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Diastereoselective Bromocyclization of *O*-Allyl-*N*-tosyl-hydroxylamines

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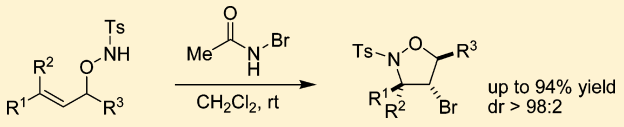
Supporting Information

ABSTRACT: The intramolecular bromoamination of *O*-allyl-*N*-tosyl-hydroxylamines results in the formation of isoxazolidines via selective 5-*endo-tet* cyclization. This process occurs *trans*-selectively in high yield and diastereoselectivity. The obtained bromo-isoxazolidines provide access to other useful building blocks, such as 2-azido-aminoalcohols, diaminoalcohols, and aziridines.



INTRODUCTION

Electrophilic activation of unsaturated hydrocarbons bearing internal nucleophiles has been widely used for the preparation of different heterocycles in organic synthesis.[1] In this respect amines,[2] carbamates,[3] amides,[4] urea derivatives,[5] imines,[6] oximes,[7] oxime ethers,[8] hydrazines,[9] hydroxamic acids,[10] and hydroxylamines[11] have been utilized in such cyclization reactions with various electrophiles. This approach was successfully employed for the preparation of various pharmacologically active compounds and synthetic building blocks.[12]

Substituted isoxazolidines have been synthesized via 1,3-dipolar cycloadditions of nitrones with alkenes[13] or metal-catalyzed cyclization reactions[14] and are important precursors to β-amino alcohols,[15] β-amino ketones,[16] β-amino acids,[17] and 3-isoxazolidones.[18] Studer[19] and Togo[20] independently developed an *exo*-selective bromocyclization of *O*-homoallyl-hydroxylamine derivatives leading to bromo-isoxazolidines. However, isoxazolidines with a bromo-substituent on a stereogenic center have not been investigated in detail. Therefore, we were interested in the behavior of *O*-allyl-*N*-tosyl-hydroxylamines toward electrophilic activation. Herein, we present the bromocyclization of *O*-allyl-*N*-tosyl-hydroxylamines, which proceeds to diastereomerically pure bromo-isoxazolidines via 5-*endo-tet* ring closure.

RESULTS AND DISCUSSION

The *O*-allyl-*N*-tosyl-hydroxylamines were readily prepared by Mitsunobu reaction[21] starting from allylic alcohols **1a**−**k** using *N*-hydroxyphthalimide as nucleophile following a modified protocol by Saito.[22] Subsequent hydrazinolysis of the *O*-allyl-*N*-phthalimido-hydroxylamines **2a**−**k** and reprotection with *p*-TsCl gave the corresponding *O*-allyl-*N*-tosyl-hydroxylamines **3a**−**k** (Scheme 1).

Initially, we screened different halonium sources and solvents for the intramolecular halocyclization of **3a** (Table 1). Utilizing brominating agents like *N*-bromosuccinimide (NBS), 1,3-dibromo-5,5-dimethylhydantoin (DBDMH), bis(2,4,6-trimethylpyridine)bromine(I) hexafluorophosphate ($Br^+(coll)_2PF_6^-$), or *N*-bromoacetamide (NBA), bromo-isoxazolidine **4a** was formed in complete diastereoselectivity and high yields (Table 1, entries 1−4). The formation of the five-membered ring as well as the relative *trans*-configuration between the phenyl- and bromo-substituent were confirmed by X-ray analysis.[23]

N-Bromoacetamide in dichloromethane or in acetonitrile led to a comparable outcome (91% vs 88% yield, Table 1, entries 4 and 9). In contrast, employing toluene or THF as solvents drastically increased reaction time and lowered the yield of **4a** to 79 and 35%, respectively (entries 5 and 6). To our surprise, the use of *N*-chlorosuccinimide (NCS) and 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) did not lead to any observable reaction within 24 h (entries 10 and 11).

After optimal reaction conditions for the selective bromocyclization of *O*-allyl-*N*-tosyl-hydroxylamines were found, the scope of this reaction was investigated. As depicted in Table 2, *trans*-alkenes bearing aromatic substituents smoothly undergo diastereoselective (dr > 98:2) cyclization to the corresponding *trans*-aryl-bromo-isoxazolidines **4a**, **4c**, and **4d** (Table 2, entries 1, 3, and 4). Thus, electron-rich aromatic systems can be employed without difficulty. In contrast, *p*-NO_2-phenyl-substituted alkene **3e** did not undergo cyclization, which is consistent with the assumption of an electrophilic attack of the double bond. Cyclization of substituted *cis*-styrene derivatives **3b** and **3f** (Table 2, entries 2 and 6) diastereoselectively led to the corresponding *cis*-aryl-bromo-isoxazolidines **4b** and **4f**, in yields of 83 and 65%, respectively. These *cis*-alkenes required longer reaction times, which can be rationalized by considering $A^{1,3}$-strain interactions.[24]

Treatment of **3c** with NBA under optimized conditions afforded **4c** as a single diastereomer exemplifying the influence of an existing stereocenter on the stereochemical outcome. The high selectivity may be explained by unfavorable steric interactions in one of the two assumed transition states as

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Scheme 1. Synthesis of Bromo-isoxazolidines Starting from Allylic Alcohols

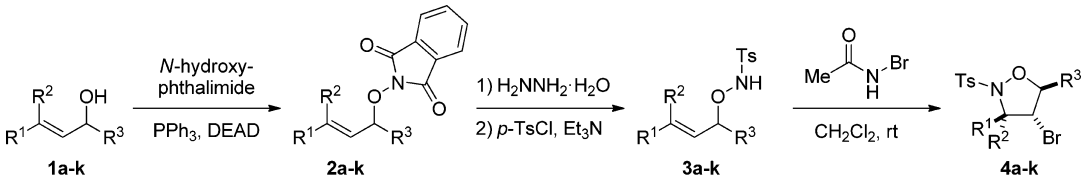
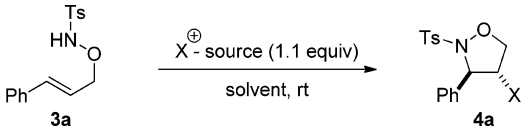


Table 1. Optimizing Conditions for the Intramolecular Bromocyclization of 3a



entry	$X^{\oplus}$-source	solvent	time (h)	yield (%)[a]	dr[b]
1	NBS	CH_2Cl_2	1.5	85	>98:2
2	DBDMH	CH_2Cl_2	1	86	>98:2
3	$Br^{\oplus}(coll)_2PF_6^{\ominus}$	CH_2Cl_2	2	81	>98:2
4	NBA	CH_2Cl_2	1	91	>98:2
5	NBA	toluene	22	79	>98:2
6	NBA	THF	18	35	>98:2
7	NBA	acetone	1.5	74	>98:2
8	NBA	EtOAc	4	85	>98:2
9	NBA	MeCN	0.5	88	>98:2
10	NCS	CH_2Cl_2	24	0[c]	–
11	DCDMH	CH_2Cl_2	24	0[c]	–

[a]Reaction performed on a 0.25 mmol scale (0.05 M), isolated yield. [b]Determined by ^{1}H NMR analysis of crude reaction mixture. [c]No reaction observed within 24 h.

shown in Scheme 2. Since all bromo-isoxazolidines **4a−d** and **4f** were obtained as single diastereomers, overall *trans*-addition by S_N2-attack of a bromonium intermediate is assumed. Besides styrene derivatives, we scrutinized the behavior of mono- and dialkyl substituted derivatives **3g−i**. Bromocyclization of methylbutenyl- and *trans*-hexenyl derivatives **3g** and **3h** led to isoxazolidines **4g** and **4h** in 84 and 70% yield, respectively (Table 2, entries 7 and 8). In contrast, similar treatment of *cis*-hexenyl hydroxylamine **3i** afforded a complex mixture of products (Table 2, entry 9). While rapid consumption of starting material upon addition of the brominating agent was observed, nucleophilic ring closure is presumably unfavored for steric reasons. Therefore, intermolecular nucleophile attack may dominate. Cyclohexenyl derivative **3j** smoothly underwent diastereoselective cyclization to the corresponding bicycle **4j** in 91% yield. The octahydrobenzo[*c*]isoxazole structure of **4j** could be confirmed by X-ray analysis.[23] Surprisingly, treatment of the closely related cyclopentenyl derivate **3k** with NBA gave a mixture of products from which only **4k** could be isolated in a yield of 26%.

Focusing on the mechanism of the bromocyclization initial ^{1}H NMR studies revealed that 1.1 equiv NBA added to **3b** in $CDCl_3$ led to the disappearance of the NH-signal at 7.07 ppm accompanied by a highfield shift of the *β*-styrene proton from 5.78 ppm to 5.66 ppm. Concomitant formation of acetamide (CH_3CONH_2) was observed. After a while, bromo-isoxazolidine **4b** was formed, and at the same time, disappearance of the putative *N*-bromo-species was monitored (Scheme 3). In addition, treatment of *p*-NO_2-phenyl-substituted derivative **3e** with 1.0 equiv NBA in $CDCl_3$ provided *N*-brominated hydroxylamine derivative **5**, which does not undergo cyclization and could be isolated (Scheme 4).[25] Reaction of this intermediate with **3a** cleanly led to isoxazolidine **4a** with back-formation of alkene **3e** within 15 min.

These observations suggest that in the first place an *N*-bromo-species is formed, which then undergoes either intra- or intermolecular bromination of the double bond. Subsequent nucleophilic opening of the bromonium intermediate leads to the final product.

The bromo-isoxazolidines can be further transformed into various synthetic building blocks. Since direct nucleophilic displacement of the bromo-substituent of **4a** with azide sources such as $TMSN_3$/TBAF,[26] or NaN_3 in DMF was unsuccessful, the N−O bond was cleaved first (Scheme 5). Hydrogenation of **4a** in the presence of 10 mol % Pd/C as catalyst provided the corresponding bromo-aminoalcohol **6** in almost quantitative yield after two days. Azidation of **6** afforded diastereomerically pure 2-azido-aminoalcohol **8**, which could be quantitatively converted into diamino-alcohol *syn*-**9** by hydrogenation on Pd/C. At this stage, the relative configuration of *syn*-**9** could be verified by comparison of its ^{1}H NMR spectrum with the one of literature-known diamino-alcohol *anti*-**9**.[27] Additionally, treatment of bromo-aminoalcohol **6** with K_2CO_3 in acetonitrile led to *trans*-configured aziridine **7** in a yield of 81%.[28]

CONCLUSION

In conclusion, we have developed a new method for the efficient synthesis of bromo-isoxazolidines by diastereoselective bromocyclization of *O*-allyl-*N*-tosyl-hydroxylamines, which are derived from easily available allylic alcohols. For this stereospecific process, highly substituted and cyclic alkenes can also be employed. The reaction presumably proceeds via an *N*-bromo intermediate, which leads to inter- or intramolecular, electrophilic activation of the alkene moiety. The utility of the new method was further exemplified by transformation of the bromo-isoxazolidines into 2-azido-aminoalcohols, diaminoalcohols, and aziridines.

