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Access to Optically Active 3-Aminopiperidines by Ring Expansion of Prolinols: Thermodynamic versus Kinetic Control

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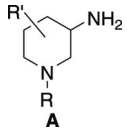
Keywords: Amines / Ring expansion / Nitrogen heterocycles / Diastereoselectivity

3-Aminopiperidines are of great interest because they can possess a wide range of biological activity depending on the nitrogen substituents. Different approaches their synthesis are presented and the most efficient is a ring expansion of prolinols induced by XtalFluor-E (diethylaminodifluorosulfinium tetrafluoroborate) in the presence of tetrabutylammonium azide, via an aziridinium intermediate, followed by the reduction of the corresponding azide. Under kinetic conditions, a 2-(azidomethyl)pyrrolidine/3-azidopiperidine ratio of 0:100 can be attained depending on the substituents present on the prolinol.

Introduction

3-Aminopiperidines of type **A** are present in a great number of natural and/or biologically active compounds (Figure 1). Because these compounds exhibit a wide range of biological activity,[1] the development of regio- and stereoselective methods to access optically active 3-aminopiperidines **A** are of great interest.



A

Figure 1. 3-Aminopiperidines **A**.

To obtain 3-aminopiperidines **A**, a range of synthetic methods have been employed such as Curtius,[2] Hofmann,[3] Neber,[4] and [3,3]-σ Overman rearrangements,[5] cyclization of methyl 4-nitrobutanoate,[6] reduction of 3-aminopyridines,[7] and reductive amination of piperidin-3-ones (Scheme 1).[8] However, syntheses of 3-aminopiperidines using these methods are either lengthy or not stereoselective. Ring enlargement of prolinols via an aziridinium intermediate was achieved in the presence of an azide, but this approach led to a mixture of five- and six-membered rings in a ratio 40:60.[9] When the reaction was performed in the presence of an amine, ring enlargement was not observed and only the five-membered ring was obtained.[10] Unsaturated 3-aminopiperidines were formed by ring expansion of unsaturated prolinols by opening of an aziridinium intermediate by either an azide or by amines, and amides.[11] However, to access piperidines **A**, a reduction step is necessary.

Here, we would like to report our studies on direct access to 3-aminopiperidines **A** by ring expansion of prolinols **B** under kinetic and thermodynamic conditions (Scheme 2).

Results and Discussion

To synthesize optically active 3-aminopiperidines using the ring enlargement of prolinols, two strategies were implemented (Scheme 3). In the first strategy, the amino group was present on the prolinol prior to ring expansion and the C–Nu bond of the piperidine **D**, formed during the ring expansion, was cleaved (Strategy 1). In the second strategy, the amino group was introduced during the ring expansion of the prolinol by attack of external amino derivatives (Strategy 2).

Strategy 1

The synthesis of 3-aminopiperidines would incorporate the dehalogenation of 3-amino-5-chloropiperidines **II** (Scheme 4). The latter could be synthesized by ring expansion of 4-aminoprolinol **III**, derived from the commercially available 4-*trans*-hydroxy-L-proline (**1**).

Prolinols **III** (Compounds **5**–**7**), the precursors of 3-amino-5-chloropiperidines **II**, were synthesized in six steps (Scheme 5). Esterification of 4-*trans*-hydroxy-L-proline (**1**) ($SOCl_2$, MeOH, room temp., 24 h; quant.) followed by *N*-benzylation (BnBr, Et_3N, CH_2Cl_2, reflux, 6 h) produced methyl ester **2** in 89% yield. Introduction of the amino group at C4 was accomplished in three steps. Mesylation of the hydroxyl group (MsCl, Et_3N, CH_2Cl_2, 0 °C to room

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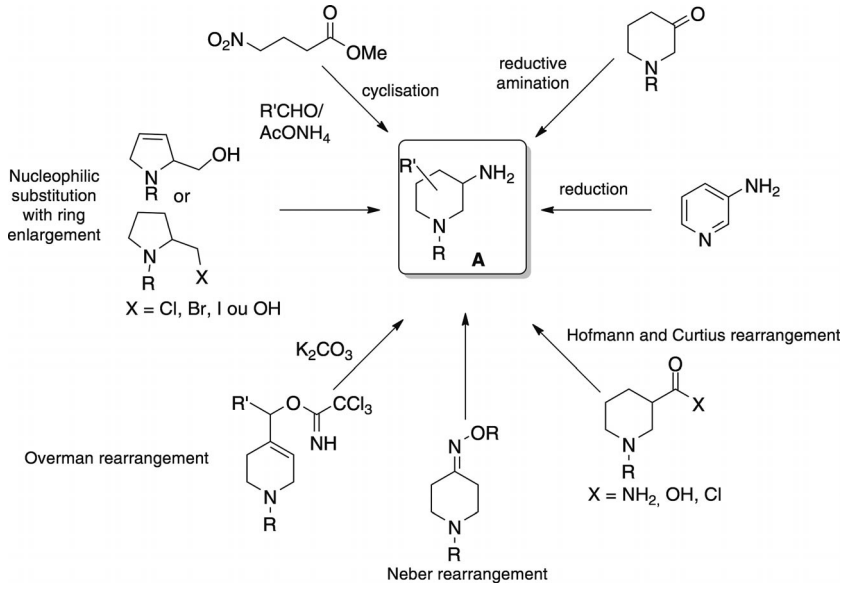
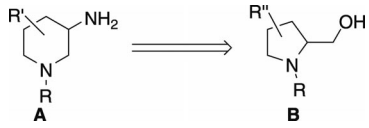
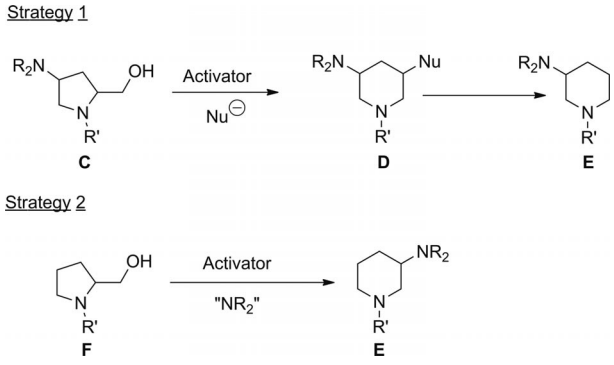


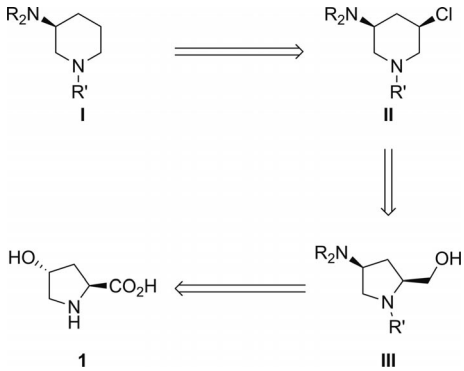
Scheme 1. Previous syntheses of 3-aminopiperidines.



Scheme 2. Retrosynthetic analysis to access **A** from prolinols **B**.



Scheme 3. Strategies for the preparation of 3-aminopiperidines.

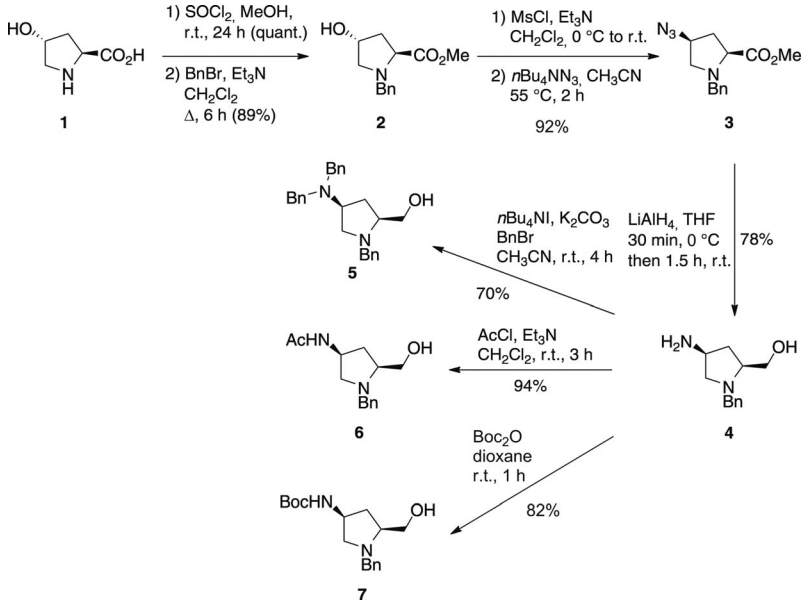


Scheme 4. Retrosynthetic analysis.

temp., 1.5 h; quant.) and nucleophilic displacement of the resulting mesylate by an azide was achieved to provide azido derivative **3** (nBu_4NN_3, CH_3CN, 55 °C, 2 h; 92%) with inversion of configuration.[12] Azido derivative **3** was then reduced to the desired 4-aminoprolinol **4** ($LiAlH_4$, THF) in 78% yield. Compound **4** was transformed into 4-(dibenzylamino)prolinol **5** (BnBr, nBu_4NI, K_2CO_3, CH_3CN, room temp., 4 h; 70%), 4-(acetamido)prolinol **6** (AcCl, Et_3N, CH_2Cl_2; 94%),[12] and the 4-(*N*-*tert*-butylcarbamate)-substituted prolinol **7** (Boc_2O, dioxane, room temp.; 82%) in good yields and with excellent diastereoselectivities (>99%).

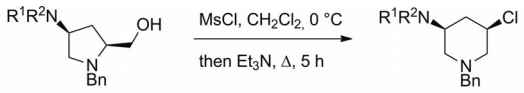
To access 3-aminopiperidines, ring expansion of prolinols using MsCl and Et_3N[13] followed by cleavage of the C–Cl bond was envisaged. Thus, prolinols **5**–**7** were treated with mesyl chloride (Et_3N, CH_2Cl_2) for 5 h in CH_2Cl_2 at reflux, to isolate 3-amino-5-chloropiperidines **8**–**10** in good yields and good diastereoselectivities (>99%).[13] The results are reported in Table 1.

To obtain the target 3-aminopiperidines **A**, cleavage of the C–Cl bond under a range of conditions was examined (Scheme 6). When piperidine **9** was treated with Pd/C or $Pd(OH)_2$ under 1 atm or 20 bars of H_2 (H-cube), at room temp. or at 40 °C, starting material was recovered. When a halogen–metal exchange using *t*BuLi (3 equiv.) (THF, –78 °C, 45 min) or Zn (NH_4Cl, MeOH, room temp., 20 h) was attempted, starting material was also recovered. Under radical conditions (Bu_3SnH, AIBN, toluene, reflux),[14] degradation of 3-amino-5-chloropiperidines **9** and **10** was observed [Scheme 6, Equations (1) and (2)]. The use of $LiAlH_4$ (2 equiv.)[15] led to ring opening of piperidine **9** to produce allylic amine **13** in 51% yield. The formation of this product can be explained by the basic conditions used to produce amide **9′**; fragmentation provided unsaturated enamide **9′′**, which was then reduced by $LiAlH_4$ [Scheme 6, Equation (3)].



Scheme 5. Preparation of prolinols **5**–**7**.

Table 1. Preparation of 3-amino-5-chloropiperidines.



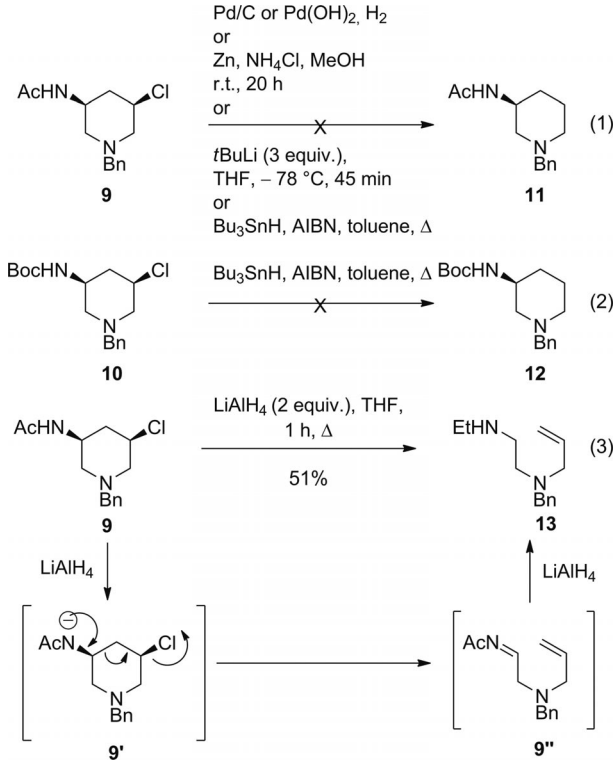
Entry	Substrate	R^1	R^2	**8**–**10** (yield)
1	**5**	Bn	Bn	**8** (63%)
2	**6**	Ac	H	**9** (70%)
2	**7**	Boc	H	**10** (90%)

When 3-chloro-5-(dibenzylamino)piperidine **8** was treated with $LiAlH_4$ (2 or 4 equiv.), the conversion of starting material **8** was incomplete (50–87%) and the expected 3-aminopiperidine **14** was isolated in low yields (21–24%; Table 2, entries 1–2). When 10 equiv. of $LiAlH_4$ were used, the conversion of starting material **8** was complete, and aminopiperidine **14** as well as pyrrolidine **15** were formed in 63 and 16% yields, respectively (ratio **14**/**15** = 80:20; Table 2, entry 3). Under these conditions, two processes can compete: one is the direct reduction of the chloride, and the second is the formation of aziridinium intermediate **16**, which can be attacked by a hydride at either the C2 or C2′ position.

Although this first strategy allows access to 3-aminopiperidines by reduction of 3-(dialkylamino)-5-chloropiperidine with $LiAlH_4$, a mixture of five- and six-membered rings was obtained.

Strategy 2

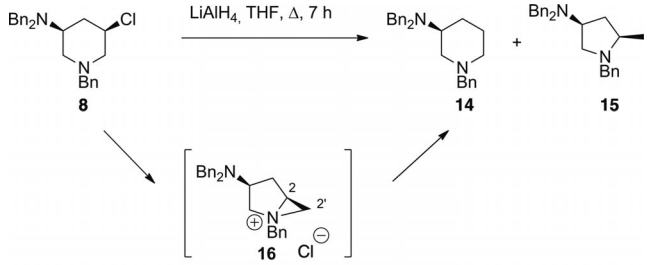
A second strategy for obtaining 3-aminopiperidines from prolinols was then examined. Two sets of conditions were tested for the ring expansion: thermodynamic and kinetic conditions.



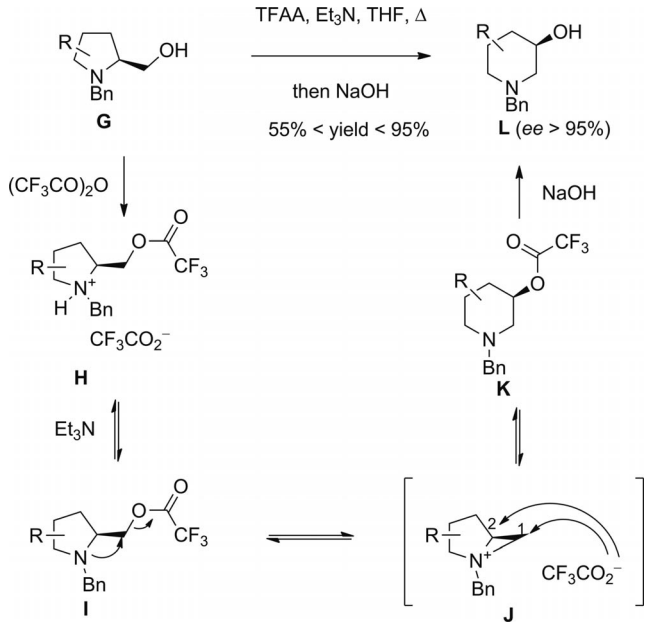
Scheme 6. Attempts to cleave the C–Cl bond.

Previously, we have shown that under thermodynamic conditions, prolinols **G** were transformed into 3-hydroxypiperidines **L** in good yields and excellent enantiomeric excess when treated with trifluoroacetic anhydride (TFAA), Et_3N and NaOH.[16] This ring enlargement took place via an aziridinium intermediate **J** (Scheme 7).[17]

Table 2. Reduction of piperidine **8**.



entry	$LiAlH_4$ (equiv)	τ_c in **8**	**14**	**15**
1	2	87%	21%	-
2	4	50%	24%	-
3	10	100%	67%	16%

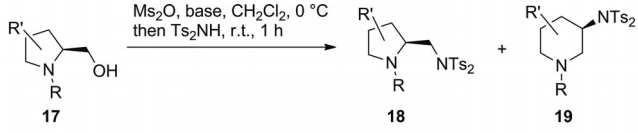


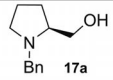
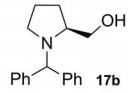
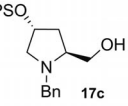
Scheme 7. Ring expansion of prolinols **G** to 3-hydroxypiperidines **L**.

The ring expansion of optically active prolinols to 3-hydroxypiperidines under thermodynamic conditions implies that the leaving group ($^-OCOCF_3$) in proline ester **I** has to be nucleophilic. Thus, ditosylamide (Ts_2N^-) was considered as a leaving group as well as a nucleophile for the rearrangement of prolinols to 3-aminopiperidines.[18]

When prolinol **17a** was treated sequentially with Ms_2O at 0 °C and Ts_2NH, after 1 h at room temp., 2-[(ditosylamino)methyl]pyrrolidine (**18a**) was the only observed product (50%) (Table 3, entry 1). As the ring expansion of *N*-alkylprolinols to *N*-alkyl-3-hydroxypiperidines was favored by increasing the steric hindrance at N1 and/or C4, prolinols **17b** and **17c** were prepared and treated with Ms_2O and then with Ts_2NH in THF at room temp. After treatment of prolinol **17b** with Ms_2O in the presence of *N*,*N*-diisopropylethylamine (DIPEA) at 0 °C, and addition of Ts_2NH, pyrrolidine **18b** and piperidine **19b** were obtained in 83% yield in a ratio of 80:20 (Table 3, entry 2). When a sterically hindered group was present at C4, as in prolinol **17c**, pyrrolidine **18c** and piperidine **19c** were isolated in 54% yield in a 60:40 ratio (Table 3, entry 3).

Table 3. Kinetic control.



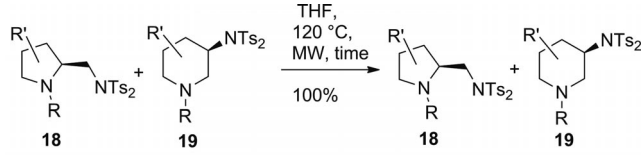
Entry	Substrate	Base	Yield	Ratio **18**/**19**
1	 **17a**	Et_3N	50%	100/0
2	 **17b**	DIPEA	83%	80/20
3	 **17c**	DIPEA	54%	60/40

To determine the thermodynamic ratios of pyrrolidines **18** and piperidines **19**, the obtained mixtures of five- and six-membered rings were heated at 120 °C under microwave irradiation. The results are reported in Table 4. When pyrrolidine **18a** was heated at 120 °C in THF under microwave irradiation for 8 h, a 1:1 ratio of pyrrolidine **18a** and piperidine **19a** was observed (Table 4, entry 1). A further increase in temperature induced decomposition of the products. When the mixture of pyrrolidine **18b** and piperidine **19b** (**18b**/**19b** = 80:20) was heated at 120 °C under microwave irradiation, a ratio of 40:60 for **18b**/**19b** was observed in favor of 3-(ditosylamino)piperidine **19b** (Table 4, entry 2). The ratio of pyrrolidine **18c** and piperidine **19c** obtained during the ring expansion of prolinol **17c** at room temp. corresponds to the thermodynamic ratio, as this ratio was 70:30 when the mixture of **18c** and **19c** (**18c**/**19c** = 60:40) was heated at 120 °C (Table 4, entry 3).

