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On the Synthesis and Reactivity of Enantiopure Azetidines

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β-Amino alcohols with an (*E*)-vinylsilane moiety were cyclized in the presence of *N*-bromosuccinimide to afford diastereomerically pure azetidines. The chemo- and stereoselectivities of this bromocyclization are discussed. AM1 calculations support the observed chemoselectivity. The reactivity of the azetidines towards fluorinated reagents was studied.

Introduction

The electrophile-induced intramolecular cyclization between a heteroatom and an olefin is a well-known process to synthesize various oxygen[1] or nitrogen[2] heterocycles. It was expected that the presence of a silyl substituent on the double bond could influence the regioselectivity of such cyclizations. Thus, functionalized vinylsilanes are recognized to favour *exo* processes for the formation of cyclic ethers[3] and amines.[4] Indeed, the cyclization of homoallylic alcohols substituted by a vinylsilane terminator led to the regioselective formation of oxetanes,[3f] and the cyclization of δ-amino vinylsilanes allowed the regioselective synthesis of pyrrolidines.[4a] To date, electrophile-induced intramolecular cyclizations of homoallylic amino vinylsilanes to obtain azetidine rings have not been reported.

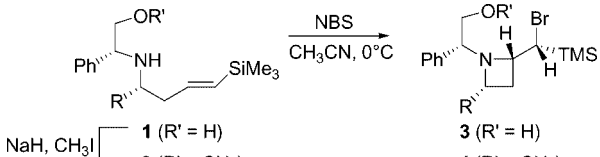
In the course of our studies about the enantioselective synthesis of pipecolic acid[5a] and proline[5b] derivatives from unsaturated and silylated β-amino alcohols,[5c] we focused on the use of these electrophile-induced cyclizations to produce azetidines.[6] These molecules are attractive synthetic targets because of their use as ligands, their presence in natural products and their potent biological and pharmaceutical activities.[7] As a consequence, the asymmetric synthesis of these compounds has attracted much attention in recent years.[8]

In the present study, we explored the scope and the limits of the cyclizations of amino alcohols with a γ-vinylsilane group by using *N*-bromosuccinimide as the electrophilic reagent. We also describe the transformations of the resulting azetidines into various heterocycles and new amino alcohols.

Results and Discussion

Formation of Azetidines

Amino alcohols **1a**–**d** and their *O*-methyl derivatives **2a**–**d** were cyclized by their treatment with *N*-bromosuccinimide to afford azetidines **3a**–**d** and **4a**–**d**, respectively, and some recovered starting material (Scheme 1). These reactions occurred in a regio- and diastereoselective manner, and the configurations of the resulting stereogenic centres have been established by X-ray analysis of compound **3d**[6] and **4d**.[9] The best experimental conditions were: addition of 1.05 equiv. of *N*-bromosuccinimide to a 0.1 M solution of **1** or **2** at 0 °C in acetonitrile.[10]



Starting material	R	Yield of **3**	Yield of **4**
1a or **2a**	Ph	75%	52%
1b or **2b**	Pr	70%	39%
1c or **2c**	*i*Pr	55%	43%
1d or **2d**	*t*Bu	53%	66%

Scheme 1.

Azetidines **3** and **4** were formed in moderate to good yields as single diastereomers. The diastereoselective formations of azetidines **3** and **4** were interpreted by considering the intramolecular attack of the nitrogen atom on the bromonium intermediate **A**, affording a 4-*exo*-*tet* cyclization product (Scheme 2).[11]

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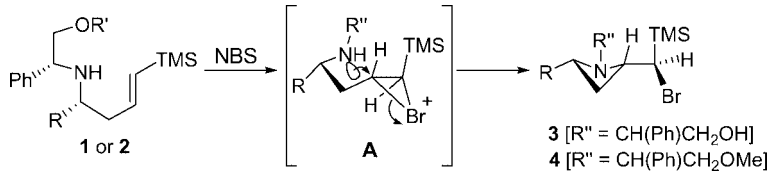


Scheme 2.

Calculations have been performed to obtain some information on the site selectivity of the bromination with respect to the two faces of the vinylsilane. Although ab initio calculations (STO3G) ascertained the traditional almost symmetrical alkene-bromonium structure, semi-empirical AM1 calculations[12,13] led to a very unsymmetrical α-bromo-β-cationic structure (Figure 1). Such a situation seemed to account for the strong hyperconjugation between the C_α–Si bond and the empty p orbital on the cationic C_β atom.[14] Evidence for this well-known effect was given by the unusual length (ca. 2.37 Å) of the C_α–Si bond. Discrimination between the attack of Br^+ on either side of the double bond arose from a quite important (3.4 kcal/mol) energy difference between the two stereoisomers; the attack on the bromine atom occurred on the side of the C=C bond opposite the incoming nitrogen atom. As a result, two conformations of the vinylsilane corresponding to the two different diastereomeric cations **A** and **B** showed different steric interactions particularly with the α-(hydroxymethyl)benzyl moiety.[15] Moreover, progress towards the cyclized products did not show any further steric hindrance. Indeed, calculations still confirmed an energy difference of 2.9 kcal/mol between the cyclized azetidinium compounds **C** and **D** (Figure 2). The energy difference may be explained by the pyramidalisation of C_β, spreading the $C_\alpha HBr$–$SiMe_3$ and phenyl groups apart and decreasing the associated steric hindrance.