EXPERIMENTAL SECTION

General Methods. All syntheses involving air- and moisture-sensitive compounds were carried out using standard Schlenk-type glassware under an atmosphere of argon. Solvents were dried under argon using a commercial purification system. Unless stated otherwise all chemicals were used as supplied. ^{1}H and ^{13}C NMR spectra were recorded at room temperature on commercial 400 and 500 MHz instruments. The chemical shift δ is given relative to TMS and referenced to the residual solvent signal. The attributions of the chemical shifts were determined by means of COSY, HSQC, HMQC, and NOE experiments. Melting points are not corrected. High resolution mass spectra (HRMS) were obtained with an ESI-TOF spectrometer. IR spectra were recorded using a NaCl disk (Film). X-ray data sets were collected using a diffractometer using Mo Kα radiation (λ = 0.71073 Å, graphite monochromator) at 133 K. For structure solution and refinement, the programs of the SHELXS-97 series were used.[29] All reactions were monitored by thin layer chromatography (TLC). Flash chromatography was carried out using silica gel (0.040−0.063 mm). *N*-Bromoacetamide (NBA),[30] bis(2,4,6-

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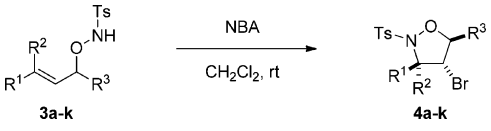
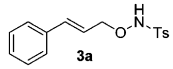
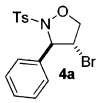
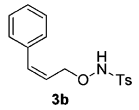
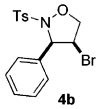
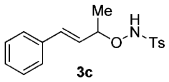
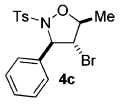
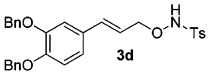
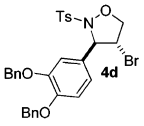
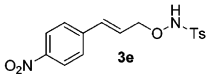
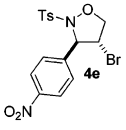
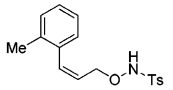
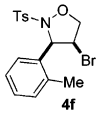
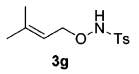
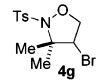
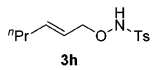
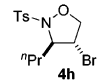
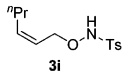
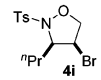
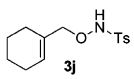
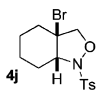
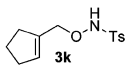
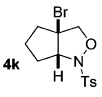
Table 2. Intramolecular Bromocyclization of Various *O*-Allyl-*N*-tosyl-hydroxylamines[a]



entry	substrate	product	time	yield (%)[b]	dr[c]
1[d]	 **3a**	 **4a**	1 h	94	> 98:2
2	 **3b**	 **4b**	19 h	83	> 98:2
3	 **3c**	 **4c**	3 h	86	> 98:2 (*anti*/*anti*)
4	 **3d**	 **4d**	3 h	84	> 98:2
5	 **3e**	 **4e**	4 d	0[e]	-
6	 **3f**	 **4f**	2 d	65	> 98:2
7	 **3g**	 **4g**	2 h	84	-
8	 **3h**	 **4h**	20 h	70	> 98:2
9	 **3i**	 **4i**	7 d	0[e]	-
10	 **3j**	 **4j**	5 h	91	> 98:2
11	 **3k**	 **4k**	32 h	26	nd[f]

[a]Conditions: Substrate (0.50 mmol), NBA (1.1 equiv), CH_2Cl_2 (0.05 M), rt. [b]Isolated yield. [c]Determined by ^1H NMR analysis of the crude reaction mixture. [d]Performed on a 3.30 mmol scale. [e]Complex mixture obtained. [f]Several byproducts were formed as indicated by ^1H NMR analysis of the crude reaction mixture. These could not be isolated in pure form. Therefore, exact determination of the dr was not possible.

trimethylpyridine)bromine(I) hexafluorophosphate,[31] (*E*)-benzyl 3-(3,4-bis(benzyloxy)phenyl)-acrylate,[32] cyclohex-1-en-1-ylmethanol (**1j**),[33] cyclopent-1-en-1-ylmethanol (**1k**),[34] and (*E*)-4-phenylbut-3-en-2-ol (**1c**)[35] were prepared according to literature procedures. (*Z*)-3-(2-Tolyl)prop-2-en-1-ol (**1f**)[36] was prepared by partial hydrogenation of the corresponding propargylic alcohol using Lindlar's catalyst[37] according to the reported method for (*Z*)-3-phenylprop-2-en-1-ol (**1b**)[38] with slight modifications.

General Procedure for the Preparation of *O*-Allyl-*N*-phthalimido-hydroxylamines (GP1). A modified procedure by Saito[22] was used: To a stirred solution of the allylic alcohol (1.0 equiv), triphenylphosphine (1.1 equiv), and *N*-hydroxyphthalimide (1.1 equiv) in tetrahydrofuran (0.25 M) diethyl azodicarboxylate (40% in toluene, 1.1 equiv) was added dropwise at 0 °C. After complete addition, the reaction was stirred at rt for the time given. The solvent was removed in vacuo, and the crude reaction mixture was purified by column chromatography on silica gel.

General Procedure for the Preparation of *O*-Allyl-*N*-tosyl-hydroxylamines (GP2). To a stirred solution of the *O*-allyl-*N*-phthalimido-hydroxylamine (1.0 equiv) in dichloromethane or tetrahydrofuran (0.25 M) hydrazine monohydrate (1.1 to 3.0 equiv) was added. The resulting suspension was stirred at rt until all starting material was gone (TLC), before water was added. The aqueous phase was extracted three times with dichloromethane, and the combined organic layers were washed with brine. After drying with sodium sulfate, filtration, and evaporation of the solvent, the crude product was directly used without further purification.

The crude material was suspended in dichloromethane (0.25 M), triethylamine (1.2 equiv), and *p*-TsCl (1.1 equiv) was added subsequently at rt. After reaction completion, as indicated by TLC analysis, water was added, and the aqueous phase was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over sodium sulfate. After filtration and evaporation of the solvent, the crude product was purified by column chromatography on silica gel.

General Procedure for the Bromocyclisation of *O*-Allyl-*N*-tosyl-hydroxylamines (GP3). To a solution of the *O*-allyl-*N*-tosyl-hydroxylamine (1.0 equiv) in dichloromethane (0.05 M) protected from light *N*-bromoacetamide (1.1 equiv) was added in one portion. The solution was stirred at rt until the reaction was complete, as indicated by TLC analysis. $Na_2S_2O_5$-solution (10%) in water was added, and the aqueous layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried over sodium sulfate. After filtration and evaporation of the solvent, the crude product was purified by column chromatography on silica gel.

(*E*)-3-(3,4-Bis(benzyloxy)phenyl)prop-2-en-1-ol (1d).[39] To a stirred solution of (*E*)-benzyl 3-(3,4-bis(benzyloxy)phenyl)acrylate[32] (10.0 g, 22.2 mmol, 1.0 equiv) in toluene (67 mL) was added dropwise DIBAL-H (1.5 M in toluene, 37.0 mL, 55.5 mmol, 2.5 equiv) at −78 °C over a time period of approximately 1 h. After complete addition, the resulting yellow solution was stirred at −78 °C for 1 h and then warmed to 0 °C and stirred for another hour at this temperature. Then water (50 mL) was added dropwise. Finally the reaction mixture was diluted with water (300 mL) and diethyl ether (300 mL). The aqueous phase was extracted with diethyl ether (3 × 100 mL). The combined organic phases were dried over sodium sulfate, filtered, and concentrated to dryness. Recrystallization of the crude product from hexanes/dichloromethane (−18 °C) afforded **1d** as colorless solid. Yield: 7.27 g (21.0 mmol, 94%); ^1H NMR (500 MHz, $CDCl_3$) δ = 4.27 (dd, J = 5.9, 1.3 Hz, 2 H, CH_2CO), 4.69 (s, 1 H, OH), 5.16 (s, 2 H, CH_2Ph), 5.17 (s, 2 H, CH_2Ph), 6.18 (td, J = 15.8, 5.9 Hz, 1 H, Ar—CH=C—H), 6.49 (d, J = 15.9 Hz, 1 H, Ph—CH=C—H), 6.87−6.92 (m, 2 H, Ar−H), 7.02 (m$_c$, 1 H, Ar−H), 7.27−7.49 (m, 10 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 63.7 (CH_2O), 71.2 (CH_2Ph), 71.3 (CH_2Ph), 112.9, 114.9, 120.2, 126.8, 127.2, 127.3, 127.8, 128.5, 130.4 137.2, 148.8, 149.0 ppm.

(*Z*)-3-(2-Tolyl)prop-2-en-1-ol (1f).[36] A stirred suspension of Lindlar's catalyst (5% Pd (poisoned with lead) on $CaCO_3$, 2.13 g, 1.00 mmol) and quinoline (3.55 mL, 30.0 mmol) in toluene (30 mL) was saturated with hydrogen. Subsequently, 3-(2-methylphenylprop)-2-yn-1-ol[40] (2.94 g, 20.0 mmol) was added, and the reaction mixture was

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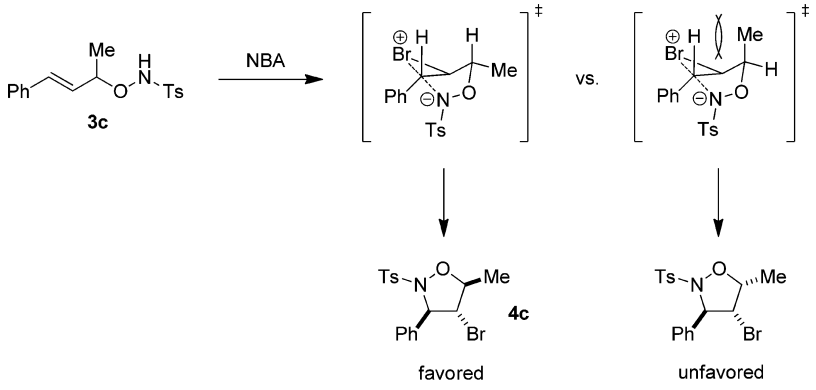
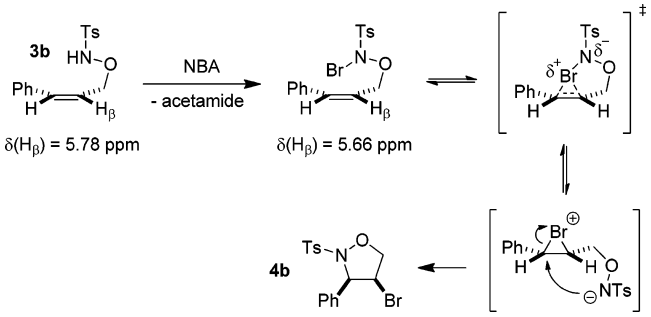
Scheme 2. Rationale for the Stereochemical Outcome of the Cyclization of 3c