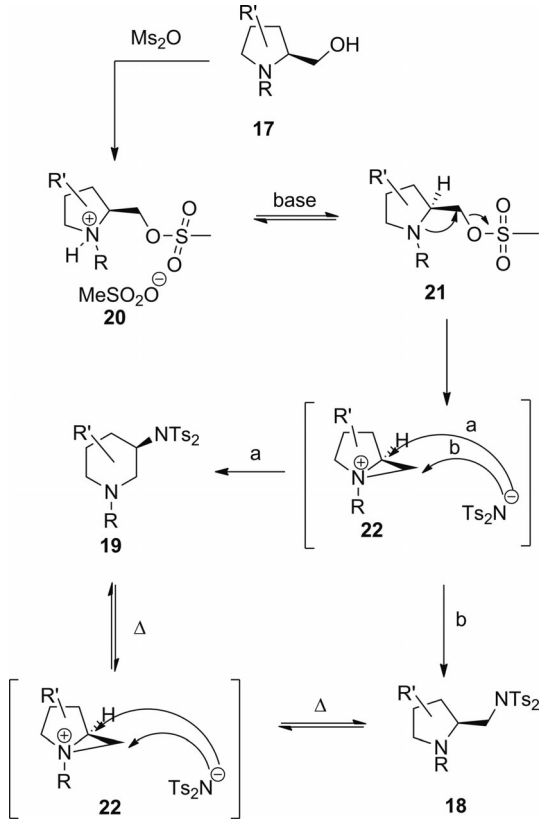
The best yields of 3-aminopiperidines **19** were obtained from prolinols **17b** substituted at N1 by a sterically hindered group. When treated with Ms_2O in the presence of a base followed by the addition of Ts_2NH and then heating of the crude mixture at 120 °C under microwave irradiation for 4–8 h, a mixture of pyrrolidines **18** and piperidines **19** was obtained. It is worth noting that **18** and **19** are issued from an aziridinium intermediate **22**, which can be attacked by Ts_2N^- (Scheme 8).

Because *N*-alkylprolinols were transformed into a mixture of 2-[(ditosylamino)methyl]pyrrolidines and 3-(ditosylamino)piperidines under thermodynamic conditions, kinetic conditions were examined in an attempt to decrease the ratio of five- to six-membered rings. Kinetic conditions should produce a six-membered ring if the aziridinium salt intermediate could be irreversibly formed and not be attacked by the leaving group ^-OLG liberated in the reaction media (Scheme 7). In addition, the use of substituents favoring nucleophilic attack at the more hindered electro-

Table 4. Thermodynamic control.

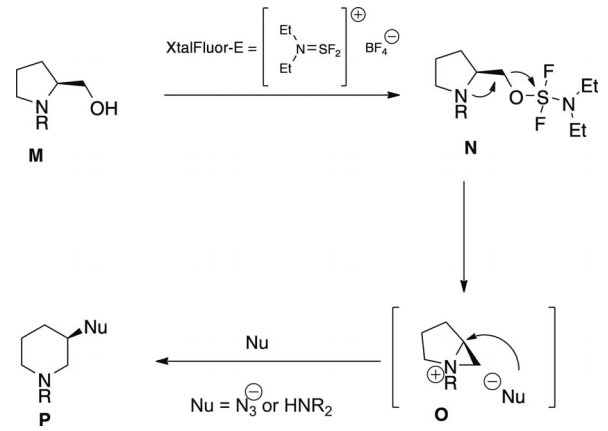


Entry	18/19	Time	Ratio 18/19
1	**18a** (100:0) **19a**	8 h	50/50
2	**18b** (80:20) **19b**	8 h	40/60
3	**18c** (60:40) **19c**	4 h	70/30



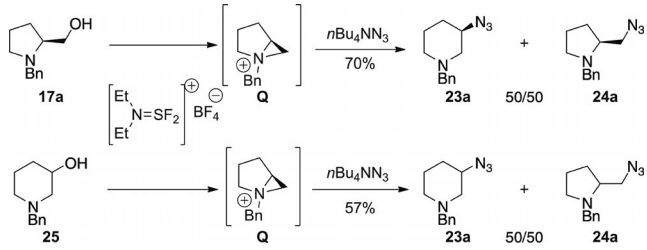
Scheme 8. Mechanism for the formation of **18** and **19** from **17**.

philic center of the aziridinium intermediate was required. XtalFluor-E (diethylaminodifluorosulfinium tetrafluoroborate), which is a good activator of hydroxyl groups and a poor nucleophile, was considered to be an appropriate reagent with which to irreversibly provide the desired aziridinium, which could then be attacked by an external nitrogen reagent such as an azide or amine (Scheme 9).[19]



Scheme 9.

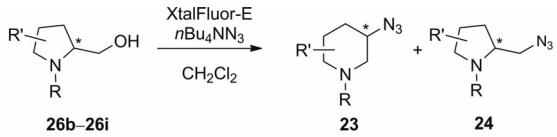
Thus, prolinol **17a** was treated with nBu$_4$NN$_3$ (1.1 equiv.) at 0 °C in CH_2Cl_2, followed by XtalFluor-E (1.1 equiv.) (Scheme 10). After 10 min, 3-azidopiperidine **23a** and 2-(azidomethyl)pyrrolidine **24a** were formed in 70% yield and a 1:1 ratio. The same ratio **23a**/**24a** was produced when 3-hydroxypiperidine **25** was treated with XtalFluor-E and nBu$_4$NN$_3$. Because the same ratio of **23a**/**24a** was obtained from prolinol **17a** and 3-hydroxypiperidine **25**, we can assume that aziridinium **Q** was completely formed and then attacked by the azide (Scheme 10).[20]



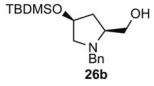
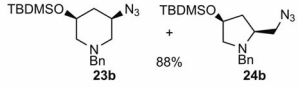
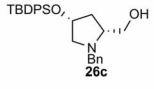
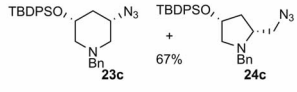
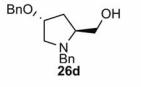
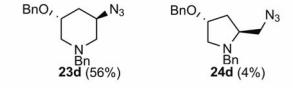
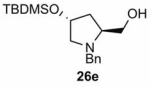
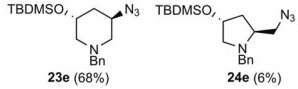
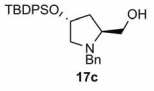
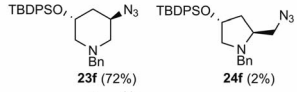
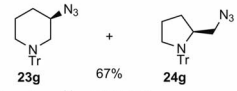
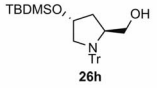
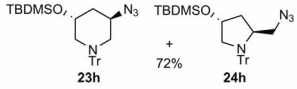
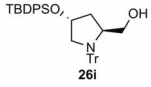
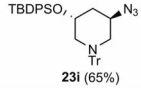
Scheme 10.

Because of above result, as previously reported,[20] prolinols with sterically hindered groups at C4 and at N1 were examined with the aim of increasing the piperidine/pyrrolidine ratio.[21] The results are reported in Table 5. *N*-Alkylprolinols substituted at C4 by a protected hydroxyl group were examined. When *cis*-prolinols **26b** and **26c** were treated with nBu$_4$NN$_3$, followed by the addition of XtalFluor-E, the piperidine/pyrrolidine (**23**/**24**) ratio was 60:40 irrespective of the size of the silyl protecting group (TBDMS or TBDPS; Table 5, entries 1 and 2). The piperidine/pyrrolidine ratio was increased in the case of *trans*-prolinols **26d**–**i**; a ratio of 85:15 to 97:3 in **23**/**24** was obtained when the protecting group of the hydroxyl at C4 was varied (Bn, TBDMS, or TBDPS; Table 5, entries 3–8). The combination of steric hindrance at C4 and at N1 in prolinols such as in **26i** led to the formation of only piperidine **23i** in 65% yield (Table 5, entry 8).

Table 5. Ring expansion of 4-hydroxyprolinol derivatives.



26b–26i 23 24

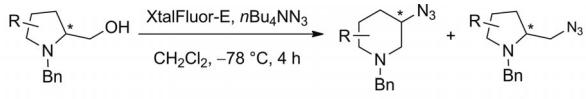
Entry	Substrate	Conditions	Products **23**, **24** (yield)	Ratio
1	 **26b**	2.5 h 0 °C	 **23b** + 88% **24b**	60/40
2	 **26c**	4.5 h –78 °C	 **23c** + 67% **24c**	60/40
3	 **26d**	4.5 h –78 °C	 **23d** (56%) **24d** (4%)	94/6
4	 **26e**	4.5 h –78 °C	 **23e** (68%) **24e** (6%)	92/8
5	 **17c**	4.5 h –78 °C	 **23f** (72%) **24f** (2%)	97/3
6	 **26g**	4.5 h –78 °C	 **23g** + 67% **24g**	85/15
7	 **26h**	30 min –78 °C	 **23h** + 72% **24h**	86/14
8	 **26i**	30 min 0 °C	 **23i** (65%)	100/0

A difference in reactivity was also observed for *cis*- and *trans*-prolinols **27** when a fluorine atom was present at C4 (Table 6). Thus, the use of prolinol **27a** led to the formation of a mixture of piperidine **28a** and pyrrolidine **29a** in a 1:1 ratio (Table 6, entry 1). In contrast, a very good piperidine/pyrrolidine **28b**/**29b** ratio of 93:7 was obtained from *trans*-prolinol **27b** (Table 6, entry 2). In addition, when the 4,4′-difluoroprolinol **27c** was examined, a piperidine/pyrrolidine **28c**/**29c** ratio of 91:9 was observed and the products were isolated in 66% yield (Table 6, entry 3).

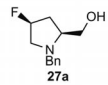
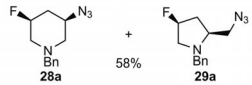
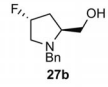
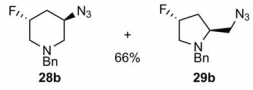
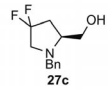
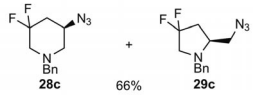
Surprisingly, and contrary to prolinols substituted at C4 by a protected hydroxyl group or a fluorine atom, the ring opening of aziridinium intermediates produced from *cis*-prolinols was more regioselective than those produced from *trans*-prolinols when the latter were substituted at C4 by an amino group. The results are reported in Table 7.

When *N*-benzyl groups were present at N1 and the protecting groups on the nitrogen at C4 were varied (*N*,*N*-dibenzyl, *N*-*tert*-butylcarbamate), *trans*-4-protected aminoprolinols **30a** and **30b** were transformed into the corresponding 3-azidopiperidine **31** and 2-(azidomethyl)pyrrolidine **32** in a 50:50 to 57:43 ratio (Table 7, entries 1 and 2). By increasing the steric hindrance at N1, such as for prolinol **30c**, the ratio of piperidine **31c**/pyrrolidine **32c** was increased to 80:20. The best piperidine/pyrrolidine ratio was

Table 6. Ring expansion of 4-fluoroprolinol derivatives.

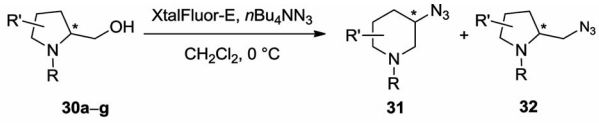


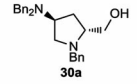
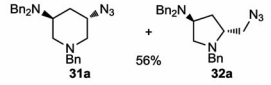
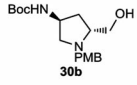
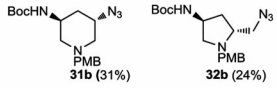
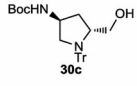
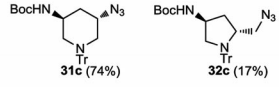
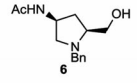
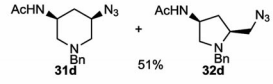
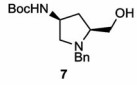
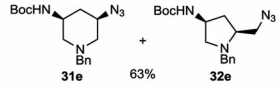
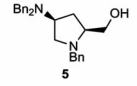
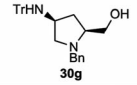
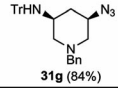
27a–c 28 29

Entry	Substrate	Products **28**, **29** (yield)	Ratio
1	 **27a**	 **28a** + 58% **29a**	50/50
2	 **27b**	 **28b** + 66% **29b**	93/7
3	 **27c**	 **28c** + 66% **29c**	91/9

obtained from *cis*-4-protected aminoprolinols **5**–**7**, and **30g** (Table 7, entries 4–7). The result for prolinol **6** was similar to the result obtained for prolinol **30c**. In the case of the 4-(*N*-*tert*-butylcarbamate)-substituted prolinol **7**, the ratio of **31e**/**32e** was 90:10. For *N*,*N*-dibenzyl derivative **5**, as well as for *N*-trityl derivative **30g**, the corresponding 3-azidopiperidines were the only product formed, and were isolated in 51–84% yields (Table 7, entries 4–7).

Table 7. Ring expansion of 4-aminoprolinol derivatives.

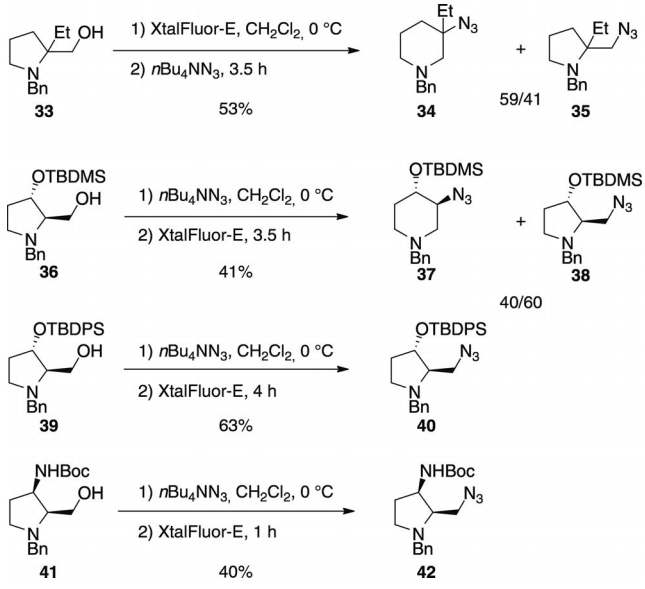


Entry	Substrate	Conditions	Products **31**, **32** (yield)	Ratio
1	 **30a**	4.5 h	 **31a** + 56% **32a**	50/50
2	 **30b**	4.5 h	 **31b** (31%) **32b** (24%)	57/43
3	 **30c**	2.5 h	 **31c** (74%) **32c** (17%)	80/20
4	 **6**	4 h	 **31d** + 51% **32d**	82/18
5	 **7**	15 min	 **31e** + 63% **32e**	90/10
6	 **5**	4.5 h	 **31f** (57%)	100/0
7	 **30g**	4.5 h	 **31g** (84%)	100/0

The difference in reactivity between the *cis*- and *trans*-prolinols substituted at C4 might be due to steric hindrance as well as to electronic effects, which could influence the strength of the C–N bonds of the formed aziridiniums (Figure 2).

Figure 2. Regioselectivity of the ring opening of the aziridinium intermediate.

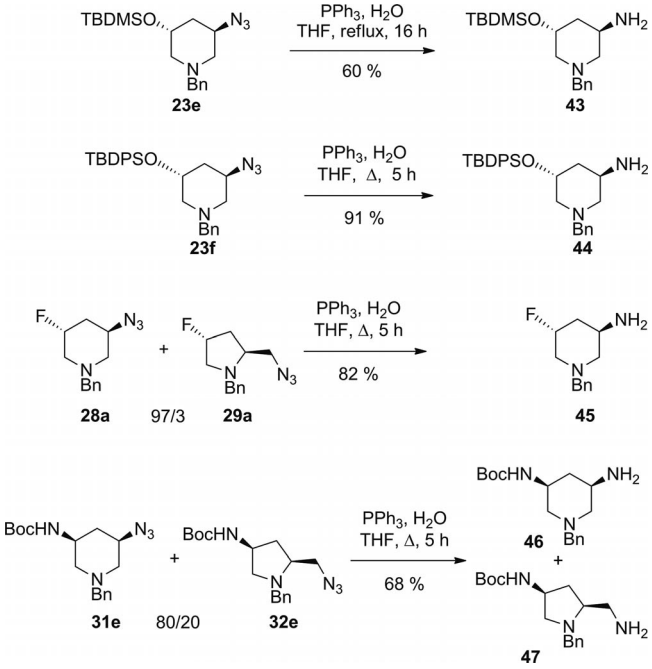
Prolinols with a quaternary center at C2 or substituted at C3 were also examined (Scheme 11). When prolinol **33** was treated with XtalFluor-E and nBu$_4$NN$_3$, a mixture of piperidine **34** and pyrrolidine **35** (separable by flash chromatography) was obtained in a 59:41 ratio favoring the former. When C3-substituted prolinols **36**, **39**, and **41** were treated with nBu$_4$NN$_3$ and XtalFluor-E, the major, or only products isolated were the corresponding pyrrolidines **38**, **40**, and **42**.



Scheme 11.

It should be noted that substituted 3-aminopiperidines **A** can be easily obtained from 3-azidopiperidines by using the chemoselective Staudinger reaction (PPh_3, H_2O, THF) to reduce the azido group.[22] Some examples are shown in Scheme 12. By using the ring expansion of prolinols associ-

ated with a Staudinger reduction, orthogonally protected 3-aminopiperidines can be obtained.



Scheme 12. Staudinger reduction.

Conclusions

We have shown that *N*-alkylprolinols can be transformed into aziridinium intermediates under thermodynamic (MsCl, Et_3N, Δ or Ms_2O, Ts_2NH, Δ) and kinetic conditions (XtalFluor-E, nBu_4NN_3, 0 °C or –78 °C). We have also shown that kinetic conditions led to a better piperidine/pyrrolidine ratio. The best ratio was obtained when a sterically hindered group was present at C4 and/or N1, and was dependent on the nature of the substituent at C4. Theoretical calculations are in progress to understand these phenomena and will be reported in due course.

Experimental Section

General Experimental Methods: Solvents were distilled. Anhydrous THF was obtained by distillation from sodium and benzophenone; CH_2Cl_2 was dried by distillation from CaH_2. Prolinols **17a**,[24] **17b**,[21b] **17c**,[16g] **26**,[20] **27**,[20] **30**,[20] and **36**[24] were obtained by using existing procedures. Other reagents were obtained from commercial suppliers and used as received. Petroleum ether (PE) had a boiling range 40–60 °C. All reactions were conducted under argon. TLC was performed on Merck 60F254 silica gel plates and visualized either with a UV lamp (254 nm) or by using a solution of $KMnO_4/K_2CO_3$/NaOH in water followed by heating. Flash chromatography was performed on silica gel (230–400 mesh). Infrared (IR) spectra were recorded with a Bruker TENSOR 27 (FTIR). ^1H NMR spectra at 400 MHz and ^{13}C NMR at 100 MHz were recorded with a Bruker AVANCE 400. ^1H NMR spectroscopic data are reported as follows: chemical shift (ppm) from $SiMe_4$ as an internal standard, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of nonequivalent resonances) and integration. ^{13}C NMR spectroscopic data are reported as follows: chemical shift (ppm) from $SiMe_4$ with the solvent as an internal indicator ($CDCl_3$: δ = 77.0 ppm; [D_6]DMSO: δ = 39.5 ppm), multiplicity with respect to proton (deduced from DEPT experiments, s = quaternary C, d = CH, t = CH_2, q = CH_3). High resolution mass spectra (HRMS) were performed by the Groupe de Spectrométrie de Masse de l'Université Pierre et Marie Curie (Paris, France). Optical rotations were measured with a Perkin–Elmer 343 polarimeter in a 10-cm cell.