Because of the presence of different heteroatoms (bromine, silicon, oxygen and nitrogen), these azetidines dis-

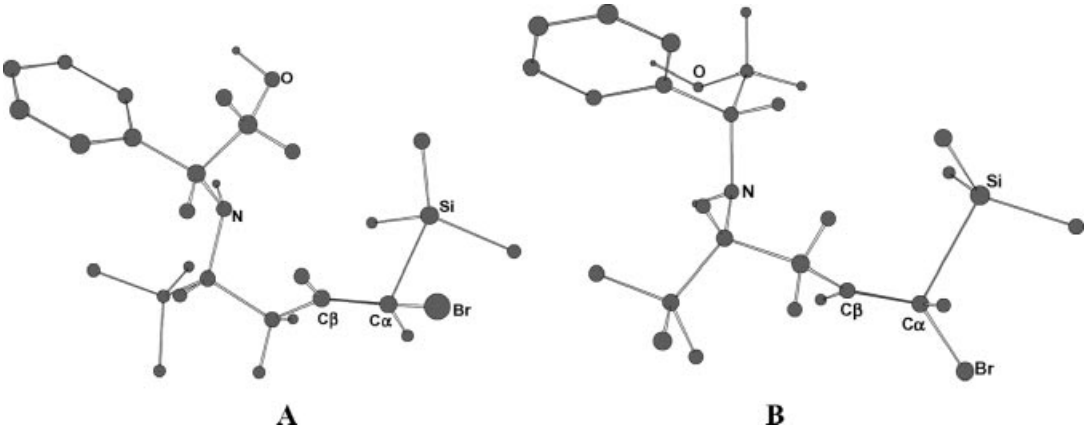


Figure 1. AM1-calculated structures for both **A** (favored) and **B** (disfavored) bromonium ions.

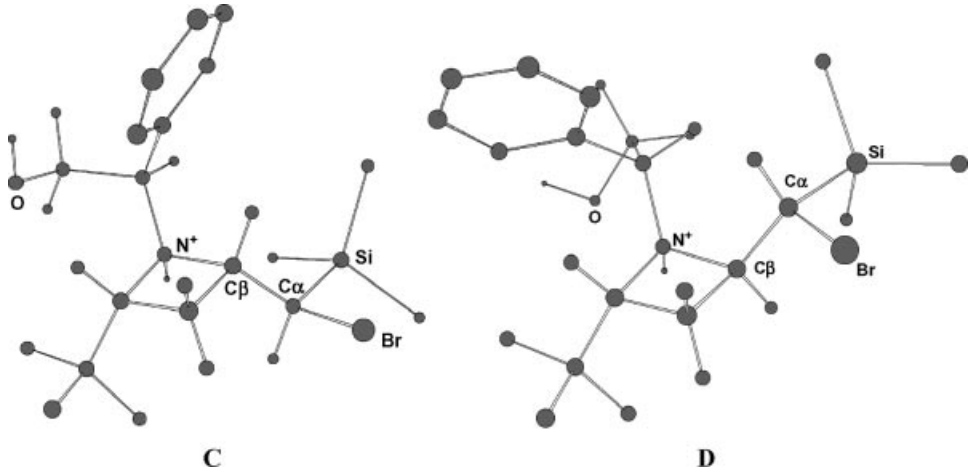


Figure 2. AM1-calculated structures for both **C** (favored) and **D** (disfavored) azetidinium ions.

closed a very intriguing reactivity upon their interaction with fluorinated reagents.

Reaction of Azetidines with Tetrabutylammonium Fluoride

Compounds **3** and **4** were treated with tetrabutylammonium fluoride in dry THF. Whereas amino ethers **4** were desilylated to afford a complex mixture of products,[16,17] azetidines **3**, under the same conditions gave bicyclic compounds **5**. The product **5a** (R = Ph) was recrystallized and an X-ray analysis[18] of this compound (Figure 3) showed a *cis* relative configuration for each heterocycle, thus establishing an (*S*) absolute configuration at the ring junction (Scheme 3).

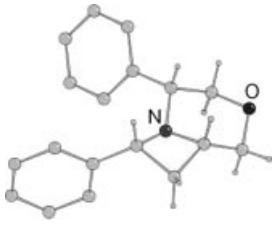
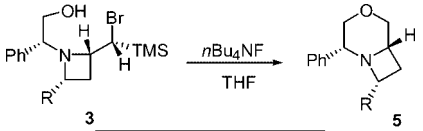


Figure 3. X-ray structure of **5a**.



Product	R	Yield of 5
5a	Ph	65%
5b	Pr	51%
5c	*i*Pr	54%
5d	*t*Bu	45%

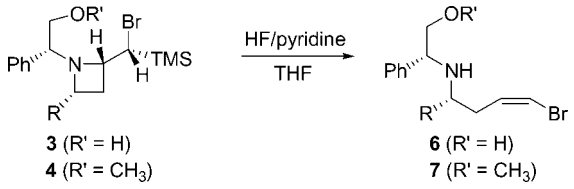
Scheme 3.

From a mechanistic point of view, the intramolecular cyclization described above can be viewed as a simple desilylation by the fluoride ion, generating a negative charge on the carbon atom. The resulting carbenoid may evolve through a subsequent acid/base reaction in an inter- or intramolecular manner with the hydroxy group, and further displacement of the bromine atom by the alcoholate in an S_N2-type reaction can occur. The integrity of the stereogenic centre at the ring junction was not altered by this process. (Scheme 4).

Interestingly, when the hydroxy function of the starting material was protected in **4** (R′ = CH_3), no cyclization could occur; a mixture of products resulting probably from the non-selective reactivity of the carbenoid species at the workup stage was observed. We decided then to test the desilylation under acidic conditions.