Scheme 3. Potential Mechanism of the Intramolecular Bromocyclization



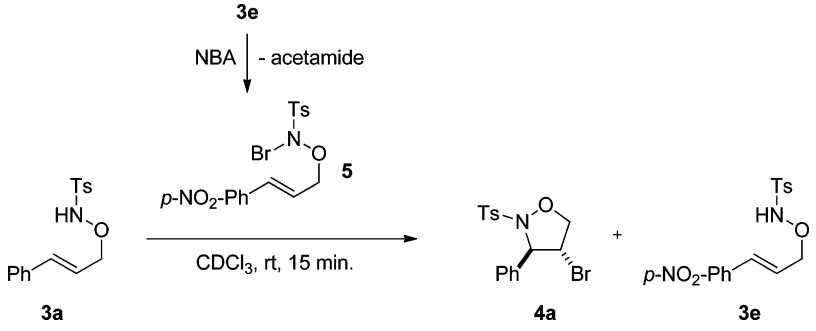
stirred in a hydrogen atmosphere at rt for 4 h. The mixture was filtered through a pad of Celite and concentrated in vacuo. Purification by flash column chromatography (SiO_2, dichloromethane/toluene 4:1) provided **1f** as brownish oil. Yield: 1.97 g (13.3 mmol, 67%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.28 (s, 3 H, Me), 4.29 (d, J = 6.5 Hz, 2 H, CH_2O), 5.92 (dt, J = 11.5, 6.6 Hz, 1 H, Ar—CH=C<u>H</u>), 6.63 (d, J = 11.5 Hz, 1 H, Ar—C<u>H</u>=CH), 7.07–7.09 (m, 1 H, Ar–H), 7.15–7.20 (m, 3 H, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.8 (Me), 59.6 (CH_2O), 125.4, 127.5, 129.0, 129.9, 130.2 (Ar—<u>C</u>H=CH), 130.8 (Ar—CH=<u>C</u>H), 135.5, 136.2 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3326 (s), 3096 (m), 3060 (m), 3018 (m), 2922 (m), 2863 (m), 1917 (w), 1809 (w), 1640 (w), 1601 (w), 1573 (w), 1486 (s), 1458 (s), 1308 (m), 1223 (m), 1041 (vs), 1017 (vs), 787 (s), 757 (s), 737 (s), 578 (w); HRMS (ESI) m/z calcd for $[C_{10}H_{12}NaO]^+$ 171.0780, found 171.0772.

2-(Cinnamyloxy)isoindoline-1,3-dione (2a).[41] Cinnamyl alcohol (**1a**) (2.15 g, 16.0 mmol) was allowed to react with PPh_3 (4.62 g, 17.6 mmol), *N*-hydroxyphthalimide (2.87 g, 17.6 mmol), and diethyl azodicarboxylate (40% in toluene, 8.00 mL, 17.6 mmol) according to **GP1** (2.5 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate 8:2 to 7:3) afforded **2a** as colorless solid. Yield: 4.26 g (15.2 mmol, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.82 (dd, J = 7.6, 1.0 Hz, 2 H, CH_2O), 6.42 (td, J = 15.8, 7.1 Hz, 1 H, Ph—CH=C—<u>H</u>), 6.63 (d, J = 15.8 Hz, 1 H, Ph—C<u>H</u>=C—H), 7.17–7.35 (m, 5 H, Ar–H), 7.65–7.78 (m, 4 H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 78.6, 122.0, 123.5, 126.9, 128.4, 128.6, 128.8, 134.4, 135.7, 137.4, 163.8 (NC=O) ppm.

(*Z*)-2-[(3-Phenylallyl)oxy]isoindoline-1,3-dione (2b). (*Z*)-3-Phenylprop-2-en-1-ol (**1b**)[38] (2.00 g, 14.9 mmol) was allowed to react with PPh_3 (4.30 g, 16.4 mmol), *N*-hydroxyphthalimide (2.67 g, 16.4 mmol), and diethyl azodicarboxylate (40% in toluene, 7.46 mL, 16.4 mmol) according to **GP1** (3 h reaction time). Flash column chromatography (SiO_2, dichloromethane) afforded **2b** as colorless solid. Yield: 3.71 g (13.3 mmol, 89%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.96 (dd, J = 7.0, 1.5 Hz, 2 H, CH_2O), 6.05 (dt, J = 11.7, 7.0 Hz, 1 H, Ph—CH=C<u>H</u>), 6.79 (d, J = 11.7 Hz, 1 H, PhC<u>H</u>=CH), 7.22–7.33 (m, 5 H, Ar–H), 7.70–7.80 (m, 5 H, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 74.3 (CH_2O), 123.4, 124.0 (Ph—CH=<u>C</u>H), 127.7, 128.3, 128.7, 128.8, 134.4, 135.6, 135.7 (Ph—<u>C</u>H=CH), 163.5 (NC=O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3081 (m), 3059 (m), 3027 (m), 2962 (m), 2926 (m), 2896 (m), 2252 (w), 1957 (w), 1891 (w), 1844 (w), 1789 (s), 1731 (vs), 1610 (m), 1467 (m), 1375 (s), 1186 (m), 1128 (m), 980 (m), 877 (m), 700 (m), 518 (m); HRMS (ESI) m/z calcd for $[C_{17}H_{13}NNaO_3]^+$ 302.0788, found 302.0785; mp 58 °C.

(*E*)-2-[(4-Phenylbut-3-en-2-yl)oxy]isoindoline-1,3-dione (2c).[42] (*E*)-4-Phenylbut-3-en-2-ol (**1c**)[35] (3.71 g, 25.0 mmol) was allowed to react with PPh_3 (7.21 g, 27.5 mmol), *N*-hydroxyphthalimide (4.49 g, 27.5 mmol), and diethyl azodicarboxylate (40% in toluene, 12.5 mL, 27.5 mmol) according to **GP1** (3 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate/dichloromethane 7:2:1) and crystallization from dichloromethane/*n*-pentane (−18 °C) afforded **2c** as colorless solid. Yield: 3.75 g (12.8 mmol, 51%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.58 (d, J = 6.4 Hz, 3 H, Me), 5.00 (qd, J = 8.8, 6.4 Hz, 1 H, Me<u>H</u>CO), 6.31 (dd, J = 15.9, 8.8 Hz, 1 H, Ph—CH=C—<u>H</u>), 6.51 (d, J = 15.9 Hz, 1 H, Ph—C<u>H</u>=C—H), 7.19–7.34 (m, 5 H, Ar–H), 7.69–7.78 (m, 4 H, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.3, 84.9, 123.3, 126.7, 128.0, 128.1, 128.5, 128.7, 134.2, 134.9, 135.8, 164.0 (NC=O) ppm.

Scheme 4. Intermolecular Bromination by *N*-Bromo-hydroxylamine 5



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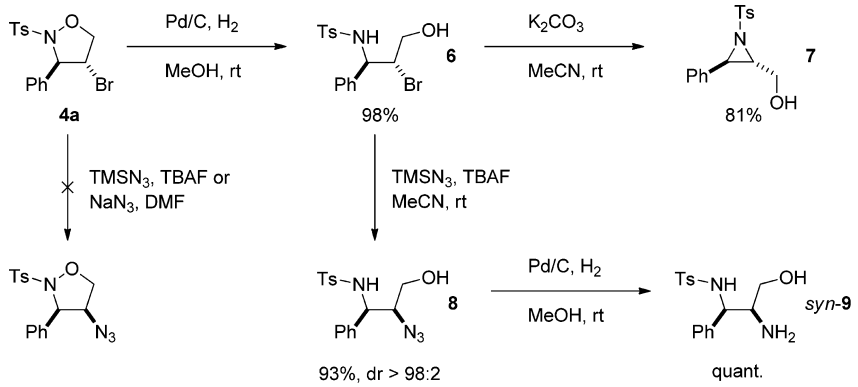
Scheme 5. Subsequent Transformations Starting from Bromo-isoxazolidine 4a



***(E)*-2-[(3-(3,4-Bis(benzyloxy)phenyl)allyl)oxy]isoindoline-1,3-dione (2d).** (*E*)-3-(3,4-Bis(benzyloxy)phenyl)prop-2-en-1-ol (**1d**)[39] (5.00 g, 14.4 mmol) was allowed to react with PPh_3 (4.16 g, 15.9 mmol), *N*-hydroxyphthalimide (2.59 g, 15.9 mmol), and diethyl azodicarboxylate (40% in toluene, 7.20 mL, 15.9 mmol) according to **GP1** (2.5 h reaction time). Flash column chromatography (SiO_2, dichloromethane/hexanes 7:3) afforded **2d** as colorless solid. Yield: 4.63 g (9.42 mmol, 65%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.83 (dd, *J* = 7.2, 0.9 Hz, 2 H, CH_2CO), 5.15 (s, 2 H, $C\underline{H}_2Ph$), 5.16 (s, 2 H, $C\underline{H}_2Ph$), 6.28 (td, *J* = 15.7, 7.2 Hz, 1 H, Ar—CH=C—H), 6.56 (d, *J* = 15.8 Hz, 1 H, Ph—CH=C—H), 7.01–7.03 (m, 1 H, Ar–H), 7.28–7.48 (m, 10 H, Ar–H), 7.69–7.74 (m, 2 H, Ar–H), 7.77–7.83 (m, 2 H, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 71.1, 71.3, 78.7, 113.1, 114.6, 120.1, 120.9, 123.4, 127.2, 127.3, 127.8, 127.8, 128.4, 128.5, 128.8, 129.5, 134.4, 137.0, 137.1, 137.2, 148.9, 149.4, 163.8 (NC=O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3063 (m), 3032 (m), 2936 (m), 2871 (m), 2251 (w), 1954 (w), 1787 (m), 1731 (s), 1511 (s), 1427 (m), 1265 (m), 970 (m), 699 (m), 619 (w); HRMS (ESI) *m*/*z* calcd for $[C_{31}H_{25}NNaO_5]^+$ 514.1625, found 514.1615; mp 118 °C.