Methyl (2*S*,4*R*)-1-Benzyl-4-hydroxypyrrolidine-2-carboxylate (2):[12] To a suspension of *trans*-4-hydroxy-L-proline (1.60 g, 12.2 mmol, 1.0 equiv.) in MeOH (30 mL) was added $SOCl_2$ (1.1 mL, 14.6 mmol, 1.2 equiv.) at 0 °C. After 18 h at room temp., the mixture was concentrated under reduced pressure. To a solution of the residue in CH_2Cl_2 (15 mL) were added Et_3N (6.82 mL, 48.6 mmol, 4.0 equiv.) and benzyl bromide (1.72 mL, 14.6 mmol, 1.2 equiv.). After 6 h at reflux temperature, the reaction mixture was hydrolyzed with a saturated aqueous solution of Na_2CO_3 (20 mL). The aqueous layer was extracted with CH_2Cl_2 and the combined organic phases were dried with $MgSO_4$ and filtered. The solvent was removed in vacuo to afford an oil, which was purified by flash column chromatography on silica gel (EtOAc) to give **2** (2.53 g, 10.8 mmol, 89%) as a colorless oil. $[\alpha]_D^{20}$ = –66.0 (*c* = 0.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3401, 2949, 2805, 1731, 1436, 1199, 1173, 1084, 1028 cm^{-1}. ^1H NMR: δ = 7.32–7.21 (m, 5 H), 4.43 (dddd, *J* = 7.0, 7.0, 3.6, 3.6 Hz, 1 H), 3.88 (d, *J* = 12.8 Hz, 1 H), 3.65 (d, *J* = 12.9 Hz, 1 H), 3.64 (s, 3 H), 3.59 (dd, *J* = 7.8, 7.8 Hz, 1 H), 3.31 (dd, *J* = 10.2, 5.7 Hz, 1 H), 2.45 (dd, *J* = 10.2, 4.0 Hz, 1 H), 2.30 (br. s, 1 H), 2.23 (m, 1 H), 2.06 (ddd, *J* = 13.4, 8.0, 3.2 Hz, 1 H) ppm. ^{13}C NMR: δ = 174.1 (s), 138.0 (s), 129.1 (d, 2 C), 128.3 (d, 2 C), 127.3 (d), 70.1 (d), 63.7 (d), 61.1 (t), 58.2 (t), 51.8 (q), 40.0 (t) ppm. MS: *m*/*z* (%) = 235 (0.5) [$M^{+\cdot}$], 176 (45), 158 (2), 104 (2), 92 (8), 91 (100), 65 (10).

Methyl (2*S*,4*S*)-4-Azido-1-benzylpyrrolidine-2-carboxylate (3):[12] To a solution of **2** (467 mg, 2.0 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) at 0 °C, was added Et_3N (1.22 mL, 8.8 mmol, 4.4 equiv.) followed by MsCl (0.13 mL, 4.4 mmol, 2.2 equiv.). The reaction mixture was stirred for 1.5 h. The reaction mixture was diluted with CH_2Cl_2 and washed with saturated aqueous sodium hydrogen carbonate, H_2O, and brine. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure to afford the crude product (600 mg). To a solution of the methanesulfonate ester (600 mg, 2.0 mmol, 1 equiv.) previously synthesized in CH_3CN (5 mL), was added tetra-*n*-butylammonium azide (1.41 g, 5.0 mmol, 2.5 equiv.). The stirred solution was heated at 55 °C for 2 h, diluted with EtOAc, and washed with H_2O and brine. The combined aqueous washings were extracted with EtOAc, the combined organic fractions were dried with Na_2SO_4, and the solvent was removed under reduced pressure to afford an oil that was purified by flash column chromatography on silica gel (PE/Et_2O, 60:40) to obtain the desired compound **3** (475 mg, 1.8 mmol, 92%). $[\alpha]_D^{20}$ = –53.6 (*c* = 0.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2100, 1733, 1454, 1436, 1266, 1200, 1174, 1138 cm^{-1}. ^1H NMR: δ = 7.35–7.23 (m, 5 H), 4.02 (d, *J* = 13.2 Hz, 1 H), 3.90 (m, 1 H), 3.71 (s, 3 H), 3.55 (d, *J* = 13.2 Hz, 1 H), 3.34 (dd, *J* = 9.3, 6.3 Hz, 1 H), 3.06 (app. d, *J* = 10.3 Hz, 1 H), 2.63 (dd, *J* = 10.3, 5.8 Hz, 1 H), 2.51 (ddd, *J* = 14.1, 9.3, 7.8 Hz, 1 H), 2.14 (dddd, *J* = 14.0, 6.3, 3.0, 0.8 Hz, 1 H) ppm. ^{13}C NMR: δ = 173.2 (s), 137.6 (s), 129.0 (d, 2 C), 128.3 (d, 2 C), 127.3 (d), 63.7 (d), 58.5 (d), 58.0 (t), 57.7 (t), 52.0 (q), 35.8 (t) ppm. MS: *m*/*z* (%) = 260 (0.1) [$M^{+\cdot}$], 201 (19), 173 (9), 92 (8), 91 (100), 65 (10).

[(2*S*,4*S*)-4-Amino-1-benzylpyrrolidin-2-yl]methanol (4):[12] To a stirred suspension of $LiAlH_4$ (0.278 g, 7.3 mmol, 4.0 equiv.) in

THF (20 mL) at 0 °C, was added dropwise a solution of **3** (0.475 g, 1.8 mmol, 1 equiv.) in THF (10 mL). The reaction mixture was stirred at 0 °C for 0.5 h and then for 1.5 h at room temp. The system was cooled to 0 °C and H_2O (0.15 mL) was added dropwise. After 5 min stirring, an aqueous solution of NaOH (3.75 M, 0.15 mL) was added. After 5 min of stirring, H_2O (0.34 mL) was added and the mixture was stirred at room temp. for 1 h. The white granular precipitate was removed by suction filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure to afford **4** (288 mg, 1.4 mmol, 78%). $[\alpha]_D^{20}$ = –48.0 (*c* = 4.7, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3665–2650, 1584, 1495, 1453, 1377, 1029 cm^{-1}. ^1H NMR: δ = 7.33–7.22 (m, 5 H), 3.97 (d, *J* = 13.2 Hz, 1 H), 3.68 (dd, *J* = 10.9, 2.9 Hz, 1 H), 3.49–3.41 (m, 3 H), 2.89 (m, 1 H), 2.73 (ddd, *J* = 9.8, 1.4, 1.4 Hz, 1 H), 2.53 (dd, *J* = 9.8, 5.1 Hz, 1 H), 2.28 (ddd, *J* = 13.5, 9.8, 6.6 Hz, 1 H), 2.23–2.06 (br. s, 3 H), 1.64 (dddd, *J* = 13.4, 5.2, 2.2, 1.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 139.3 (s), 128.6 (d, 2 C), 128.3 (d, 2 C), 127.3 (d), 63.8 (d), 62.7 (t), 61.6 (t), 58.0 (t), 49.4 (d), 37.9 (t) ppm. MS: *m*/*z* (%) = 206 (0.1) [$M^{+\cdot}$], 176 (5), 175 (38), 158 (18), 92 (8), 91 (100), 72 (6), 65 (11), 56 (7).

[(2*S*,4*S*)-1-Benzyl-4-(dibenzylamino)pyrrolidin-2-yl]methanol (5):[20] *n*Bu_4NI (123 mg, 0.33 mmol, 0.3 equiv.), BnBr (0.29 mL, 2.44 mmol, 2.2 equiv.) and K_2CO_3 (462 mg, 3.33 mmol, 3 equiv.) were added to a solution of **4** (229 mg, 1.11 mmol, 1 equiv.) in CH_3CN (11 mL). After 4 h at room temp., H_2O (10 mL) was added to the mixture, which was then extracted with EtOAc. The organic layer was dried with $MgSO_4$, filtered and then concentrated under reduced pressure. After purification by flash column chromatography on silica gel (PE/EtOAc, 80:20), **5** (300 mg, 0.78 mmol, 70%) was isolated as a yellow oil. $[\alpha]_D^{20}$ = –47.0 (*c* = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3408, 1493, 1452, 1365, 1125, 1047, 1027 cm^{-1}. ^1H NMR: δ = 7.36–7.16 (m, 15 H), 3.99 (d, *J* = 13.6 Hz, 1 H), 3.80 (dd, *J* = 11.0, 4.2 Hz, 1 H), 3.65–3.51 (m, 5 H), 3.38 (m, 1 H), 3.16 (d, *J* = 13.1 Hz, 1 H), 3.08 (dd, *J* = 10.5, 3.4 Hz, 1 H), 2.61 (m, 1 H), 2.40 (dd, *J* = 10.5, 8.9 Hz, 1 H), 2.13 (ddd, *J* = 16.5, 9.7, 7.1 Hz, 1 H), 1.95 (ddd, *J* = 15.0, 8.4, 7.1 Hz, 1 H) ppm. ^{13}C NMR: δ = 140.0 (s, 2 C), 139.0 (s), 128.8 (d, 4 C), 128.5 (d, 2 C), 128.4 (d, 2 C), 128.2 (d, 4 C), 127.2 (d), 126.8 (d, 2 C), 64.6 (d), 60.6 (t), 58.2 (t), 57.0 (t), 56.3 (d), 54.5 (t, 2 C), 29.2 (t) ppm. HRMS (ESI): calcd. for $C_{26}H_{31}ON_2$ [M + H^+] 387.2431; found 387.2429.

***N*-[(3*S*,5*S*)-1-Benzyl-5-(hydroxymethyl)pyrrolidin-3-yl]ethanamide (6):**[12] To a stirring solution of **4** (206 mg, 1.0 mmol, 1 equiv.) in CH_2Cl_2 (5 mL), was added AcCl (70 µL, 1.0 mmol, 1 equiv.) and Et_3N (160 µL, 1.1 mmol, 1.1 equiv.). The reaction mixture was stirred at room temp. for 3 h. The mixture was taken up in Et_2O and washed with H_2O, dried with $MgSO_4$, and concentrated under reduced pressure. The crude material was purified by flash chromatography on silica gel (EtOAc/MeOH, 90:10) to obtain the desired compound **6** (233 mg, 0.94 mmol, 94%). $[\alpha]_D^{20}$ = –53.4 (*c* = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3286, 1637, 1543, 1453, 1374, 1295, 1043, 912 cm^{-1}. ^1H NMR: δ = 7.35–7.23 (m, 5 H), 6.38 (br. s, 1 H), 4.34 (m, 1 H), 3.90 (d, *J* = 13.0 Hz, 1 H), 3.60 (dd, *J* = 11.2, 3.1 Hz, 1 H), 3.44 (d, *J* = 13.1 Hz, 1 H), 3.40 (dd, *J* = 11.4, 1.9 Hz, 1 H), 2.90 (dd, *J* = 10.0, 1.5 Hz, 1 H), 2.86–2.66 (m, 2 H), 2.56 (dd, *J* = 10.0, 5.1 Hz, 1 H), 2.40 (ddd, *J* = 14.1, 9.9, 7.8 Hz, 1 H), 1.91 (s, 3 H), 1.65 (dddd, *J* = 14.1, 5.4, 1.9, 1.9 Hz, 1 H) ppm. ^{13}C NMR: δ = 169.3 (s), 138.4 (s), 128.8 (d, 2 C), 128.5 (d, 2 C), 127.4 (d), 63.1 (d), 61.4 (t), 61.1 (t), 58.1 (t), 47.6 (d), 35.5 (t), 23.4 (q) ppm. MS: *m*/*z* (%) = 217 (10) [$M^{+\cdot}$ – $CH_2OH^{\cdot}$], 158 (37), 92 (8), 91 (100), 65 (17), 56 (6).

***tert*-Butyl [(3*S*,5*S*)-1-Benzyl-5-(hydroxymethyl)pyrrolidin-3-yl]carbamate (7):**[20] Di-*tert*-butyl dicarbonate (152 mg, 0.70 mmol, 1.2 equiv.) was added to a solution of **4** (120 mg, 0.58 mmol, 1 equiv.) in dioxane (8 mL). After 1 h at room temp., H_2O (10 mL) was added to the reaction mixture, and the solution was extracted with Et_2O. The organic layer was dried with Na_2SO_4, filtered and then concentrated under reduced pressure. After purification by flash column chromatography on silica gel (CH_2Cl_2 to CH_2Cl_2/MeOH, 90:10), **7** (146 mg, 0.48 mmol, 82%) was isolated as a yellow oil. M.p. 105 °C. $[\alpha]_D^{20}$ = –38.0 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1694, 1498, 1366, 1250, 1167, 906 cm^{-1}. ^1H NMR: δ = 7.37–7.23 (m, 5 H), 5.15 (br. s, 1 H), 4.08 (m, 1 H), 3.92 (d, *J* = 13.1 Hz, 1 H), 3.63 (dd, *J* = 11.1, 3.0 Hz, 1 H), 3.44–3.34 (m, 2 H), 2.90 (d, *J* = 10.0 Hz, 1 H), 2.75 (m, 1 H), 2.53 (dd, *J* = 9.6, 5.6 Hz, 1 H), 2.37 (m, 1 H), 1.66 (dd, *J* = 14.1, 5.7 Hz, 1 H), 1.41 (s, 9 H) ppm. ^{13}C NMR: δ = 155.4 (s), 138.4 (s), 128.8 (d, 2 C), 128.5 (d, 2 C), 127.3 (d), 79.2 (s), 63.3 (d), 61.2 (t, 2 C), 58.0 (t), 48.7 (d), 35.7 (t), 28.4 (q, 3 C) ppm. HRMS (ESI): calcd. for $C_{17}H_{27}O_3N_2$ [M + H^+] 307.2010; found 307.2006.

(3*S*,5*R*)-1-Benzyl-3-chloro-5-(dibenzylamino)piperidine (8): To a solution of **5** (240 mg, 0.62 mmol, 1 equiv.) in CH_2Cl_2 (8 mL) at 0 °C were added Et_3N (0.27 mL, 2.48 mmol, 4 equiv.) and mesyl chloride (0.16 mL, 2.05 mmol, 3.3 equiv.) dropwise. After stirring at reflux for 5 h, H_2O was added to the reaction mixture, which was then extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE/EtOAc, 80:20), **8** (159 mg, 0.39 mmol, 63%) was isolated as a yellow oil. $[\alpha]_D^{20}$ = +6.3 (*c* = 2.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 1494, 1453, 1364, 1169, 1063, 1028, 972, 909 cm^{-1}. ^1H NMR: δ = 7.34–7.18 (m, 15 H), 3.84 (dddd, *J* = 11.6, 11.6, 4.4, 4.4 Hz, 1 H), 3.63 (s, 4 H), 3.60 (d, *J* = 12.9 Hz, 1 H), 3.50 (d, *J* = 12.9 Hz, 1 H), 3.06 (dd, *J* = 10.9, 4.5 Hz, 1 H), 2.99 (app. d, *J* = 10.6 Hz, 1 H), 2.87 (m, 1 H), 2.44 (ddd, *J* = 11.9, 4.3, 3.6 Hz, 1 H), 2.10–1.96 (m, 2 H), 1.64 (ddd, *J* = 12.0, 12.0, 12.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 140.1 (s, 3 C), [128.9, 128.4, 128.3, 127.3, 126.9 (d, 15 C)], 62.2 (t), 61.0 (t), 54.8 (d), 54.7 (t), 54.6 (d), 54.3 (t, 2 C), 37.2 (t) ppm. HRMS (ESI): calcd. for $C_{26}H_{30}N_2Cl$ [M + H^+] 405.2092; found 405.2095.

***N*-[(3*S*,5*R*)-1-Benzyl-5-chloropiperidin-3-yl]ethanamide (9):** To a solution of **6** (227 mg, 0.92 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) at 0 °C were added Et_3N (0.52 mL, 3.66 mmol, 4 equiv.) and mesyl chloride (0.15 mL, 1.92 mmol, 2.1 equiv.) dropwise. After stirring at reflux for 5 h, water was added and the reaction mixture was extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. After purification by flash chromatography on silica gel (CH_2Cl_2/MeOH, 98:2), **9** (170 mg, 0.64 mmol, 70%) was isolated as a yellow oil. $[\alpha]_D^{20}$ = +3.0 (*c* = 10.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3018, 1658, 1548, 1372, 1215, 1042 cm^{-1}. ^1H NMR: δ = 7.37–7.23 (m, 5 H), 6.00 (br. s, 1 H), 4.16–4.00 (m, 2 H), 3.60 (d, *J* = 13.5 Hz, 1 H), 3.56 (d, *J* = 13.4 Hz, 1 H), 2.90 (m, 1 H), 2.80 (m, 1 H), 2.47–2.25 (m, 2 H), 2.10 (m, 1 H), 1.95 (s, 3 H), 1.61 (m, 1 H) ppm. ^{13}C NMR: δ = 169.3 (s), 137.4 (s), 128.8 (d, 2 C), 128.4 (d, 2 C), 127.4 (d), 62.0 (t), 60.1 (t), 57.4 (t), 53.8 (d), 45.1 (d), 39.5 (t), 23.5 (q) ppm. MS: *m*/*z* (%) = 209 (7) [$M^{+\cdot}$ – CH_3CONH_2], 207 (20) [$M^{+\cdot}$ – CH_3CONH_2], 172 (19), 92 (10), 91 (100), 65 (19). HRMS (ESI): calcd. for $C_{14}H_{20}N_2OCl$ [M + H^+] 267.1259; found 267.1258.

***tert*-Butyl [(3*S*,5*R*)-1-Benzyl-5-chloropiperidin-3-yl]carbamate (10):** To a solution of **7** (259 mg, 0.85 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) at 0 °C were added Et_3N (0.48 mL, 3.4 mmol, 4 equiv.) and mesyl chloride (0.14 mL, 1.79 mmol, 2.1 equiv.) dropwise. After stirring at reflux for 5 h, H_2O was added to the reaction mixture, which was then extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. After

purification by flash chromatography on silica gel (CH_2Cl_2/MeOH, 98:2), **10** (266 mg, 0.82 mmol, 90%) was isolated as a yellow oil. $[\alpha]_D^{20}$ = +7.0 (*c* = 2.8, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3326, 2975, 1689, 1508, 1454, 1366, 1248, 1166, 1068, 787 cm^{-1}. ^1H NMR: δ = 7.34–7.23 (m, 5 H), 4.68 (br. s, 1 H), 3.96 (m, 1 H), 3.78 (m, 1 H), 3.61 (d, *J* = 13.4 Hz, 1 H), 3.53 (d, *J* = 12.7 Hz, 1 H), 3.06–2.89 (m, 2 H), 2.42 (m, 1 H), 2.17 (dd, *J* = 9.5, 9.5 Hz, 1 H), 1.93 (dd, *J* = 9.3, 9.3 Hz, 1 H), 1.42 (m, 1 H), 1.41 (s, 9 H) ppm. ^{13}C NMR: δ = 155.0 (s), 137.4 (s), 128.9 (d, 2 C), 128.4 (d, 2 C), 127.3 (d), 79.6 (s), 62.0 (t), 60.1 (t), 57.9 (t), 53.3 (d), 46.7 (d), 41.0 (t), 28.4 (q, 3 C) ppm. MS: *m*/*z* (%) = 324 (0.1) [M^+], 209 (11), 207 (31), 172 (23), 171 (7), 92 (10), 91 (100), 65 (9), 57 (22).

***N*-Allyl-*N*-benzyl-*N*-ethylethane-1,2-diamine (13):** To a suspension of $LiAlH_4$ (25 mg, 0.64 mmol, 2 equiv.) in THF (3 mL) was added a solution of **9** (85 mg, 0.32 mmol, 1 equiv.) in THF (3 mL) at 0 °C. After being stirred at reflux for 1 h, H_2O (16 μL), NaOH (3.75 M, 16 μL), and H_2O (36 μL) were added dropwise at 0 °C. The white granular precipitate was removed by suction filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure. After purification by flash chromatography on silica gel (CH_2Cl_2/MeOH, 80:20), **13** (36 mg, 0.16 mmol, 51%) was isolated. IR (neat): $\tilde{\nu}$ = 2962, 2930, 2803, 1642, 1453, 1371, 1261, 1116, 1073, 1028, 993, 917 cm^{-1}. ^1H NMR: δ = 7.33–7.20 (m, 5 H), 5.88 (dddd, *J* = 17.2, 10.2, 6.5, 6.5 Hz, 1 H), 5.22–5.12 (m, 2 H), 3.58 (s, 2 H), 3.10 (dd, *J* = 6.5, 1.5 Hz, 1 H), 3.09 (dd, *J* = 6.5, 1.5 Hz, 1 H), 2.70–2.59 (m, 4 H), 2.55 (q, *J* = 7.2 Hz, 2 H), 1.07 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR: δ = 139.6 (s), 135.7 (d), 128.8 (d, 2 C), 128.2 (d, 2 C), 126.7 (d), 117.5 (t), 58.4 (t), 57.2 (t), 53.4 (t), 47.3 (t), 44.0 (t), 15.3 (q) ppm. MS: *m*/*z* (%) = 218 (0.02) [M^+], 160 (33), 127 (3), 92 (8), 91 (100).

