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Iodoamination of Alkenyl Sulfonamides by Potassium Iodide and Hydrogen Peroxide in Aqueous Medium

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Dedication ((optional))

Abstract A procedure for the iodoamination of unfunctionalized olefins tethered to a tosyl-protected NH-group has been developed. The combined use of KI and H_2O_2 in aqueous medium was effective for the preparation of iodomethyl-substituted nitrogen-containing heterocycles. The selective *exo-trig* iodocyclization provided 1,2-bifunctional 5-, 6-, and 7-membered cyclic skeletons.

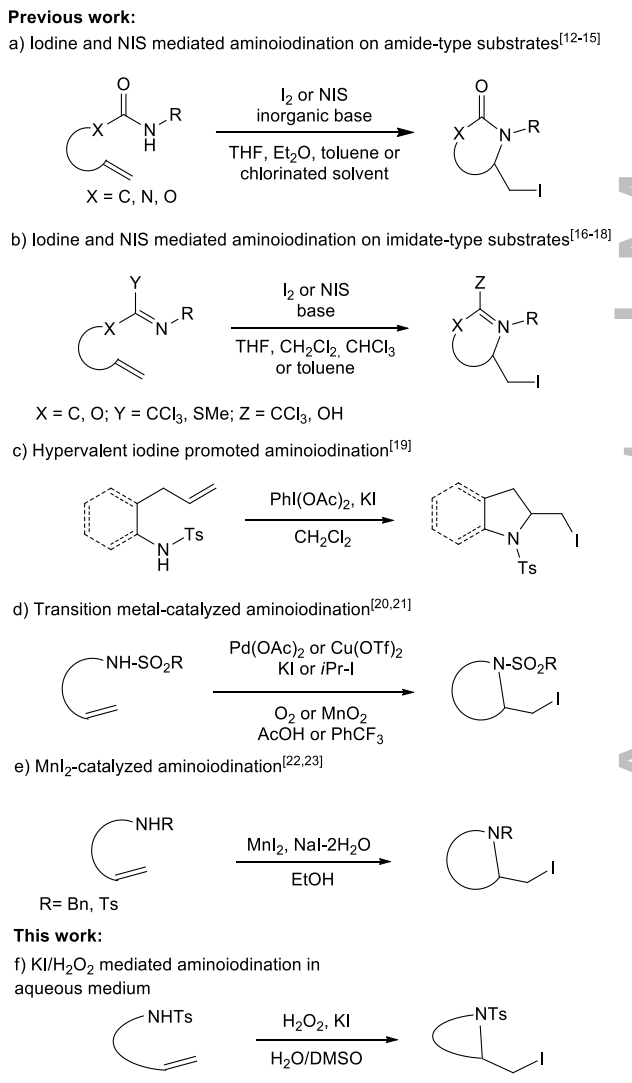
Keywords Cyclization • amination • nitrogen heterocycles • synthetic methods • sulfonamides

Introduction

The development of efficient synthetic protocols which allow the formation of more than one bond in a single step plays a central role in organic synthesis. Recently, haloamination of carbon-carbon double bond involving an intramolecular carbon-nitrogen bond formation received great attention as fruitful methodology for the synthesis of nitrogen-containing heterocycles.[1-3] The usefulness of heterocycles containing a vicinal haloamine moiety as versatile synthetic intermediates[4-7] or as potential medicinal agents[8,9] is well established.

Among the alkene halocyclizations, iodoamination reactions represent a powerful tool for the preparation of heterocycles suitable for further introduction of functionalities.[10,11] The formation of a carbon-iodine bond provides high added value to the process as proven by the multi-faceted conversions which can undergo. While the most efficient procedures for the access to vicinal chloro- and bromoamines are based on transition metal-catalyzed reactions, direct formation of vicinal iodoamines from aminoalkenes can be typically realized by initial activation of the carbon-carbon double bond with different sources of electrophile. Molecular iodine and *N*-iodosuccinimide (NIS) have been widely used with amide-type substrates (Scheme 1a)[12-15] as well as with alkenyl imidates (Scheme 1b).[16-18] Alternatively, KI in the presence of a hypervalent iodine derivatives (Scheme 1c)[19] or a transition metal-catalyst (Scheme 1d)[20-21] were proven to be effective for this goal. Also NaI, combined with MnI_2 as catalyst, has been proven a useful source of iodine for iodoamination of unfunctionalized olefins (Scheme 1e).[22-23] It is worth noting also the iodocyclization of alkenyl carbamates performed with Bu_4NI as iodine source with $NaNO_2$ as catalyst and molecular oxygen as oxidant.[24]

The importance of the development of a mild and easy synthesis of vicinal iodoamine moieties is also due to their role as core scaffolds in various structures of bioactive compounds. In particular, some antitumor, anti-infective, and anti-inflammatory agents feature iodomethyl substituted nitrogen-containing heterocycles (Figure 1).[25-26]



Scheme 1. Synthetic procedure for aminoiodination

Following our previous investigations on heterocyclization reactions in domino processes,[27-30] we focused our attention on the search of alternative conditions for intramolecular amination reactions combined with iodine functionalization (Scheme 1f). Herein we report selected mild conditions relying on the use of KI as iodine source and H_2O_2 as oxidant agent which act in water at room temperature providing iodomethyl-substituted heterocycles. Although it is known that H2O2 has been used combined to tetrabutylammonium iodide to promote an

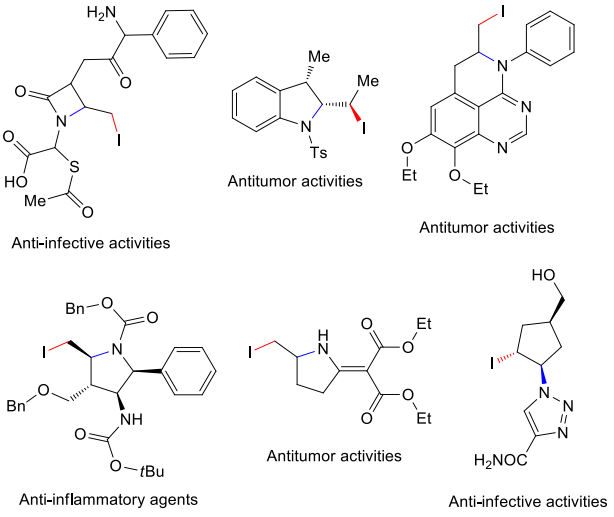


Figure 1. Selected bioactive vicinal iodoamine derivatives

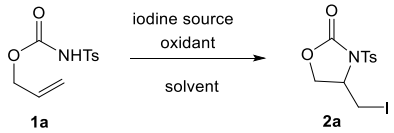
amination reaction,[31] to the best of our knowledge the possibility to perform iodoamination reactions by the use of KI/H2O2 is unknown in the literature.