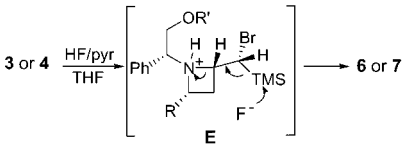
Reaction of Azetidines with HF/Pyridine

Surprisingly, azetidines **3** and **4** reacted with a mixture HF/pyridine to lead to the amino alcohols **6** and **7**, respectively, bearing a (*Z*)-bromovinyl function, in good to excellent yields (Scheme 5).



Scheme 5.

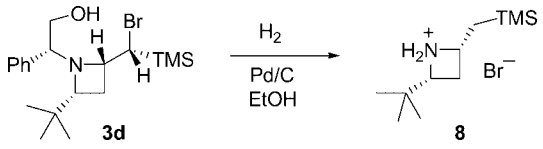
This totally stereoselective reaction might take place, by an E2 mechanism; protonation of the nitrogen atom would give the ammonium intermediate **E**, and opening of the azetidine ring in an *anti* elimination by attack of the fluoride ion on the TMS group would result in the selective formation of the (*Z*) isomer (Schemes 5 and 6).[19] Likewise, the β-elimination of N_3SiMe_3[20] and $BrSiMe_3$[21] are known to take place with *anti* stereochemistry. In contrast, ring-opening elimination[22] or substitution[23] of four-membered cyclic ammonium ions have been only scarcely described.



Product	R	Yield
6a	Ph	95 %
6b	Pr	82 %
6c	*i*Pr	94 %
6d	*t*Bu	86 %
7a	Ph	97 %
7b	Pr	92 %
7c	*i*Pr	50 %
7d	*t*Bu	95 %

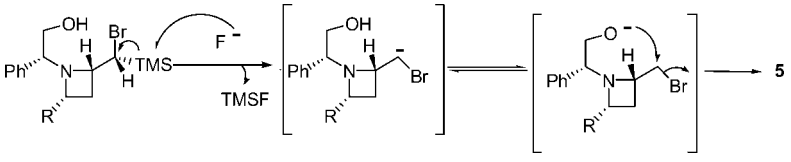
Scheme 6.

Next, in order to obtain the free azetidines, we focused on their hydrogenolysis. This reaction was tested on compound **3d**, which reacted with hydrogen to afford product **8**. Two reactions occurred under these conditions: a debenzylation and a hydrodehalogenation, as indicated in Scheme 7.



Scheme 7.

This result shows that it is possible to synthesize in four steps, starting from phenyl glycinol, enantiopure *cis*-2,4-dialkylated azetidines.



Scheme 4.

Conclusions

We have described the one-pot formation of polysubstituted enantiopure azetidines by a totally regio- and diastereoselective *N*-bromosuccinimide-induced intramolecular cyclization. These compounds show their highly stimulating reactivity when submitted to various reagents. The new β-amino alcohols possessing a bromovinyl function are potential intermediates for the synthesis of new heterocycles. Studies are underway to elucidate the mechanistic peculiarities of the behaviour of these azetidines.

Experimental Section

General Methods: ^{1}H and ^{13}C NMR spectra ($CDCl_3$ solution) were recorded with a Bruker ARX 250 spectrometer at 250 MHz and 62.9 MHz, respectively; chemical shifts are reported in ppm from TMS. Optical rotations were determined with a Perkin–Elmer 141 instrument. All reactions were carried out under argon. Column chromatography was performed with silica gel (230–400 mesh) by using various mixtures of ethyl acetate (AcOEt) or diethyl ether (Et_2O) and cyclohexane (CH). Melting points are uncorrected. THF was distilled from sodium/benzophenone ketyl. Compositions of stereoisomeric mixtures were determined by NMR analysis of crude products before any purification.

General Procedure for the Methylation of Amino Alcohols: A solution of amino alcohol (1.6 mmol) in anhydrous THF (3 mL) was added to a solution of sodium hydride (2 mmol) in THF (12 mL) at 0 °C. After stirring at room temp. for 1.5 h, iodomethane (4.1 mmol) was added dropwise and the mixture was stirred until the complete disappearance of the starting material. After addition of water, extraction with Et_2O was followed by drying the organic layers with $MgSO_4$. After concentration under reduced pressure, the crude material was purified by chromatography with silica gel (CH/AcOEt, 95:5) to give the amino ethers.

[(1*R*)-2-Methoxy-1-phenylethyl][(1*R*,3*E*)-1-phenyl-4-(trimethylsilyl)-but-3-en-1-yl]amine (2a): Oil (384 mg, 68% yield). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.22–7.06 (m, 10 H, Ar), 5.87 (dt, J = 6.5 and 18.5 Hz, 1 H, C*H*=CHTMS), 5.70 (d, J = 18.5 Hz, 1 H, CH=C*H*TMS), 3.92 (dd, J = 4.5 and 7.0 Hz, 1 H, NC*H*Ph), 3.72 (t, J = 6.5 Hz, 1 H, NC*H*Ph), 3.50–3.40 (m, 2 H, CH_2O), 3.23 (s, 3 H, OCH_3), 2.46 (dt, J = 3.5 and 6.5 Hz, 2 H, CH_2), 2.26 (s, 1 H, NH), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 144.5 (Ar), 143.3 (*C*H=CHTMS), 141.7 5 (Ar), 133.8 (CH=*C*HTMS), 128.1, 128.0, 127.7, 127.1, 127.0, 126.6 (Ar), 77.0 (CH_2O), 60.6 (OCH_3), 60.2 (NCHPh), 58.9 (NCHPh), 44.7 (CH_2), –1.2 (TMS) ppm. $C_{22}H_{31}NOSi$ (353.57): calcd. C 74.73, H 8.84, N 3.96; found C 74.63, H 10.22, N 3.37.