(*S*)-1-Benzyl-3-(dibenzylamino)piperidine (14) and (3*S*,5*R*)-1-Benzyl-3-(dibenzylamino)-5-methylpyrrolidine (15): To a suspension of $LiAlH_4$ (69 mg, 1.8 mmol, 10 equiv.) in THF (3 mL) was added a solution of **8** (73 mg, 0.18 mmol, 1 equiv.) in THF (3 mL) at 0 °C. After stirring at reflux for 1 h, H_2O (38 μL), NaOH (3.75 M, 38 μL), and H_2O (89 μL) were added dropwise at 0 °C. The white granular precipitate was removed by suction filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE/EtOAc, 90:10), **14** (45 mg, 0.12 mmol, 67%) and **15** (11 mg, 0.03 mmol, 16%) were isolated. **14**: $[\alpha]_D^{20}$ = –15.0 (*c* = 1.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2930, 1493, 1453, 1363, 1160, 1134, 1052, 1028, 962, 914 cm^{-1}. ^1H NMR: δ = 7.38–7.16 (m, 15 H), 3.64 (s, 4 H), 3.53 (d, *J* = 13.2 Hz, 1 H), 3.46 (d, *J* = 13.2 Hz, 1 H), 3.05 (ddd, *J* = 10.6, 2.0, 2.0 Hz, 1 H), 2.81 (dddd, *J* = 10.7, 10.7, 3.7, 3.7 Hz, 1 H), 2.74 (app. d, *J* = 10.9 Hz, 1 H), 1.96 (dd, *J* = 10.4, 10.4 Hz, 1 H), 1.90 (m, 1 H), 1.79 (ddd, *J* = 11.7, 11.7, 2.5 Hz, 1 H), 1.65 (app. d, *J* = 13.2 Hz, 1 H), 1.45 (ddddd, *J* = 12.7, 12.7, 12.7, 3.8, 3.8 Hz, 1 H), 1.32 (m, 1 H) ppm. ^{13}C NMR: δ = 140.8 (s, 2 C), 138.3 (s), {129.1, 128.4, 128.2, 127.0, 126.9, 126.7 (d, 15 C)}, 63.3 (t), 56.2 (t), 55.6 (d), 54.4 (t, 2 C), 53.7 (t), 26.2 (t), 24.9 (t) ppm. MS: *m*/*z* (%) = 279 (15) [$M^{+\cdot}$ – $Ph^{\cdot}$], 236 (12), 174 (6), 134 (16), 92 (8), 91 (100), 65 (11). HRMS (ESI): calcd. for $C_{26}H_{31}N_2$ [M + H^+] 371.2482; found 371.2479. **15**: ^1H NMR: δ = 7.35–7.16 (m, 15 H), 4.05 (d, *J* = 13.5 Hz, 1 H), 3.66–3.54 (m, 4 H), 3.31 (dddd, *J* = 8.7, 8.7, 6.7, 2.3 Hz, 1 H), 3.03–2.94 (m, 2 H), 2.31 (dqd, *J* = 9.9, 6.5, 5.1 Hz, 1 H), 2.14–1.95 (m, 2 H), 1.58 (m, 1 H), 1.19 (d, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR: δ = 140.6 (s, 2 C), 140.1 (s), {128.6, 128.5, 128.2, 128.1, 126.7, 126.6 (d, 15 C)}, 59.3 (d), 58.0 (t), 56.6 (t), 55.9 (d), 54.7 (t, 2 C), 36.1 (t), 18.7 (q) ppm.

(*S*)-*N*-[(1-Benzylpyrrolidin-2-yl)methyl]-4-methyl-*N*-tosylbenzenesulfonamide (18a): To a solution of prolinol **17a**[23] (850 mg, 4.45 mmol, 1 equiv.) and Ms_2O (1.07 g, 5.79 mmol, 1.3 equiv.) in CH_2Cl_2 (50 mL) at 0 °C was added Et_3N (1.86 mL, 13.35 mmol, 3 equiv.). After 5 min at 0 °C, bis(*p*-toluene)sulfimide (1.59 g, 4.90 mmol, 1.1 equiv.) was added. After 1 h of stirring at room temp., the reaction mixture was washed with an aqueous solution of NaOH (2.5 M, 2 × 5 mL) and H_2O (5 mL). The organic layers were dried with $MgSO_4$ and the solvent was evaporated in vacuo. After purification by flash chromatography on silica gel (PE/EtOAc, 80:20), **18a** (1.10 g, 2.21 mmol, 50%) was isolated as a colorless oil. $[\alpha]_D^{20}$ = –3.4 (*c* = 5.8, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2793, 1596, 1494, 1452, 1368, 1307, 1291, 1162, 1120, 1084, 1043, 996, 908, 812, 777, 723 cm^{-1}. ^1H NMR: δ = 7.92 (d, *J* = 7.6 Hz, 4 H), 7.42–7.25 (m, 9 H), 4.06 (d, *J* = 13.5 Hz, 1 H), 3.79–3.63 (m, 2 H), 3.50 (d, *J* = 13.5 Hz, 1 H), 3.16 (dddd, *J* = 8.6, 7.3, 4.8, 4.0 Hz, 1 H), 2.97 (m, 1 H), 2.48 (s, 6 H), 2.32 (m, 1 H), 1.93 (m, 1 H), 1.83–1.65 (m, 3 H) ppm. ^{13}C NMR: δ = 144.8 (s, 2 C), 139.5 (s), 137.0 (s, 2 C), 129.6 (d, 4 C), 128.9 (d, 2 C), 128.6 (d, 4 C), 128.4 (d, 2 C), 126.9 (d), 62.4 (d), 59.3 (t), 54.3 (t), 52.6 (t), 28.6 (t), 23.2 (t), 21.7 (q, 2 C) ppm. MS: *m*/*z* (%) = 174 (9), 173 (72) [$M^{+\cdot}$ – $HNTs_2$], 172 (36), 158 (6), 144 (3), 117 (1), 104 (4), 96 (18), 92 (13), 91 (100), 82 (13), 77 (2), 65 (13), 55 (8).

(*R*)-*N*-(1-Benzylpiperidin-3-yl)-4-methyl-*N*-tosylbenzenesulfonamide (18a) and (*S*)-*N*-[(1-Benzylpyrrolidin-2-yl)methyl]-4-methyl-*N*-tosylbenzenesulfonamide (19a): A solution of **18a** (75 mg, 0.15 mmol, 1 equiv.) in THF (50 mL) was heated under microwave irradiation for 8 h at 120 °C. The solvent was evaporated in vacuo and a mixture of **18a** and **19a** (75 mg, 0.15 mmol, 100%) was isolated. **18a**: ^1H NMR: δ = 7.91–7.80 (4 H), 7.34–7.18 (m, 9 H), 4.01 (d, *J* = 13.4 Hz, 1 H), 3.72–3.60 (m, 2 H), 3.45 (d, *J* = 13.3 Hz, 1 H), 3.10 (dddd, *J* = 8.7, 7.3, 5.1, 3.9 Hz, 1 H), 2.92 (m, 1 H), 2.45 (s, 6 H), 2.26 (m, 1 H), 1.88 (m, 1 H), 1.79–1.51 (m, 3 H) ppm. ^{13}C NMR: δ = 144.8 (s, 2 C), 138.2 (s), 136.9 (s, 2 C), 129.6 (d, 4 C), 128.9 (d, 2 C), 128.4 (d, 4 C), 128.2 (d, 2 C), 126.9 (d), 62.4 (d), 59.3 (t), 54.3 (t), 52.6 (t), 28.6 (t), 23.2 (t), 21.7 (q, 2 C) ppm. **19a**: ^1H NMR: δ = 7.91–7.80 (4 H), 7.34–7.18 (m, 9 H), 4.22 (dddd, *J* = 12.3, 10.9, 4.0, 3.6 Hz, 1 H), 3.52 (d, *J* = 13.1 Hz, 1 H), 3.32 (d, *J* = 13.2 Hz, 1 H), 2.77 (m, 1 H), 2.67 (dd, *J* = 11.0, 10.2 Hz, 1 H), 2.57 (m, 1 H), 2.42 (s, 6 H), 2.26 (m, 1 H), 1.97 (ddd, *J* = 11.9, 11.5, 2.7 Hz, 1 H), 1.79–1.51 (m, 3 H) ppm. ^{13}C NMR: δ = 144.6 (s, 2 C), 138.2 (s), 136.9 (s, 2 C), 129.5 (d, 4 C), 128.8 (d, 2 C), 128.4 (d, 4 C), 128.2 (d, 2 C), 128.1 (d), 62.7 (t), 61.0 (d), 56.6 (t), 53.2 (t), 28.9 (t), 25.7 (t), 21.7 (q, 2 C) ppm.

(*S*)-*N*-[(1-Benzhydrylpyrrolidin-2-yl)methyl]-4-methyl-*N*-tosylbenzenesulfonamide (18b) and (*R*)-*N*-(1-Benzhydrylpiperidin-3-yl)-4-methyl-*N*-tosylbenzenesulfonamide (19b): To a solution of prolinol **17b**[21b] (375 mg, 1.43 mmol, 1 equiv.) and Ms_2O (323 mg, 1.86 mmol, 1.3 equiv.) in CH_2Cl_2 (10 mL) at 0 °C was added DIPEA (0.72 mL, 4.29 mmol, 3 equiv.). After 5 min at 0 °C, bis(*p*-toluene)sulfimide (509 mg, 1.57 mmol, 1.1 equiv.) was added. After 1 h stirring at room temp., the reaction mixture was washed with an aqueous solution of NaOH (2.5 M, 2 × 5 mL) and H_2O (5 mL). The organic layers were dried with $MgSO_4$ and the solvent was evaporated in vacuo. After purification by flash chromatography on silica gel (CH_2Cl_2) a mixture of **18b** and **19b** (677 mg, 1.19 mmol, 83%, **18b**/**19b** = 80:20) was isolated. **18b**: ^1H NMR: δ = 7.68 (d, *J* = 8.3 Hz, 4 H), 7.44–7.12 (m, 14 H), 4.78 (s, 1 H), 3.69 (m, 1 H), 3.47 (dd, *J* = 14.6, 4.3 Hz, 1 H), 3.34 (m, 1 H), 2.96 (m, 1 H), 2.43 (s, 6 H), 2.38 (m, 1 H), 1.89–1.32 (m, 4 H) ppm. **19b**: ^1H NMR: δ = 7.79 (d, *J* = 8.4 Hz, 4 H), 7.44–7.12 (m, 14 H), 4.37 (dddd, *J* = 11.4, 11.4, 3.2, 3.2 Hz, 1 H), 4.26 (s, 1 H), 2.82–2.72 (m, 2 H), 2.61 (dd, *J* = 11.3, 10.4 Hz, 1 H), 2.42 (s, 6 H), 2.17 (dddd, *J* = 12.3, 12.3, 12.3, 4.8 Hz, 1 H), 1.89–1.32 (m, 4 H) ppm. **18b** + **19b**: ^{13}C NMR: δ = 144.6 (s), 144.5 (s), 142.8 (s), 142.4 (s),

137.0 (s), 129.6 (d), 129.5 (d), 128.6 (d), 128.5 (d), 128.4 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.8 (d), 126.9 (d), 126.7 (d), 126.6 (d), 75.9 (d), 72.4 (d), 61.2 (d), 59.7 (d), 56.0 (t), 52.1 (t), 51.6 (t), 51.5 (t), 29.5 (t), 26.9 (t), 25.8 (t), 23.5 (t), 21.7 (q) ppm.

***N*-{[(2*S*,4*R*)-1-Benzyl-4-(*tert*-butyldiphenylsilyloxy)pyrrolidin-2-yl]methyl}-4-methyl-*N*-tosylbenzenesulfonamide (18c) and *N*-[(3*R*,5*R*)-1-Benzyl-5-(*tert*-butyldiphenylsilyloxy)piperidin-3-yl]-4-methyl-*N*-tosylbenzenesulfonamide (19c):** To a solution of prolinol **17c**[16g] (200 mg, 0.45 mmol, 1 equiv.) and Ms_2O (102 mg, 0.58 mmol, 1.3 equiv.) in CH_2Cl_2 (10 mL) at 0 °C was added DIPEA (0.23 mL, 1.35 mmol, 3 equiv.). After 5 min at 0 °C, bis(*p*-toluene)sulfimide (161 mg, 0.49 mmol, 1.1 equiv.) was added. After 1 h stirring at room temp., the reaction mixture was washed with an aqueous solution of NaOH (2.5 M, 2 × 5 mL) and H_2O (5 mL). The organic layers were dried with $MgSO_4$ and the solvent was evaporated in vacuo. After purification by flash chromatography on silica gel (PE/EtOAc, 80:20) a mixture of **18c** and **19c** (184 mg, 0.24 mmol, 54% **18c/19c** = 60:40) was isolated. **18c**: ^{1}H NMR: δ = 7.91–7.23 (23 H), 4.31 (m, 1 H), 4.19–3.98 (m, 1 H), 3.83 (d, J = 13.3 Hz, 1 H), 3.62 (d, J = 13.3 Hz, 1 H), 3.53 (m, 1 H), 2.97 (m, 1 H), 2.54–2.24 (m, 8 H), 2.00–1.82 (m, 2 H), 1.15–1.05 (m, 9 H) ppm. **19c**: ^{1}H NMR: δ = 7.91–7.23 (23 H), 4.91 (m, 1 H), 4.19–3.98 (m, 1 H), 3.41 (d, J = 13.3 Hz, 1 H), 3.35 (d, J = 13.3 Hz, 1 H), 2.81–2.66 (m, 2 H), 2.61 (m, 1 H), 2.54–2.24 (m, 6 H), 2.00–1.82 (m, 3 H), 1.15–1.05 (m, 9 H) ppm.

General Procedure for Rearrangement of Prolinols Induced by XtalFluor-E: To a solution of prolinols in CH_2Cl_2 (0.06 M) was added nBu$_4$NN$_3$ (1.1 equiv.) and XtalFluor-E (1.1 equiv.) at 0 °C or –78 °C. The mixture was stirred for 15 min to 4 h at 0 °C or –78 °C. After addition of NaOH (3.75 M), the mixture was extracted with CH_2Cl_2 (×2), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the residue by flash chromatography on silica gel afforded the 3-azidopiperidine derivative.

(*R*)-3-Azido-1-benzylpiperidine (23a) and (*S*)-2-(Azidomethyl)-1-benzylpyrrolidine (24a):[20] Following the general procedure with nBu$_4$NN$_3$ (164 mg, 0.58 mmol, 1.1 equiv., 0 °C, 2 h) and XtalFluor-E (134 mg, 0.58 mmol, 1.1 equiv.), the transformation of **17a** (100 mg, 0.52 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (petroleum ether/Et_2O, 80:20) to give a mixture of **23a** and **24a** (78 mg, 0.36 mmol, 70%, **23a/24a** = 50:50). **23a**: IR (neat): $\tilde{\nu}$ = 2091, 1453, 1267 cm^{-1}. ^{1}H NMR: δ = 7.36–7.21 (m, 5 H), 3.52 (s, 2 H), 3.47 (dddd, J = 9.0, 9.0, 5.1, 5.1 Hz, 1 H), 2.82 (dd, J = 10.8, 2.8 Hz, 1 H), 2.60 (ddd, J = 10.1, 4.4, 4.4 Hz, 1 H), 2.15–2.05 (m, 2 H), 1.98 (m, 1 H), 1.74 (m, 1 H), 1.56 (m, 1 H), 1.38 (m, 1 H) ppm. MS: m/z (%) = 216 (0.2) [M$^+$], 174 (0.5), 160 (17), 91 (100); **24a**: IR (neat): $\tilde{\nu}$ = 2091, 1453, 1267 cm^{-1}. ^{1}H NMR: δ = 7.36–7.21 (m, 5 H), 3.99 (d, J = 12.8 Hz, 1 H), 3.42 (d, J = 12.8 Hz, 1 H), 3.27 (dd, J = 12.4, 5.8 Hz, 1 H), 3.16 (dd, J = 12.4, 3.9 Hz, 1 H), 2.96 (ddd, J = 9.4, 7.3, 2.7 Hz, 1 H), 2.75 (m, 1 H), 2.23 (m, 1 H), 2.98 (m, 1 H), 1.83–1.66 (m, 3 H) ppm. **23a** + **24a**: ^{13}C NMR: δ = 139.4 (s), 137.9 (s), 129.1 (d), 128.8 (d), 128.3 (d), 128.2 (d), 127.2 (d), 127.0 (d), 63.2 (d), 63.0 (t), 59.4 (t), 57.5 (t), 57.3 (d), 54.6 (t), 54.5 (t), 53.0 (t), 29.6 (t), 28.9 (t), 23.3 (t), 23.1 (t) ppm.

(3*R*,5*S*)-3-Azido-1-benzyl-5-(*tert*-butyldimethylsilyloxy)piperidine (23b) and (2*S*,4*S*)-2-(Azidomethyl)-1-benzyl-4-(*tert*-butyldimethylsilyloxy)pyrrolidine (24b):[20] Following the general procedure with nBu$_4$NN$_3$ (98 mg, 0.34 mmol, 1.1 equiv., 0 °C, 2.5 h) and XtalFluor-E (79 mg, 0.34 mmol, 1.1 equiv.), the transformation of **26b**[20] (79 mg, 0.25 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 95:5) to give a mixture of **23b** and **24b** (76 mg, 0.22 mmol, 88%, **23b/24b** = 60:40). **23b**: IR (neat): $\tilde{\nu}$ = 2952, 2929, 2856, 2094, 1470, 1253, 1100, 835, 775 cm^{-1}. ^{1}H NMR: δ = 7.37–7.18 (m, 5 H), 3.74 (dddd, J = 9.5, 9.5, 4.7, 4.7 Hz, 1 H), 3.59 (d, J = 13.4 Hz, 1 H), 3.48 (d, J = 13.4 Hz, 1 H), 3.41–3.25 (m, 2 H), 2.94–2.80 (m, 2 H), 1.87–1.75 (m, 2 H), 1.69 (ddd, J = 14.0, 5.7, 4.0 Hz, 1 H), 0.84 (s, 9 H), 0.02 (s, 3 H), 0.00 (s, 3 H) ppm. MS (EI): m/z (%) = 304 (0.4) [M$^{+\cdot}$ – N$_3^{\cdot}$], 290 (1), 157 (1), 133 (19), 132 (20), 91 (100), 75 (50), 73 (19); **24b**: IR (neat): $\tilde{\nu}$ = 2952, 2929, 2856, 2094, 1470, 1253, 1100, 835, 775 cm^{-1}. ^{1}H NMR: δ = 7.37–7.18 (m, 5 H), 4.27 (dddd, J = 5.8, 5.8, 3.1, 3.1 Hz, 1 H), 3.99 (d, J = 13.5 Hz, 1 H), 3.45 (d, J = 13.4 Hz, 1 H), 3.33 (m, 1 H), 2.94–2.80 (m, 2 H), 2.45 (dd, J = 10.3, 5.4 Hz, 1 H), 2.27–2.12 (m, 2 H), 1.51 (m, 1 H), 0.85 (s, 9 H), 0.00 (s, 3 H), –0.025 (s, 3 H) ppm. MS (EI): m/z (%) = 290 (9) [M$^{+\cdot}$ – CH$_2$N$_3^{\cdot}$], 157 (19), 91 (100), 75 (87); **23b** + **24b**: ^{13}C NMR: δ = 139.3 (s), 137.6 (s), 128.9 (d), 128.5 (d), 128.3 (d),128.3 (d), 127.3 (d), 126.9 (d), 71.0 (d), 66.9 (d), 62.7 (d), 62.4 (t), 62.2 (t), 60.5 (t), 59.3 (t), 56.6 (t), 55.7 (d), 54.9 (t), 39.6 (t), 39.3 (t), 25.9 (q), 25.8 (q), 19.2 (s), 18.1 (s), –4.8 (q) –4.7 (q) ppm.