Results and Discussion

O-Allyl-*N*-tosylcarbamate (**1a**) was investigated in preliminary experiments aimed to explore new conditions for the feasibility of the iodoamination reaction. Various combinations of iodine sources and oxidant agents in different solvents used to afford the oxazolidinone product **2a** are collected in Table 1. A stoichiometric amount of molecular iodine or NIS in acetonitrile at room temperature furnished the iodoamination product in unsatisfactory yields in a complex crude mixture, in the latter case also due to the formation of the *O*-(2,3-diiodopropyl)-*N*-tosyl-carbamate (Table 1, entries 1 and 2). The same acyclic diiodinated compound was obtained as by-product when the reaction was carried out in the presence of NIS and $CuCl_2$ as the oxidant in oxygen atmosphere (Table 1, entry 3). A iodocyclizative process was observed when I_2 and NIS were combined with PIFA, although the product resulted in the 3-unsubstituted 4-iodomethyloxazolidinone, isolated in both cases in moderate yields (Table 1, entries 4 and 5). Conversely, the use of PIFA was effective if used with KI as iodine source, providing **2a** in 81% yield (Table 1, entry 6).

Other hypervalent iodine derivatives such as PIDA and $PhI(mcba)_2$ were a good choice as promoter to afford **2a**, although with a slight decrease in yield (Table 1, entries 7 and 8). Following these preliminary results, we focused on other conditions based on the presence of KI as iodine source. Using molecular iodine in O_2 atmosphere combined with benzoquinone as further oxidant in acetonitrile, no formation of **2a** was observed and carbamate **1a** was completely recovered (Table 1, entry 9). Also MnO_2 was tested as additive in the reaction mixture under oxygen atmosphere but **2a** was achieved in low yield (Table 1, entry 10). Intriguingly, a consistent improvement of the outcome of the reaction was detected when H_2O_2 was used as the sole oxidant in the presence of KI and CH_3CN as the solvent. These conditions determined a neat conversion of **1a**, providing the desired iodoamination product in 79% yield (Table 1, entry 11). Use of DMF or dioxane led to a remarkable decrease of the yield (Table 1, entries 12 and 13), while water associated to DMSO or CH_3CN as a co-solvent was gratifyingly proven to be a good medium to obtain the complete conversion of the substrate into **2a** in mild conditions (Table 1, entries 14 and 15). Working in the conditions of Table 1, entry 14, the crude mixture resulted cleaner than the corresponding reaction carried out with I_2 or NIS as iodine source. Besides, the product obtained might be collected through an easy filtration, due to its lower solubility in the DMSO/H_2O mixture compared to the starting material.

Table 1. Optimization of the reaction conditions.



1a **2a**

Entry	Iodine source	Oxidant	Solvent[a]	Time (h)	2a[b] (% yield)
1	I_2	-	CH_3CN	30	52
2	NIS	-	CH_3CN	18	29[c]
3[d]	NIS	$CuCl_2$ (5 mol%), O_2	CH_3CN	24	49[c]
4	I_2	PIFA	CH_3CN	4	-[e]
5	NIS	PIFA	CH_3CN	6	-[e]
6	KI	PIFA	CH_3CN	3	81
7	KI	PIDA	CH_3CN	8	68
8	KI	$PhI(mcba)_2$	CH_3CN	20	73
9	KI	BQ (20 mol%), O_2	CH_3CN	48	-
10	KI	MnO_2 (20 mol%), O_2	CH_3CN	48	31
11[f]	KI	H_2O_2	CH_3CN	24	79
12[f]	KI	H_2O_2	DMF	24	32
13[f]	KI	H_2O_2	Dioxane	24	54
14[f]	**KI**	**H_2O_2**	**H_2O/ DMSO[g]**	**24**	**78**
15[f]	KI	H_2O_2	H_2O/CH_3CN[h]	24	67

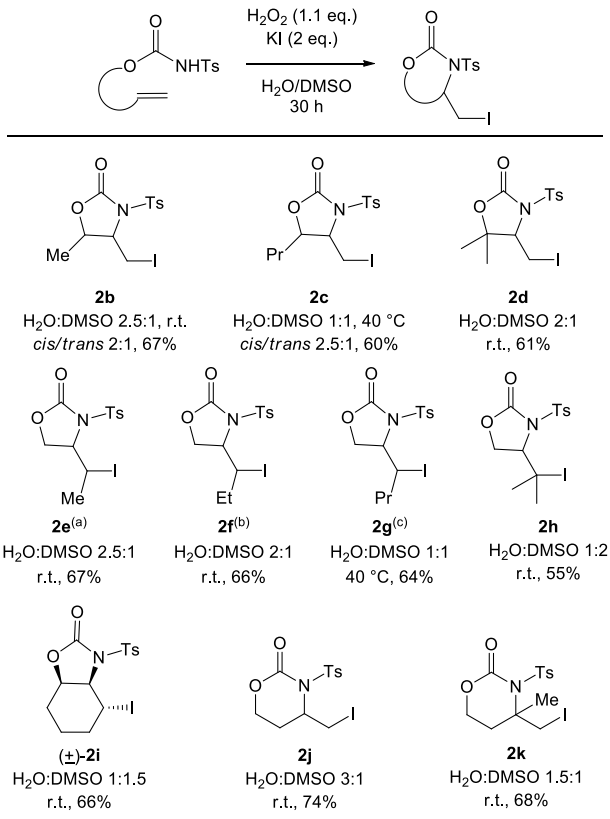
[a] The reactions were carried out at room temperature unless otherwise stated. [b] Yields of purified products. [c] *O*-(2,3-Diiodopropyl)-*N*-tosyl-carbamate has been isolated in 57% yield (entry 2) and 37% yield (entry 3). [d] The reaction was performed in CH_3CN at reflux under O2 atmosphere. [e] 3-Unsubstituted 4-iodomethyl-oxazolidin-2-one has been isolated in 54% yield (entry 4) and 43% yield (entry 5). [f] The reaction was carried out at room temperature using a 30% solution of H_2O_2 in water. [g] In 3:1 ratio. [h] In 2:1 ratio.

The result obtained with KI/H_2O_2 in water as solvent at room temperature prompted us to explore the substrate scope of the

iodoamination reaction in the conditions of Table 1, entry 19. Initially, variously substituted alkenyl carbamates were envisaged and the results of the iodocyclization reactions are reported in Table 2. The presence of substituents on the allylic moiety is compatible with reaction conditions, as demonstrated by the formation of compounds **2b-h**, although a mild heating in some cases was required. Compounds **2b** and **2c** were obtained as a mixture of *cis/trans* diastereoisomers, easily separated and fully characterized.

The (*R**,*R**)-configuration of a representative iodo-derivative arising from *O*-allyl-carbamates mono-substituted at terminal position was confirmed by X-ray analysis of compound **2f** (Figure 2),[A] achieved by iodocyclization of the *O*-pent-2-enyl carbamate in the (*Z*)-configuration. The *O*-2-cyclohexenyl-*N*-tosyl-carbamate furnished exclusively the bicyclic oxazolidinone **2i** in 66% yield. The reaction conditions are also suitable for the iodoamination of *O*-alk-3-enyl carbamates, which provided the 1,3-oxazin-2-one products **2j** and **2k**.

Table 2. Reaction of iodoamination of alkenyl carbamates

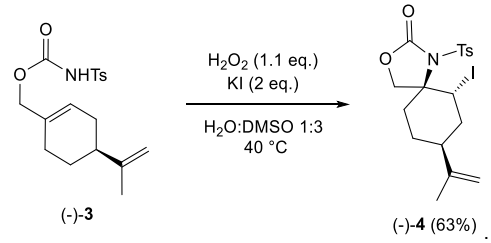


[a] Starting from a mixture of (*E*/*Z*)-**1e**. [b] Starting from (*Z*)-**1f**. [c] Starting from (*E*)-**1g**.