***(E)*-2-[(3-(4-Nitrophenyl)allyl)oxy]isoindoline-1,3-dione (2e).** *p*-NO_2-Cinnamyl alcohol (**1e**) (5.0 g, 27.9 mmol) was allowed to react with PPh_3 (8.05 g, 30.7 mmol), *N*-hydroxyphthalimide (5.01 g, 30.7 mmol), and diethyl azodicarboxylate (40% in toluene, 13.9 mL, 30.7 mmol) according to **GP1** (2.5 h reaction time). The product **2e** directly precipitated from the reaction mixture. The solid was collected by filtration and washed with hexanes. Yield: 7.68 g (23.7 mmol, 85%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.90 (dd, *J* = 6.6, 1.1 Hz, 2 H, CH_2O), 6.64 (td, *J* = 16.0, 6.6 Hz, 1 H, Ph—CH=C—H), 6.76 (d, *J* = 16.0 Hz, 1 H, Ph—CH=C—H), 7.51–7.53 (m, 2 H, Ar–H), 7.73–7.75 (m, 2 H, Ar–H), 7.82–7.84 (m, 2 H, Ar–H), 8.16–8.18 (m, 2 H, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 78.0, 123.6, 124.0, 127.0, 127.4, 128.8, 134.3, 134.6, 142.1, 147.5, 163.7 (NC=O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3103 (w), 2938 (w), 1925 (w), 1847 (w), 1786 (m), 1737 (vs), 1594 (m), 1517 (s), 1340 (vs), 1182 (m), 1131 (m), 1105 (m), 1079 (m), 971 (s), 877 (m), 859 (m), 818 (m), 784 (m), 745 (m), 695 (s); HRMS (ESI) *m*/*z* calcd for $[C_{17}H_{12}N_2NaO_5]^+$ 347.0638, found 347.0640; mp 223 °C.

***(Z)*-2-[(3-(2-Tolyl)allyl)oxy]isoindoline-1,3-dione (2f).** (*Z*)-3-(2-Tolyl)prop-2-en-1-ol (**1f**)[36] (1.76 g, 11.9 mmol) was allowed to react with PPh_3 (3.43 g, 13.1 mmol), *N*-hydroxyphthalimide (2.13 g, 13.1 mmol), and diethyl azodicarboxylate (40% in toluene, 5.90 mL, 13.1 mmol) according to **GP1** (2.0 h reaction time). Flash column chromatography (SiO_2, dichloromethane) afforded **2f** as colorless solid. Yield: 2.68 g (11.2 mmol, 94%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.14 (s, 3 H, Me), 4.84 (dd, *J* = 7.1, 1.3 Hz, 2 H, CH_2O), 6.10 (td, *J* = 15.5, 7.1 Hz, 1 H, Ph—CH=C—H), 6.86 (d, *J* = 11.5 Hz, 1 H, Ph—CH=CH), 7.07–7.26 (m, 4 H, Ar–H), 7.71–7.82 (m, 4 H, Ar–H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.6, 74.2, 123.4, 124.1, 125.6, 127.9, 128.8, 129.0, 129.8, 134.4, 134.5, 135.3, 136.1, 163.5 (NC=O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3061 (m), 3027 (m), 2947 (m), 1891 (w), 1845 (w), 1788 (s), 1731 (s), 1466 (m), 1376 (m), 1186 (m), 980 (m), 701 (m), 518 (m); HRMS (ESI) *m*/*z* calcd for $[C_{18}H_{15}NNaO_3]^+$ 316.0944, found 316.0930; mp 121 °C.

2-[(3-Methylbut-2-en-1-yl)oxy]isoindoline-1,3-dione (2g).[43] 3-Methylbut-2-en-1-ol (1.38 g, 16.0 mmol) was allowed to react with PPh_3 (4.62 g, 17.6 mmol), *N*-hydroxyphthalimide (2.87 g, 17.6 mmol), and diethyl azodicarboxylate (40% in toluene, 8.00 mL, 17.6 mmol) according to **GP1** (3.0 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate 8:2) afforded **2g** as colorless solid. Yield: 3.09 g (12.6 mmol, 79%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.72 (s, 3 H, Me), 1.75 (s, 3 H, Me), 4.70 (d, *J* = 7.7 Hz, 2 H, CH_2O), 5.49–5.54 (m, 1 H, C=C—H), 7.72–7.74 (m, 2 H, Ar–H), 7.80–7.81 (m, 2 H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 18.0, 25.9, 74.0, 117.1, 123.3, 128.9, 134.3, 143.5, 163.7 (NC=O) ppm.

***(E)*-2-(Hex-2-en-1-yloxy)isoindoline-1,3-dione (2h).** (*E*)-Hex-2-en-1-ol (5.00 g, 49.9 mmol) was allowed to react with PPh_3 (14.4 g, 54.9 mmol), *N*-hydroxyphthalimide (8.96 g, 54.9 mmol), and diethyl azodicarboxylate (40% in toluene, 25.0 mL, 54.9 mmol) according to **GP1** (2.5 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1) afforded **2h** as colorless solid. Yield: 11.7 g (47.5 mmol, 95%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.75 (t, *J* = 7.4 Hz, 3 H, Me), 1.24–1.34 (m, 2 H, $CH_3C\underline{H}_2CH_2$), 1.95–1.99 (m, 2 H, $CH_3CH_2C\underline{H}_2$), 4.62 (d, *J* = 6.8 Hz, 2 H, CH_2O), 5.68–5.80 (m, 2 H, H—C=C—H), 7.70–7.73 (m, 2 H, Ar–H), 7.77–7.80 (m, 2 H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.4, 21.7, 34.1, 78.5, 122.9, 123.3, 128.8, 134.3, 140.6, 163.7 (NC=O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3030 (m), 2959 (s), 2931 (s), 2873 (m), 1789 (s), 1730 (s), 1466 (m), 1376 (m), 1186 (m), 1130 (m), 973 (s), 912 (s), 877 (s), 732 (s), 701 (s), 517 (m); HRMS (ESI) *m*/*z* calcd for $[C_{14}H_{15}NNaO_3]^+$ 268.0950, found 268.0946; mp 67 °C.

***(Z)*-2-(Hex-2-en-1-yloxy)isoindoline-1,3-dione (2i).** (*Z*)-Hex-2-en-1-ol (5.00 g, 49.9 mmol) was allowed to react with PPh_3 (14.4 g, 54.9 mmol), *N*-hydroxyphthalimide (8.96 g, 54.9 mmol), and diethyl azodicarboxylate (40% in toluene, 25.0 mL, 54.9 mmol) according to **GP1** (2.5 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1) afforded **2i** as colorless, viscous liquid. Yield: 11.1 g (45.1 mmol, 90%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.78 (t, *J* = 7.4 Hz, 3 H, Me), 1.24–1.32 (m, 2 H, $CH_3C\underline{H}_2CH_2$), 2.01–2.06 (m, 2 H, $CH_3CH_2C\underline{H}_2$), 4.76 (d, *J* = 6.6 Hz, 2 H, CH_2O), 5.68–5.78 (m, 2 H, H—C=C—H), 7.70–7.73 (m, 2 H, Ar–H), 7.78–7.82 (m, 2 H, Ar–H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.4, 22.4, 29.3, 72.8, 122.0, 123.3, 128.8, 134.3, 138.8, 163.7 (NC=O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3025 (m), 2960 (s), 2932 (s), 2872 (m), 1789 (s), 1730 (s), 1467 (m), 1375 (m), 1186 (m), 1130 (m), 975 (s), 877 (s), 702 (s), 518 (m); HRMS (ESI) *m*/*z* calcd for $[C_{14}H_{15}NNaO_3]^+$ 268.0950, found 268.0943.

2-(Cyclohex-1-en-1-ylmethoxy)isoindoline-1,3-dione (2j). Cyclohex-1-en-1-ylmethanol (**1j**)[33] (3.00 g, 26.7 mmol) was allowed to react with PPh_3 (7.72 g, 29.4 mmol), *N*-hydroxyphthalimide (4.80 g, 29.4 mmol), and diethyl azodicarboxylate (40% in toluene, 12.2 mL, 29.4 mmol) according to **GP1** (1.5 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1) afforded **2j** as

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colorless solid. Yield: 5.55 g (21.6 mmol, 81%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.51−1.55 (m, 2 H), 1.62−1.67 (m, 2 H, Cy), 1.91−1.98 (m, 2 H, Cy), 2.25−2.31 (m, 2 H, Cy), 4.49 (s, 2 H, CH_2O), 5.73−5.76 (m, 1 H, C═C—H), 7.70−7.74 (m, 2 H, Ar−H), 7.78−7.82 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.8, 22.3, 25.3, 26.2, 82.7 (CH_2O), 123.3, 128.9, 131.2, 132.5, 134.3, 163.6 (NC═O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 2997 (m), 2932 (s), 2859 (s), 2835 (s), 1845 (m), 1789 (s), 1767 (s), 1725 (s), 1466 (m), 1448 (m), 1435 (m), 1374 (s), 1186 (s), 1132 (m), 971 (s), 877 (m), 701 (s), 519 (m); HRMS (ESI) m/z calcd for $[C_{15}H_{15}NNaO_3]^+$ 280.0944, found 280.0942; mp 75 °C.

2-(Cyclopent-1-en-1-ylmethoxy)isoindoline-1,3-dione (2k). Cyclopent-1-en-1-ylmethanol (**1k**)[34] (2.80 g, 28.5 mmol) was allowed to react with PPh_3 (8.23 g, 31.4 mmol), *N*-hydroxyphthalimide (5.12 g, 31.4 mmol), and diethyl azodicarboxylate (40% in toluene, 14.3 mL, 31.4 mmol) according to **GP1** (2.5 h reaction time). Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1) afforded **2k** as colorless solid. Yield: 6.62 g (27.2 mmol, 96%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.87−1.93 (m, 2 H, Cy), 2.26−2.32 (m, 2 H, Cy), 2.51−2.57 (m, 2 H, Cy), 4.70 (s, 2 H, CH_2O), 5.75−5.78 (m, 1 H, C═C—H), 7.71−7.74 (m, 2 H, Ar−H), 7.77−7.82 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 23.5, 32.6, 32.9, 76.2 (CH_2O), 123.3, 128.9, 133.8, 134.3, 138.2, 163.5 (NC═O) ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3063 (m), 2953 (s), 2870 (s), 2849 (s), 1846 (m), 1788 (s), 1730 (s), 1611 (m), 1465 (m), 1374 (s), 1186 (s), 1132 (m), 1017 (m), 972 (s), 915 (m), 701 (s), 517 (m); HRMS (ESI) m/z calcd for $[C_{14}H_{13}NNaO_3]^+$ 266.0788, found 266.0790; mp 80 °C.