(3*S*,5*R*)-3-Azido-1-benzyl-5-(*tert*-butyldiphenylsilyloxy)piperidine (23c) and (2*R*,4*R*)-2-(Azidomethyl)-1-benzyl-4-(*tert*-butyldiphenylsilyloxy)pyrrolidine (24c):[20] Following the general procedure with nBu$_4$NN$_3$ (47 mg, 0.17 mmol, 1.1 equiv., –78 °C, 4.5 h) and XtalFluor-E (38 mg, 0.17 mmol, 1.1 equiv.), the transformation of **26c**[20] (67 mg, 0.15 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 90:10 to 80:20) to give a mixture of **23c** and **24c** (47 mg, 0.10 mmol, 67%, **23c/24c** = 60:40). **23c**: IR (neat): $\tilde{\nu}$ = 2095, 1471, 1454, 1427, 1272, 1172, 1105, 909, 822 cm^{-1}. ^{1}H NMR: δ = 7.66–7.57 (m, 4 H), 7.46–7.22 (m, 10 H), 7.15 (m, 1 H), 3.75 (dddd, J = 9.5, 9.5, 4.5, 4.5 Hz, 1 H), 3.46 (s, 2 H), 3.22 (dddd, J = 10.8, 10.8, 4.4, 4.4 Hz, 1 H), 2.90–2.78 (m, 2 H), 2.16 (m, 1 H), 1.90 (dd, J = 10.1, 10.1 Hz, 1 H), 1.43–1.27 (m, 2 H), 1.03 (s, 9 H) ppm. **24c**: IR (neat): $\tilde{\nu}$ = 2095, 1471, 1454, 1427, 1272, 1172, 1105, 909, 822 cm^{-1}. ^{1}H NMR: δ = 7.66–7.57 (m, 4 H), 7.46–7.22 (m, 10 H), 7.15 (m, 1 H), 4.28 (dddd, J = 5.3, 5.3, 2.6, 2.6 Hz, 1 H), 4.01 (d, J = 13.4 Hz, 1 H), 3.45–3.30 (m, 3 H), 2.96 (ddd, J = 10.5, 1.8, 1.8 Hz, 1 H), 2.83 (m, 1 H), 2.30 (dd, J = 10.3, 5.1 Hz, 1 H), 2.09 (m, 1 H), 1.83 (dd, J = 10.4, 10.4 Hz, 1 H), 1.04 (s, 9 H) ppm. **23c** + **24c**: ^{13}C NMR: δ = 139.3 (s), 137.5 (s), 135.8 (d), 135.7 (d), 135.7 (d), 134.9 (s), 133.9 (s), 129.8 (d), 129.8 (d), 129.7 (d), 129.6 (d), 128.9 (d), 128.5 (d), 128.3 (d), 127.7 (d), 127.6 (d), 127.6 (d), 127.2 (d), 127.0 (d), 72.0 (d), 67.5 (d), 62.8 (d), 62.2 (t), 62.1 (t), 60.0 (t), 59.3 (t), 55.7 (t), 55.6 (d), 55.0 (t), 39.2 (t), 38.9 (t), 26.9 (q), 26.9 (q), 19.12 (s) ppm.

(3*R*,5*R*)-3-Azido-1-benzyl-5-(benzyloxy)piperidine (23d) and (2*S*,4*R*)-2-(Azidomethyl)-1-benzyl-4-(benzyloxy)pyrrolidine (24d):[20] Following the general procedure with nBu$_4$NN$_3$ (105 mg, 0.37 mmol, 1.1 equiv., –78 °C, 4.5 h) and XtalFluor-E (88 mg, 0.37 mmol, 1.1 equiv.), the transformation of **26d**[25] (100 mg, 0.34 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (petroleum ether/Et_2O, 90:10 to 80:20) to give a mixture of **23d** (61 mg, 0.19 mmol, 56%) and **24d** (4 mg, 0.01 mmol, 4%). **23d**: $[\alpha]_D^{20}$ = –62.0 (c = 1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2096, 1495, 1454, 1271, 1153, 1093, 1028 cm^{-1}. ^{1}H NMR: δ = 7.41–7.22 (m, 10 H), 4.51 (d, J = 11.9 Hz, 1 H), 4.46 (d, J = 11.9 Hz, 1 H), 3.84 (m, 1 H), 3.77 (m, 1 H), 3.64 (d, J = 13.2 Hz, 1 H), 3.54 (d, J = 13.3 Hz, 1 H), 2.65–2.55 (m, 2 H), 2.50–2.40 (m, 2 H), 1.89–1.77 (m, 2 H) ppm. ^{13}C NMR: δ = 138.5 (s), 137.4 (s), 129.1 (d, 2 C), 128.4 (d, 2 C), 128.3 (d, 2 C), 127.6 (d, 2 C), 127.3 (d, 2 C), 71.6 (d), 70.6 (t), 62.5 (t), 56.4 (t), 56.2 (t), 55.3 (d), 34.8 (t) ppm. HRMS (ESI): calcd. for $C_{19}H_{23}ON_4$ [M + H$^+$] 323.1866; found 323.1868; **24d**: $[\alpha]_D^{20}$ = –13.0 (c = 0.3, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2098, 1495, 1454, 1366, 1334, 1274, 1106, 1067 cm^{-1}. ^{1}H NMR: δ

= 7.37–7.22 (m, 10 H), 4.67 (d, *J* = 11.8 Hz, 1 H), 4.43 (d, *J* = 11.7 Hz, 1 H), 4.10 (m, 1 H), 4.04 (d, *J* = 12.9 Hz, 1 H), 3.47 (d, *J* = 12.9 Hz, 1 H), 3.37 (dd, *J* = 12.6, 5.1 Hz, 1 H), 3.26 (dd, *J* = 10.3, 5.6 Hz, 1 H), 3.18 (dd, *J* = 12.1, 3.8 Hz, 1 H), 3.09–3.00 (m, 1 H), 2.42 (dd, *J* = 10.3, 5 Hz, 1 H), 2.11–1.94 (m, 2 H) ppm. ^{13}C NMR: δ = 138.9 (s), 138.2 (s), 129.1 (d, 2 C), 128.4 (d, 2 C), 128.4 (d, 2 C), 127.6 (d, 3 C), 127.1 (d), 76.7 (d), 71.3 (t), 62.3 (d), 59.7 (t), 59.3 (t), 53.6 (t), 35.9 (t) ppm. HRMS (ESI): calcd. for $C_{19}H_{23}ON_4$ [M + H$^+$] 323.1866; found 323.1867.

(3*R*,5*R*)-3-Azido-1-benzyl-5-(*tert*-butyldimethylsilyloxy)piperidine (23e) and (2*S*,4*R*)-2-(Azidomethyl)-1-benzyl-4-(*tert*-butyldimethylsilyloxy)pyrrolidine (24e):[20] Following the general procedure with *n*Bu$_4$NN$_3$ (276 mg, 1.02 mmol, 1.1 equiv., –78 °C, 4.5 h) and Xtal-Fluor-E (222 mg, 1.02 mmol, 1.1 equiv.), the transformation of **26e**[26] (300 mg, 0.93 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (CH_2Cl_2 then CH_2Cl_2/MeOH, 98:2) to give **23e** (213 mg, 0.62 mmol, 66%) and a mixture of **23e** and **24e** (25 mg, 0.07 mmol, 8%, **23e/24e** = 77:23), **23e/24e** = 98:2. **23e**: $[\alpha]_D^{20}$ = +56.0 (*c* = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2095, 1253, 835, 774 cm^{-1}. ^{1}H NMR: δ = 7.30–7.16 (m, 5 H), 3.99 (dddd, *J* = 7.8, 7.8, 4.1, 4.1 Hz, 1 H), 3.76 (dddd, *J* = 5.4, 5.4, 3.8, 3.8 Hz, 1 H), 3.60 (d, *J* = 13.4 Hz, 1 H), 3.46 (d, *J* = 13.5 Hz, 1 H), 2.63 (d, *J* = 12.8 Hz, 1 H), 2.55 (dd, *J* = 11.7, 5.4 Hz, 1 H), 2.37 (d, *J* = 10.1 Hz, 1 H), 2.12 (dd, *J* = 11.3, 8.2 Hz, 1 H), 1.82 (ddd, *J* = 13.2, 4.3, 4.3 Hz, 1 H), 1.57 (ddd, *J* = 12.8, 8.5, 3.9 Hz, 1 H), 0.83 (s, 9 H), 0.00 (s, 3 H), –0.02 (s, 3 H) ppm. ^{13}C NMR: δ = 137.6 (s), 128.9 (d, 2 C), 128.3 (d, 2 C), 127.2 (d), 65.3 (d), 62.3 (t), 60.1 (t), 55.9 (t), 55.7 (d), 37.9 (t), 25.8 (q, 3 C), 18.1 (s), –4.7 (q), –4.8 (q) ppm. MS: *m*/*z* (%) = 347 (0.1) [M$^{+\cdot}$], 132 (23), 91 (100), 75 (40). HRMS (ESI): calcd. for $C_{18}H_{31}ON_4Si$ [M + H$^+$] 347.2262; found 347.2254; **24e**: ^{1}H NMR: δ = 7.30–7.19 (m, 5 H), 4.28 (dddd, *J* = 10.5, 10.5, 10.5, 5.5 Hz, 1 H), 3.97 (d, *J* = 12.9 Hz, 1 H), 3.46 (d, *J* = 13.2 Hz, 1 H), 3.28 (dd, *J* = 12.8, 5.4 Hz, 1 H), 3.13–3.07 (m, 2 H), 3.03 (dddd, *J* = 12.0, 4.7, 3.8, 3.8 Hz, 1 H), 2.26 (dd, *J* = 10.1, 5.6 Hz, 1 H), 1.93–1.80 (m, 2 H), 0.83 (s, 9 H), 0.00 (s, 3 H), –0.02 (s, 3 H) ppm.

(3*R*,5*R*)-3-Azido-1-benzyl-5-(*tert*-butyldiphenylsilyloxy)piperidine (23f) and (2*S*,4*R*)-2-(Azidomethyl)-1-benzyl-4-(*tert*-butyldiphenylsilyloxy)pyrrolidine (24f):[20] Following the general procedure with *n*Bu$_4$NN$_3$ (51 mg, 0.18 mmol, 1.1 equiv., –78 °C, 4.5 h) and Xtal-Fluor-E (41 mg, 0.18 mmol, 1.1 equiv.), the transformation of **17c**[16g] (72 mg, 0.16 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (petroleum ether/Et_2O, 95:5) to give **23f** (55 mg, 0.12 mmol, 72%) and **24f** (2 mg, 0.004 mmol, 2%). **23f**: $[\alpha]_D^{20}$ = +42.0 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2093, 1463, 1427, 1258, 1106, 1036, 1028, 821 cm^{-1}. ^{1}H NMR: δ = 7.65–7.60 (m, 4 H), 7.44–7.22 (m, 11 H), 4.07 (dddd, *J* = 7.1, 7.1, 3.9, 3.9 Hz, 1 H), 3.83 (dddd, *J* = 7.3, 7.3, 3.6, 3.6 Hz, 1 H), 3.51 (d, *J* = 13.5 Hz, 1 H), 3.46 (d, *J* = 13.2 Hz, 1 H), 2.61 (d, *J* = 11.4 Hz, 1 H), 2.51–2.20 (m, 3 H), 1.78 (dddd, *J* = 7.1, 7.1, 4.1, 4.1 Hz, 1 H), 1.64 (dddd, *J* = 8.0, 8.0, 4.1, 4.1 Hz, 1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR: δ = 137.8 (s), 135.7 (d), 135.7 (d), 134.1 (s), 133.9 (s), 129.8 (d, 2 C), 129.7 (d, 2 C), 128.9 (d, 2 C), 128.3 (d, 2 C), 127.7 (d, 2 C), 127.6 (d, 2 C), 127.1 (d), 66.4 (d), 62.3 (t), 59.4 (t), 56.4 (t), 55.4 (d), 37.5 (t), 27.0 (q, 3 C), 19.2 (s) ppm. HRMS (ESI): calcd. for $C_{28}H_{35}ON_4Si$ [M + H$^+$] 471.2575; found 471.2573; **24f**: $[\alpha]_D^{20}$ = +10.0 (*c* = 0.8, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2096, 1427, 1273, 1105, 910, 822 cm^{-1}. ^{1}H NMR: δ = 7.66–7.57 (m, 5 H), 7.44–7.20 (m, 10 H), 4.34 (dddd, *J* = 6.6, 5.1, 5.1, 4.1 Hz, 1 H), 4.0 (d, *J* = 13.8 Hz, 1 H), 3.57 (d, *J* = 13.1 Hz, 1 H), 3.21 (dd, *J* = 11.9, 4.9 Hz, 1 H), 3.15–3.03 (m, 3 H), 2.44 (dddd, *J* = 5.6, 5.0, 0.6, 0.6 Hz, 1 H), 1.93 (m, 1 H), 1.74 (dddd, *J* = 7.0, 7.0, 7.0, 7.0 Hz, 1 H), 1.05 (s, 9 H) ppm. ^{13}C NMR: δ = 139.3 (s), 135.7 (d, 2 C), 135.7 (d, 2 C), 134.0 (s), 133.9 (s), 129.7 (d), 129.7 (d), 128.7 (d, 2 C), 128.3 (d, 2 C), 127.7 (d, 2 C), 127.7 (d, 2 C), 127.0 (d), 71.6 (d), 62.4 (d), 62.2 (t), 59.8 (t), 54.0 (t), 39.0 (t), 26.7 (q, 3 C), 19.1 (s) ppm. HRMS (ESI): calcd. for $C_{28}H_{35}ON_4Si$ [M + H$^+$] 471.2575; found 471.2572.

(*R*)-3-Azido-1-tritylpiperidine (23g) and (*S*)-2-(Azidomethyl)-1-tritylpyrrolidine (24g):[20] Following the general procedure with *n*Bu$_4$NN$_3$ (91 mg, 0.32 mmol, 1.1 equiv., –78 °C, 4.5 h) and Xtal-Fluor-E (73 mg, 0.32 mmol, 1.1 equiv.), the transformation of **26g**[27] (100 mg, 0.29 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 99:1 + 0.5% Et_3N) to give a mixture of **23g** and **24g** (72 mg, 0.20 mmol, 67%, **23g/24g** = 88:12). **23g**: ^{1}H NMR ([D$_6$]DMSO at 120 °C): δ = 7.67–6.95 (m, 15 H), 3.83 (dddd, *J* = 8.3, 8.3, 3.9, 3.9 Hz, 1 H), 2.98–2.70 (m, 2 H), 1.94–1.68 (m, 5 H), 1.31 (m, 1 H) ppm. **24g**: ^{1}H NMR ([D$_6$]DMSO at 120 °C): δ = 7.67–6.95 (m, 15 H), 3.50–3.42 (m, 2 H), 3.34 (m, 1 H), 3.25 (m, 1 H), 1.53–1.41 (m, 2 H), 1.03–0.70 (m, 4 H) ppm.

[(2*S*,4*R*)-4-(*tert*-Butyldimethylsilyloxy)-1-tritylpyrrolidin-2-yl]methanol (26h): To a solution of methyl (2*S*,4*R*)-4-hydroxy-1-tritylpyrrolidine-2-carboxylate[28] (720 mg, 1.86 mmol, 1.0 equiv.) in CH_2Cl_2 (15 mL) were added Et_3N (0.69 mL, 4.83 mmol, 2.6 equiv.), DMAP (30 mg, 0.25 mmol, 0.13 equiv.) and TBDMSCl (450 mg, 3.0 mmol, 1.6 equiv.). After 18 h at room temp., a solution of Na_2CO_3 (40 mL) was added to the reaction mixture. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), then the organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE to PE/EtOAc, 90:10 + 0.5% Et_3N), methyl (2*S*,4*R*)-4-(*tert*-butyldimethylsilyloxy)-1-tritylpyrrolidine-2-carboxylate (773 mg, 1.54 mmol, 83%) was isolated as a colorless oil. $[\alpha]_D^{20}$ = +4.5 (*c* = 1.1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 29, 2856, 1744, 1489, 1448, 1251, 1195, 1165, 1117, 1029, 1005, 898, 835 cm^{-1}. ^{1}H NMR: δ = 7.60 (m, 6 H), 7.31 (m, 6 H), 7.22 (m, 3 H), 4.55 (dddd, *J* = 8.9, 6.6, 6.6, 6.6 Hz, 1 H), 3.92 (dd, *J* = 9.1, 1.9 Hz, 1 H), 3.62 (s, 3 H), 3.61 (dd, *J* = 9.9, 6.8 Hz, 1 H), 2.57 (dd, *J* = 10.0, 6.5 Hz, 1 H), 1.78 (ddd, *J* = 12.3, 6.4, 1.8 Hz, 1 H), 1.03 (ddd, *J* = 12.3, 9.1, 9.1 Hz, 1 H), 0.84 (s, 9 H), 0.00 (s, 3 H), –0.02 (s, 3 H) ppm. ^{13}C NMR: δ = 176.6 (s), 143.7 (s, 3 C), 129.5 (d, 6 C), 127.6 (d, 6 C), 126.3 (d, 3 C), 76.7 (s), 70.7 (d), 60.9 (d), 56.2 (t), 51.6 (q), 39.5 (t), 25.8 (q, 3 C), 17.9 (s), –4.8 (q, 2 C) ppm. HRMS (ESI): calcd. for $C_{31}H_{39}NO_3SiNa$ [M + Na$^+$] 524.2591; found 524.2579. To a suspension of $LiAlH_4$ (219 mg, 5.73 mmol, 3.7 equiv.) in THF (15 mL) at 0 °C, was added dropwise a solution of the previously synthesized methyl (2*S*,4*R*)-4-(*tert*-butyldimethylsilyloxy)-1-tritylpyrrolidine-2-carboxylate (773 mg, 1.54 mmol, 1.0 equiv.) in THF (10 mL). After 2.5 h at room temp., H_2O (0.12 mL), NaOH (3.75 M, 0.12 mL) and H_2O (0.28 mL) were added dropwise at 0 °C. After 30 min at room temp., the white granular precipitate was removed by suction filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure to give **26h** (444 mg, 0.94 mmol, 61%) as a colorless oil. $[\alpha]_D^{20}$ = +52.0 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 53, 2928, 2883, 2855, 1488, 1471, 1462, 1448, 1386, 1251, 1121, 1032, 912, 895, 834, 773, 742, 733 cm^{-1}. ^{1}H NMR: δ = 7.65 (m, 6 H), 7.35 (m, 6 H), 7.24 (m, 3 H), 4.53 (dddd, *J* = 8.4, 7.3, 7.0, 6.8 Hz, 1 H), 3.64–3.49 (m, 3 H), 3.31 (dddd, *J* = 8.8, 6.1, 2.9, 2.9 Hz, 1 H), 2.56 (dd, *J* = 11.0, 6.7 Hz, 1 H), 2.06 (dd, *J* = 7.1, 4.7 Hz, 1 H), 1.79 (ddd, *J* = 12.1, 7.3, 2.4 Hz, 1 H), 0.90–0.80 (m, 10 H), 0.00 (s, 3 H), –0.02 (s, 3 H) ppm. ^{13}C NMR: δ = 144.0 (s, 3 C), 129.7 (d, 6 C), 127.9 (d, 6 C), 126.3 (d, 3 C), 77.2 (s), 71.0 (d), 66.0 (t), 60.2 (d), 58.0 (t), 38.7 (t), 25.8 (q, 3 C), 17.9 (s), –4.8 (q), –4.8 (q) ppm. HRMS (ESI): calcd. for $C_{30}H_{40}NO_3Si$ [M + H$^+$] 474.2823; found 474.2818.

(3*R*,5*R*)-3-Azido-5-(*tert*-butyldimethylsilyloxy)-1-tritylpiperidine (23h) and (2*S*,4*R*)-2-(Azidomethyl)-4-(*tert*-butyldimethylsilyloxy)-1-tritylpyrrolidine (24h): Following the general procedure with nBu$_4$NN$_3$ (178 mg, 0.63 mmol, 1.1 equiv., –78 °C, 30 min) and XtalFluor-E (143 mg, 0.63 mmol, 1.1 equiv.), the transformation of **26h** (269 mg, 0.57 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/EtOAc, 90:10) to give a mixture of **23h** and **24h** (205 mg, 0.41 mmol, 72%, **23h**/**24h** = 86:14). **23h**: IR (neat): $\tilde{\nu}$ = 2098, 1489, 1470, 1448, 1253, 1184, 1144, 1090, 1013, 858, 835, 774, 743 cm^{-1}. ^{1}H NMR ([D$_6$]-DMSO at 120 °C): δ = 7.67–7.26 (m, 15 H), 4.35 (dddd, J = 7.7, 7.7, 3.8, 3.8 Hz, 1 H), 4.11 (m, 1 H), 2.70–2.50 (m, 2 H), 2.29 (m, 1 H), 2.03 (m, 2 H), 1.69 (ddd, J = 13.5, 8.0, 4.2 Hz, 1 H), 1.05 (s, 9 H), 0.22 (s, 3 H), 0.18 (s, 3 H) ppm.