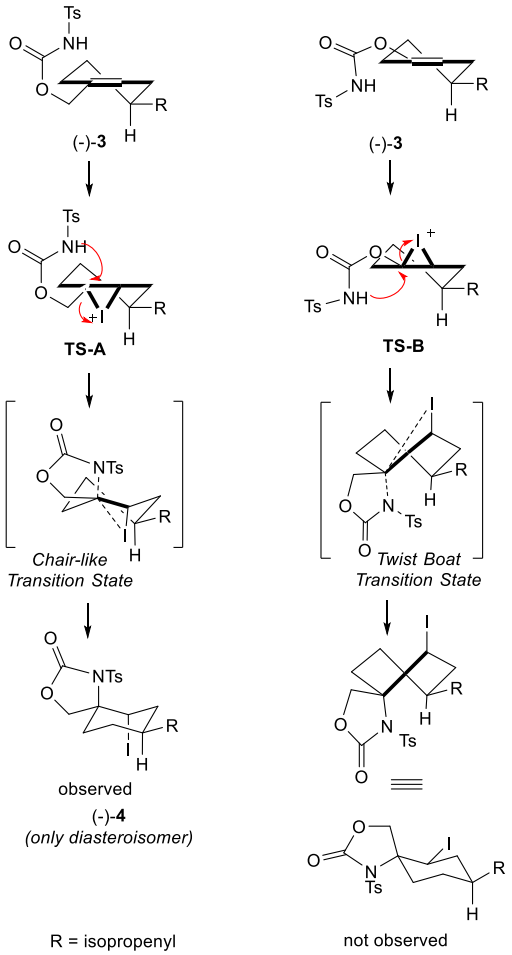
[A] CCDC 1868155 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

Figure 2. Molecular structure of the (*R*,*R*) enantiomer of **2f** at room temperature, as derived from single crystal X-ray diffraction. The methyl of the tosyl group is rotationally disordered with site occupation factors of 0.64(7) and 0.36(7). Thermal ellipsoids are drawn at the 30% probability level. Configurational descriptors of the stereogenic centres are also shown.

Interestingly, the treatment of the optically active carbamate **3** with H_2O_2 and KI in H_2O/DMSO 1:3 at 40 °C resulted selectively in an *exo*-cyclization, providing the spiro-compound **4** as the sole product (Scheme 2).



Scheme 2. Iodoamination of the optically active carbamate **3**



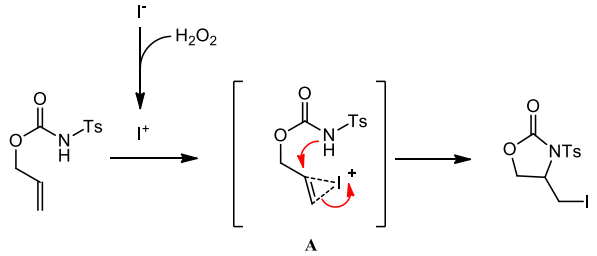
Scheme 3. Selective formation of the sole diastereoisomer (-)-**4**.

The stereoselective reaction path is due to the difference arisen from the torsional strain of the two plausible transition states having a substituent on the pseudo equatorial position (Scheme 3).[32-33] The stability of the chair-like transition state (from **TS-A**) rather than the twist-boat state (from **TS-B**) afforded only the *trans*-diaxial addition product (-)-**4**.

The configuration was unambiguously assigned by X-ray diffraction analysis (Figure 3). [B]

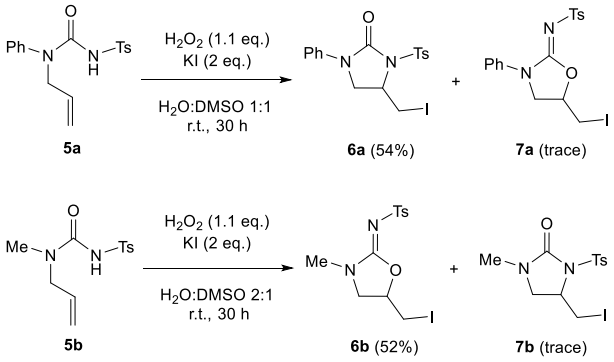
Figure 3. Molecular structure of 4 at room temperature, as derived from single crystal X-ray diffraction. Thermal ellipsoids are drawn at the 30% probability level. Configurational descriptors of the stereogenic centres are also shown.

Based on the observed results and literature data,[10,11] a plausible mechanism for the iodocyclization is shown in Scheme 4 taking carbamate **1a** as example. The I^+ species generated *in situ* from KI and H_2O_2 suggested the formation of the electrophilic iodinated intermediate **A**,[34-41] from which the *anti*-attack by the nucleophilic tosylamino group afforded the 4-iodomethyl oxazolidinone product.



Scheme 4. Proposed iodoamination reaction mechanism

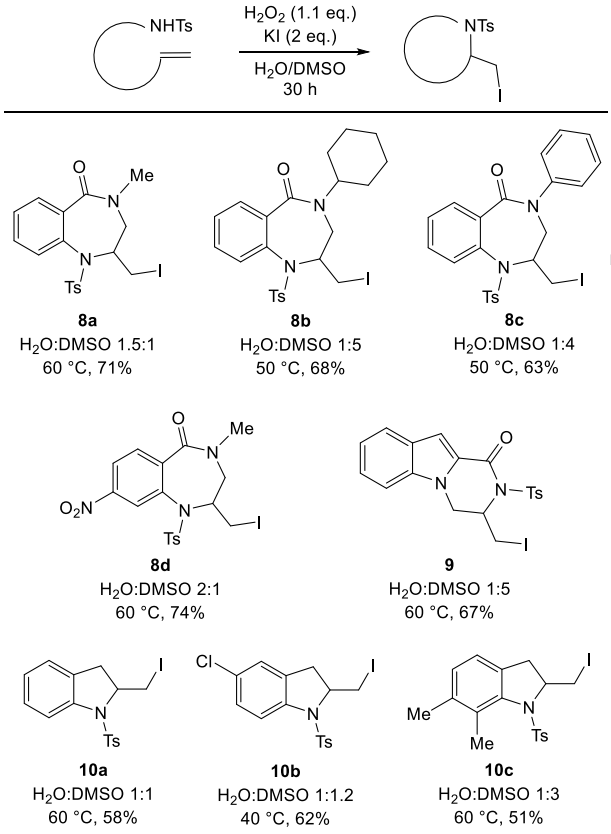
The use of H_2O_2 and KI for the iodocyclization of *N*-allyl-*N'*-tosylureas resulted in a different outcome of the reaction depending on the substituent on the nitrogen atom. If the phenyl-substituted urea **5a** provided the 4-iodomethyl-imidazolidinone **6a** as the major product, the *N*-allyl-*N*-methyl-urea **5b** followed mainly a iodoalkoxylation process giving the 2-imino-oxazolidine **6b** in 52% yield (Scheme 5). In both cases, minor products were detected in the crude mixtures, specifically arising from iodoalkoxylation (imino-oxazolidine **7a** from **5a**) and iodoamination (imidazolidinone **7b** from **5b**) reactions. The possibility of C-O vs C-N bond formation in intramolecular reactions of secondary ureas is well known in literature.[42-44] However, the low selectivity achieved in cyclization of compounds **5a,b** decreases the interest from the synthetic point of view for the application of this procedure to alkenyl ureas.