[(1*R*)-2-Methoxy-1-phenylethyl][(1*S*,3*E*)-1-propyl-4-(trimethylsilyl)-but-3-en-1-yl]amine (2b): Oil (306 mg, 60% yield). $[\alpha]_D^{20}$ = –83 (c = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.34–7.15 (m, 5 H, Ar), 5.92 (dt, J = 7.0 and 18.5 Hz, 1 H, C*H*=CHTMS), 5.67 (d, J = 18.5 Hz, 1 H, CH=C*H*TMS), 4.00 (dd, J = 5.0 and 7.5 Hz, 1 H, NCHPh), 3.33 (m, 2 H, CH_2O), 3.27 (s, 3 H, OCH_3), 2.38 (dt, J = 7.5 and 17.5 Hz, 1 H, NC*H*-Pr), 2.19 (t, J = 5.0 Hz, 2 H, CH_2C=C), 1.75 (s, 1 H, NH), 1.40–1.23 (m, 1 H, CH*H*CH$_2$), 1.23–1.14 (m, 3 H, CH*HCH*$_2$), 0.71 (t, J = 6.0 Hz, 3 H, CH_3), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 143.5 (*C*H=CHTMS), 141.8 (Ar), 133.6 (CH=*C*HTMS), 128.4, 127.9, 127.4 (Ar), 78.3 (CH_2O), 59.8 (NCHPh), 58.8 (OCH_3), 53.3 (NCH-Pr), 40.5 (CH_2), 37.7 (CH_2), 19.2 (CH_2), 14.3 (CH_3), –1.1 (TMS) ppm. $C_{19}H_{33}NOSi$ (319.56): calcd. C 71.41, H 10.41, N 4.38; found C 71.12, H 10.65, N 4.14.

[(1*R*,3*E*)-1-Isopropyl-4-(trimethylsilyl)but-3-en-1-yl][(1*R*)-2-methoxy-1-phenylethyl]amine (2c): Oil (434 mg, 85% yield). $[\alpha]_D^{20}$ = –87 (c = 0.9, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.34–7.14 (m, 5 H, Ar), 5.94 (dt, J = 7.5 and 17.5 Hz, 1 H, C*H*=CHTMS), 5.67 (d, J = 17.5 Hz, 1 H, CH=C*H*TMS), 3.98 (t, J = 7.5 Hz, 1 H, NCHPh), 3.33–3.28 (m, 2 H, CH_2O), 3.27 (s, 3 H, OCH_3), 2.24–2.15 (m, 3 H, NC*H*-iPr and CH_2), 1.69 (s, 1 H, NH), 1.52–1.45 [m, 1 H, C*H*(CH_3)$_2$], 0.78 (d, J = 10 Hz, 3 H, CH_3), 0.75 (d, J = 10 Hz, 3 H, CH_3), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 144.4 (*C*H=CHTMS), 142.0 (Ar), 133.0 (CH=*C*HTMS), 128.2, 128.1, 127.3 (Ar), 78.3 (CH_2O), 60.3 (NCHPh), 59.6 (NCH*i*Pr), 58.8 (OCH_3), 37.8 (CH_2), 31.0 (*C*HMe$_2$), 19.2 (CH_3), 18.6 (CH_3), –1.0 (TMS) ppm. $C_{19}H_{33}NOSi$ (319.56): calcd. C 71.41, H 10.41, N 4.38; found C 70.61, H 10.47, N 4.13.

[(1*R*,3*E*)-1-*tert*-Butyl-4-(trimethylsilyl)but-3-en-1-yl][(1*R*)-2-methoxy-1-phenylethyl]amine (2d): Oil (469 mg, 88% yield). $[\alpha]_D^{20}$ = –101 (c = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.15–7.32 (m, 5 H, Ar), 6.06 (dt, J = 6.5 and 18.5 Hz, 1 H, C*H*=CHTMS), 5.63 (d, J = 18.5 Hz, 1 H, CH=C*H*TMS), 4.07 (dd, J = 4.5 and 8.5 Hz, 1 H, NCHPh), 3.43–3.32 (m, 2 H, CH_2O), 3.31 (s, 3 H, OCH_3), 2.50–2.42 (m, 1 H, C*H*H C=C), 2.21–1.94 (m, 2 H, CH*H*C=C and *t*BuC*H*), 1.59 (s, 1 H, NH), 0.77 (s, 9 H, *t*Bu), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 146.9 (*C*H=CHTMS), 141.6 (Ar), 130.9 (*C*H=CHTMS), 128.6, 128.2, 127.4 (Ar), 78.4 (CH_2O), 62.2 (N*C*H*t*Bu), 60.1 (NCHPh), 58.9 (OCH_3), 39.0 (CH_2), 35.4 (*C*Me$_3$), 27.4 (C*Me$_3$*), –1.1 (TMS) ppm. $C_{20}H_{35}NOSi$ (333.58): calcd. C 72.01, H 10.58, N 4.20; found C 71.98, H 10.59, N 4.39.

General Procedure for the Syntheses of Azetidines 3 and 4: *N*-Bromosuccinimide (0.23 mmol) was added at 0 °C to a solution of the required amino alcohol (0.21 mmol) in acetonitrile (4 mL). The mixture was stirred at 0 °C for 15 min, and aqueous NaOH (10%, 3 mL) was added. The aqueous layer was extracted with Et_2O, and the organic layers were combined, dried with $MgSO_4$ and concentrated under reduced pressure. The residue was then chromatographed on silica gel.