(3*R*,5*R*)-3-Azido-5-(*tert*-butyldiphenylsilyloxy)-1-tritylpiperidine (23i):[20] Following the general procedure with nBu$_4$NN$_3$ (78 mg, 0.28 mmol, 1.1 equiv., 0 °C, 30 min) and XtalFluor-E (63 mg, 0.28 mmol, 1.1 equiv.), the transformation of **26i**[20] (79 mg, 0.25 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et$_2$O, 98:2 + 0.5% Et$_3$N) to give **23i** (68 mg, 0.11 mmol, 65%). $[\alpha]_D^{20}$ = +24.0 (c = 0.7, CHCl$_3$). IR (neat): $\tilde{\nu}$ = 2098, 1448, 1428, 1110 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO at 120 °C): δ = 7.72–7.13 (m, 25 H), 4.39 (dddd, J = 6.8, 6.8, 2.7, 2.7 Hz, 1 H), 3.96 (dddd, J = 4.8, 4.8, 2.7, 2.7 Hz, 1 H), 2.69 (d, J = 11.5 Hz, 1 H), 2.53 (m, 1 H), 2.07 (d, J = 11.5 Hz, 1 H), 1.97–1.76 (m, 2 H), 1.52 (dddd, J = 8.6, 8.6, 4.3, 4.3 Hz, 1 H), 1.07 (s, 9 H) ppm. HRMS (ESI): calcd. for C$_{40}$H$_{42}$ON$_4$NaSi [M + Na$^+$] 645.3020; found 645.3025.

(3*R*,5*S*)-3-Azido-1-benzyl-5-fluoropiperidine (28a) and (2*S*,4*S*)-2-(Azidomethyl)-1-benzyl-4-fluoropyrrolidine (29a):[20] Following the general procedure with nBu$_4$NN$_3$ (75 mg, 0.26 mmol, 1.1 equiv., –78 °C, 4 h) and XtalFluor-E (60 mg, 0.26 mmol, 1.1 equiv.), the transformation of **27a**[20] (51 mg, 0.24 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et$_2$O, 80:20) to give a mixture of **28a** and **29a** (33 mg, 0.14 mmol, 58%, **28a**/**29a** = 50:50). **28a**: IR (neat): $\tilde{\nu}$ = 2094, 1454, 1273, 1089, 1071, 1028 cm^{-1}. ^{1}H NMR: δ = 7.37–7.22 (m, 5 H), 4.61 (ddddd, J = 48.1, 9, 9, 4.5, 4.5 Hz, 1 H), 3.6 (s, 2 H), 3.47 (m, 1 H), 3.02 (m, 1 H), 2.87 (m, 1 H), 2.94–1.93 (m, 3 H), 1.56 (m, 1 H) ppm. MS: m/z (%) = 234 (0.1) [M$^{+\cdot}$], 178 (12), 102 (30), 91 (100), 88 (35), 65 (24); **29a**: IR (neat): $\tilde{\nu}$ = 2094, 1454, 1273, 1089, 1071, 1028 cm^{-1}. ^{1}H NMR: δ = 7.37–7.22 (m, 5 H), 5.07 (app. d, J = 54.2 Hz, 1 H), 4.08 (d, J = 13.3 Hz, 1 H), 3.43 (d, J = 13.1 Hz, 1 H), 3.40–3.18 (m, 3 H), 2.87 (m, 1 H), 2.94–1.93 (m, 3 H) ppm. MS: m/z (%) = 178 (20) [M$^{+\cdot}$ – CH$_2$N$_3^{\cdot}$], 91 (100), 65 (13); **28a** + **29a**: ^{13}C NMR: δ = 138.3 (s), 137.1 (s), 129.0 (d), 128.7 (d), 128.4 (d), 127.5 (d), 127.3 (d), 92.1 (dd, J = 177 Hz), 86.3 (dd, J = 174.6 Hz), 62.3 (d), 62.1 (t), 60.4 (dt, J = 21.6 Hz), 58.7 (t), 56.6 (dt, J = 21.2 Hz), 56.6 (dt, J = 24.8 Hz), 54.9 (dd, J = 11.6 Hz), 54.2 (t), 36.6 (dt, J = 22.4 Hz), 36.0 (dt, J = 20 Hz) ppm.

(3*R*,5*R*)-3-Azido-1-benzyl-5-fluoropiperidine (28b) and (2*S*,4*R*)-2-(Azidomethyl)-1-benzyl-4-fluoropyrrolidine (29b):[20] Following the general procedure with nBu$_4$NN$_3$ (153 mg, 0.54 mmol, 1.1 equiv., –78 °C, 4 h) and XtalFluor-E (123 mg, 0.54 mmol, 1.1 equiv.), the transformation of **27b**[20] (103 mg, 0.49 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et$_2$O, 90:10) to give a mixture of **28b** and **29b** (76 mg, 0.32 mmol, 66%, **28b**/**29b** = 93:7). **28b**: IR (neat): $\tilde{\nu}$ = 2926, 2097, 1454, 1257, 1152, 1055, 1029, 989, 930 cm^{-1}. ^{1}H NMR: δ = 7.36–7.24 (m, 5 H), 4.84 (ddddd, J = 47.2, 5.3, 5.3, 3.0, 3.0 Hz, 1 H), 3.84 (dddd, J = 8.5, 8.5, 4.1, 4.1 Hz, 1 H), 3.61 (s, 2 H), 2.90–2.77 (m, 2 H), 2.43 (ddd, J = 29.2, 12.4, 2.1 Hz, 1 H), 2.28–2.21 (m, 2 H), 1.68 (dddd, J = 32.1, 13.2, 9.5, 3.1 Hz, 1 H) ppm. ^{13}C NMR: δ = 137.0 (s), 129.0 (d, 2 C), 128.4 (d, 2 C), 127.4 (d), 86.5 (dd, J = 173.4 Hz), 62.2 (t), 56.3 (t), 56.0 (dt, J = 21.2 Hz), 54.4 (dd, J = 3.6 Hz), 34.8 (dt, J = 21.2 Hz) ppm. MS m/z (%) = 234 (0.2) [M$^{+\cdot}$], 178 (13), 132 (7), 102 (32), 91 (100), 88 (37), 65 (23); **29b**: IR (neat): $\tilde{\nu}$ = 2926, 2097, 1454, 1257, 1152, 1055, 1029, 989, 930 cm^{-1}. MS m/z (%) =178 (15) [M$^{+\cdot}$ – CH$_2$N$_3^{\cdot}$], 91 (100), 65 (14).

(*R*)-5-Azido-1-benzyl-3,3-difluoropiperidine (28c) and (*S*)-2-(Azidomethyl)-1-benzyl-4,4-difluoropyrrolidine (29c):[20] Following the general procedure with nBu$_4$NN$_3$ (159 mg, 0.56 mmol, 1.1 equiv., –78 °C, 4 h) and XtalFluor-E (128 mg, 0.56 mmol, 1.1 equiv.), the transformation of **27c**[20] (115 mg, 0.51 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et$_2$O, 90:10) to give a mixture of **28c** and **29c** (85 mg, 0.34 mmol, 66%, **28c**/**29c** = 91:9). **28c**: IR (neat): $\tilde{\nu}$ = 2099, 1454, 1281, 1253, 1188, 1103, 1084, 1012, 976, 918, 820 cm^{-1}. ^{1}H NMR: δ = 7.41–7.21 (m, 5 H), 3.76–3.60 (m, 3 H), 3.0–2.88 (m, 2 H), 2.47–2.32 (m, 2 H), 2.17 (dd, J = 10.0 Hz, 1 H), 1.76 (m, 1 H) ppm. ^{13}C NMR: δ = 136.5 (s), 128.9 (d, 2 C), 128.6 (d, 2 C), 127.7 (d), 119.5 (dds, J = 243.0, 243.0 Hz), 61.5 (t), 57.4 (ddt, J = 29.2, 25.6 Hz), 55.9 (t), 54.4 (dd, J = 9.2 Hz), 37.9 (ddt, J = 24.0, 24.0 Hz) ppm. MS m/z (%) = 252 (0.1) [M$^{+\cdot}$], 196 (15), 120 (25), 106 (23), 91 (100), 65 (20); **29c**: IR (neat): $\tilde{\nu}$ = 2099, 1454, 1281, 1253, 1188, 1103, 1084, 1012, 976, 918, 820 cm^{-1}. ^{1}H NMR: δ = 7.41–7.21 (m, 5 H), 4.08 (d, J = 13.3 Hz, 1 H), 3.46 (m, 1 H), 3.39 (dd, J = 13.2 Hz, 1 H), 3.31–3.20 (m, 2 H), 3.05 (m, 1 H), 2.73–2.52 (m, 2 H), 2.27 (m, 1 H) ppm. MS m/z (%) = 196 (11) [M$^{+\cdot}$ – CH$_2$N$_3^{\cdot}$], 91 (100), 65 (14).

(3*S*,5*S*)-5-Azido-1-benzyl-3-(dibenzylamino)piperidine (31a) and (3*S*,5*R*)-5-(Azidomethyl)-1-benzyl-3-(dibenzylamino)pyrrolidine (32a):[20] Following the general procedure with nBu$_4$NN$_3$ (31 mg, 0.11 mmol, 1.1 equiv., 0 °C, 4.5 h) and XtalFluor-E (25 mg, 0.11 mmol, 1.1 equiv.), the transformation of **30a**[20] (40 mg, 0.10 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et$_2$O, 70:30) to give a mixture of **31a** and **32a** (23 mg, 0.06 mmol, 56%, **31a**/**32a**: 50:50). **31a**: IR (neat): $\tilde{\nu}$ = 2096, 1493, 1453, 1364, 1275, 1153, 1072, 1050, 1028, 967 cm^{-1}. ^{1}H NMR: δ = 7.34–7.17 (m, 15 H), 3.69–3.46 (m, 6 H), 3.39 (m, 1 H), 3.20 (m, 1 H), 3.05–2.97 (m, 2 H), 2.83 (m, 1 H), 2.26 (dd, J = 9.1, 9.1 Hz, 1 H), 2.00 (m, 1 H), 1.87 (ddd, J = 13.1, 8.8, 5.6 Hz, 1 H) ppm. **32a**: IR (neat): $\tilde{\nu}$ = 2096, 1493, 1453, 1364, 1275, 1153, 1072, 1050, 1028, 967 cm^{-1}. ^{1}H NMR: δ = 7.34–7.17 (m, 15 H), 3.94 (d, J = 12.9 Hz, 1 H), 3.80 (dddd, J = 3.2, 3.2, 3.2, 3.2 Hz, 1 H), 3.69–3.46 (m, 4 H), 3.39 (m, 1 H), 3.25 (dd, J = 12.4, 5.6 Hz, 1 H), 3.14 (dd, J = 12.7, 4.0 Hz, 1 H), 2.83 (m, 1 H), 2.26 (dd, J = 9.1, 9.1 Hz, 1 H), 2.00 (m, 1 H), 1.61 (ddd, J = 13.5, 11.6, 3.8 Hz, 1 H) ppm. **31a** + **32a**: ^{13}C NMR: δ = 140.2 (s), 139.7 (s), 138.8 (s), 137.5 (s), 129.0 (d), 128.8 (d), 128.7 (d), 128.4 (d), 128.4 (d), 128.3 (d), 128.2 (d), 127.1 (d), 126.9 (d), 62.7 (t), 62.2 (d), 59.1 (t), 58.7 (d), 57.4 (t), 56.4 (d), 55.8 (t), 54.5 (t), 54.4 (t), 51.7 (d), 32.2 (t), 30.5 (t) ppm.

***tert*-Butyl [(3*S*,5*S*)-5-Azido-1-(4-methoxybenzyl)piperidin-3-yl]carbamate (31b) and *tert*-Butyl [(3*S*,5*R*)-5-(Azidomethyl)-1-(4-methoxybenzyl)pyrrolidin-3-yl]carbamate (32b):**[20] Following the general procedure with nBu$_4$NN$_3$ (47 mg, 0.17 mmol, 1.1 equiv., 0 °C, 4.5 h) and XtalFluor-E (38 mg, 0.17 mmol, 1.1 equiv.), the transformation of **30b**[20] (50 mg, 0.15 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/EtOAc, 70:30 to 60:40) to give **31b** (17 mg, 0.05 mmol, 31%) as a yellow solid and **32b** (13 mg, 0.04 mmol, 24%) as a yellow solid. **31b**: M.p. 83 °C. $[\alpha]_D^{20}$ = +1.0 (c = 1.0, CHCl$_3$). IR (neat): $\tilde{\nu}$ = 3351, 2928, 2099, 1710, 1512, 1366, 1300, 1249, 1172, 821 cm^{-1}.

^{1}H NMR: δ = 7.19 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 5.05 (br. s, 1 H), 3.96 (m, 1 H), 3.81 (s, 3 H), 3.62 (m, 1 H), 3.50 (d, J = 13.3 Hz, 1 H), 3.45 (d, J = 12.8 Hz, 1 H), 2.88 (m, 1 H), 2.57 (m, 1 H), 2.30 (m, 1 H), 2.17–1.91 (m, 2 H), 1.50–1.44 (m, 10 H) ppm. ^{13}C NMR: δ = 159.0 (s), 155.0 (s), 130.2 (d, 2 C), 129.2 (s), 113.8 (d, 2 C), 79.5 (s), 61.8 (t), 57.1 (t), 57.0 (t), 55.3 (d), 54.6 (q), 45.3 (d), 34.7 (t), 28.5 (q, 3 C) ppm. HRMS (ESI): calcd. for $C_{18}H_{28}O_3N_5$ [M + H$^+$] 362.2187; found 362.2179; **32b**: M.p. 66–70 °C. $[\alpha]_D^{20}$ = +15.0 (c = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3339, 2927, 2099, 1698, 1513, 1366, 1298, 1249, 1172, 1037 cm^{-1}. ^{1}H NMR: δ = 7.21 (d, J = 8.5 Hz, 2 H), 6.85 (d, J = 8.5 Hz, 2 H), 4.42 (br. s, 1 H), 4.14 (m, 1 H), 3.92 (d, J = 13.1 Hz, 1 H), 3.80 (s, 3 H), 3.41 (d, J = 13.0 Hz, 1 H), 3.32–3.21 (m, 2 H), 3.15 (dd, J = 12.7, 3.8 Hz, 1 H), 2.91 (m, 1 H), 2.18–2.04 (m, 2 H), 1.74 (ddd, J = 12.5, 8.3, 8.3 Hz, 1 H), 1.42 (s, 9 H) ppm. ^{13}C NMR: δ = 158.8 (s), 155.3 (s), 130.5 (s), 129.8 (d, 2 C), 113.8 (d, 2 C), 79.5 (s), 61.6 (d), 59.8 (t), 58.0 (t), 55.3 (q), 54.0 (t), 48.5 (d), 36.3 (t), 28.4 (q, 3 C) ppm. HRMS (ESI): calcd. for $C_{18}H_{28}O_3N_5$ [M + H$^+$] 362.2187; found 362.2178.

***tert*-Butyl [(3*S*,5*S*)-5-Azido-1-tritylpiperidin-3-yl]carbamate (31c) and *tert*-Butyl [(3*S*,5*S*)-5-Azido-1-tritylpiperidin-3-yl]carbamate (32c):**[20] Following the general procedure with nBu$_4$NN$_3$ (69 mg, 0.24 mmol, 1.1 equiv., 0 °C, 2.5 h) and XtalFluor-E (55 mg, 0.24 mmol, 1.1 equiv.), the transformation of **30c**[20] (100 mg, 0.22 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/EtOAc, 90:10 to 80:20) to give **31c** (79 mg, 0.16 mmol, 74%) as a white solid and **32c** (18 mg, 0.04 mmol, 17%) as a colorless oil. **31c**: M.p. 100 °C. $[\alpha]_D^{20}$ = –50.0 (c = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2099, 1695, 1491, 1448, 1391, 1366, 1250, 1164, 1045, 1028 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO at 120 °C): δ = 7.50–7.44 (m, 5 H), 7.33–7.25 (m, 7 H), 7.22–7.14 (m, 3 H), 6.49 (br. s, 1 H), 4.09 (m, 1 H), 3.95 (dddd, J = 11.8, 7.9, 7.9, 3.7 Hz, 1 H), 2.48–2.17 (m, 3 H), 1.94 (m, 1 H), 1.76 (m, 1 H), 1.60 (dddd, J = 12.5, 7.8, 4.9 Hz, 1 H), 1.43 (s, 9 H) ppm. HRMS (ESI): calcd. for [M + Na$^+$] 506.2527; found 506.2519; **32c**: IR (neat): $\tilde{\nu}$ = 2099, 1695, 1491, 1448, 1391, 1366, 1250, 1164, 1045, 1028 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO at 120 °C): δ = 7.56–7.48 (m, 6 H), 7.35–7.25 (m, 6 H), 7.25–7.15 (m, 3 H), 5.21 (br. s, 1 H), 4.04 (m, 1 H), 3.78–3.40 (m, 3 H), 3.27 (m, 1 H), 2.66 (dd, J = 7.2, 7.2 Hz, 1 H), 2.37 (m, 1 H), 1.95–1.77 (m, 1 H), 1.35 (s, 9 H) ppm.

***N*-[(3*S*,5*R*)-5-Azido-1-benzylpiperidin-3-yl]ethanamide (31d) and *N*-[(3*S*,5*S*)-5-(Azidomethyl)-1-benzylpyrrolidin-3-yl]ethanamide (32d):** Following the general procedure with nBu$_4$NN$_3$ (54 mg, 0.19 mmol, 1.1 equiv., 0 °C, 4 h) and XtalFluor-E (44 mg, 0.19 mmol, 1.1 equiv.), the transformation of **6** (43 mg, 0.17 mmol, 1 equiv) afforded an oil that was purified by flash column chromatography on silica gel (Et$_2$O/MeOH, 98:2) to give a mixture of **31d** and **32d** (24 mg, 0.09 mmol, 51%, **31d**/**32d** = 82:18). **31d**: ^{1}H NMR: δ = 7.37–7.23 (m, 5 H), 6.23 (br. s, 1 H), 4.13 (m, 1 H), 3.69 (m, 1 H), 3.56 (s, 2 H), 2.68–2.53 (m, 2 H), 2.50–2.21 (m, 2 H), 1.99 (m, 1 H), 1.97 (s, 3 H), 1.55 (m, 1 H) ppm. ^{13}C NMR: δ = 169.3 (s), 137.3 (s), 128.9 (d, 2 C), 128.4 (d, 2 C), 127.4 (d), 62.3 (t), 57.4 (t), 56.2 (t), 56.1 (d), 44.1 (d), 33.8 (t), 23.5 (q) ppm. MS: m/z(%) = 215 (5) [M$^{+\cdot}$ – AcNH$^{\cdot}$], 214 (35), 186 (3), 184 (4), 158 (13), 92 (9), 91 (100), 68 (25), 65 (13); **32d**: ^{1}H NMR: δ = 7.37–7.23 (m, 5 H), 4.34 (m, 1 H), 3.99 (d, J = 13.1 Hz, 1 H), 3.46 (dd, J = 12.8, 3.8 Hz, 1 H), 3.40 (d, J = 13.1 Hz, 1 H), 3.18 (dd, J = 12.9, 3.1 Hz, 1 H), 2.80 (m, 2 H), 2.50–2.21 (m, 2 H), 1.95 (s, 3 H), 1.64 (dddd, J = 14.0, 5.4, 1.8, 1.8 Hz, 1 H) ppm. ^{13}C NMR: δ = 169.3 (s), 137.3 (s), 128.9 (d, 2 C), 128.4 (d, 2 C), 127.4 (d), 61.9 (d), 60.3 (t), 58.2 (t), 53.0 (t), 47.4 (d), 36.1 (t), 23.5 (q) ppm. MS: m/z(%) = 217 (6) [M$^{+\cdot}$ – CH$_2$N$_3^{\cdot}$], 158 (27), 157 (14), 92 (8), 91 (100), 65 (16).