***(E)*-*N*-(Cinnamyloxy)-4-toluenesulfonamide (3a).** Phthalimide **2a** (0.905 g, 3.24 mmol) was reacted with hydrazine monohydrate (472 μL, 9.72 mmol) in dichloromethane for 1.5 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (0.701 g, 3.56 mmol) and Et_3N (541 μL, 3.89 mmol) for 15 h. Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1 to 8:2) afforded **3a** as colorless solid. Yield: 0.606 g (1.99 mmol, 62%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.40 (s, 3 H, Me), 4.58 (dd, J = 6.8, 1.1 Hz, 2 H, CH_2O), 6.20 (td, J = 15.9, 6.8 Hz, 1 H, Ph—CH═C—H), 6.60 (d, J = 15.9, 1 H, Ph—CH═C—H), 7.16 (s, 1 H, NH), 7.23−7.36 (m, 7 H, Ar−H), 7.81−7.83 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.6 (Me), 77.8 (CH_2O), 122.8, 126.6, 128.1, 128.5, 128.5, 129.7, 133.5, 135.6, 136.1, 144.8 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3222 (m), 3058 (w), 3027 (w), 2924 (w), 2874 (w), 1597 (m), 1334 (m), 1167 (vs), 1091 (m), 968 (m), 814 (m), 728 (m), 693 (m), 545 (m); HRMS (ESI) m/z calcd for $[C_{16}H_{17}NNaO_3S]^+$ 326.0821, found 326.0810; mp 103 °C.

***(Z)*-*N*-[(3-Phenylallyl)oxy]-4-toluenesulfonamide (3b).** Phthalimide **2b** (1.50 g, 5.37 mmol) was reacted with hydrazine monohydrate (782 μL, 16.1 mmol) in dichloromethane for 2 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (1.16 g, 5.91 mmol) and Et_3N (905 μL, 6.45 mmol) for 18 h. Flash column chromatography (SiO_2, dichloromethane/toluene 6:4) afforded **3b** as colorless solid. Yield: 0.733 g (2.42 mmol, 45%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.44 (s, 3 H, Me), 4.75 (dd, J = 6.7, 1.5 Hz, 2 H, CH_2O), 5.80 (dt, J = 11.8, 6.7 Hz, 1 H, Ph—CH═CH), 6.66 (d, J = 11.8 Hz, 1 H, Ph—CH═CH), 7.00 (s, 2 H, NH), 7.19−7.21 (m, 2 H, Ar−H), 7.27−7.36 (m, 5 H, Ar−H), 7.80−7.82 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.7 (Me), 73.8 (CH_2O), 125.3 (Ph—CH═CH), 127.6, 128.3, 128.6, 128.7, 129.7, 133.6 (Ph—CH═CH), 133.8, 136.0, 144.9 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3218 (m), 3057 (w), 3026 (w), 2921 (w), 2851 (w), 1737 (w), 1645 (w), 1597 (w), 1333 (m), 1167 (vs), 1092 (m), 1019 (m), 813 (m), 725 (s), 702 (s), 544 (m); HRMS (ESI) m/z calcd for $[C_{16}H_{17}NNaO_3S]^+$ 326.0821, found 326.0813; mp 77 °C.

***(E)*-*N*-[(4-Phenylbut-3-en-2-yl)oxy]-4-toluenesulfonamide (3c).** Phthalimide **2c** (2.00 g, 6.82 mmol) was reacted with hydrazine monohydrate (1.00 mL, 20.5 mmol) in dichloromethane for 2.5 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (1.48 g, 7.50 mmol) and Et_3N (1.14 mL, 8.18 mmol) for 24 h. Flash column chromatography (SiO_2, dichloromethane/toluene 7:3) afforded **3c** as colorless solid. Yield: 1.66 g (5.23 mmol, 77%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.35 (d, J = 6.5 Hz, 3 H, C═C—Me), 2.41 (s, 3 H, Ar−CH_3), 4.66−4.71 (m, 1 H, MeHCO), 6.06 (dd, J = 15.9, 7.7 Hz, 1 H, Ph—CH═C—H), 6.59 (d, J = 15.9, 1 H, Ph—CH═C—H), 7.03 (s, 1 H, NH), 7.23−7.37 (m, 7 H, Ar−H), 7.81−7.83 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.2, 21.6, 83.1, 126.6, 127.9, 128.4, 128.5, 129.6, 133.3, 133.6, 136.2, 144.6 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3380 (m), 3225 (m), 3081 (m), 3059 (m), 2981 (m), 2932 (m), 2869 (m), 1949 (w), 1918 (w), 1807 (w), 1752 (w), 1597 (m), 1337 (s), 1166 (s), 968 (m), 812 (m), 718 (m), 665 (m), 585 (m); HRMS (ESI) m/z calcd for $[C_{17}H_{19}NNaO_3S]^+$ 340.0983, found 340.0971; mp 101 °C.

***(E)*-*N*-[(3-(3,4-Bis(benzyloxy)phenyl)allyl)oxy]-4-toluenesulfonamide (3d).** Phthalimide **2d** (2.50 g, 5.09 mmol) was reacted with hydrazine monohydrate (740 μL, 15.3 mmol) in dichloromethane for 3 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (1.10 g, 5.60 mmol) and Et_3N (851 μL, 6.10 mmol) for 20 h. Flash column chromatography (SiO_2, in dichloromethane/hexanes 6:4 to *n*-pentane/diethyl ether 1:1) afforded **3d** as colorless solid. Yield: 1.11 g (2.15 mmol, 42%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.42 (s, 3 H, Me), 4.56 (d, J = 6.9 Hz, 2 H, CH_2O), 5.17 (s, 4 H, 2 × CH_2Ph), 6.04 (td, J = 15.7, 6.9 Hz, 1 H, Ph—CH═C—H), 6.51 (d, J = 15.8, 1 H, Ph—CH═C—H), 6.87−6.91 (m, 2 H, Ar−H), 6.99−7.02 (m, 1 H, Ar−H), 7.07 (s, 1 H, NH), 7.27−7.49 (m, 12 H, Ar−H), 7.81−7.83 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.6, 71.1, 71.3, 77.9, 113.0, 114.7, 120.6, 121.0, 127.2, 127.3, 127.8, 127.8, 128.4, 128.4, 128.5, 129.7, 129.8, 133.6, 135.5, 137.0, 137.1, 144.8, 148.9, 149.1 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3225 (m), 3088 (m), 3064 (m), 3032 (m), 2928 (m), 2871 (m), 1952 (w), 1917 (w), 1877 (w), 1809 (w), 1598 (m), 1512 (s), 1380 (s), 1334 (s), 1265 (s), 1018 (s), 739 (s), 698 (s), 565 (m), 544 (m); HRMS (ESI) m/z calcd for $[C_{30}H_{29}NNaO_5S]^+$ 538.1664, found 538.1660; mp 106 °C.

***(E)*-*N*-[(3-(4-Nitrophenyl)allyl)oxy]-4-toluenesulfonamide (3e).** Phthalimide **2e** (2.55 g, 7.86 mmol) was reacted with hydrazine monohydrate (1.14 mL, 23.6 mmol) in dichloromethane for 24 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (1.70 g, 8.65 mmol) and Et_3N (1.32 mL, 9.44 mmol) for 24 h. Flash column chromatography (SiO_2, toluene/diethyl ether 98:2) afforded **3e** as yellow solid. Yield: 0.845 g (2.43 mmol, 31%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.43 (s, 3 H, Me), 4.65 (dd, J = 6.4, 1.0 Hz, 2 H, CH_2O), 6.41 (td, J = 16.0, 6.4 Hz, 1 H, Ph—CH═C—H), 6.66 (d, J = 16.0 Hz, 1 H, Ph—CH═C—H), 7.33−7.35 (m, 2 H, Ar−H), 7.47−7.50 (m, 2 H, Ar−H), 7.81−7.83 (m, 2 H, Ar−H), 8.15−8.17 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.6, 77.1, 123.9, 127.2, 128.1, 128.5, 129.8, 132.6, 133.4, 142.6, 145.1, 147.2 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3221 (m), 3107 (w), 3076 (w), 2926 (w), 2868 (w), 1923 (w), 1787 (w), 1729 (m), 1596 (m), 1515 (s), 1344 (vs), 1166 (s), 1108 (m), 1091 (m), 971 (m), 911 (m), 862 (m), 813 (m), 730 (s), 647 (w), 558 (m), 553 (m); HRMS (ESI) m/z calcd for $[C_{16}H_{16}N_2NaO_5S]^+$ 371.0672, found 371.0660; mp 116 °C.

***(Z)*-*N*-[(3-(2-Tolyl)allyl)oxy]-4-toluenesulfonamide (3f).** Phthalimide **2f** (2.00 g, 6.82 mmol) was reacted with hydrazine monohydrate (1.22 mL, 25.1 mmol) in dichloromethane for 1.5 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (1.81 g, 9.19 mmol) and Et_3N (1.40 mL, 10.0 mmol) for 20 h. Flash column chromatography (SiO_2, dichloromethane/toluene 6:4) afforded **3f** as colorless solid. Yield: 1.15 g (3.63 mmol, 53%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.26 (s, 3 H, Me), 2.44 (s, 3 H, Me), 4.59 (dd, J = 6.8, 1.4 Hz, 2 H, CH_2O), 5.86 (td, J = 11.6, 6.8 Hz, 1 H, Ph—CH═C—H), 6.72 (d, J = 11.6, 1 H, Ph—CH═C—H), 7.05−7.07 (m, 1 H), 7.15−7.22 (m, 4 H), 7.30−7.32 (m, 2 H, Ar−H), 7.79−7.81 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.7, 21.6, 73.6, 125.3, 125.5, 127.7, 128.5, 128.9, 129.6, 129.8, 133.1, 133.5, 135.0, 136.1, 144.8 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3220 (m), 3065 (w), 3023 (w), 2921 (w), 1920 (w), 1486 (w), 1456 (w), 1380 (w), 1333 (m), 1166 (s), 1019 (m), 945 (w), 899 (w), 747 (m), 543 (m); HRMS (ESI) m/z calcd for $[C_{17}H_{19}NNaO_3S]^+$ 340.0978, found 340.0972; mp 94 °C.

***N*-[(3-Methylbut-2-en-1-yl)oxy]-4-toluenesulfonamide (3g).** Phthalimide **2g** (2.45 g, 10.0 mmol) was reacted with hydrazine monohydrate (551 μL, 11.0 mmol) in tetrahydrofuran for 6 h according to **GP2**. After workup the crude material was stirred with *p*-

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TsCl (2.16 g, 11.0 mmol) and Et_3N (1.67 mL, 12.0 mmol) for 22 h. Flash column chromatography (SiO_2, hexanes/ethyl acetate 8:2) and subsequent crystallization from toluene (−18 °C) afforded **3g** as colorless solid. Yield: 0.731 g (2.86 mmol, 29%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.70 (s, 3 H, C═C—Me), 1.73 (s, 3 H, C═C—Me), 2.43 (s, 3 H, Ar−C$\underline{H}_3$), 4.45 (d, J = 7.5, 2 H, CH_2O), 5.24−7.31 (m, 1 H, C═C—H), 7.31−7.34 (m, 2 H, Ar−H), 7.78−7.81 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 18.1, 21.6, 25.8, 73.4, 117.9, 128.5, 129.6, 133.7, 141.2, 144.7 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3223 (m), 3067 (w), 2976 (m), 2933 (m), 1921 (w), 1787 (w), 1729 (m), 1671 (m), 1597 (w), 1449 (w), 1400 (m), 1379 (m), 1335 (s), 1166 (vs), 1091 (m), 942 (m), 814 (m), 726 (m), 544 (m); HRMS (ESI) m/z calcd for $[C_{12}H_{17}NNaO_3S]^+$ 278.0821, found 278.0805; mp 61 °C.