Scheme 5. Iodoamination reactions of allyl ureas

Further extension of the reaction scope was attempted taking into account other alkenyl sulphonamides. The iodomethyl-substituted heterocyclic products, obtained by reaction with KI and H_2O_2 using H_2O/DMSO in a ratio depending on the solubility of the substrates, are collected in Table 3.

Table 3. Reaction of iodoamination of alkenyl tosylamines



N-Allyl 2-tosylamino-benzamides, already used by our group for the synthesis of benzodiazepine scaffolds,[45] were proven compatible with the iodoamination process, giving the 2-iodomethyl-substituted 1,2,3,4-tetrahydro-benzodiazepin-5-one derivatives **8a-d** in 63-74% yield. Satisfyingly, this procedure also represents a valuable alternative for the

[B] CCDC 1868135 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

synthesis of these compounds, previously reported in the literature by displacement with KI of the first-formed chloromethyl derivative.[46] The iodocyclization conditions were found effective also for the conversion of the 1-allyl-indole-2-*N*-tosylcarboxamide into the iodomethyl-substituted pyrazino[1,2-*a*]indole **9**. It is noteworthy the reluctance of these substrates to afford haloamination processes in palladium-catalyzed reactions,[47] as further proof of the fruitfulness of the KI/H_2O_2 system. Finally, we explored the behaviour of 2-allyl-*N*-tosylanilines, already successfully undergone to iodoamination in palladium-catalyzed conditions.[21] Treatment of these substrates with the standard iodocyclization conditions provided the iodo-indolines **10a-c**, although in moderate yields.

Conclusions

In summary, we have developed an efficient iodoamination procedure on alkenes bearing a secondary sulphonamide group based on the use of KI/H2O2 system. The current methodology allows to achieve easily different kind of iodomethyl-substituted nitrogen containing heterocycles by totally selective exo-cyclization which involves halogenation and the formation of an intramolecular C-N bond. This iodoamination reaction proceeds smoothly in water needing the minimum amount of DMSO as co-solvent to solubilize the substrates.

Experimental Section

Analytical Instruments

Melting points were determined in a Stuart Scientific melting point apparatus in open capillary tubes and are uncorrected. Chemicals were obtained from Sigma Aldrich and used without further purification. HPLC analyses were carried out on a Kromasil 5-AmyCoat column (4.6 mm i.d. × 250 mm, 5 µm, AkzoNobel). ESI mass spectra were recorded on a LCQ Advantage spectrometer from Thermo Finningan and a LCQ Fleet spectrometer from Thermo Scientific. The NMR spectroscopic experiments were carried out either on a Bruker AVANCE 400 (400 and 101 MHz for ^1H and ^{13}C, respectively), on a Varian OXFORD 300 MHz (300 and 75 MHz for ^1H and ^{13}C, respectively), or on a Bruker Avance 300 MHz spectrometers (300 and 75 MHz for ^1H and ^{13}C, respectively). Optical rotations were measured on a Perkin–Elmer 343 polarimeter at 20 °C (concentration in g/100 mL). Chemical shifts δ are given in ppm relative to the $CHCl_3$ internal standard, and the coupling constants *J* are reported in Hertz (Hz).

General Procedure for the Aminoiodination Reaction. To a solution of the appropriate olefins (1 equiv.) in a mixture of DMSO and water (0.1M), potassium iodide (2 equiv.) was added at room temperature, followed by the addition of a solution of 30% H_2O_2 (1.1 equiv) in water. The reaction was monitored by TLC. Then, the reaction mixture was quenched with $Na_2S_2O_3$ (1M), and ethyl acetate was added. The organic layer was separated and washed with brine (6 x 15 mL). Afterwards, the organic phase was dried over Na_2SO_4, filtered and evaporated under reduced pressure. The purification by flash silica gel column chromatography afforded the corresponding products.

4-(Iodomethyl)-3-tosyloxazolidin-2-one (2a). Compound **2a** was prepared according to the general procedure (H_2O/DMSO 3:1, 30h, room temperature) and isolated as white solid (yield 78%) after flash column chromatography (hexane:EtOAc 3:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.54-4.44 (m, 1H), 4.36 (t, *J* = 8.8 Hz, 1H), 4.09 (dd, *J* = 9.1, 3.9 Hz, 1H), 3.60 (dd, *J* = 10.3, 2.3 Hz, 1H), 3.49-3.28 (m, 1H), 2.39 (s, 3H). The data are in good agreement with those reported in the literature.[20]

***Cis*-4-(Iodomethyl)-5-methyl-3-tosyloxazolidin-2-one (*cis*-2b).** Compound ***cis*-2b** was prepared according to the general procedure (H_2O/DMSO 2.5:1, 30h, room temperature) and isolated as white solid (yield 45%) after flash column chromatography (hexane:EtOAc 2:1). IR: 3428, 2975, 1778, 1359, 1163, 1135, 819, 666, 594, 572, 541 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 4.91-4.79 (m, 1H), 4.54 (td, *J* = 7.2, 2.2 Hz, 1H), 3.58-3.40 (m, 2H), 2.48 (s, 3H), 1.61 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.2 (s), 145.9 (s), 134.7 (s), 129.9 (d), 128.7 (d), 75.0 (d), 59.3 (d), 21.8 (q), 13.5 (q), -0.5 (t). MS: (ESI) *m/z* 418.05 [M+Na$^+$]. Anal. calcd for $C_{12}H_{14}NIO_4S$: C, 36.47; H, 3.57; N, 3.54. Found: C, 36.69; H, 3.32; N, 3.77.

***Trans*-4-(Iodomethyl)-5-methyl-3-tosyloxazolidin-2-one (*trans*-2b).** Compound ***trans*-2b** was prepared according to the general procedure (H_2O/DMSO 2.5:1, 30h, room temperature) and isolated as white solid (yield 22%) after flash column chromatography (hexane:EtOAc 2:1). M.p. 146-147 °C. IR: 3435, 2984, 1785, 1595, 1359, 1166, 1131 1088, 816, 665, 596, 568, 539 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.36 (dd, *J* = 6.3, 3.0 Hz, 1H), 4.02 (dt, *J* = 8.9, 2.7 Hz, 1H), 3.57 (dd, *J* = 10.3, 2.6 Hz, 1H), 3.31 (t, *J* = 9.7 Hz, 1H), 2.39 (s, 3H), 1.31 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0 (s), 145.0 (s), 134.6 (s), 129.9 (d), 128.5 (d), 77.3 (d), 62.8 (d), 21.7 (q), 21.1 (q), 6.5 (t). MS: (ESI) *m/z* 418.12 [M+Na$^+$]. Anal. calcd for $C_{12}H_{14}NIO_4S$: C, 36.47; H, 3.57; N, 3.54. Found: C, 36.31; H, 3.80; N, 3.72.

