32-7.28 (m, 1H), 7.20-7.15 (m, 1H), 7.14-7.09 (m, 4H), 7.03-6.99 (m, 2H), 6.90-6.87 (m, 2H), 4.31 (dd, *J* = 15.7, 1.8 Hz, 1H, H^4), 4.19 (d, *J* = 15.7 Hz, 1H, H^4), 3.92-3.88 (m, 1H, H^2), 3.56 (dd, *J* = 9.7, 7.0 Hz, 1H, H^1), 3.47 (dd, J = 9.7, 3.5 Hz, 1H, H^1), 2.46 (s, 3H); *E isomer* 7.63 (d, *J* = 8.2 Hz, 2H), 7.39-7.33 (m, 2H), 7.32-7.28 (m, 1H), 7.25-7.21 (m, 1H), 7.14-7.09 (m, 4H), 6.95-6.92 (m, 2H), 6.85-6.81 (m, 2H), 4.23-4.20 (m, 1H, $H^{2'}$), 4.15-4.12 (m, 1H, $H^{4'}$), 3.94 (d, *J* = 14.5 Hz, 1H, $H^{4'}$), 3.69 (dd, *J* = 10.0, 7.5 Hz, 1H, $H^{1'}$), 3.48-3.44 (m, 1H, $H^{1'}$), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ *Z isomer* 143.9, 141.5, 137.3, 136.9, 132.5, 129.8, 128.6, 128.5, 128.1, 128.0, 127.9, 127.2, 126.8, 57.2 (C^1), 53.4 (C^4), 48.0 (C^2), 21.6; *E isomer* 143.9, 141.0, 137.4, 136.6, 132.6, 129.8, 128.7, 128.5, 128.0, 127.9, 127.8, 127.3, 127.0, 55.2 ($C^{1'}$), 52.2 ($C^{4'}$), 49.0 ($C^{2'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2924 (sp^3 C-H), 2848 (sp^3 C-H), 1601 (C=C), 1343 (sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{24}H_{22}ClNO_2SNa$ $[M+Na]^+$ 446.0952, found 446.0953.



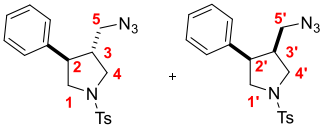
4-(chloro(phenyl)methylene)-3-methyl-3-phenyl-1-tosyl pyrrolidine (4ab). According to general procedure C1, isolated as a white solid (63.0 mg, 0.144 mmol, 72%) as a single isomer *Z*. With general procedure C2 (60.4 mg, 0.138 mmol, 68%). R_f 0.46 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.18-7.14 (m, 3H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.08-7.05 (m, 2H), 7.02 (t, *J* = 7.8 Hz, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 4.32-4.23 (m, 2H, $2H^4$), 3.49 (d, *J* = 9.3 Hz, 1H, H^1), 3.25 (d, *J* = 9.3 Hz, 1H, H^1), 2.48 (s, 3H), 1.30 (s, 3H, H^6); ^{13}C NMR ($CDCl_3$) δ 144.8, 143.9, 142.2, 137.0, 131.9 (C^5), 129.8, 128.6, 128.4, 128.2, 128.0, 127.7, 127.1 (C^3), 126.7, 126.3, 65.1 (C^1), 54.7 (C^4), 50.1 (C^2), 23.7 (C^6), 21.7; FTIR (ν_{max} cm^{-1}) 2929 (sp^3 C-H), 2838 (sp^3 C-H), 1601 (C=C), 1338 (sulfone), 1162 (sulfone); HRMS (ESI+) calculated for $C_{25}H_{24}ClNO_2SNa$ $[M+Na]^+$ 460.1109, found 460.1089; M.p.: 151-153 °C.