(*E*)-*N*-(Hex-2-en-1-yloxy)-4-toluenesulfonamide (3h). Phthalimide **2h** (3.68 g, 15.0 mmol) was reacted with hydrazine monohydrate (2.18 mL, 45.0 mmol) in dichloromethane for 2.5 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (3.25 g, 16.5 mmol) and Et_3N (2.51 mL, 18.0 mmol) for 14 h. Flash column chromatography (SiO_2, dichloromethane/hexanes 8:2 to pure dichloromethane) afforded **3h** as colorless solid. Yield: 1.54 g (5.70 mmol, 38%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.88 (t, J = 7.4 Hz, 3 H, C$\underline{H}_3$CH$_2$CH$_2$), 1.34−1.42 (m, 2 H, CH$_3$C$\underline{H}_2$CH$_2$), 1.97−2.02 (m, 2 H, CH$_3$CH$_2$C$\underline{H}_2$), 2.43 (s, 3 H, Ar−C$\underline{H}_3$), 4.38 (d, J = 6.8 Hz, 2 H, CH_2O), 5.49 (ttd, J = 15.1, 6.8, 1.4 Hz, 1 H, $\underline{H}$C═CHCH$_2$O), 5.70−5.77 (m, 1 H, HC═C$\underline{H}$CH$_2$O), 7.08 (s, 1 H, NH), 7.31−7.33 (m, 2 H, Ar−H), 7.79−7.81 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.6, 21.6, 21.9, 34.3, 77.9, 123.6, 128.5, 129.6, 133.6, 138.1, 144.7 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3222 (m), 2958 (m), 2929 (m), 2872 (m), 1597 (w), 1459 (w), 1397 (w), 1377 (w), 1335 (m), 1166 (vs), 1091 (m), 1019 (m), 971 (m), 898 (w), 812 (m), 724 (m), 545 (w); HRMS (ESI) m/z calcd for $[C_{13}H_{19}NKO_3S]^+$ 308.0717, found 308.0704; mp 58 °C.

(*Z*)-*N*-(Hex-2-en-1-yloxy)-4-toluenesulfonamide (3i). Phthalimide **2i** (3.68 g, 15.0 mmol) was reacted with hydrazine monohydrate (2.18 mL, 45.0 mmol) in dichloromethane for 3 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (3.25 g, 16.5 mmol) and Et_3N (2.51 mL, 18.0 mmol) for 18 h. Flash column chromatography (SiO_2, dichloromethane/*n*-pentane 8:2) afforded **3i** as colorless solid. Yield: 2.16 g (8.02 mmol, 54%); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.90 (t, J = 7.4 Hz, 3 H, C$\underline{H}_3$CH$_2$CH$_2$), 1.34−1.42 (m, 2 H, CH$_3$C$\underline{H}_2$CH$_2$), 2.03−2.08 (m, 2 H, CH$_3$CH$_2$C$\underline{H}_2$), 2.43 (s, 3 H, Ar−C$\underline{H}_3$), 4.51 (d, J = 7.1 Hz, 2 H, CH_2O), 5.45−5.52 (m, 1 H, $\underline{H}$C═CHCH$_2$O), 5.63−5.69 (m, 1 H, HC═C$\underline{H}$CH$_2$O), 7.04 (s_{br}, 1 H, NH), 7.32−7.33 (m, 2 H, Ar−H), 7.79−7.81 (m, 2 H, Ar−H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.7, 21.7, 22.7, 29.6, 72.6, 122.9, 128.6, 129.8, 133.8, 136.9, 144.9 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3222 (m), 3023 (w), 2959 (m), 2930 (m), 2871 (m), 1597 (w), 1457 (w), 1400 (m), 1380 (w), 1333 (m), 1166 (s), 1091 (m), 1019 (m), 944 (m), 892 (w), 813 (m), 720 (m), 545 (w); HRMS (ESI) m/z calcd for $[C_{13}H_{19}NNaO_3S]^+$ 292.0978, found 292.0951; mp 55 °C.

***N*-(Cyclohex-1-en-1-ylmethoxy)-4-toluenesulfonamide (3j).** Phthalimide **2j** (3.00 g, 11.7 mmol) was reacted with hydrazine monohydrate (1.70 mL, 35.0 mmol) in dichloromethane for 4 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (2.52 g, 12.8 mmol) and Et_3N (1.95 mL, 14.0 mmol) for 20 h. Flash column chromatography (SiO_2, *n*-pentane/diethyl ether 8:2) afforded **3j** as colorless solid. Yield: 2.05 g (7.29 mmol, 62%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.50−1.61 (m, 4 H, Cy), 1.92−2.03 (m, 4 H, Cy), 2.42 (s, 3 H, Ar−C$\underline{H}_3$), 4.23 (s, 2 H, CH_2O), 5.70 (m_c, 1 H, C═CH), 7.18 (s, 1 H, NH), 7.30−7.32 (m, 2 H, Ar−H), 7.79−7.81 (m, 2 H, Ar−H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.5, 21.9, 22.3, 25.0, 26.1, 82.0, 128.4, 128.4, 129.5, 132.7, 133.8, 144.6 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3223 (s), 2950 (w), 2999 (m), 2927 (s), 2858 (s), 2837 (s), 2736 (w), 2676 (w), 2588 (w), 2515 (w), 1917 (w), 1804 (w), 1725 (w), 1670 (w), 1597 (m), 1334 (s), 1166 (s), 1092 (m), 1019 (m), 950 (w), 735 (s), 544 (m); HRMS (ESI) m/z calcd for $[C_{14}H_{19}NNaO_3S]^+$ 304.0983, found 304.0985; mp 53 °C.

***N*-(Cyclopent-1-en-1-ylmethoxy)-4-toluenesulfonamide (3k).** Phthalimide **2k** (3.00 g, 12.3 mmol) was reacted with hydrazine monohydrate (658 μL, 13.6 mmol) in tetrahydrofuran for 3.0 h according to **GP2**. After workup the crude material was stirred with *p*-TsCl (2.67 g, 13.6 mmol) and Et_3N (2.06 mL, 14.8 mmol) for 18 h. Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1) and subsequent crystallization from toluene (−18 °C) afforded **3k** as colorless solid. Yield: 1.75 g (6.54 mmol, 53%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.82−1.92 (m, 2 H, Cy), 2.25−2.36 (m, 4 H, Cy), 2.44 (s, 3 H, Ar−C$\underline{H}_3$), 4.51 (s, 2 H, CH_2O), 5.66 (m_c, 1 H, C═CH), 7.07 (s, 1 H, NH), 7.32−7.34 (m, 2 H, Ar−H), 7.80−7.82 (m, 2 H, Ar−H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.6, 23.2, 32.4, 33.0, 75.9, 128.5, 128.6, 130.5, 133.7, 138.8, 144.7 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3223 (s), 3046 (w), 2950 (m), 2927 (m), 2848 (m), 1918 (w), 1727 (w), 1597 (m), 1401 (m), 1334 (s), 1167 (vs), 1092 (m), 1030 (m), 740 (s), 544 (m); HRMS (ESI) m/z calcd for $[C_{13}H_{17}NKO_3S]^+$ 306.0561, found 306.0561; mp 73 °C.

***trans*-4-Bromo-3-phenyl-2-(4-toluenesulfonyl)isoxazolidine (4a).** *O*-Allyl-*N*-tosyl-hydroxylamine **3a** (1.00 g, 3.30 mmol) was allowed to react with *N*-bromoacetamide (0.500 g, 3.63 mmol) for 1 h according to **GP3**. Flash column chromatography (SiO_2, dichloromethane) afforded **4a** as colorless solid. Yield: 1.18 g (3.09 mmol, 94%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.47 (s, 3 H, Me), 4.16 (dd, J = 9.6, 8.4 Hz, 1 H, C$\underline{H}$HO), 4.23−4.28 (m, 1 H, C$\underline{H}$Br), 4.36 (dd, J = 8.3, 6.4 Hz, 1 H, CH$\underline{H}$O), 5.17 (d, J = 7.0 Hz, 1 H, NCH), 7.33−7.42 (m, 5 H, Ar−H), 7.48−7.52 (m, 2 H, Ar−H), 7.87−7.89 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.7 (Me), 49.4 (C$\underline{H}$Br), 70.1 (NC), 75.9 (OCH_2), 126.7, 128.6, 128.9, 129.4, 129.8, 132.2, 137.2, 145.5 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3064 (w), 3032 (w), 2951 (w), 2924 (w), 2884 (w), 1921 (w), 1810 (m), 1597 (m), 1494 (m), 1455 (m), 1364 (m), 1337 (m), 1166 (s), 1089 (m), 986 (m), 910 (w), 815 (w), 670 (s), 572 (s), 549 (w); HRMS (ESI) m/z calcd for $[C_{16}H_{16}BrNNaO_3S]^+$ 405.9906, found 405.9910; mp 98 °C.

***cis*-4-Bromo-3-phenyl-2-(4-toluenesulfonyl)isoxazolidine (4b).** *O*-Allyl-*N*-tosyl-hydroxylamine **3b** (0.152 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 19 h according to **GP3**. Flash column chromatography (SiO_2, dichloromethane/toluene 1:1) afforded **4b** as colorless solid. Yield: 0.126 g (0.417 mmol, 83%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.47 (s, 3 H, Me), 4.25 (dd, J = 9.4, 3.1 Hz, 1 H, C$\underline{H}$HO), 4.68 (dd, J = 9.4, 4.9 Hz, 1H, CH$\underline{H}$O), 4.91 (ddd, J = 6.3, 4.9, 3.1 Hz, 1H, C$\underline{H}$Br), 5.51 (d, J = 6.3 Hz, 1 H, NCH), 7.33−7.41 (m, 7 H, Ar−H), 7.89−7.91 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.7 (Me), 52.3 (C$\underline{H}$Br), 65.6 (NC), 77.1 (OCH_2), 127.6, 128.2, 128.3, 129.3, 129.8, 132.3, 136.6, 145.5 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3090 (w), 3063 (w), 3033 (w), 2922 (w), 2871 (w), 1595 (m), 1495 (w), 1360 (s), 1329 (w), 1161 (s), 1088 (m), 1007 (m), 907 (w), 813 (w), 671 (s), 546 (m); HRMS (ESI) m/z calcd for $[C_{16}H_{16}BrNKO_3S]^+$ 421.9645, found 421.9620; mp 142 °C.