***Cis*-4-(Iodomethyl)-5-propyl-3-tosyloxazolidin-2-one (*cis*-2c).** Compound ***cis*-2c** was prepared according to the general procedure (H_2O/DMSO 1:1, 24h, 40 °C) and isolated as white solid (yield 28%) after flash column chromatography (hexane:EtOAc 5:1 to 2:1). M.p.: 130-131° C. IR: 3435, 2973, 1788, 1366, 1160, 657, 560 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 4.70-4.54 (m, 1H), 4.55-4.39 (m, 1H), 3.51-3.40 (m, 2H), 2.39 (s, 3H), 2.04-1.98 (m, 1H), 1.85-1.79 (m, 1H), 1.80-1.46 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.4 (s), 145.0 (s), 135.0 (s), 130.0 (d), 128.9 (d), 78.8 (d), 59.1 (d), 29.6 (t), 21.9 (q), 19.3 (t), 13.8 (q), -0.0 (t). MS: (ESI) *m/z* 424.82 [M$^+$],

446.54 [M+Na$^+$]. Anal. calcd for $C_{14}H_{18}NIO_4S$: C, 39.73; H, 4.29; N, 3.31. Found: C, 39.65; H, 4.08; N, 3.59.

***Trans*-4-(Iodomethyl)-5-propyl-3-tosyloxazolidin-2-one (*trans*-2c)**. Compound ***trans*-2c** was prepared according to the general procedure (H_2O/DMSO 1:1, 24h, 40 °C) and isolated as white solid (yield 32%) after flash column chromatography hexane:EtOAc 5:1 to 2:1). M.p. 118-119 °C. IR: 3437, 2969, 1786, 1361, 1158, 655, 563 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 4.39-4.24 (m, 1H), 4.15 (dt, *J* = 8.8, 2.8 Hz, 1H), 3.64 (dd, *J* = 10.3, 2.8 Hz, 1H), 3.42 (dd, *J* = 10.2, 8.8 Hz, 1H), 2.48 (s, 3H), 1.74-1.27 (m, 4H), 0.95 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.93 (s), 134.6 (s), 129.9 (d), 128.5 (d), 80.4 (d), 61.2 (d), 36.0 (t), 21.7 (q), 17.3 (d), 13.5 (q), 7.0 (t). MS: (ESI) *m/z* 424.82 [M$^+$], 446.54 [M+Na$^+$]. Anal. calcd for $C_{14}H_{18}NIO_4S$: C, 39.73; H, 4.29; N, 3.31. Found: C, 39.46; H, 4.55; N, 3.04.

4-(Iodomethyl)-5,5-dimethyl-3-tosyloxazolidin-2-one (2d). Compound **2d** was prepared according to the general procedure (H_2O/DMSO 2:1, 30h, room temperature) and isolated as white solid (yield 56%) after flash chromatography (hexane:EtOAc 3:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 4.17 (dd, *J* = 7.6, 1.9 Hz, 1H), 3.59-3.41 (m, 2H), 2.46 (s, 3H), 1.61 (s, 3H), 1.39 (s, 3H). The data are in good agreement with those reported in the literature.[24]

4-(1-Iodopropyl)-3-tosyloxazolidin-2-one (2e). Compound **2e** was prepared according to the general procedure (H_2O/DMSO 2.5:1, 30h, room temperature) and isolated as white solid (yield 67%) after flash column chromatography (hexane:EtOAc 2:1). M.p. 164-165 °C. IR: 2998, 1781, 1602, 1346, 1174, 1126 1075, 810, 603, 575, 549 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.81-4.62 (m, 1H), 4.33 (t, *J* = 9.0 Hz, 1H), 4.14 (dd, *J* = 9.0, 3.7 Hz, 1H), 3.90 (dq, *J* = 6.6, 3.1 Hz, 1H), 2.39 (s, 3H), 1.77 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6 (s), 145.9 (s), 134.6 (s), 129.8 (d), 128.8 (d), 66.4 (t), 61.2 (d), 29.2 (d), 23.1 (q), 21.7 (q). MS: (ESI) *m/z* 418.26 [M+Na$^+$]. Anal. calcd for $C_{12}H_{14}NIO_4S$: C, 36.47; H, 3.57; N, 3.54. Found: C, 36.61; H, 3.30; N, 3.69.

4-(1-Iodopropyl)-3-tosyloxazolidin-2-one (2f). Compound **2f** was prepared according to the general procedure (H_2O/DMSO 2:1, 30h, room temperature) and isolated as white solid (yield 66%) after flash column chromatography (hexane:EtOAc 1:1). M.p. 146-146 °C. IR: 3435, 2971, 2873, 2850, 1784, 1369, 1356, 1175, 1164, 1116, 668, 596, 540 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.9 Hz, 2H), 7.40 (d, *J* = 7.9 Hz, 2H), 5.02-4.95 (m, 1H), 4.60-4.50 (m, 1H), 4.48-4.36 (m, 2H), 2.48 (s, 3H), 1.62-1.45 (m, 2H), 1.01 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6 (s), 146.5 (s), 134.8 (s), 130.3 (d), 128.7 (d), 66.8 (t), 61.0 (d), 37.5 (d), 24.1 (t), 22.1 (q), 14.6 (q). MS: (ESI) *m/z* 432.38 [M+Na$^+$]. Anal. calcd for $C_{13}H_{16}NIO_4S$: C, 38.15; H, 3.94; N, 3.42. Found: C, 37.98; H, 4.17; N, 3.15.

4-(1-Iodobutyl)-3-tosyloxazolidin-2-one (2g). Compound **2g** was prepared according to the general procedure (H_2O/DMSO 1:1, 24h, 40 °C) and isolated as white solid (yield 64%) after flash column chromatography (hexane:EtOAc 4:1). M.p. 136-137 °C. IR: 3439, 2965, 1784, 1352, 1121, 645, 565 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 4.73-4.56 (m, 1H), 4.32 (t, *J* = 9.0 Hz, 1H), 4.16 (dd, *J* = 9.0, 3.8 Hz, 1H), 4.09-3.98 (m, 1H), 2.39 (s, 3H), 1.73-1.28 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6 (s), 145.8 (s), 134.6 (s), 129.7 (d), 128.8 (d), 66.6 (t), 60.1 (d), 38.6 (d), 37.3 (t), 22.7 (t), 21.7 (q), 13.1 (q). MS: (ESI) *m/z* 446.21 [M+Na$^+$]. Anal. calcd for $C_{14}H_{18}NIO_4S$: C, 39.73; H, 4.29; N, 3.31. Found: C, 39.56; H, 4.47; N, 3.06.

4-(2-Iodopropan-2-yl)-3-tosyloxazolidin-2-one (2h). Compound **2h** was prepared according to the general procedure (H_2O/DMSO 1:2, 30h, room temperature) and isolated as white solid (yield 55%) after flash chromatography (hexane:EtOAc 2.5:1). M.p. 156-160 °C (decomp.). IR: 3396, 2921, 1783, 1165, 1160, 665, 554, 538 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 4.79 (dd, *J* = 8.0, 1.6 Hz, 1H), 4.63 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.38 (dd, *J* = 9.7, 7.9 Hz, 1H), 2.48 (s, 3H), 2.16 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 145.9, 134.7, 129.8, 128.5, 69.8, 67.0, 48.9, 35.4, 30.0, 21.7. MS: (ESI) *m/z* 432,24 [M+Na$^+$]. Anal. calcd for $C_{13}H_{16}NIO_4S$: C, 38.15; H, 3.94; N, 3.42. Found: C, 38.21; H, 3.72; N, 3.59.