(2*R*)-2-{(2*S*,4*R*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-4-phenylazetidin-1-yl}-2-phenylethanol (3a): White solid (66 mg, 75% yield). M.p. 87 °C. $[\alpha]_D^{20}$ = 20 (c = 2.5, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.38–7.35 (m, 2 H, Ar), 7.19–7.04 (m, 6 H, Ar), 6.91–6.85 (m, 2 H, Ar), 3.75–3.67 (m, 2 H, CHBr and C*H*HO), 3.49 (dd, J = 4.5 and 8.3 Hz, 1 H, CH*H*O), 3.36–3.06 (m, 4 H, NC*H*CBr, 2 N*C*HPh and OH), 2.12–1.86 (m, 2 H, CCH_2C), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 143.8, 135.6, 129.4, 128.5, 128.4, 128.1, 127.7, 127.6 (Ar), 67.3 (NCHPh), 62.6 (CH_2O), 60.8 (*C*HCBr), 58.7 (NCHPh), 49.1 (CBr), 32.1 (CH_2), –2.1 (TMS) ppm. $C_{21}H_{28}BrNOSi$ (418.44): calcd. C 60.28, H 6.74, N 3.35; found C 60.25, H 6.82, N 3.31.

(2*R*)-2-{(2*S*,4*S*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-4-propylazetidin-1-yl}-2-phenylethanol (3b): White solid (36.3 mg, 45% yield). M.p. 58 °C. $[\alpha]_D^{20}$ = –36 (c = 1.15, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.32–7.09 (m, 5 H, Ar), 3.75–3.52 (m, 3 H, CHBr and CH_2O), 3.52–3.35 (m, 1 H, NCHPh), 3.25–3.05 (m, 1 H, NC*H*CBr), 3.05–2.85 (m, 1 H, NC*H*Pr), 1.73 (t, J = 7.8 Hz, 2 H, CHCH_2CH), 1.50–0.85 (m, 4 H, 2 CH_2), 0.71 (t, J = 7.3 Hz, 3 H, CH_3), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 136.9, 129.2, 128.5, 128.1 (Ar), 67.4 (N*C*HPh), 63.4 (CH_2O), 59.6 (CHBr), 58.2 (N*C*HCBr), 48.9 (N*C*HPr), 38.5 (CH_2), 27.5 (CH_2), 18.3 (CH_2), 14.2 (Me), –2.0 (TMS) ppm. $C_{18}H_{30}BrNOSi$ (384.43): calcd. C 56.24, H 7.87, N 3.64; found C 56.44, H 8.15, N 3.65.

(2*R*)-2-{(2*S*,4*S*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-4-isopropylazetidin-1-yl}-2-phenylethanol (3c): White solid (44.4 mg, 55% yield). M.p. 63 °C. $[\alpha]_D^{20}$ = –44 (*c* = 1.18, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.56–7.03 (m, 5 H, Ar), 3.66–3.51 (m, 3 H, CHBr and CH_2O), 3.37–3.28 (m, 2 H, N*C*HPh and OH), 3.02 (td, *J* = 2.3 and 8.0 Hz, 1 H, NC*H*CBr), 2.84–2.76 (m, 1 H, NC*H*iPr), 1.81 (q, *J* = 7.5 Hz, 1 H, CHC*H*HCH), 1.46–1.23 (m, 2 H, CHCH*H*CH and C*H*Me_2), 0.86 (d, *J* = 5.0 Hz, 3 H, Me), 0.47 (d, *J* = 5.0 Hz, 3 H, Me), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 137.2, 129.1, 128.5, 128.1 (Ar), 68.3 (N*C*HPh), 64.1 (N*C*H*i*Pr), 63.8 (CH_2O), 59.3 (NCH), 49.1 (CHBr), 31.0 [*C*H($Me)_2$], 21.8 (CH_2), 18.8 (Me), 17.0 (Me), –2.0 (TMS) ppm. $C_{18}H_{30}BrNOSi$ (384.43): calcd. C 56.24, H 7.87, N 3.64; found C 56.74, H 8.08, N 3.07.

(2*R*)-2-{(2*S*,4*S*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-4-*tert*-butylazetidin-1-yl}-2-phenylethanol (3d): White solid (44.3 mg, 53% yield). M.p. 71 °C. $[\alpha]_D^{20}$ = –106 (*c* = 0.8, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.25–6.95 (m, 5 H, Ar), 3.75 (t, *J* = 10.5 Hz, 1 H, C*H*HO), 3.55 (m, 2 H, CHBr and OH), 3.43–3.28 (m, 2 H, CH*H*O and NCHPh), 3.21 (td, *J* = 2.3 and 8.0 Hz, 1 H, NCHCBr), 2.66 (t, *J* = 8.3 Hz, 1 H, C*H*t*B*u), 1.80 (q, *J* = 7.5 Hz, 1 H, CHCH_2CH), 1.53–1.43 (m, 1 H, CHCH_2CH), 0.67 (s, 9 H, *t*Bu), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 136.6, 129.6, 128.5, 128.1 (Ar), 68.2 (N*C*H*t*Bu), 66.3 (N*C*HPh), 62.7 (CH_2O), 58.0 (NCH), 48.5 (CHBr), 34.1 (*C*Me_3), 27.0 (CMe_3), 24.0 (CH_2), –2.0 (TMS) ppm. $C_{19}H_{32}BrNOSi$ (398.45): calcd. C 57.27, H 8.09, N 3.52; found C 57.33, H 8.23, N 3.41.