4-Bromo-5-methyl-3-phenyl-2-(4-toluenesulfonyl)-isoxazolidine (4c). *O*-Allyl-*N*-tosyl-hydroxylamine **3c** (0.159 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 3 h according to **GP3**. Flash column chromatography (SiO_2, dichloromethane) afforded **4c** as colorless solid. Yield: 0.170 g (0.428 mmol, 86%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.33 (d, J = 6.0 Hz, 3 H, OCH$\underline{Me}$), 2.46 (s, 3 H, Ar−Me), 3.74 (dd, J = 9.7, 8.1 Hz, 1 H, C$\underline{H}$Br), 4.32 (qd, J = 9.8, 6.0 Hz, 1 H, OC$\underline{H}$Me), 5.20 (d, J = 8.07 Hz, 1 H, NCH), 7.34−7.42 (m, 5 H, Ar−H), 7.51−7.52 (m, 2 H, Ar−H), 7.86−7.88 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 14.4 (OCH$\underline{Me}$), 21.7 (Ar−Me), 56.2 (CHBr), 70.5 (NC), 83.2 (OCH_2), 126.7, 128.6, 128.9, 129.4, 129.8, 132.2, 137.2, 145.5 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3089 (m), 3065 (m), 3034 (m), 2981 (m), 2933 (m), 2871 (w), 1953 (w), 1920 (w), 1807 (w), 1759 (w), 1597 (m), 1494 (m), 1455 (m), 1364 (s), 1337 (s), 1167 (s), 1092 (m), 1001 (m), 912 (w), 814 (w), 670 (s), 579 (s), 535 (w); HRMS (ESI) m/z calcd for $[C_{17}H_{18}BrNNaO_3S]^+$ 420.0063, found 420.0053; mp 140 °C.

***trans*-3-(3,4-Bis(benzyloxy)phenyl)-4-bromo-2-(4-toluenesulfonyl)isoxazolidine (4d).** *O*-Allyl-*N*-tosyl-hydroxylamine **3d** (0.258 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 3 h according to **GP3**.

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Flash column chromatography (SiO_2, hexanes/ethyl acetate, 9:1 to 8:2) afforded **4d** as light yellow solid. Yield: 0.246 g (0.413 mmol, 83%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.47 (s, 3 H, Me), 4.13 (dd, J = 9.6, 8.1 Hz, 1 H, CHHO), 4.16−4.21 (m, 1 H, CHBr), 4.32 (dd, J = 8.0, 6.2 Hz, 1 H, CHHO), 5.11 (d, J = 6.8 Hz, 1 H, NCH), 5.18 (s, 2 H, CH_2Ph), 5.19 (s, 2 H, CH_2Ph), 6.97 (d, J = 8.3 Hz, 1 H), 7.05 (dd, J = 8.3, 2.0 Hz, 1 H), 7.13 (d, J = 2.0 Hz, 1 H), 7.31−7.51 (m, 12 H, Ar−H), 7.28−7.31 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.6 (Me), 49.4 (CHBr), 69.8 (NC), 71.1 (CH_2Ph), 71.3 (CH_2Ph), 75.7 (OCH_2), 113.4, 114.8, 119.9, 127.1, 127.4, 127.7, 127.7, 128.3, 128.4, 129.3, 129.7, 130.1, 132.1, 136.9, 137.1, 145.4, 149.1, 149.3 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3088 (m), 3065 (m), 3032 (m), 1953 (w), 1921 (w), 1876 (w), 1810 (w), 1732 (w), 1596 (s), 1514 (s), 1455 (m), 1413 (m), 1365 (m), 1335 (m), 1264 (m), 1166 (m), 1018 (m), 911 (m), 741 (m), 668 (s), 592 (s), 547 (w); HRMS (ESI) m/z calcd for $[C_{30}H_{28}BrNNaO_5S]^+$ 618.0744, found 618.0763; mp 108 °C.

***cis*-4-Bromo-3-(2-tolyl)-2-(4-toluenesulfonyl)isoxazolidine (4f).** *O*-Allyl-*N*-tosyl-hydroxylamine **3f** (0.159 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 49 h according to **GP3**. Flash column chromatography (SiO_2, toluene/dichloromethane 6:4) afforded **4f** as colorless solid. Yield: 0.129 g (0.325 mmol, 65%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.39 (s, 3 H, Me), 2.46 (s, 3 H, Me), 4.30 (dd, J = 9.6, 2.5 Hz, 1 H, CHHO), 4.77 (dd, J = 9.6, 4.8 Hz, 1H, CHHO), 5.04 (ddd, J = 6.4, 4.8, 2.5 Hz, 1H, CHBr), 5.70 (d, J = 6.5 Hz, 1 H, NCH), 7.17−7.19 (m, 3 H, Ar−H), 7.37−7.39 (m, 2 H, Ar−H), 7.58−7.60 (m, 1 H, Ar−H), 7.88−7.90 (m, 2 H, Ar−H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.8 (Me), 21.7 (Me), 51.3 (CHBr), 62.5 (NC), 77.8 (OCH_2), 125.9, 127.3, 128.2, 129.3, 129.8, 130.1, 132.5, 124.8, 135.5, 145.5 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3099 (m), 3061 (m), 3033 (w), 2925 (m), 2882 (w), 1918 (w), 1810 (w), 1735 (w), 1653 (w), 1596 (m), 1491 (m), 1469 (m), 1342 (s), 1165 (vs), 1089 (m), 1006 (m), 976 (w), 907 (w), 815 (w), 750 (m), 675 (s), 554 (m); HRMS (ESI) m/z calcd for $[C_{17}H_{18}BrNNaO_3S]^+$ 418.0083, found 418.0080; mp 194 °C.

4-Bromo-3,3-dimethyl-2-(4-toluenesulfonyl)isoxazolidine (4g). *O*-Allyl-*N*-tosyl-hydroxylamine **3g** (0.128 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 2 h according to **GP3**. Flash column chromatography (SiO_2, hexanes/ethyl acetate 9:1) afforded **4g** as colorless solid. Yield: 0.140 g (0.418 mmol, 84%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.49 (s, 3 H, Me), 1.79 (s, 3 H, Me), 2.44 (s, 3 H, Ar−Me), 4.01 (t, J = 7.9 Hz, 1 H, CHBr), 4.59 (t, J = 8.3 Hz, 1 H, CHHO), 4.70 (t, J = 8.2 Hz, 1 H, CHHO), 7.32−7.34 (m, 2 H, Ar−H), 7.82−7.84 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.7 (Me), 22.3 (Me), 25.3 (Me), 51.3 (CHBr), 69.6 (NC), 75.2 (OCH_2), 129.0, 129.5, 134.7, 144.9 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3066 (m), 2988 (m), 2942 (m), 2895 (m), 1919 (w), 1807 (w), 1733 (w), 1646 (w), 1597 (m), 1493 (m), 1464 (m), 1332 (s), 1166 (vs), 1157 (vs), 1089 (m), 925 (w), 839 (w), 813 (w), 672 (s), 567 (m), 548 (w); HRMS (ESI) m/z calcd for $[C_{12}H_{16}BrNNaO_3S]^+$ 355.9929, found 355.9937; mp 59 °C.

***trans*-4-Bromo-3-propyl-2-(4-toluenesulfonyl)isoxazolidine (4h).** *O*-Allyl-*N*-tosyl-hydroxylamine **3h** (0.135 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 20 h according to **GP3**. Flash column chromatography (SiO_2, toluene/dichloromethane 1:1) afforded **4h** as colorless solid. Yield: 0.121 g (0.348 mmol, 70%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.99 (t, J = 7.3 Hz, 3 H, $CH_3CH_2CH_2$), 1.52−1.60 (m, 2 H, $CH_3CH_2CH_2$), 1.75−1.80 (m, 2 H, $CH_3CH_2CH_2$), 2.45 (s, 3 H, Ar−Me), 4.03−4.08 (m, 2 H, CHBr and CHHO), 4.18−4.25 (m, 2 H, NCH and CHHO), 7.34−7.37 (m, 2 H, Ar−H), 7.85−7.87 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.8 ($CH_3CH_2CH_2$), 19.3 ($CH_3CH_2CH_2$), 21.7 (Ar−Me), 36.5 ($CH_3CH_2CH_2$), 46.1 (CHBr), 67.4 (NC), 75.8 (OCH_2), 129.2, 129.7, 132.6, 145.2 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3066 (m), 3032 (m), 2960 (s), 2933 (s), 2873 (s), 2736 (w), 2587 (w), 1921 (w), 1806 (w), 1732 (w), 1652 (w), 1597 (s), 1493 (m), 1458 (m), 1362 (s), 1335 (s), 1166 (vs), 1088 (m), 975 (m), 906 (m), 815 (m), 670 (s), 576 (m), 539 (w); HRMS (ESI) m/z calcd for $[C_{13}H_{18}BrNNaO_3S]^+$ 372.0063, found 372.0064; mp 53 °C.

***cis*-3a-Bromo-1-(4-toluenesulfonyl)octahydrobenzo[*c*]-isoxazole (4j).** *O*-Allyl-*N*-tosyl-hydroxylamine **3j** (0.141 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 5 h according to **GP3**. Flash column chromatography (SiO_2, dichloromethane/toluene 1:1) afforded **4j** as colorless solid. Yield: 0.163 g (0.454 mmol, 91%, dr >98:2); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.50−1.69 (m, 4 H, Cy), 1.95−2.09 (m, 3 H, Cy), 2.23−2.31 (m, 1 H, Cy), 2.46 (s, 3 H, Me), 3.52 (d, J = 7.9 Hz, 1 H, CHHO), 3.77 (d, J = 7.9 Hz, 1 H, CHHO), 3.73−3.76 (m, 1 H, NCH), 7.36−7.38 (m, 2 H, Ar−H), 7.83−7.85 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 19.0, 21.1, 21.7, 24.4, 35.3, 59.8, 64.6, 78.8, 129.6, 129.8, 130.8, 145.4 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3066 (w), 2940 (s), 2882 (s), 2863 (m), 1923 (w), 1809 (w), 1727 (w), 1597 (m), 1492 (w), 1447 (m), 1361 (s), 1334 (s), 1169 (vs), 1089 (m), 976 (m), 921 (m), 814 (m), 727 (m), 668 (m), 613 (m), 537 (w); HRMS (ESI) m/z calcd for $[C_{14}H_{18}BrNNaO_3S]^+$ 384.0063, found 384.0063. mp 103 °C.