4-Iodo-3-tosylhexahydrobenzo[d]oxazol-2(3*H*)-one (2i). Compound **2i** was prepared according to the general procedure (H_2O/DMSO 1:1.5, 30h, room temperature) and isolated as white solid (yield 66%) after flash chromatography (hexane:EtOAc 3:1). M.p.: 171-172 °C. IR: 3294, 2940, 1787, 1175, 1163, 671, 558, 541 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 5.00 (dd, *J* = 8.0, 3.9 Hz, 1H), 4.77 (dd, *J* = 11.1, 6.2 Hz, 1H), 4.67 (dd, *J* = 6.5, 3.6 Hz, 1H), 2.48 (s, 3H), 2.28 – 1.58 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.9 (s), 129.8 (d), 128.6 (d), 74.2 (d), 63.3 (d), 28.9 (t), 25.6 (d), 25.1 (t), 21.7 (q), 18.1 (t). MS: (ESI) *m/z* 444.32 [M+Na$^+$]. Anal. calcd for $C_{14}H_{16}NIO_4S$: C, 39.92; H, 3.83; N, 3.33. Found: C, 40.13; H, 3.55; N, 3.24.

4-(Iodomethyl)-3-tosyl-1,3-oxazinan-2-one (2j). Compound **2j** was prepared according to the general procedure (H_2O/DMSO 3:1, 30h, room temperature) and isolated as white solid (yield 74%) after flash chromatography (hexane:EtOAc 2:1). M.p.: 127-128 °C. IR: 3324, 1722, 1358, 1271, 1170, 1143, 669, 612, 542, 533 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 4.75-4.57 (m, 1H), 4.33-4.14 (m, 2H), 3.69 (dd, *J* = 10.1, 3.0 Hz, 1H), 3.24 (t, *J* = 10.6 Hz, 1H), 2.53-2.42 (m, 1H), 2.36 (s, 3H), 2.22-2.06 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0 (s), 145.4 (s), 135.2 (s), 129.5 (d), 129.1 (d), 63.9 (t), 55.4 (d), 26.0 (t), 21.7 (q), 5.3 (t). MS: (ESI) *m/z* 418.51 [M+Na$^+$]. Anal. calcd for $C_{12}H_{14}NIO_4S$: C, 36.47; H, 3.57; N, 3.54. Found: C, 36.41; H, 3.75; N, 3.39.

4-(Iodomethyl)-4-methyl-3-tosyl-1,3-oxazinan-2-one (2k). Compound **2k** was prepared according to the general procedure (H_2O/DMSO 1.5:1, 30h, room temperature) and isolated as colorless oil (yield 68%) after flash chromatography (hexane:EtOAc 4:1). IR: 2936, 1755, 1342, 1176, 667, 562, 546 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.1 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 4.30 (d, *J* = 10.4 Hz, 1H), 4.23-4.15 (m, 2H), 3.89 (d, *J* = 10.4 Hz, 1H), 2.57-2.45 (m, 1H), 2.42 (s, 3H), 2.11-1.96 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 144.9, 136.6, 129.4, 129.1, 64.0, 62.6, 38.3, 25.8, 21.6, 13.0. MS: (ESI) *m/z* 432.45 [M+Na$^+$]. Anal. calcd for $C_{13}H_{16}NIO_4S$: C, 38.15; H, 3.94; N, 3.42. Found: C, 37.99; H, 4.13; N, 3.53.

(5*S*,6*R*,8*S*)-6-Iodo-8-(prop-1-en-2-yl)-1-tosyl-3-oxa-1-azaspiro[4.5]decan-2-one (4). Compound **4** was prepared according to the general procedure (H_2O/DMSO 1:3, 24h, 40 °C) and isolated as white solid (yield 63%) after flash chromatography (hexane:EtOAc 3:1). M.p.: 160-164 °C (decomp.). IR: 3358, 3261, 2959, 2922, 1785, 1188, 1168, 1084, 667, 562, 545 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 5.46 (dd, *J* = 13.6, 4.1 Hz, 1H), 5.17 (s, 1H), 5.01 (s, 1H), 4.48 (d, *J* = 8.3 Hz, 1H), 4.31 (d, *J* = 8.7 Hz, 1H), 3.03 (td, *J* = 13.8, 3.2 Hz, 1H), 2.93-2.82 (m, 1H), 2.46 (s, 3H), 2.33-1.99 (m, 4H), 1.83 (s, 3H), 1.71-1.56 (m, 1H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 151.0 (s), 145.5 (s), 143.1 (s), 135.1 (s), 129.7 (d), 129.2 (d), 112.7 (t), 71.5 (t), 70.0 (s), 40.5 (d), 39.2 (t), 34.2 (d), 30.5 (t), 24.6 (t), 22.5 (q), 21.7 (q). MS: (ESI) *m/z* 498,23 [M]$^+$. $[\alpha]^D_{20}$: -17 (c: 0.1 in $CHCl_3$). Anal. calcd for $C_{18}H_{22}NIO_4S$: C, 45.48; H, 4.67; N, 2.95. Found: C, 45.44; H, 4.89; N, 3.11.

4-(Iodomethyl)-1-phenyl-3-tosylimidazolidin-2-one (6a). Compound **6a** was prepared according to the general procedure (H_2O/DMSO 1:1, 30h, room temperature) and isolated as pale yellow solid (yield 54%) after flash chromatography (hexane:EtOAc 2.5:1). M.p. 148-149 °C. IR: 3023, 2958, 1716, 1599, 1504, 1359, 1170, 1131, 751, 666, 592, 554 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.4 Hz, 2H), 7.53-7.43 (m, 2H), 7.35 (t, *J* = 8.0 Hz, 4H), 7.14 (t, *J* = 7.4 Hz, 1H), 4.54 (tt, *J* = 8.8, 3.2 Hz, 1H), 4.09 (t, *J* = 9.4 Hz, 1H), 3.78 (dd, *J* = 10.2, 2.7 Hz, 1H), 3.68 (dd, *J* = 9.6, 3.7 Hz, 1H), 3.54 (dd, *J* = 10.2, 8.4 Hz, 1H). 7.54-7.44 (m, 2H), 7.41-7.32 (m, 4H), 7.14 (t, *J* = 7.4 Hz, 1H), 4.72-4.41 (m, 1H), 4.09 (t, *J* = 9.4 Hz, 1H), 3.73 (ddd, *J* = 29.8, 9.9, 3.2 Hz, 1H), 3.54 (dd, *J* = 10.2, 8.4 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.1 (s), 145.2 (s), 137.9 (s), 135.5 (s), 129.7 (d), 129.0 (d), 128.5 (d), 124.6 (d), 118.9 (d), 52.9 (d), 49.6 (t), 21.6 (q), 9.3 (t). MS: (ESI) *m/z* 479.20 [M+Na$^+$]. Anal. calcd for $C_{17}H_{17}N_2IO_3S$: C, 44.75; H, 3.76; N, 6.14. Found: C, 44.97; H, 3.50; N, 5.88.