Major Z:E = 67:33 Minor

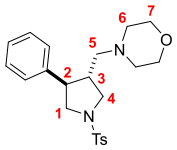
4-(chloro(phenyl)methylene)-3-(4-methoxyphenyl)-2-methyl-1-tosylpyrrolidine (4ac). According to general procedure C1, isolated as a yellow solid (70.8 mg, 0.151 mmol, 84%) of a mixture of non separable isomers *Z:E* (67:33). With general procedure C2 (65.2 mg, 0.139 mmol, 70%). R_f 0.36 (30% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *Z isomer* 7.55 (d, *J* = 8.2 Hz, 2H), 7.40-7.35 (m, 2H), 7.23-7.10 (m, 5H), 6.63 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 8.7 Hz, 2H), 4.56 (d, *J* = 15.7 Hz, 1H, H^4), 4.24-4.17 (m, 1H, H^4), 4.00-3.93 (m, 1H, H^1), 3.76 (s, 3H, OMe), 3.52 (br s, 1H, H^2), 2.41 (s, 3H), 1.36 (d, *J* = 6.4 Hz, 3H, H^6); *E isomer* 7.57 (d, *J* = 8.2 Hz, 2H), 7.40-7.35 (m, 1H), 7.23-7.10 (m, 6H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.68 (d, *J* = 8.7 Hz, 2H), 4.24-4.17 (m, 1H, $H^{4'}$), 4.12 (dd, *J* = 14.5, 1.7 Hz, 1H, $H^{4'}$), 4.00-3.93 (m, 2H, $H^{1'}$, $H^{2'}$), 3.78 (s, 3H, OMe), 2.41 (s, 3H), 1.46 (d, J = 6.4 Hz, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *Z isomer* 158.2, 143.1, 137.0, 136.4, 133.6, 132.5 (C^5), 129.4, 128.1, 128.0, 127.9, 127.8, 127.1, 113.9, 129.0 (C^3), 66.3 (C^1), 55.1 (C^2), 55.0 (OMe), 52.2 (C^4), 21.9 (C^6), 21.4; *E isomer* 158.3, 143.4, 137.3, 135.7, 134.8, 132.5, 132.5 ($C^{5'}$), 129.6, 128.7, 128.5, 128.2 ($C^{3'}$), 127.9, 127.8, 127.2, 114.0, 64.3 ($C^{1'}$), 56.5 ($C^{2'}$), 55.2 (OMe), 51.4 ($C^{4'}$), 22.7 ($C^{6'}$), 21.5; FTIR (ν_{max} cm^{-1}) 2927 (sp^3 C-H), 2833 (sp^3 C-H), 1596 (C=C), 1341 (sulfone), 1242 (ether, C-O), 1159 (sulfone); HRMS (ESI+) calculated for $C_{26}H_{26}ClNO_3SNa$ $[M+Na]^+$ 490.1214, found 490.1214.

3-methyl-4-phenyl-1-tosyl-1H-pyrrole (5). In a microwave tube were placed the pyrrolidine **4a** (79 mg, 0.23 mmol, 1 equiv.), KOH (127 mg, 2.26 mmol, 10 equiv.) and EtOH (2.2 mL, 0.1 M). The tube was sealed under an argon atmosphere and the reaction mixture was stirred at 80 °C for 18 h. The mixture was concentrated *in vacuo*. The residue was taken in H_2O and the aqueous phase was extracted with CH_2Cl_2 (3x). The organic phase was dried over $MgSO_4$, filtered and solvent was removed under reduced pressure. The crude was placed in a microwave tube and MnO_2 (197 mg, 2.26 mmol, 10 equiv.) and toluene (2.2 mL, 0.1 M) were added. The tube was sealed and stirred at 100 °C for 2 h. The mixture was filtered through a plug of celite. The filtrate was concentrated *in vacuo*. The crude was purified by silica flash column chromatography (95/5 to 9/1 hexane/EtOAc) to yield the desired pyrrole **5** as a clear orange oil (50.1 mg, 0.16 mmol, 71%). Spectral data were in agreement with literature values.[34]