***cis*-3a-Bromo-1-(4-toluenesulfonyl)hexahydro-1*H*-cyclopenta[*c*]isoxazole (4k).** *O*-Allyl-*N*-tosyl-hydroxylamine **3k** (0.134 g, 0.500 mmol) was allowed to react with *N*-bromoacetamide (75.9 mg, 0.550 mmol) for 32 h according to **GP3**. Flash column chromatography (SiO_2, toluene/dichloromethane 6:4) afforded **4k** as colorless oil. Yield: 0.046 g (0.131 mmol, 26%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.85−1.98 (m, 3 H, Cy), 2.15−2.21 (m, 1 H, Cy), 2.21−2.36 (m, 2 H, Cy), 2.45 (s, 3 H, Me), 4.02 (d, J = 9.0 Hz, 1 H, CHHO), 4.27 (d, J = 9.0 Hz, 1 H, CHHO), 4.68 (dd, J = 7.2, 3.5 Hz, 1 H, NCH), 7.35−7.37 (m, 2 H, Ar−H), 7.86−7.87 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.7, 26.0, 33.8, 43.9, 67.7, 73.9, 81.1, 129.3, 129.8, 132.3, 145.3 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3066 (w), 3031 (w), 2963 (s), 2926 (m), 2874 (m), 1726 (w), 1597 (m), 1493 (w), 1448 (m), 1362 (s), 1338 (s), 1165 (vs), 1091 (m), 922 (m), 815 (m), 739 (m), 717 (m), 672 (m), 552 (m), 534 (m); HRMS (ESI) m/z calcd for $[C_{13}H_{16}BrNNaO_3S]^+$ 369.9906, found 369.9907.

(*E*)-*N*-Bromo-*N*-[(3-(4-nitrophenyl)allyl)oxy]-4-toluenesulfonamide (5). To a solution of *O*-allyl-*N*-tosyl-hydroxylamine **3e** (50.0 mg, 0.144 mmol) in $CDCl_3$ (1.0 mL) protected from light *N*-bromoacetamide (19.8 mg, 0.144 mmol) was added in one portion. The solution was stirred at rt for 10 min and then rapidly (contact time <1 min) filtered over a small plug (SiO_2, $CDCl_3$) to afford unstable (decomposition upon light exposure and evaporation of the solvent observed) **5** as light yellow solution in $CDCl_3$: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.45 (s, 3 H, Me), 4.52 (dd, J = 6.7, 1.1 Hz, 2 H, CH_2O), 6.25 (td, J = 15.9, 6.7 Hz, 1 H, Ph—CH=C—H), 6.66 (d, J = 16.0 Hz, 1 H, Ph—CH=C—H), 7.37−7.39 (m, 2 H, Ar−H), 7.46−7.48 (m, 2 H, Ar−H), 7.91−7.93 (m, 2 H, Ar−H), 8.18−8.20 (m, 2 H, Ar−H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.8, 75.8, 124.0, 125.9, 127.3, 127.9, 129.7, 131.1, 133.9, 142.1, 146.6, 147.4 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3106 (w), 3076 (w), 2927 (w), 2856 (w), 2449 (w), 2257 (w), 1922 (w), 1792 (w), 1732 (w), 1596 (m), 1517 (s), 1363 (s), 1344 (s), 1171 (vs), 1188 (m) 1110 (m), 1087 (m), 957 (m), 861 (m), 815 (m), 743 (m), 661 (w), 567 (m).

***N*-(*trans*-2-Bromo-3-hydroxy-1-phenylpropyl)-4-toluenesulfonamide (6).** A suspension of isoxazolidine **4a** (0.375 g, 0.980 mmol) and palladium on charcoal (10% Pd, 0.104 g, 977 μmol) in methanol (9.8 mL) was stirred at rt in an atmosphere of hydrogen (1 atm) for 2 d. After reaction completion, as indicated by TLC analysis, the reaction mixture was filtered over Celite, and the resulting solution was concentrated to dryness. Flash column chromatography of the crude product (SiO_2, dichloromethane/ethyl acetate 9:1) afforded **6** as colorless solid. Yield: 0.368 g (0.958 mmol, 98%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.35 (s, 3 H, Me), 2.60 (t, J = 6.7 Hz, 1 H, OH), 3.71−3.77 (m, 1 H, CHHO), 4.01 (ddd, J = 12.6, 5.7, 4.2 Hz, 1 H, CHHO), 4.29 (td, J = 6.5, 4.4 Hz, 1 H, CHBr), 4.74 (dd, J = 8.6, 6.6 Hz, 1 H, NCH), 5.78 (d, J = 8.7 Hz, 1 H, NH), 7.02−7.22 (m, 7 H, Ar−H), 7.53−7.55 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.5 (Me), 57.8 (CHBr), 59.8 (NCH), 63.6 (CH_2O), 127.1, 128.2, 128.4, 129.4, 137.0, 143.5 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3503 (m), 3275 (m), 3063 (w), 3033 (w), 2925 (w), 2880 (w), 1597 (m), 1495 (w), 1455 (m), 1426 (m), 1323 (s), 1158 (vs), 1092 (m), 1057 (m), 1020 (m), 912 (m), 812 (m), 701 (m), 680 (m), 570 (m), 543 (w); HRMS

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(ESI) m/z calcd for $[C_{16}H_{18}BrNNaO_3S]^+$ 408.0062, found 408.0080; mp 119 °C.

***trans*-1-(4-Toluenesulfonyl)-3-phenyl-2-aziridinemethanol (7).**[28] To a stirred solution of bromo-aminoalcohol **6** (0.100 g, 0.260 mmol) in acetonitrile (7.8 mL) was added potassium carbonate (39.5 mg, 0.286 mmol) in one portion. The resulting suspension was stirred at rt for 19 h. Then the reaction mixture was suction filtered, and the filter cake was rinsed once with acetonitrile (15 mL). After evaporation of the solvent, the crude product was purified by flash column chromatography (SiO_2, dichloromethane/ethyl acetate 9:1) to obtain **7** as colorless solid. Yield: 64.3 mg (0.212 mmol, 81%); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 2.40 (s, 3 H, Me), 3.11−3.23 (m, 2 H), 4.02 (d, J = 4.3 Hz, 1 H), 4.18 (ddd, J = 13.3, 8.5, 4.7 Hz, 1 H), 4.31 (ddd, J = 13.1, 9.7, 3.1 Hz, 1 H), 7.11−7.19 (m, 2 H, Ar−H), 7.23−7.31 (m, 5 H, Ar−H), 7.79−7.85 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 21.5 (Me), 46.3, 54.6, 60.6, 126.4, 127.1, 128.3, 128.6, 129.6, 134.5, 137.0, 144.3 ppm.

***N*-(*cis*-2-Azido-3-hydroxy-1-phenylpropyl)-4-toluenesulfonamide (8).** To a stirred solution of bromoaminoalcohol **6** (0.192 g, 0.500 mmol) in acetonitrile (3.5 mL) $TMSN_3$ (99.0 μL, 0.750 mmol) and TBAF (1 M in tetrahydrofuran, 700 μL, 0.700 mmol) were added. The resulting solution was stirred at rt for 1 h, and then water (20 mL) and ethyl acetate (20 mL) were added. The aqueous phase was extracted with ethyl acetate (3 × 10 mL), and the combined organic phases washed with brine (30 mL) and dried over sodium sulfate. After filtration and evaporation of the solvent, the crude product was purified by flash column chromatography (SiO_2, hexanes/ethyl acetate 6:4) to furnish **8** as colorless solid. Yield: 0.161 g (0.465 mmol, 93%, dr >98:2); ^{1}H NMR (500 MHz, CD_3OD) δ = 2.39 (s, 3 H, Me), 3.44 (dd, J = 11.2, 4.2 Hz, 1 H, CHHO), 3.52 (td, J = 7.0, 4.4 Hz, 1 H, CHN_3), 3.62 (dd, J = 11.2, 4.7 Hz, 1 H, CHHO), 4.72 (d, J = 7.1 Hz, 1 H, PhCHN), 7.19−7.27 (m, 7 H, Ar−H), 7.53−7.55 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, CD_3OD) δ = 21.5 (Me), 60.4 (CHN_3), 61.6 (CH_2O), 67.0 (PhCHN), 127.9, 128.8, 129.4, 129.6, 130.6, 137.7, 139.8, 144.3 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3462 (m), 3279 (m), 3064 (w), 3032 (w), 2924 (w), 2889 (w), 2106 (vs), 1917 (w), 1804 (w), 1599 (m), 1495 (w), 1454 (m), 1326 (m), 1157 (s), 1092 (m), 1050 (w), 1020 (w), 910 (m), 814 (m), 702 (m), 551 (w); HRMS (ESI) m/z calcd for $[C_{16}H_{18}N_4KO_3S]^+$ 385.0731, found 385.0738; mp 122 °C.

***N*-(*cis*-2-Amino-3-hydroxy-1-phenylpropyl)-4-toluenesulfonamide (*syn*-9).** A suspension of azidoaminoalcohol **8** (0.100 g, 0.289 mmol) and palladium on charcoal (10% Pd, 30.7 mg, 28.9 μmol) in methanol (2.9 mL) was stirred at rt under an atmosphere of hydrogen (1 atm) for 40 min. Filtration over Celite and evaporation of the solvent afforded *syn*-**9** as colorless oil. Yield: 92.5 mg (0.289 mmol, quant); ^{1}H NMR (500 MHz, CD_3OD) δ = 2.37 (s, 3 H, Me), 3.24 (dd, J = 11.2, 6.6 Hz, 1 H, CHHO), 3.30 (dd, J = 11.3, 4.7 Hz, 1 H, CHHO), 3.39 (td, J = 6.4, 5.0 Hz, 1 H, CHN_3), 4.01 (d, J = 5.3 Hz, 1 H, PhCHN), 7.15−7.25 (m, 7 H, Ar−H), 7.57−7.59 (m, 2 H, Ar−H); ^{13}C NMR (125 MHz, CD_3OD) δ = 21.4 (Me), 57.1 (PhCHN), 61.1 ($CHNH_2$), 62.4 (CH_2O), 128.1, 128.3, 128.5, 129.3, 130.6, 139.5, 142.5, 144.5 ppm; IR (Film, cm^{-1}) $\tilde{\nu}$ = 3247 (m), 3055 (m), 3041 (m), 2938 (m), 2871 (m), 1597 (m), 1494 (m), 1455 (m), 1393 (m), 1154 (vs), 1089 (m), 1059 (w), 985 (w), 848 (m), 703 (m); HRMS (ESI) m/z calcd for $[C_{16}H_{21}N_2O_3S]^+$ 321.1267, found 321.1286. mp 198 °C (decomp).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds, and crystallographic information files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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†Responsible for X-ray analysis.

Notes

The authors declare no competing financial interest.

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