***tert*-Butyl [(3*S*,5*R*)-5-Azido-1-benzylpiperidin-3-yl]carbamate (31e) and [*tert*-Butyl (3*S*,5*S*)-5-(Azidomethyl)-1-benzylpyrrolidin-3-yl]-carbamate (32e):**[20] Following the general procedure with nBu$_4$NN$_3$ (103 mg, 0.36 mmol, 1.1 equiv., 0 °C, 15 min) and XtalFluor-E (83 mg, 0.36 mmol, 1.1 equiv.), the transformation of **7** (100 mg, 0.33 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (CH$_2$Cl$_2$/MeOH, 98:2) to give a mixture of **31e** and **32e** (68 mg, 0.21 mmol, 63%, **31e**/**32e** = 90:10). **31e**: IR (neat): $\tilde{\nu}$ = 2095, 1693, 1496, 1365, 1250, 1165, 1070 cm^{-1}. ^{1}H NMR ([D$_6$]DMSO at 120 °C): δ = 7.37–7.21 (m, 5 H), 6.17 (br. s, 1 H), 3.67–3.49 (m, 4 H), 2.91 (dd, J = 10.9, 4.2 Hz, 1 H), 2.84 (dd, J = 10.7, 4.1 Hz, 1 H), 2.09 (dd, J = 10.8, 10.8 Hz, 1 H), 1.97 (dd, J = 10.8, 10.8 Hz, 1 H), 1.90 (dd, J = 10.8, 10.8 Hz, 1 H), 1.40 (s, 9 H), 1.31 (ddd, J = 12.0, 12.0, 12.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 155.1 (s), 137.4 (s), 128.9 (d, 2 C), 128.4 (d, 2 C), 127.3 (d), 79.5 (s), 62.3 (t), 57.9 (t), 56.3 (t), 56.1 (d), 45.6 (d), 35.1 (t), 28.4 (q, 3 C) ppm.

(3*S*,5*R*)-5-Azido-1-benzyl-3-(dibenzylamino)piperidine (31f):[20] Following the general procedure with nBu$_4$NN$_3$ (94 mg, 0.33 mmol, 1.1 equiv., 0 °C, 4.5 h) and XtalFluor-E (76 mg, 0.33 mmol, 1.1 equiv.), the transformation of **5** (116 mg, 0.30 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/EtOAc, 95:5) to give **31f** (70 mg, 0.17 mmol, 57%). $[\alpha]_D^{20}$ = +4.0 (c = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2091, 1494, 1453, 1254, 1065 cm^{-1}. ^{1}H NMR: δ = 7.34–7.18 (m, 15 H), 3.72 (d, J = 14.0 Hz, 2 H), 3.61 (d, J = 14.0 Hz, 2 H), 3.58 (d, J = 13.1 Hz, 1 H), 3.49 (d, J = 13.1 Hz, 1 H), 3.36 (dddd, J = 13.4, 9.0, 9.0, 4.2 Hz, 1 H), 3.0 (ddd, J = 10.4, 2.1, 21 Hz, 1 H), 2.93 (ddd, J = 12.3, 2.9, 2.9 Hz, 1 H), 2.86 (m, 1 H), 2.25 (m, 1 H), 1.98 (dd, J = 10.4, 10.4 Hz, 1 H), 1.77 (dd, J = 10.7, 10.7 Hz, 1 H), 1.41 (ddd, J = 11.7, 11.7, 11.7 Hz, 1 H) ppm. ^{13}C NMR: δ = 140.10 (s, 2 C), 137.7 (s), 128.7 (d, 2 C), 128.4 (d, 4 C), 128.3 (d, 2 C), 128.3 (d, 4 C), 127.2 (d), 126.9 (d, 2 C), 62.5 (t), 57.5 (d), 57.0 (t), 54.7 (t), 54.4 (t, 2 C), 54.0 (d), 32.0 (t) ppm. HRMS (ESI): calcd. for $C_{20}H_{30}N_5$ [M + H$^+$] 412.2496; found 412.2497.

(3*S*,5*R*)-5-Azido-1-benzyl-3-(tritylamino)piperidine (31g):[20] Following the general procedure with nBu$_4$NN$_3$ (31 mg, 0.11 mmol, 1.1 equiv., 0 °C, 4.5 h) and XtalFluor-E (25 mg, 0.11 mmol, 1.1 equiv.), the transformation of **30g**[20] (43 mg, 0.10 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/EtOAc, 60:40 + 0.5% Et$_3$N) to give **31g** (38 mg, 0.08 mmol, 84%). $[\alpha]_D^{20}$ = +12.0 (c = 1.8, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2093, 1490, 1448, 1069, 1028, 902 cm^{-1}. ^{1}H NMR: δ = 7.58–7.07 (m, 20 H), 3.35 (d, J = 13.2 Hz, 1 H), 3.30 (d, J = 13.2 Hz, 1 H), 3.18 (dddd, J = 10.3, 10.3, 4.5, 4.5 Hz, 1 H), 2.74 (dd, J = 10.9, 4.3 Hz, 1 H), 2.64 (dddd, J = 10.4, 7.8, 7.8, 3.9 Hz, 1 H), 2.22 (dd, J = 11.0, 3.8 Hz, 1 H), 1.79 (dd, J = 10.2, 10.2 Hz, 1 H), 1.55 (br. s, 1 H), 1.42 (m, 1 H), 0.95 (ddd, J = 11.3, 11.3, 11.3 Hz, 1 H) ppm. ^{13}C NMR: δ = 146.9 (s, 3 C), 137.6 (s), 129.0 (d, 2 C), 128.6 (d, 6 C), 128.3 (d, 2 C), 127.9 (d, 6 C), 127.1 (d), 126.4 (d, 3 C), 71.3 (s), 62.3 (t), 60.0 (t), 57.0 (t), 56.4 (d), 48.9 (d), 38.3 (t) ppm. HRMS (ESI): calcd. for $C_{31}H_{32}N_5$ [M + H$^+$] 474.2652; found 474.2646.

(1-Benzyl-2-ethylpyrrolidin-2-yl)methanol (33): To a solution of methyl (*S*)-1-benzylpyrrolidine-2-carboxylate[16g] (876 mg, 4.0 mmol, 1 equiv.) in THF (10 mL) at –78 °C was added dropwise a solution of LDA (1 M in THF, 4.4 mL, 4.4 mmol, 1.1 equiv.). After 30 min at –78 °C, EtI (0.38 mL, 4.8 mmol, 1.2 equiv.) was added dropwise. The temperature was raised slowly to room temp. during 3 h and then a saturated aqueous solution of NaHCO$_3$ was added to the reaction mixture, which was then extracted with EtOAc. The organic layer was then dried with MgSO$_4$, filtered, and

concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE/EtOAc, 95:5 to 90:10), methyl 1-benzyl-2-ethylpyrrolidine-2-carboxylate (759 mg, 3.07 mmol, 77%) was isolated as a yellow oil. IR (neat): $\tilde{\nu}$ = 2967, 2803, 1722, 1454, 1224, 1170, 1134, 1108 cm^{-1}. ^1H NMR: δ = 7.37–7.18 (m, 5 H), 3.96 (d, J = 13.9 Hz, 1 H), 3.73 (s, 3 H), 3.29 (d, J = 13.7 Hz, 1 H), 2.90 (m, 1 H), 2.50 (ddd, J = 8.7, 7.5, 7.5 Hz, 1 H), 2.22 (m, 1 H), 2.02 (dq, J = 14.6, 7.3 Hz, 1 H), 1.88–1.70 (m, 3 H), 1.63 (dq, J = 13.8, 7.4 Hz, 1 H), 0.96 (dd, J = 7.4, 7.4 Hz, 3 H) ppm. ^{13}C NMR: δ = 175.0 (s), 140.5 (s), 128.3 (d, 2 C), 128.2 (d, 2 C), 126.6 (d), 71.1 (s), 53.4 (t), 51.4 (t), 51.0 (q), 33.3 (t), 27.6 (t), 21.7 (t), 8.7 (q) ppm. MS: m/z(%) = 247 (0.1) [$M^{+\cdot}$], 189 (7), 188 (54), 92 (8), 91 (100), 65 (10). HRMS (ESI): calcd. for $C_{15}H_{22}NO_2$ [M + H^+] 248.16451; found 248.16404. To a suspension of $LiAlH_4$ (233, 6.14 mmol, 2 equiv.) in THF (20 mL) at 0 °C was added dropwise a solution of the previously synthesized methyl 1-benzyl-2-ethylpyrrolidine-2-carboxylate (759 mg, 3.07 mmol, 1 equiv.) in THF (15 mL). After 2 h at room temp., H_2O (0.12 mL), NaOH (3.75 m, 0.12 mL), and water (0.28 mL) were added dropwise at 0 °C. After 1 h at room temp., the mixture was filtered through a pad of Celite, the filtrate was concentrated under reduced pressure and **33** (405 mg, 1.85 mmol, 60%) was isolated as an oil. IR (neat): $\tilde{\nu}$ = 3416, 2963, 2878, 2804, 1454, 1412, 1365, 1308, 1141, 1054, 1027 cm^{-1}. ^1H NMR: δ = 7.35–7.21 (m, 5 H), 3.83 (d, J = 13.0 Hz, 1 H), 3.74 (d, J = 10.5 Hz, 1 H), 3.37 (d, J = 10.7 Hz, 1 H), 3.34 (d, J = 13.3 Hz, 1 H), 2.91 (ddd, J = 9.1, 7.5, 3.0 Hz, 1 H), 2.51 (ddd, J = 9.1, 9.1, 7.7 Hz, 1 H), 1.93 (ddd, J = 12.7, 10.0, 5.3 Hz, 1 H), 1.82 (m, 1 H), 1.76–1.60 (m, 2 H), 1.60–1.40 (m, 2 H), 0.91 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR: δ = 140.0 (s), 128.6 (d, 2 C), 128.4 (d, 2 C), 127.0 (d), 66.5 (s), 63.6 (t), 51.9 (t), 51.3 (t), 31.4 (t), 24.5 (t), 22.3 (t), 8.7 (q) ppm. MS: m/z (%) = 219 (0.04) [$M^{+\cdot}$], 189 (5), 188 (37), 98 (4), 92 (8), 91 (100), 65 (9). HRMS (ESI): calcd. for $C_{14}H_{22}NO$ [M + H^+] 220.16959; found 220.16885.

3-Azido-1-benzyl-3-ethylpiperidine (34) and 2-(Azidomethyl)-1-benzyl-2-ethylpyrrolidine (35): Following the general procedure with n-Bu_4NN_3 (94 mg, 0.33 mmol, 1.1 equiv., 0 °C, 3.5 h) and Xtal-Fluor-E (76 mg, 0.33 mmol, 1.1 equiv.), the transformation of **33** (65 mg, 0.30 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et_2O, 98:2 to 90:10) to give **34** (23 mg, 0.09 mmol, 31%) and **35** (16 mg, 0.07 mmol, 22%). **34**: IR (neat): $\tilde{\nu}$ = 2940, 2093, 1763, 1455, 1310, 1275, 1124, 875 cm^{-1}. ^1H NMR: δ = 7.36–7.22 (m, 5 H), 3.54 (d, J = 13.0 Hz, 1 H), 3.48 (d, J = 13.0 Hz, 1 H), 2.65–2.50 (m, 2 H), 2.24–2.09 (m, 2 H), 1.78 (m, 1 H), 1.70–1.52 (m, 4 H), 1.40 (m, 1 H), 0.89 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR: δ = 138.1 (s), 129.0 (d, 2 C), 128.2 (d, 2 C), 127.1 (d), 63.0 (t), 63.0 (s), 60.4 (t), 53.4 (t), 33.0 (t), 30.8 (t), 22.2 (t), 7.6 (q) ppm. MS: m/z(%) = 244 (0.1) [$M^{+\cdot}$], 188 (3), 160 (19), 92 (13), 91 (100), 70 (37), 65 (15). HRMS (ESI): calcd. for $C_{14}H_{21}N_4$ [M + H^+] 245.1761; found 245.1755; **35**: IR (neat): $\tilde{\nu}$ = 2965, 2925, 2095, 1726, 1494, 1453, 1360, 1282, 1153 cm^{-1}. ^1H NMR: δ = 7.37–7.18 (m, 5 H), 3.75 (d, J = 13.4 Hz, 1 H), 3.69 (d, J = 13.4 Hz, 1 H), 3.39 (d, J = 12.3 Hz, 1 H), 3.25 (d, J = 12.5 Hz, 1 H), 2.72–2.66 (m, 2 H), 1.85–1.46 (m, 6 H), 0.95 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR: δ = 140.7 (s), 128.2 (d, 2 C), 128.2 (d, 2 C), 126.6 (d), 65.3 (s), 56.8 (t), 52.3 (t), 51.5 (t), 32.6 (t), 26.6 (t), 22.0 (t), 8.8 (q) ppm. MS: m/z(%) = 188 (36) [$M^{+\cdot}$ –$CH_2N_3^{\cdot}$], 130 (4), 104 (7), 92 (8), 91 (100), 65 (13). HRMS (ESI): calcd. for $C_{14}H_{21}N_4$ [M + H^+] 245.1761; found 245.1755.

(3*S*,4*S*)-3-Azido-1-benzyl-4-(*tert*-butyldimethylsilyloxy)piperidine (37) and (2*R*,3*S*)-2-(Azidomethyl)-1-benzyl-3-(*tert*-butyldimethylsilyloxy)pyrrolidine (38): Following the general procedure with n-Bu_4NN_3 (97 mg, 0.34 mmol, 1.1 equiv., 0 °C, 3.5 h) and Xtal-Fluor-E (78 mg, 0.34 mmol, 1.1 equiv.), the transformation of **36**[24] (100 mg, 0.31 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et_2O, 95:5) to give a mixture of **37** and **38** (44 mg, 0.13 mmol, 41%, **37**/**38**, 40:60). **37**: IR (neat): $\tilde{\nu}$ = 2953, 2929, 2857, 2100, 1471, 1454, 1372, 1295, 1254, 1103, 1048, 907, 834 cm^{-1}. ^1H NMR: δ = 7.29–7.13 (m, 5 H), 3.43 (s, 2 H), 3.37 (m, 1 H), 3.28 (ddd, J = 9.7, 8.1, 4.3 Hz, 1 H), 2.84 (m, 1 H), 2.65 (dddd, J = 11.6, 4.2, 4.2, 2.0 Hz, 1 H), 1.98 (ddd, J = 11.4, 11.4, 2.8 Hz, 1 H), 1.86 (m, 1 H), 1.76 (m, 1 H), 1.56 (m, 1 H), 0.83 (s, 9 H), 0.04 (s, 3 H), 0.00 (s, 3 H) ppm. **38**: IR (neat): $\tilde{\nu}$ = 2953, 2929, 2857, 2100, 1471, 1454, 1372, 1295, 1254, 1103, 1048, 907, 834, 775 cm^{-1}. ^1H NMR: δ = 7.29–7.13 (m, 5 H), 4.08 (ddd, J = 6.2, 2.9, 2.9 Hz, 1 H), 3.90 (d, J = 13.0 Hz, 1 H), 3.44 (d, J = 13.0 Hz, 1 H), 3.18 (dd, J = 12.8, 5.4 Hz, 1 H), 3.06 (dd, J = 12.9, 3.8 Hz, 1 H), 2.84 (m, 1 H), 2.55 (ddd, J = 5.4, 3.5, 3.5 Hz, 1 H), 2.48 (ddd, J = 10.7, 8.9, 7.0 Hz, 1 H), 1.86 (m, 1 H), 1.56 (m, 1 H), 0.82 (s, 9 H), 0.00 (s, 3 H), –0.02 (s, 3 H) ppm. MS: m/z (%) = 291 (14), 290 (61) [$M^{+\cdot}$ – $CH_2N_3^{\cdot}$], 92 (8), 91 (100), 75 (12), 73 (40). **37** + **38**: ^{13}C NMR: δ = 139.2 (s), 138.0 (s), 128.9 (d), 128.8 (d), 128.3 (d), 127.2 (d), 127.1 (d), 74.8 (d), 73.3 (d), 72.5 (d), 64.4 (d), 62.3 (t), 59.6 (t), 55.4 (t), 52.0 (t), 51.9 (t), 50.8 (t), 33.5 (t), 33.3 (t), 25.8 (q), 25.8 (q), 18.0 (s), –4.5 (q), –4.6 (q), –4.8 (q),–4.9 (q) ppm.

[(2*R*,3*R*)-1-Benzyl-3-(*tert*-butyldiphenylsilyloxy)pyrrolidin-2-yl]methanol (39): To a suspension of *trans*-3-hydroxy-L-proline (1.4 g, 10.69 mmol, 1.0 equiv.) in MeOH (70 mL) was added $SOCl_2$ (1.54 mL, 21.37 mmol, 2.0 equiv.) at 0 °C. After 2 d at room temp., the reaction mixture was concentrated under reduced pressure. To a solution of the crude material in CH_2Cl_2 (40 mL) were added Et_3N (5.78 mL, 42.11 mmol, 3.9 equiv.) and benzyl bromide (1.51 mL, 12.70 mmol, 1.2 equiv.). After 18 h at room temp., a saturated solution of $NaHCO_3$ (15 mL) was added to the reaction mixture. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL), the organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE/EtOAc, 50:50), methyl (2*S*,3*S*)-1-benzyl-3-hydroxypyrrolidine-2-carboxylate (1.81 g, 7.7 mmol, 72%) was isolated as a pale-yellow oil. $[\alpha]_D^{20}$ = –52.2 (c = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 49, 2810, 1731, 1436, 1201, 1170, 1134, 1075, 989 cm^{-1}. ^1H NMR: δ = 7.34–7.22 (m, 5 H), 4.41 (ddd, J = 6.6, 2.9, 2.9 Hz, 1 H), 3.92 (d, J = 12.8 Hz, 1 H), 3.68 (s, 3 H), 3.64 (d, J = 12.8 Hz, 1 H), 3.23 (d, J = 3.7 Hz, 1 H), 2.99 (ddd, J = 8.6, 8.6, 2.8 Hz, 1 H), 2.73–2.59 (m, 2 H), 2.18 (m, 1 H), 1.75 (dddd, J = 13.4, 7.4, 2.6, 2.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 173.1 (s), 137.9 (s), 129.2 (d, 2 C), 128.3 (d, 2 C), 127.3 (d), 75.5 (d), 74.2 (d), 58.6 (t), 52.0 (q), 51.0 (t), 33.3 (t) ppm. MS: m/z = 235 (0.8) [M^+], 176 (40), 92 (8), 91 (100), 65 (11). To a solution of methyl (2*S*,3*S*)-1-benzyl-3-hydroxypyrrolidine-2-carboxylate (500 mg, 2.13 mmol, 1 equiv.) in CH_2Cl_2 (10 mL) were added Et_3N (0.36 mL, 2.60 mmol, 1.2 equiv.), DMAP (16 mg, 0.13 mmol, 0.6 equiv.), and TBDPSCl (0.68 mL, 2.60 mmol, 1.2 equiv.). After 18 h at room temp., a saturated solution of Na_2CO_3 (20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the organic layer was dried with $MgSO_4$, filtered, and then concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE/EtOAc, 90:10), methyl (2*S*,3*S*)-1-benzyl-3-(*tert*-butyldiphenylsilyloxy)pyrrolidine-2-carboxylate (693 mg, 1.47 mmol, 69) was isolated as a colorless oil. $[\alpha]_D^{20}$ = –14.0 (c = 1.1, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 32, 2857, 1737, 1428, 1202, 1111, 1061, 1028, 822 cm^{-1}. ^1H NMR: δ = 7.65–7.59 (m, 4 H), 7.44–7.20 (m, 11 H), 4.47 (ddd, J = 6.1, 2.8, 2.8 Hz, 1 H), 3.87 (d, J = 13.0 Hz, 1 H), 3.68 (d, J = 13.0 Hz, 1 H), 3.45 (s, 3 H), 3.34 (d, J = 3.3 Hz, 1 H), 2.96 (ddd, J = 8.7, 7.7, 2.3 Hz, 1 H), 2.73 (ddd, J = 10.2, 8.6, 6.8 Hz, 1 H), 1.87 (dddd, J = 13.1, 10.3, 7.7, 6.4 Hz, 1 H), 1.69 (dddd, J = 13.0, 6.6, 2.3, 2.3 Hz,

1 H), 1.06 (s, 9 H) ppm. ^{13}C NMR: δ = 173.2 (s), 138.2 (s), 133.8 (s), 133.4 (s), {135.9, 135.8, 134.8, 129.7, 129.2, 128.2, 127.6, 127.6, 127.1 (d, 15 C)}, 76.7 (d), 74.8 (d), 59.2 (t), 51.7 (t), 51.6 (q), 34.3 (t), 26.9 (q, 3 C), 19.1 (s) ppm. MS: *m*/*z*(%) = 414 (13) [$M^{+\cdot}$ – $COOCH_3^{\cdot}$], 199 (17), 135 (8), 120 (6), 92 (8), 91 (100), 77 (11), 65 (11), 57 (17). HRMS (ESI): calcd. for $C_{29}H_{36}NO_3Si$ [M + H^+] 474.2459; found 474.2458. To a solution of methyl (2*S*,3*S*)-1-benzyl-3-(*tert*-butyldiphenylsilyloxy)pyrrolidine-2-carboxylate (693 mg, 1.47 mmol, 1.0 equiv.) in THF (20 mL) at 0 °C, was added DIBAL-H (1 M in CH_2Cl_2, 4.83 mL, 4.83 mmol, 3.3 equiv.). After 2.5 h at room temp., an aqueous saturated solution of potassium sodium tartrate (20 mL) was added at 0 °C. After stirring for 2 h, the mixture was extracted with EtOAc (3 × 20 mL), then the organic layers were dried with $MgSO_4$ and concentrated under reduced pressure to afford **39** (464 mg, 1.04 mmol, 71%) as a yellow oil. $[\alpha]_D^{20}$ = –20.0 (*c* = 0.4, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 57, 1428, 1106, 1043, 821 cm^{-1}. ^{1}H NMR: δ = 7.67–7.62 (m, 4 H), 7.46–7.21 (m, 11 H), 4.26 (ddd, *J* = 5.5, 2.3, 2.3 Hz, 1 H), 3.91 (d, *J* = 13.0 Hz, 1 H), 3.55 (d, *J* = 13.0 Hz, 1 H), 3.29 (dd, *J* = 11.0, 3.8 Hz, 1 H), 3.02 (dd, *J* = 11.0, 2.4 Hz, 1 H), 2.89 (ddd, *J* = 8.8, 6.8, 1.6 Hz, 1 H), 2.76–2.68 (m, 2 H), 2.45 (br. s, 1 H), 1.78–1.60 (m, 2 H), 1.07 (s, 9 H) ppm. ^{13}C NMR: δ = 139.1 (s), 134.1 (s), 134.0 (s), {135.8, 135.8, 129.8, 129.7, 128.8, 128.4, 127.7, 127.2 (d, 15 C)}, 76.8 (d), 74.1 (d), 60.1 (t), 59.1 (t), 52.2 (t), 34.6 (t), 27.0 (q, 3 C), 19.1 (s) ppm. HRMS (ESI): calcd. for $C_{28}H_{36}NO_2Si$ [M + H^+] 446.2510; found 446.2511.