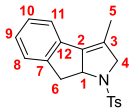


Major dr = 70:30 Minor

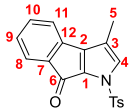
3-(azidomethyl)-4-phenyl-1-tosylpyrrolidine (6). In a microwave tube was placed the pyrrolidine **4a** (70 mg, 0.2 mmol, 1 equiv.) in DMF (2 mL, 0.1 M). Sodium azide (65 mg, 1.0 mmol, 5 equiv.) was added and the tude was sealed under an argon atmosphere. The reaction mixture was then stirred at 80 °C for 18 h. The mixture was diluted in EtOAc and washed two times with 1N NaOH. The organic phase was dried over $MgSO_4$, filtered and solvent was removed *in vacuo.* The crude was purified by silica flash column chromatography (9/1 to 8/2 hexane/EtOAc) to yield the desired pyrrolidine **6** (colorless oil, 51.7 mg, 0.15 mmol, 73%) as a mixture of non separable diastereoisomers (dr = 70:30). R_f 0.11 (10% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.77 (d, *J* = 8.0 Hz, 2H), 7.40-7.38 (m, 2H), 7.32-7.24 (m, 3H), 7.10 (d, *J* = 7.2 Hz, 2H), 3.72 (dd, *J* = 10.2, 8.1 Hz, 1H, H^1), 3.69-3.66 (m, 1H, H^4), 3.32-3.26 (m, 2H, H^1 and H^5), 3.19-3.16 (m, 1H, H^4), 3.13 (dd, *J* = 12.5, 7.4 Hz, 1H, H^5), 2.94 (q, *J* = 8.1 Hz, 1H, H^2), 2.48 (s, 3H), 2.40-2.34 (m, 1H, H^3); *minor diastereoisomer* 7.81 (d, *J* = 8.0 Hz, 2H), 7.40-7.38 (m, 2H), 7.32-7.24 (m, 3H), 7.04 (d, *J* = 7.2 Hz, 2H), 3.69-3.65 (m, 1H, $H^{1'}$), 3.63-3.59 (m, 1H, $H^{1'}$), 3.56 (dd, *J* = 10.5, 7.2 Hz, 1H, $H^{4'}$), 3.47 (q, *J* = 6.6 Hz, 1H, $H^{2'}$), 3.32-3.26 (m, 1H, $H^{4'}$), 2.88 (dd, *J* = 12.2, 6.1 Hz, 1H, $H^{5'}$), 2.64 (dd, J = 12.2, 8.9 Hz, 1H, $H^{5'}$), 2.47 (s, 3H), 2.46-2.43 (m, 1H, $H^{3'}$); ^{13}C NMR ($CDCl_3$) *major diastereoisomer* δ 143.8, 138.6, 133.5, 129.8, 129.0, 127.6, 127.5, 127.3, 54.5 (C^1), 51.6 (C^5), 51.1 (C^4), 47.2 (C^2), 45.9 (C^3), 21.6; *minor diastereoisomer* 143.8, 137.6, 133.7, 129.9, 128.8, 127.7, 127.5, 127.4, 52.2 ($C^{1'}$), 50.4 ($C^{5'}$), 50.0 ($C^{4'}$), 45.3 ($C^{2'}$), 42.4 ($C^{3'}$), 21.6; FTIR (ν_{max} cm^{-1}) 2924 (sp^3 C-H), 2096 (sp^3 C-H), 1341 (sulfone), 1159 (sulfone); HRMS (ESI+) calculated for $C_{18}H_{20}N_4O_2SNa$ $[M+Na]^+$ 379.1197, found 379.1187.