(*Z*)-*N*-(5-(Iodomethyl)-3-methyloxazolidin-2-ylidene)-4-methylbenzenesulfonamide (6b). Compound **6b** was prepared according to the general procedure (H_2O/DMSO 2:1, 30h, room temperature) and isolated as white solid (yield 52%) after flash chromatography (hexane:EtOAc 1:1). M.p. 120-121 °C. IR: 2920, 1728, 1358, 1172, 1140, 666, 590 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 5.00-4.55 (m, 1H), 3.79 (t, *J* = 9.2 Hz, 1H), 3.37-3.22 (m, 3H), 2.96 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.6 (s), 142.8 (s), 140.3 (s), 129.4 (d), 127.6 (d), 77.1 (d), 53.5 (t), 32.1 (q), 21.9 (q), 5.1 (t). MS: (ESI) *m/z* 417.22 [M+Na$^+$]. Anal. calcd for $C_{12}H_{15}N_2IO_3S$: C, 36.56; H, 3.84; N, 7.11. Found: C, 36.29; H, 4.12; N, 6.91.

2-(Iodomethyl)-4-methyl-1-tosyl-1,2,3,4-tetrahydro-5*H*-benzo[*e*][1,4]diazepin-5-one (8a). Compound **8a** was prepared according to the general procedure (H_2O/DMSO 1.5:1, 20h, 60 °C) and isolated as white solid (yield 71%) after flash chromatography (hexane:EtOAc 1.5:1). M.p. 156-156 °C. IR: 3074, 1670, 1382, 1157, 1145, 1049, 712, 667 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.2 Hz, 1H), 7.60-7.38 (m, 5H), 7.27 (d, *J* = 7.7 Hz, 2H), 4.72-4.33 (m, 1H), 3.75-3.45 (m, 2H), 3.28-2.93 (m, 2H), 2.62 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5 (s), 144.1 (s), 135.3 (s), 134.4 (s), 133.6 (d), 132.3 (s), 131.9 (d), 130.1 (d), 129.9 (d), 129.5 (d), 127.1 (d), 61.5 (d), 52.8 (t), 34.2 (q), 21.6 (q), 4.0 (t). MS: (ESI) *m/z* 471,22 [M+Na$^+$]. Anal. calcd for $C_{18}H_{19}N_2IO_3S$: C, 45.97; H, 4.07; N, 5.96. Found: C, 45.94; H, 4.23; N, 6.19.

4-Cyclohexyl-2-(iodomethyl)-1-tosyl-1,2,3,4-tetrahydro-5*H*-benzo[*e*][1,4]diazepin-5-one (8b). Compound **8b** was prepared according to the general procedure (H_2O/DMSO 1:5, 30h, 50 °C) and isolated as white solid (yield 68%) after flash chromatography (hexane:EtOAc 7:3). M.p. = 158–159 °C. IR = 2924, 1640, 1347, 1157, 1139, 1055, 710, 662 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8 Hz, 1H), 7.47-7.38 (m, 5H), 7.17 (d, *J* = 8 Hz, 2H), 4.16-4.09 (m, 1H), 3.84-3.78 (m, 1H), 3.69 (dd, *J* = 15.5Hz, 4.5Hz, 1H), 3.53 (dd, *J* = 9.9 Hz, 3.7 Hz, 1H), 2.97 (t, *J* = 10.1 Hz, 1H), 2.73 (dd, *J* = 15.4, 11.9 Hz, 1H), 2.34 (s, 3H), 1.74-0.8 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.5 (s), 144.1 (s), 135.7 (s), 135.1 (s), 132.9 (d), 132.3 (s), 131.6 (d), 130.5 (d), 129.7 (d), 129.2 (d), 127.7 (d), 64.0 (d), 53.0 (d), 45.6 (t), 30.4 (t), 30.1 (t), 25.7 (t), 25.3 (t), 25.3 (t), 21.5 (q), 4.0 (t). MS: (ESI) *m/z* 561.45 [M+Na$^+$]. Anal. calcd for $C_{23}H_{27}N_2IO_3S$: C, 51.30; H, 5.05; N, 5.20. Found: C, 51.07; H, 5.28; N, 4.97.

2-(Iodomethyl)-4-phenyl-1-tosyl-1,2,3,4-tetrahydro-5*H*-benzo[*e*][1,4]diazepin-5-one (8c). Compound **8c** was prepared according to the general procedure (H_2O/DMSO 1:5, 30h, 50 °C) and isolated as white solid (yield 63%) after flash chromatography (hexane:EtOAc 4:1). M.p.: 87–88 °C. IR = 1653, 1398, 1350, 1170, 1087, 1050, 743, 717. ^{1}H NMR (400MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.4 Hz, 1H), 7.55-7.42 (m, 5H), 7.21-7.14 (m, 5H), 6.59 (d, *J* = 7.5 Hz, 2H), 4.46-4.40 (m, 1H), 4.02 (dd, *J* = 15.1, 4.3Hz, 1H), 3.60-3.35 (m, 2H), 3.11 (t, *J* = 9.8 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (101MHz, $CDCl_3$): δ 157.3 (s), 144.3 (s), 141.4 (s), 135.9 (s), 134.8 (s), 133.4 (d), 132.5 (s), 132.0 (d), 130.5 (d), 130.0 (d), 129.4 (d), 128.0 (d), 127.6 (d), 126.8 (d), 125.3 (d), 62.0 (d), 54.3 (t), 21.5 (q), 4.2 (t). MS: (ESI) *m/z* 555.23 [M+Na$^+$]. Anal. calcd for $C_{23}H_{21}N_2IO_3S$: C, 51.89; H, 3.98; N, 5.26. Found: C, 52.01; H, 3.81; N, 5.45.

2-(Iodomethyl)-4-methyl-8-nitro-1-tosyl-1,2,3,4-tetrahydro-5*H*-benzo[*e*][1,4]diazepin-5-one (8d). Compound **8d** was prepared

according to the general procedure (H_2O/DMSO 2:1, 24h, 60 °C) and isolated as pale yellow solid (yield 74%) after flash chromatography (hexane:EtOAc 1:1). M.p. 85-86 °C. IR: 2921, 1654, 1334, 1155, 1111, 709, 666, 583, 571 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, *J* = 2.1 Hz, 1H), 8.30 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.32-7.22 (m, 2H), 4.66-4.28 (m, 1H), 3.66-3.48 (m, 2H), 3.28-3.07 (m, 2H), 2.64 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8 (s), 140.1 (s), 134.7 (s), 133.8 (s), 131.2 (d), 130.1 (d), 129.0 (d), 127.1 (d), 123.9 (d), 61.3 (d), 52.8 (t), 34.3 (q), 21.6 (q), 4.1 (t). MS: (ESI) *m/z* 538.43[M+Na^+]. Anal. calcd for $C_{18}H_{18}N_3IO_5S$: C, 41.95; H, 3.52; N, 8.15. Found: C, 42.08; H, 3.43; N, 7.96.

3-(Iodomethyl)-2-tosyl-3,4-dihydropyrazino[1,2-*a*]indol-1(2*H*)-one (9). Compound **9** was prepared according to the general procedure (H_2O/DMSO 1:5, 6h, room temperature) and isolated as white solid (yield 67%) after flash chromatography (hexane:EtOAc 4:1). M.p. 173-174 °C. IR: 3435, 2922, 1690, 1536, 1346, 1163, 742, 715, 556 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.46-7.33 (m, 5H), 7.26-7.13 (m, 1H), 5.37-5.25 (m, 1H), 5.13 (d, *J* = 13.2 Hz, 1H), 4.33 (dd, *J* = 12.8, 3.0 Hz, 1H), 3.62-3.49 (m, 1H), 3.17 (dd, *J* = 11.6, 10.3 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3 (s), 145.5 (s), 137.3 (s), 135.8 (s), 129.6 (d), 129.0 (d), 127.3 (s), 126.4 (d), 126.1 (s), 123.2 (d), 121.6 (d), 110.0 (d), 56.9 (d), 42.8 (t), 21.7 (q), 2.8 (t). MS: (ESI) *m/z* 481.25 [M^+], 503.38 [M+Na^+]. Anal. calcd for $C_{19}H_{17}N_2IO_3S$: C, 47.51; H, 3.57; N, 5.83. Found: C, 47.59; H, 3.80; N, 5.62.