(2*R*,3*S*)-2-(Azidomethyl)-1-benzyl-3-(*tert*-butyldiphenylsilyloxy)-pyrrolidine (40): Following the general procedure with *n*Bu_4NN_3 (71 mg, 0.25 mmol, 1.1 equiv., 0 °C, 4 h) and XtalFluor-E (57 mg, 0.25 mmol, 1.1 equiv.), the transformation of **39** (100 mg, 0.23 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et_2O, 90:10) to give **40** (68 mg, 0.14 mmol, 63%) as a yellow oil. $[\alpha]_D^{20}$ = +0.3 (*c* = 1.8, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3071, 2931, 2101, 1472, 1428, 1296, 1262, 1217, 1111, 1049, 821, 756 cm^{-1}. ^{1}H NMR: δ = 7.75–7.19 (m, 15 H), 4.17 (ddd, *J* = 5.1, 2.1, 2.1 Hz, 1 H), 3.98 (d, *J* = 13.0 Hz, 1 H), 3.61 (d, *J* = 12.9 Hz, 1 H), 3.51–3.37 (m, 2 H), 2.93 (m, 1 H), 2.76 (ddd, *J* = 4.6, 4.1, 2.1 Hz, 1 H), 2.67 (m, 1 H), 1.83–1.63 (m, 2 H), 1.08 (s, 9 H) ppm. ^{13}C NMR: δ = 137.9 (s), 132.7 (s), 132.6 (s), {135.9, 135.8, 134.5, 130.3, 129.9, 129.8, 129.0, 128.9, 128.4, 127.9, 127.7, 127.6 (d, 15 C)}, 76.3 (d), 72.8 (d), 62.4 (t), 59.8 (t), 52.2 (t), 33.8 (t), 27.0 (q, 3 C), 19.1 (s) ppm. MS: *m*/*z*(%) = 413 (23) [$M^{+\cdot}$ – *t*$Bu^{\cdot}$], 354 (13), 239 (7), 197 (17), 181 (9), 159 (6), 136 (13), 135 (95), 105 (16), 92 (9), 91 (100), 77 (4), 65 (12), 57 (11). HRMS (ESI): calcd. for $C_{28}H_{35}ON_4Si$ [M + H^+] 471.2575; found 471.2574.

***tert*-Butyl [(2*S*,3*R*)-1-Benzyl-2-(hydroxymethyl)pyrrolidin-3-yl]carbamate (41):** To a solution of methyl (2*S*,3*S*)-1-benzyl-3-hydroxypyrrolidine-2-carboxylate (500 mg, 2.13 mmol, 1 equiv.) in CH_2Cl_2 (5 mL) at 0 °C were added Et_3N (1.25 mL, 9.03 mmol, 4.2 equiv.) and MsCl (0.38 mL, 4.90 mmol, 2.3 equiv.). After 2.5 h at room temp., the mixture was taken up in CH_2Cl_2 then the organic layer was washed with a saturated solution of $NaHCO_3$, H_2O, and brine. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. To a solution of the crude material (524 mg, 1.67 mmol, 1 equiv.) in CH_3CN (2 mL) was added *n*-tetrabutylammonium azide (1.19 g, 4.18 mmol, 2.5 equiv.). After 2 h at reflux, the reaction mixture was diluted with EtOAc, and washed with H_2O and brine. The aqueous layers were then extracted with EtOAc, dried Na_2SO_4, filtered, and then concentrated under reduced pressure. After purification by flash chromatography on silica gel (PE/EtOAc, 70:30), methyl (2*S*,3*R*)-3-azido-1-benzylpyrrolidine-2-carboxylate (79 mg, 0.30 mmol, 14%) was isolated as a colorless oil. ^{1}H NMR: δ = 7.35–7.21 (m, 5 H), 4.14 (ddd, *J* = 8.1, 6.7, 5.1 Hz, 1 H), 3.99 (d, *J* = 13.1 Hz, 1 H), 3.76 (s, 3 H), 3.47 (d, *J* = 12.6 Hz, 1 H), 3.46 (d, *J* = 7.0 Hz, 1 H), 3.11 (ddd, *J* = 8.9, 8.9, 3.5 Hz, 1 H), 2.40 (ddd, *J* = 9.2, 8.2, 8.2 Hz, 1 H), 2.22 (dddd, *J* = 13.4, 8.2, 8.2, 3.5 Hz, 1 H), 1.98 (dddd, *J* = 13.3, 8.7, 8.7, 5.2 Hz, 1 H) ppm. ^{13}C NMR: δ = 170.4 (s), 137.6 (s), 129.0 (d, 2 C), 128.3 (d, 2 C), 127.3 (d), 69.1 (d), 62.3 (d), 57.6 (t), 51.9 (q), 50.6 (t), 29.5 (t) ppm. To a suspension of $LiAlH_4$ (41 mg, 1.08 mmol, 4 equiv.) in THF (4 mL) at 0 °C was added dropwise a solution of methyl (2*S*,3*R*)-3-azido-1-benzylpyrrolidine-2-carboxylate (70 mg, 0.27 mmol, 1 equiv.) in THF (2 mL). After 30 min at 0 °C and 3 h at room temp., H_2O (22 μL), NaOH (22 μL, 3.75 M), and H_2O (50 μL) were added dropwise at 0 °C. After 1 h at room temp., the suspension was filtered through a pad of Celite, then concentrated under reduced pressure. To a solution of the residue (37 mg, 0.18 mmol, 1 equiv.) in dioxane (2 mL) was added Boc_2O (45 mg, 0.21 mmol, 1.2 equiv.). After 2.5 h at room temp., the reaction mixture was taken up in Et_2O, then washed with H_2O. The organic layer was dried with Na_2SO_4 then concentrated under reduced pressure. After purification by flash chromatography on silica gel (CH_2Cl_2/MeOH, 98:2), **41** (51 mg, 0.17 mmol, 62%) was isolated as a colorless oil. ^{1}H NMR: δ = 7.37–7.22 (m, 5 H), 5.26 (d, *J* = 10.0 Hz, 1 H), 4.34 (dddd, *J* = 8.8, 8.8, 8.8, 8.8 Hz, 1 H), 3.92 (d, *J* = 12.9 Hz, 1 H), 3.55–3.51 (m, 2 H), 3.44 (d, *J* = 13.5 Hz, 1 H), 2.95 (ddd, *J* = 8.6, 7.3, 1.2 Hz, 1 H), 2.81 (ddd, *J* = 8.9, 2.7, 2.7 Hz, 1 H), 2.27 (ddd, *J* = 11.0, 9.3, 6.1 Hz, 1 H), 2.16 (m, 1 H), 1.48–1.47 (m, 10 H) ppm. ^{13}C NMR: δ = 138.4 (s), 128.8 (d, 2 C), 128.4 (d, 2 C), 127.3 (d), 79.5 (s), 65.3 (d), 59.1 (t), 58.8 (t), 51.8 (d), 51.1 (t), 32.6 (t), 28.3 (q, 3 C) ppm.

***tert*-Butyl [(2*R*,3*R*)-2-(Azidomethyl)-1-benzylpyrrolidin-3-yl]carbamate (42):** Following the general procedure with *n*Bu_4NN_3 (53 mg, 0.19 mmol, 1.1 equiv., 0 °C, 1 h) and XtalFluor-E (43 mg, 0.19 mmol, 1.1 equiv.), the transformation of **41** (51 mg, 0.17 mmol, 1 equiv.) afforded an oil that was purified by flash column chromatography on silica gel (PE/Et_2O, 70:30 to 50:50) to give **42** (22 mg, 0.07 mmol, 40%). $[\alpha]_D^{20}$ = +20.0 (*c* = 1.7, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3434, 2978, 2103, 1703, 1505, 1367, 1246, 1164 cm^{-1}. ^{1}H NMR: δ = 7.35–7.23 (m, 5 H), 4.97 (br. s, 1 H), 4.33 (dddd, *J* = 9.6, 9.6, 8.3, 7.4 Hz, 1 H), 3.95 (d, *J* = 13.0 Hz, 1 H), 3.52 (d, *J* = 12.6 Hz, 1 H), 3.31 (dd, *J* = 12.9, 3.7 Hz, 1 H), 3.07–2.97 (m, 2 H), 2.94 (m, 1 H), 2.27 (ddd, *J* = 10.7, 9.3, 6.2 Hz, 1 H), 2.10 (m, 1 H), 1.68 (m, 1 H), 1.44 (s, 9 H) ppm. ^{13}C NMR: δ = 155.6 (s), 138.7 (s), 128.8 (d, 2 C), 128.4 (d, 2 C), 127.2 (d), 79.6 (s), 63.9 (d), 59.4 (t), 52.0 (d), 51.0 (t), 50.7 (t), 31.9 (t), 28.4 (q, 3 C) ppm. MS: *m*/*z*(%) = 275 (5) [$M^{+\cdot}$ – $CH_2N_3^{\cdot}$], 220 (4), 219 (29), 127 (12), 92 (9), 91 (100), 65 (10), 57 (22). HRMS (ESI): calcd. for $C_{17}H_{26}N_5O_2$ [M + H^+] 332.2081; found 332.2077.

(3*R*,5*R*)-1-Benzyl-5-(*tert*-butyldimethylsilyloxy)piperidin-3-amine (43): To a solution of **23e** (213 mg, 0.62 mmol, 1 equiv.) in THF (12 mL) were added PPh_3 (242 mg, 0.93 mmol, 1.5 equiv.) and H_2O (78 μL, 4.34 mmol, 7 equiv.). After 16 h at reflux, the mixture was concentrated under reduced pressure. After purification by flash chromatography on silica gel (CH_2Cl_2/MeOH, 90:10), **43** (117 mg, 0.37 mmol, 60%) was isolated as a colorless oil. $[\alpha]_D^{20}$ = +26.0 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2928, 2856, 1462, 1360, 1252, 1157, 1088, 880, 834, 773, 736, 698 cm^{-1}. ^{1}H NMR: δ = 7.34–7.15 (m, 5 H), 3.96 (dddd, *J* = 8.0, 8.0, 4.0, 4.0 Hz, 1 H), 3.57 (d, *J* = 13.4 Hz, 1 H), 3.42 (d, *J* = 13.4 Hz, 1 H), 3.13 (dddd, *J* = 5.4, 4.0, 4.0, 4.0 Hz, 1 H), 2.60 (dd, *J* = 10.8, 3.9 Hz, 1 H), 2.37–2.27 (m, 2 H), 2.09 (dd, *J* = 10.9, 7.6 Hz, 1 H), 1.64 (m, 1 H), 1.53 (ddd, *J* = 13.0, 8.5, 4.0 Hz, 1 H), 1.45 (br. s, 2 H), 0.84 (s, 9 H), 0.00 (s, 3 H), –0.02 (s, 3 H) ppm. ^{13}C NMR: δ = 138.5 (s), 128.8 (d, 2 C), 128.2 (d, 2 C), 126.9 (d), 65.7 (d), 62.5 (d), 60.9 (t), 60.6 (t), 46.0 (d), 42.0 (t),

25.9 (q, 3 C), 18.2 (s), –4.7 (q, 2 C) ppm. MS: *m*/*z*(%) = 320 (1) [$M^{+\cdot}$], 188 (43), 146 (73), 134 (51), 120 (11), 101 (15), 91 (100), 73 (26), 65 (6), 59 (11). HRMS (ESI): calcd. for $C_{18}H_{33}N_2OSi$ [M + H^+] 321.2357; found 321.2352.

(3*R*,5*R*)-1-Benzyl-5-(*tert*-butyldiphenylsilyloxy)piperidin-3-amine (44):[20] To a solution of **23c** (582 mg, 1.24 mmol, 1 equiv.) in THF (15 mL) were added PPh_3 (488 mg, 1.86 mmol, 1.5 equiv.) and H_2O (156 μL, 8.68 mmol, 7 equiv.). After 5 h at reflux, the mixture was concentrated under reduced pressure. After purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 90:10), **44** (500 mg, 1.13 mmol, 91%) was isolated. $[\alpha]_D^{20}$ = +33.0 (*c* = 1.3, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2930, 1427, 1109, 822 cm^{-1}. ^1H NMR: δ = 7.67–7.59 (m, 4 H), 7.43–7.20 (m, 11 H), 4.00 (dddd, *J* = 7.2, 7.2, 3.9, 3.9 Hz, 1 H), 3.45 (d, *J* = 13.8 Hz, 1 H), 3.42 (d, *J* = 13.8 Hz, 1 H), 3.26 (m, 1 H), 2.52 (d, *J* = 10.7 Hz, 1 H), 2.38 (d, *J* = 10.7 Hz, 1 H), 2.30–2.12 (m, 2 H), 2.04 (br. s, 1 H), 1.73 (dddd, *J* = 7.8, 7.8, 4.1, 4.1 Hz, 1 H), 1.50 (m, 1 H), 1.04 (s, 9 H) ppm. ^{13}C NMR: δ = 138.5 (s), 135.8 (d, 2 C), 135.7 (d, 2 C), 134.4 (s), 134.2 (s), 129.6 (d, 1 C), 129.5 (d, 1 C), 128.8 (d, 2 C), 128.2 (d, 2 C), 127.6 (d, 2 C), 127.5 (d, 2 C), 126.9 (d), 66.7 (d), 62.4 (t), 60.6 (t), 60.1 (t), 45.7 (d), 41.4 (t), 27.0 (q, 3 C), 19.2 (s) ppm. MS: *m*/*z* (%) = 188 (69) [$M^{+\cdot}$ – TBDPSO$^{\cdot}$], 146 (71), 134 (32), 91 (100). HRMS (ESI): calcd. for $C_{28}H_{37}ON_2Si$ [M + H^+] 445.2670; found 445.2671.

(3*R*,5*R*)-1-Benzyl-5-fluoropiperidin-3-amine (45):[20] To a solution of the mixture of **28a** and **29a** (56 mg, 0.24 mmol, 1 equiv.) in THF (5 mL) were added PPh_3 (94 mg, 0.36 mmol, 1.5 equiv.) and H_2O (40 μL, 1.68 mmol, 7 equiv.). After 5 h at reflux, the mixture was concentrated under reduced pressure. After purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 90:10), **45** (41 mg, 0.20 mmol, 82%) was isolated. $[\alpha]_D^{20}$ = +11.0 (*c* = 2.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3700–2750, 1600, 1454, 1340, 1306, 1152, 1028, 972, 928, 910, 814 cm^{-1}. ^1H NMR: δ = 7.36–7.21 (m, 5 H), 4.82 (ddddd, *J* = 47.4, 5.3, 5.3, 3.0, 3.0 Hz, 1 H), 3.58 (s, 2 H), 3.26 (dddd, *J* = 8.3, 8.3, 3.8, 3.8 Hz, 1 H), 2.87–2.69 (m, 2 H), 2.37 (dd, *J* = 29.6, 12.2 Hz, 1 H), 2.16–1.95 (m, 4 H), 1.48 (dddd, *J* = 23.1, 13.1, 9.5, 3.0 Hz, 1 H) ppm. ^{13}C NMR: δ = 137.5 (s), 129.1 (d, 2 C), 128.3 (d, 2 C), 127.2 (d), 87.2 (dd, *J* = 172.6 Hz), 62.4 (t), 60.8 (t), 56.5 (dt, *J* = 21.6 Hz), 44.8 (dd, *J* = 2.8 Hz), 38.4 (dt, *J* = 20.4 Hz) ppm. MS: *m*/*z* (%) = 208 (1) [$M^{+\cdot}$], 188 (16) [$M^{+\cdot}$ – $F^{\cdot}$], 146 (27), 134 (19), 91 (100), 80 (12), 65 (13). HRMS (ESI): calcd. for $C_{12}H_{18}FN_2$ [M + H^+] 209.1449; found 209.1448.

***tert*-Butyl [(3*S*,5*R*)-5-Amino-1-benzylpiperidin-3-yl]carbamate (46) and *tert*-Butyl [(3*S*,5*S*)-5-(Aminomethyl)-1-benzylpyrrolidin-3-yl]-carbamate (47):**[20] To a solution of the mixture of **31e** and **32e** (88 mg, 0.27 mmol, 1 equiv.) in THF (5 mL) were added PPh_3 (104 mg, 0.40 mmol, 1.5 equiv.) and H_2O (34 μL, 1.89 mmol, 7 equiv.). After 5 h at reflux, the mixture was concentrated under reduced pressure. After purification by flash column chromatography on silica gel (CH_2Cl_2/MeOH, 80:20) a mixture of **46** and **47** (56 mg, 0.18 mmol, 68%, **46**/**47** = 90:10) was isolated. **46**: IR (neat): $\tilde{\nu}$ = 3376–2805, 1685, 1512, 1365, 1311, 1230, 1164, 1111, 1055, 913 cm^{-1}. ^1H NMR ([D_6]DMSO at 120 °C): δ = 7.39–7.19 (m, 5 H), 6.17 (br. s, 1 H), 3.54 (d, *J* = 13.4 Hz, 1 H), 3.50 (d, *J* = 13.2 Hz, 1 H), 3.46 (m, 1 H), 2.86–2.75 (m, 3 H), 2.64 (br. s, 2 H), 1.96 (m, 1 H), 1.78 (dd, *J* = 10.2, 10.2 Hz, 1 H), 1.67 (dd, *J* = 11.7, 11.7 Hz, 1 H), 1.39 (s, 9 H), 1.0 (ddd, *J* = 11.2, 11.2, 11.2 Hz, 1 H) ppm. ^{13}C NMR: δ = 155.2 (s), 138.0 (s), 129.0 (d, 2 C), 128.3 (d, 2 C), 127.1 (d), 79.3 (s), 62.3 (t), 60.9 (t), 58.5 (t), 47.1 (d), 46.6 (d), 40.3 (t), 28.4 (q, 3 C) ppm.

Supporting Information (see footnote on the first page of this article): Characterization data of all newly synthesized compounds.

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