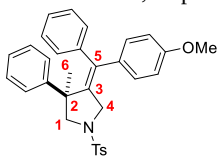
4-((4-phenyl-1-tosylpyrrolidin-3-yl)methyl)morpholine (7). In a microwave tube were placed the pyrrolidine **4a** (70 mg, 0.2 mmol, 1 equiv.), K_2CO_3 (276 mg, 2 mmol, 10 equiv.) and KI (7 mg, 0.04 mmol, 0.2 equiv.). Acetonitrile (2 mL, 0.1 M) was added and the tube was sealed under an argon atmosphere. The reaction mixture was stirred at 80 °C for 3 days. The crude was diluted with H_2O and the aqueous phase was extracted with CH_2Cl_2 (3x). The organic phase was dried over $MgSO_4$, filtered and solvent was removed *in vacuo*. The crude was purified by silica flash column chromatography (6/4 to 4/6 hexane/EtOAc) to yield the desired pyrrolidine **7** as a single diastereoisomer (white solid, 44.6 mg, 0.11 mmol, 56%). R_f 0.18 (50% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 7.28-7.25 (m, 2H), 7.24-7.20 (m, 1H), 7.08 (d, *J* = 7.4 Hz, 2H), 3.70-3.63 (m, 2H, H^1, H^4), 3.58 (t, *J* = 4.9 Hz, 4H, H^7), 3.26 (t, *J* = 9.3 Hz, 1H, H^1), 3.12 (dd, *J* = 10.2, 7.5 Hz, 1H, H^4), 2.89 (q, *J* = 8.4 Hz, 1H, H^2), 2.47 (s, 3H), 2.41-2.36 (m, 1H, H^3), 2.34-2.28 (m, 2H, H^5), 2.21-2.14 (m, 4H, H^6); ^{13}C NMR ($CDCl_3$) δ 143.5, 140.3, 133.6, 129.7, 128.7, 127.6, 127.3, 127.1, 66.8 (C^7), 61.0 (C^6), 54.6 (C^1), 53.7 (C^5), 52.6 (C^4), 48.5 (C^2), 43.4 (C^3), 21.6; FTIR (ν_{max} cm^{-1}) 2957 (sp^3 C-H), 2891 (sp^3 C-H), 2863 (sp^3 C-H), 2805 (sp^3 C-H), 1338 (sulfone), 1116 (ether, C-O), 1157 (sulfone); HRMS (ESI+) calculated for $C_{22}H_{29}N_2O_3S$ $[M+H]^+$ 401.1893, found 401.1897; M.p.: 137-139 °C.



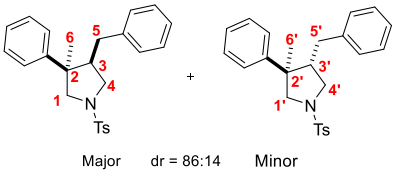
3-methyl-1-tosyl-1,2,8,8a-tetrahydroindeno[2,1-b]pyrrole (8). In a microwave tube were placed the pyrrolidine **4p** (120 mg, 0.33 mmol, 1 equiv.), KOH (185 mg, 3.3 mmol, 10 equiv.) and EtOH (3.3 mL, 0.1 M). The tube was sealed under argon and the reaction mixture was stirred at 80 °C for 18 h. The mixture was concentrated under reduced pressure. The residue was taken in H_2O, and extracted with CH_2Cl_2 (3x). The organic phase was dried over $MgSO_4$, filtered and solvent was removed *in vacuo*. The crude was purified by Florisil® flash column chromatography (95/5 to 85/15 hexane/EtOAc) to yield the desired product **8** (clear yellow solid, 101.4 mg, 0.31 mmol, 94%). R_f 0.35 (20% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.34-7.32 (m, 1H, H^8), 7.27-7.25 (m, 1H, H^{11}), 7.22-7.20 (m, 2H, H^9, H^{10}), 4.69-4.63 (m, 1H, H^1), 4.30 (dd, *J* = 13.3, 4.3 Hz, 1H, H^4), 4.24 (ddd, *J* = 13.3, 4.3, 1.7 Hz, 1H, H^4), 3.25 (dd, *J* = 15.3, 7.4 Hz, 1H, H^6), 3.06 (dd, *J* = 15.3, 7.9 Hz, 1H, H^6), 2.44 (s, 3H), 1.87 (s, 3H, H^5); ^{13}C NMR ($CDCl_3$) δ 146.7, 143.7, 139.0, 134.1, 132.9, 129.8, 128.2, 128.1, 127.1, 126.1, 123.0, 122.2, 71.7 (C^1), 64.4 (C^4), 38.1 (C^6), 21.5, 12.4 (C^5); FTIR (ν_{max} cm^{-1}) 2972 (sp^3 C-H), 2929 (sp^3 C-H), 2856 (sp^3 C-H), 1341 (sulfone), 1156 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{20}NO_2S$ $[M+H]^+$ 326.1215; found 326.1205. M.p.: 158-160 °C.