2-(Iodomethyl)-1-tosylindoline (10a). Compound **10a** was prepared according to the general procedure (H_2O/DMSO 1:1, 24h, 60 ° C) and isolated as pale yellow solid (yield 58%) after flash chromatography (hexane:EtOAc 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.20-7.07 (m, 3H), 7.00-6.93 (m, 2H), 4.30-4.24 (m, 1H), 3.58 (dd, *J* = 9.7, 3.4 Hz, 1H), 3.18 (t, *J* = 9.9 Hz, 1H), 2.86 (dd, *J* = 16.7, 9.3 Hz, 1H), 2.76 (dd, *J* = 16.7, 3.0 Hz, 1H), 2.27 (s, 3H). The data are in good agreement with those reported in the literature.[18]

5-Chloro-2-(iodomethyl)-1-tosylindoline (10b). Compound **10b** was prepared according to the general procedure (H_2O/DMSO 1:1.2, 20h, 40 °C) and isolated as white solid (yield 62%) after flash chromatography (hexane:EtOAc 10:1). ^1H NMR (300 MHz, $CDCl_3$) δ = 7.58-7.53 (m, 3H), 7.23-7.16 (m, 3H), 7.03 (s, 1H), 4.36 – 4.30 (m, 1H), 3.63 (dd, *J* = 9.7, 3.3 Hz, 1H), 3.26 (t, *J* = 9.9 Hz, 1H), 2.89-2.82 (m, 2H), 2.37 (s, 3H). The data are in good agreement with those reported in the literature.[18]

2-(Iodomethyl)-6,7-dimethyl-1-tosylindoline (10c). Compound **10c** was prepared according to the general procedure (H_2O/DMSO 1:2.5, 20h, 60 °C) and isolated as pale yellow solid (yield 51%) after flash chromatography (hexane:EtOAc 12:1). ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.3 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.96 (t, *J* = 6.9 Hz, 2H), 6.77 (d, *J* = 7.5 Hz, 1H), 4.48-4.37 (m, 1H), 3.36 (dd, *J* = 9.8, 5.1 Hz, 1H), 2.98 (t, *J* = 9.9 Hz, 1H), 2.45 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H), 2.12-1.98 (m, 2H). The data are in good agreement with those reported in the literature.[20]

General procedure for the X-ray diffraction analysis. Single-crystal X-ray diffraction experiments were carried out on a Bruker AXS three-circle diffractometer equipped with an Apex II CCD area detector. Data were collected using graphite-monochromated Mo Kα radiation (λ=0.71073 Å) at a nominal X-rays power of 50 kV x 30 mA. A 100 % complete full sphere of reflections was recorded up to a maximum resolution of 0.77 Å, resulting in 3578 (compound **2f**) and 4460 (ompound **4**) independent structure factor amplitudes. The latter were reduced with the SAINT+ software[48] and corrected for absorption using the empirical procedure implemented in SADABS.[49] The structures were solved by either iterative charge-flipping methods implemented in SUPERFLIP[50] (compound **2f**) or by direct methods (SIR92).[51] Structure refinements were carried out in the independent atom approximation with the least squares algorithm implemented in shelxl.[52] Molecular drawings were plotted with Diamond 3.0k (©1997–2014 Crystal Impact GbR, Bonn, Germany).

X-ray-quality crystals of the compound **2f** (prismatic habit, colorless) were grown by slow evaporation (~ 10 hrs) from a 1:1 mixture of hexane and CH_2Cl_2 at room temperature. The specimen used for the X-ray diffraction experiment was cut from a larger agglomerate and polished by mechanical ablation in a drop of perfluorinated oil. It showed pleochroism under polarized light (from colourless to dark grey). **2f** is chiral and crystallizes in the monoclinic centric space group $P2_1/n$ as a racemate, with one molecule per asymmetric unit and absolute configurations (*S,S*) or (*R,R*). The oxazolidin-2-one ring is slightly distorted toward a half-chair conformation. Unit cell (Å, deg, $Å^3$), as estimated from 9987 intense reflections with $4.7 \leq 2\theta \leq 56.2$ deg: a = 7.8801(2), b = 17.1890(5), c = 11.5884(3), β = 96.156(1), V = 1560.6(1).

X-ray quality crystals (prismatic habit, colorless) were grown by slow evaporation (~ 6 hrs) from a 1:1 hexane:CH_2Cl_2 mixture at room temperature. The sample chosen for the X-ray analysis was cut from a larger agglomerate and polished by mechanical ablation in a drop of perfluorinated oil. It showed pleochroism under polarized light (from colourless to dark grey). The compound is chiral and crystallizes in the orthorhombic acentric space group $P2_12_12_1$ as a pure enantiomer, with one molecule per asymmetric unit. The presence of sulphur and iodine anomalous scatterers allow to secure the absolute molecular configuration, with a Flack parameter[53] as low as 0.02(2) by classical fit to all intensities (Figure 3). The saturated six-membered ring assumes an almost perfect chair conformation, while the oxazolidin-2-one ring, analogously to compound **2f**, adopts a slightly distorted half-chair conformation. Unit cell (Å, $Å^3$), as estimated from 8060 intense reflections with $5.3 \leq 2\theta \leq 47.2$ deg: a = 8.1577(2), b = 11.8874(2), c = 20.0540(4), V = 1944.7(1).

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Author Contribution Statement

G. B. and *E. M. B.* designed the project. *S. G.* and *R. S.* performed the experiments. XRD data was acquired and analyzed by *L. L. P*. All authors contributed to writing the manuscript.

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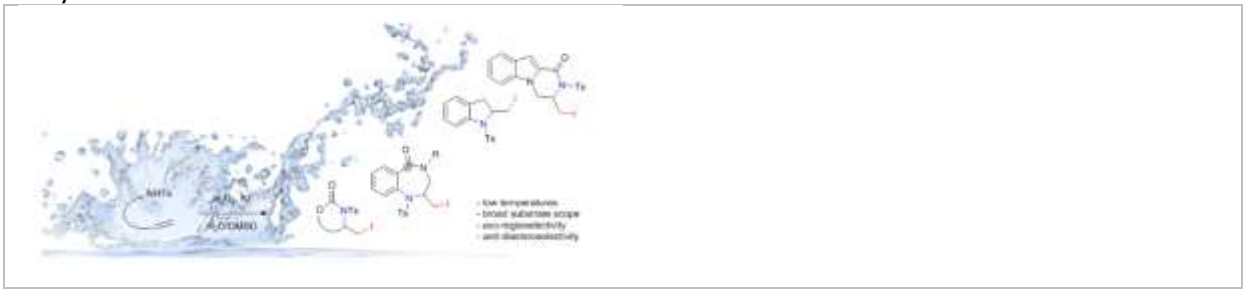

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