(2*S*,4*R*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-1-[(1*R*)-2-methoxy-1-phenylethyl)]-4-phenylazetidine (4a): Oil (47.2 mg, 52% yield). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.15–7.11 (m, 2 H, Ar), 6.92–6.81 (m, 8 H, Ar), 3.75–3.53 (m, 4 H, NCHPh, C*H*HO, NCHCBr and CHBr), 3.32 (dt, *J* = 2.5 and 7.5 Hz, 1 H, NCHPh), 3.17 (dd, *J* = 5.0 and 10.0 Hz, 1 H, CH*H*O), 3.11 (s, 3 H, OMe), 2.04 (t, *J* = 7.5 Hz, 2 H, CHCH_2CH), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 144.4, 137.8, 128.9, 127.9, 127.7, 127.5, 127.3, 126.6 (Ar), 76.6 (CH_2O), 70.2 (NCHPh), 64.2 (N*C*HCBr), 61.6 (NCHPh), 58.6 (OMe), 50.9 (CHBr), 31.9 (CH_2), –2.0 (TMS) ppm. $C_{22}H_{30}BrNOSi$ (432.47): calcd. C 61.10, H 6.99, N 3.24; found C 60.82, H 7.78, N 2.68.

(2*S*,4*S*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-1-[(1*R*)-2-methoxy-1-phenylethyl)]-4-propylazetidine (4b): Solid (32.6 mg, 39% yield). M.p. 44 °C. $[\alpha]_D^{20}$ = –45 (*c* = 1.0, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.19–7.12 (m, 5 H, Ar), 3.58–3.47 (m, 3 H, NCHPh, C*H*HO and CHBr), 3.30 (dt, *J* = 1.5 and 9.5 Hz, 1 H, NCHCBr), 3.19 (dd, *J* = 2.0 and 7.2 Hz, 1 H, CH*H*O), 3.15 (s, 3 H, OMe), 2.81 (dq, *J* = 3.0 and 7.5 Hz, 1 H, NC*H*Pr), 1.81 (dq, *J* = 2.0 and 7.5 Hz, 1 H, CHC*H*HCH), 1.67 (q, *J* = 7.5 Hz, 1 H, CHCH*H*CH), 1.00–0.80 (m, 2 H, C$H_2$$CH_3$), 0.78–0.67 (m, 2 H, C$H_2$$CH_2CH_3$), 0.49 (t, *J* = 7.0 Hz, 3 H, CH_3), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 140.7, 128.7, 128.2, 127.6 (Ar), 77.5 (CH_2O), 71.0 (NCHPh), 62.2 (N*C*HCBr), 61.9 (NCHPr), 58.7 (OMe), 51.7 (CHBr), 37.8 (*C*$H_2CH_2CH_3$), 27.3 (CH_2), 18.0 (CH_2*C*H_2CH_3), 14.1 (CH_3), –2.0 (TMS) ppm. $C_{19}H_{32}BrNOSi$ (398.45): calcd. C 57.27, H 8.10; found C 57.89, H 8.30.

(2*S*,4*R*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-4-isopropyl-1-[(1*R*)-2-methoxy-1-phenylethyl)]azetidine (4c): Solid (36 mg, 43% yield). M.p. 63 °C. $[\alpha]_D^{20}$ = –41 (*c* = 1.0, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.30–7.00 (m, 5 H, Ar), 3.61–3.54 (m, 2 H, C*H*HO and CHBr), 3.45 (dd, *J* = 3.5 and 7.7 Hz, 1 H, NCHCBr), 3.28–3.17 (m, 2 H, CH*H*O and NCHPh), 3.15 (s, 3 H, OMe), 2.79 (dt, *J* = 3.7 and 8.5 Hz, 1 H, NC*HiPr*), 1.81 (q, *J* = 10 Hz, 1 H, CHC*H*HCH), 1.52 (dq, *J* = 3.7 and 10.0 Hz, 1 H, CHCH*H*CH), 0.73 (d, *J* = 7.5 Hz, 3 H, Me), 0.70–0.50 (m, 1 H, C*H*Me_2), 0.31 (d, *J* = 7.5 Hz, 3 H, Me), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.0, 128.4, 128.2, 127.6 (Ar), 77.2 (CH_2O), 71.3 (NCHPh), 68.0 (N*C*HCBr), 61.0 (NCH*i*Pr), 58.6 (OMe), 51.5 (CHBr), 30.0 (*C*HMe_2), 21.7 (CH_2), 18.4 (Me), 16.7 (Me), –2.0 (TMS) ppm. $C_{19}H_{32}BrNOSi$ (398.45): calcd. C 57.27, H 8.10, N 3.52; found C 57.32, H 8.71, N 3.82.

(2*S*,4*R*)-2-[(1*S*)-(Bromo)(trimethylsilyl)methyl]-4-*tert*-butyl-1-[(1*R*)-2-methoxy-1-phenylethyl)]azetidine (4d): Oil (57 mg, 66% yield). $[\alpha]_D^{20}$ = –54 (*c* = 0.9, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 2 H, Ar), 7.25–7.05 (m, 3 H, Ar), 3.72 (dd, *J* = 1.8 and 7.8 Hz, 1 H, N*C*HCBr), 3.66 (dd, *J* = 2.5 and 8.0 Hz, 1 H, NCHPh), 3.54 (dd, *J* = 8.0 and 10.0 Hz, 1 H, C*H*HO), 3.36 (dd, *J* = 3.5 and 10.3 Hz, 1 H, CH*H*O), 3.34 (d, *J* = 2.0 Hz, 1 H, CHBr), 3.23 (s, 3 H, OMe), 2.88 (t, *J* = 8.3 Hz, 1 H, NC*H*t*B*u), 1.89–1.78 (m, 1 H, CHC*H*HCH), 1.69–1.58 (m, 1 H, CHCH*H*CH), 0.52 (s, 9 H, *t*Bu), 0.0 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 142.7, 128.4, 128.1, 127.0 (Ar), 75.8 (CH_2O), 73.5 (N*C*H*t*Bu), 68.4 (NCHPh), 58.6 (OMe), 57.4 (N*C*HCBr), 52.2 (CHBr), 34.4 (*C*Me_3), 26.5 (C*Me*$_3$), 23.8 (CH_2), –2.0 (TMS) ppm. $C_{20}H_{34}BrNOSi$ (412.48): calcd. C 58.24, H 8.31, N 3.40; found C 58.11, H 8.03, N 3.21.