3-methyl-1-tosylindeno[2,1-b]pyrrol-8(1H)-one (9). In a microwave tube were placed the product **8** (20 mg, 0.06 mmol, 1 equiv.) and MnO_2 (26 mg, 0.3 mmol, 5 equiv.) in toluene (0.6 mL, 0.1 M). The tube was sealed and stirred at 100 °C for 6 h in total (every hour a new portion of 5 equiv. of MnO_2 was added). The mixture was filtered through a plug of celite. The filtrate was concentrated *in vacuo*. The crude was purified by Florisil® flash column chromatography (95/5 to 9/1 hexane/EtOAc) to yield the desired pyrrole **9** as an orange solid (9.4 mg, 0.03 mmol, 47%). R_f 0.25 (20% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 8.05 (d, *J* = 8.2 Hz, 2H), 7.33-7.30 (m, 3H, H^8), 7.21 (t, *J* = 7.5 Hz, 1H, H^{10}), 7.18 (s, 1H, H^4), 7.07 (t, *J* = 7.5 Hz, 1H, H^9), 7.00 (d, *J* = 7.2 Hz, 1H, H^{11}), 2.40 (s, 3H), 2.16 (s, 3H, H^5); ^{13}C NMR ($CDCl_3$) δ 178.4 (C^6), 148.2, 145.8, 137.4, 136.6, 134.7, 133.1 (C^{10}), 130.2, 130.0, 129.9 (C^4), 128.0 (C^9), 127.9, 123.9 (C^8), 119.5 (C^{11}), 118.0 (C^3), 21.7, 10.5 (C^5); FTIR (ν_{max} cm^{-1}), 2931 (sp^3 C-H), 1697 (C=O), 1368 (sulfone), 1177 (sulfone); HRMS (ESI+) calculated for $C_{19}H_{15}NO_3SNa$ $[M+Na]^+$ 360.0665, found 360.0660; M.p.: 156-158 °C.



4-((4-methoxyphenyl)(phenyl)methylene)-3-methyl-3-phenyl-1-tosylpyrrolidine (10). In a microwave tube were placed the pyrrolidine **4ac** (100 mg, 0.23 mmol, 1 equiv.), 4-methoxyphenyl boronic acid (140 mg, 0.92 mmol, 4 equiv.), $PdCl_2(P(o\text{-tol})_3)_2$ (18 mg, 0.023 mmol, 0.1 equiv.) and Cs_2CO_3 (450 mg, 1.38 mmol, 6 equiv.) in toluene (0.5 mL, 0.4 M). The tube was sealed under an argon atmosphere and stirred at 110 °C for 18 h. The mixture was diluted in EtOAc and filtered through a plug of celite. The filtrate was concentrated *in vacuo*. The crude was purified by silica flash column chromatography (9/1 to 8/2 hexane/EtOAc) to yield the desired pyrrolidine **10** as a yellow oil (92.1 mg, 0.18 mmol, 78%). R_f 0.25 (20% EtOAc/hexane); ^{1}H NMR ($CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.16-7.14 (m, 3H), 7.12-7.10 (m, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.92 (t, *J* = 7.4 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.61 (d, *J* = 7.4 Hz, 2H), 4.06-4.01 (m, 2H, $2H^4$), 3.79 (s, 3H, OMe), 3.41 (d, *J* = 9.3 Hz, 1H, H^1), 3.17 (d, *J* = 9.3 Hz, 1H, H^1), 2.47 (s, 3H), 1.33 (s, 3H, H^6); ^{13}C NMR ($CDCl_3$) δ 158.4, 146.5, 143.6, 141.6, 140.4, 137.4, 135.1, 132.3, 129.6, 128.8, 128.7, 128.0, 127.9, 127.3, 126.4, 126.2, 126.1, 64.8 (C^1), 55.2 (OMe), 53.6 (C^4), 49.5 (C^2), 24.3 (C^6), 21.6; FTIR (ν_{max} cm^{-1}) 2926 (sp^3 C-H), 2838 (sp^3 C-H), 1606 (C=C), 1343 (sulfone), 1248 (ether C-O), 1157 (sulfone); HRMS (ESI+) calculated for $C_{32}H_{31}NO_3SNa$ $[M+Na]^+$ 532.1917, found 532.1894.



4-benzyl-3-methyl-3-phenyl-1-tosylpyrrolidine (11). In a conical flask was placed the pyrrolidine **4ac** (40 mg, 0.09 mmol) in MeOH/CH_2Cl_2 1:1 (0.05 M). The mixture was passed on a H-Cube apparatus through a cartridge of Pd/C 10% (0.5 mL/min, 60 °C, 60 bars) until complete conversion was observed by mass analysis. The crude was concentrated *in vacuo* and purified by silica flash column chromatography (85/15 to 8/2 hexane/EtOAc) to yield the pyrrolidine **11** as a mixture of two diastereoisomers dr = 86:14 (colorless oil, 26.4 mg, 0.065 mmol, 72 %). R_f 0.46 (30% EtOAc/hexane);); ^{1}H NMR ($CDCl_3$) δ *major diastereoisomer* 7.75 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.32-7.30 (m, 2H), 7.25-7.15 (m, 6H), 6.84 (d, *J* = 7.3 Hz, 2H), 3.85 (d, *J* = 9.5 Hz, 1H, H^1), 3.49 (d, *J* = 9.5 Hz, 1H, H^1), 3.41 (dd, *J* = 10.3, 6.6 Hz, 1H, H^4), 3.12 (dd, *J* = 10.3, 5.5 Hz, 1H, H^4), 2.50-2.47 (m, 1H, H^5), 2.46 (s, 3H), 2.30-2.25 (m, 1H, H^3), 1.56-1.52 (m, H^5), 1.33 (s, 3H, H^6); *minor diastereoisomer* 7.69 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.32-7.30 (m, 3H), 7.25-7.15 (m, 5H), 7.00 (d, *J* = 7.3 Hz, 2H), 3.47-3.43 (m, 2H, $H^{1'}$), 3.44-3.39 (m, 1H, $H^{4'}$), 3.17 (t, *J* = 9.8 Hz, 1H, $H^{4'}$), 2.67-

2.62 (m, 2H, $H^{3'}$, $H^{5'}$), 2.45 (s, 3H), 2.36-2.31 (m, 1H, $H^{5'}$), 1.24 (s, 3H, $H^{6'}$); ^{13}C NMR ($CDCl_3$) δ *major diastereoisomer* 143.4, 143.3, 139.8, 134.5, 129.7, 128.6, 128.5, 128.4, 127.4, 126.6, 126.5, 126.2, 58.0 (C^1), 50.8 (C^4), 50.2 (C^3), 48.6 (C^2), 35.3 (C^5), 27.5 (C^6), 21.6; *minor diastereoisomer* 143.6, 143.3, 139.8, 134.4, 129.7, 128.6, 128.3, 127.3, 126.8, 126.3, 125.9, 61.8 ($C^{1'}$), 51.6 ($C^{4'}$), 49.9 ($C^{3'}$), 47.4 ($C^{2'}$), 34.0 ($C^{5'}$), 29.7 ($C^{6'}$), 19.3; FTIR (ν_{max} cm^{-1}) 2927 (sp^3 C-H), 2886 (sp^3 C-H), 1341 (sulfone), 1154 (sulfone); HRMS (ESI+) calculated for $C_{25}H_{27}NO_2SNa$ $[M+Na]^+$ 428.1654, found 428.1643.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:.

Crystallographic data for **4l** (CIF) and **4ab** (CIF)

Photoreactor setup, numbering for the starting materials **1** and **3**, NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest. Additional data related to this publication is available at the University of Cambridge Institutional Data Repository (https://doi.org/10.17863/CAM.12885).

ACKNOWLEDGMENT

This work was supported by a postdoctoral fellowship from Pfizer (L.C. and A.G.) and the EPSRC grants EP/K009494/1 and EP/M004120/1 (S.V.L.). We also thank Dr. Andrew D. Bond for conducting X-ray crystallographic analysis.

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(15) The reaction set up usually heats the reaction media to 55 °C due to the intense generation of heat of the blue LEDs. The temperature can be decreased to 35 °C by using a fan on the top of the system (see SI).

(16) Cambridge Crystallographic Data Centre (CCDC) 1564499 contains supplementary crystallographic data for compound **4l**.

(17) Cambridge Crystallographic Data Centre (CCDC) 1564500 contains supplementary crystallographic data for compound **4ab**.

(18) Redox potential of a similar substrate was found to be $E^{1/2}$ = -0.47 V *vs* SCE (see 11a). This low reduction potential cannnot exclude an oxidative quenching of the various excited catalysts tested.

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