General Procedure for the Preparation of the Bicyclic Compounds 5: A solution of tetrabutylammonium fluoride (1 M in THF, 0.45 mmol) was added dropwise to a solution of compound **3** (0.37 mmol) in THF (4 mL). The mixture was stirred at room temperature for 24 h. After the addition of water (5 mL), the solution was extracted with Et_2O. The organic layers were dried with $MgSO_4$, filtered, and concentrated, and the crude product was flash-chromatographed.

(2*R*,6*S*,8*R*)-2,8-Diphenyl-4-oxa-1-azabicyclo[4.2.0]octane (5a): Oil (53 mg, 54% yield). $[\alpha]_D^{20}$ = –44 (*c* = 2.0, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.17–6.89 (m, 10 H, Ar), 4.04 (t, *J* = 6.7 Hz, 1 H, C*H*HO), 3.82 (dd, *J* = 2.7 and 9.5 Hz, 1 H, C*H*HO), 3.72–3.63 (m, 3 H, CH*H*O, CH*H*O and NCHPh), 3.56–3.51 (m, 1 H, NCHPh), 3.20–3.05 (m, 1 H, NCH), 2.31–2.23 (m, 2 H, CH_2) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.4, 137.4, 128.6, 128.3, 127.9, 127.8, 127.7, 127.3 (Ar), 73.6 (CH_2O), 70.7 (NCHPh), 69.6 (NCHPh), 69.4 (CH_2O), 61.5 (NCH), 35.4 (CH_2) ppm. $C_{18}H_{19}NO$ (265.35): calcd. C 81.47, H 7.22, N 5.28; found C 80.76, H 7.47, N 5.02.

(2*R*,6*S*,8*S*)-2-Phenyl-8-propyl-4-oxa-1-azabicyclo[4.2.0]octane (5b): Oil (46.2 mg, 54% yield). $[\alpha]_D^{20}$ = –93 (*c* = 1.8, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.21–7.06 (m, 5 H, Ar), 3.61 (dd, *J* = 2.7 and 9.5 Hz, 1 H, C*H*HO), 3.55 (dd, *J* = 2.0 and 9.7 Hz, 1 H, C*H*HO), 3.42 (t, *J* = 9.7 Hz, 1 H, CH*H*O), 3.38–3.28 (m, 2 H, NCHPh and CH*H*O), 3.04–2.93 (m, 1 H, NC*H*Pr), 2.88–2.75 (m, 1 H, NCH), 1.91 (td, *J* = 5.5 and 8.7 Hz, 1 H, C*H*H), 1.63 (q, *J* = 8.8 Hz, 1 H, CH*H*), 1.15–0.50 (m, 4 H, C$H_2$$CH_2CH_3$), 0.53 (t, *J* = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 139.4, 128.3, 128.2, 127.8 (Ar), 73.6 (CH_20), 70.7 (CH_20), 68.9 (NCHPh), 67.5 (N*C*HPr), 61.7 (NCH), 38.1 (*C*$H_2CH_2CH_3$), 32.9 (*C*H_2), 18.8 (CH_2*C*H_2CH_3), 14.2 (CH_3) ppm. $C_{15}H_{21}NO$ (231.33): calcd. C 77.88, H 9.15, N 6.05; found C 77.82, H 9.51, N .29.

(2*R*,6*S*,8*R*)-8-Isopropyl-2-phenyl-4-oxa-1-azabicyclo[4.2.0]octane (5c): Oil (47 mg, 55% yield). $[\alpha]_D^{20}$ = –90 (*c* = 1.5, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.32–7.18 (m, 5 H, Ar), 3.73 (dd, *J* = 2.5 and 9.5 Hz, 1 H, C*H*HO), 3.67–3.48 (m, 4 H, CH_2O, NCHPh and CH*H*O), 2.97–2.84 (m, 2 H, NCH and NCH*i*Pr), 1.85–1.78 (m, 2 H, CH_2), 1.25–1.16 (m, 1 H, C*H*Me_2), 0.71 (d, *J* = 6.7 Hz, 3 H, Me), 0.33 (d, *J* = 6.7 Hz, 3 H, Me) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 139.8, 128.4, 128.3, 128.0 (Ar), 73.8 (N*C*H*i*Pr), 73.5

(CH_2O), 70.6 (CH_2O), 69.7 (NCHPh), 61.3 (NCH), 30.5 (*C*HMe$_2$), 27.8 (CH_2), 19.5 (Me), 17.6 (Me) ppm.

(2*R*,6*S*,8*R*)-8-*tert*-Butyl-2-phenyl-4-oxa-1-azabicyclo[4.2.0]octane (5d): Oil (49 mg, 54% yield). $[\alpha]_D^{20}$ = –99 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.21–7.18 (m, 5 H, Ar), 3.70 (dd, *J* = 2.5 and 9.5 Hz, 1 H, C*H*HO), 3.66–3.40 (m, 4 H, CH*H*O, CH_2O and NCHPh), 2.85–2.74 (m, 2 H, NC*H*t Bu and NC*H*CH_2), 1.78–1.70 (m, 2 H, CH_2), 0.36 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 139.7, 128.6, 127.8, 127.6 (Ar), 78.3 (N*C*H*t*Bu), 72.7 (CH_2O), 70.1 (NCHPh), 69.9 (CH_2O), 60.6 (NCH), 31.6 (*C*tBu), 27.1 (CH_2), 25.8 (C*tBu*) ppm. $C_{16}H_{23}NO$ (245.36): calcd. C 78.32, H 9.45, N 5.71; found C 78.02, H 9.61, N 5.42.

General Procedure for the Preparation of the Brominated β-Amino Alcohols 6 and β-Amino Ethers 7: A solution of hydrofluoric acid in pyridine (35 μL) was added to a solution of azetidine (0.13 mmol) in THF (1.5 mL) at 0 °C. The mixture was stirred until the complete disappearance of the starting material. After the addition of saturated aq. $NaHCO_3$ (3 mL), the aqueous layer was extracted with Et_2O (3 × 3 mL). The organic layers were dried with $MgSO_4$, concentrated under reduced pressure, and compounds **6** and **7** were isolated.

(2*R*)-2-{[(1*R*,3*Z*)-4-Bromo-1-phenylbut-3-en-1-yl]amino}-2-phenylethanol (6a): Oil (42.7 mg, 95% yield). $[\alpha]_D^{20}$ = –47 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.26–7.12 (m, 10 H, Ar), 6.08 (d, *J* = 7.0 Hz, 1 H, CH=C*H*Br), 5.85 (q, *J* = 7.0 Hz, 1 H, C*H*=CHBr), 3.83 (dd, *J* = 4.7 and 7.2 Hz, 1 H, NCHPh), 3.72–3.64 (m, 2 H, NCHPh and C*H*HO), 3.46 (dd, *J* = 4.7 and 7.2 Hz, 1 H, CH*H*O), 2.74–2.62 (m, 1 H, C*H*HC=C), 2.56–2.44 (m, 3 H, CH*H*C=C, OH and NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 143.2, 140.9 (Ar), 131.3 (*C*H=CHBr), 128.7, 128.6, 127.7, 127.6, 127.3, 127.1 (Ar), 109.9 (CH=*C*HBr), 65.9 (CH_20), 61.6 (NCHPh), 58.9 (NCHPh), 36.8 (*C*H_2C=C) ppm. $C_{18}H_{20}BrNO$ (346.26): calcd. C 62.44, H 5.82, N 4.05; found C 62.82, H 5.96, N 3.84.

(2*R*)-2-{[(1*S*,3*Z*)-4-Bromo-1-propylbut-3-en-1-yl]amino}-2-phenylethanol (6b): Oil (33.3 mg, 82% yield). $[\alpha]_D^{20}$ = –93 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.35–7.21 (m, 5 H, Ar), 6.19 (d, *J* = 7.0 Hz, 1 H, CH=C*H*Br), 6.10 (q, *J* = 7.0 Hz, 1 H, C*H*=CHBr), 3.86 (dd, *J* = 4.5 and 8.7 Hz, 1 H, NCHPh), 3.62 (dd, *J* = 4.5 and 10.7 Hz, 1 H, C*H*HO), 3.45 (dd, *J* = 8.7 and 10.7 Hz, 1 H, CH*H*O), 2.58–2.54 (m, 1 H, NC*H*Pr), 2.30–2.25 (m, 4 H, CH_2C=C, OH and NH), 1.37–1.19 (m, 4 H, CH_2CH_2CH$_3$), 0.73 (t, *J* = 6.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.1 (Ar), 131.6 (*C*H=CHBr), 128.8, 127.8, 127.3 (Ar), 109.7 (CH=*C*HBr), 67.0 (CH_20), 61.8 (NHCHPh), 53.2 (NH*C*HPr), 37.4 (*C*H_2CH$_2$CH$_3$), 33.8 (CH_2C=C), 19.3 (CH_2*C*H_2CH$_3$), 14.2 (CH_2CH$_2$*C*H$_3$) ppm. $C_{15}H_{22}BrNO$ (312.25): calcd. C 57.70, H 7.10, N 4.49; found C 58.19, H 7.40, N 4.34.

(2*R*)-2-{[(1*R*,3*Z*)-4-Bromo-1-isopropylbut-3-en-1-yl]amino}-2-phenylethanol (6c): Oil (38.1 mg, 94% yield). $[\alpha]_D^{20}$ = –109 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.31–7.16 (m, 5 H, Ar), 6.16 (dt, *J* = 1.0 and 7.0 Hz, 1 H, CH=C*H*Br), 6.09 (q, *J* = 6.7 Hz, 1 H, C*H*=CHBr), 3.82 (dd, *J* = 4.5 and 8.5 Hz, 1 H, NCHPh), 3.60 (dd, *J* = 4.5 and 10.5 Hz, 1 H, C*H*HO), 3.45 (dd, *J* = 8.7 and 10.7 Hz, 1 H, CH*H*O), 2.38–2.26 (m, 3 H, NCH*i*Pr and CH_2C=C), 2.22 (br. s, 2 H, NH and OH), 1.64–1.51 (m, 1 H, C*H*Me$_2$), 0.82 (d, *J* = 6.7 Hz, 3 H, Me), 0.74 (d, *J* = 6.7 Hz, 3 H, Me) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.1 (Ar), 132.3 (*C*H=CHBr), 128.7, 127.7, 127.5 (Ar), 109.3 (CH=*C*HBr), 67.0 (CH_2O), 62.0 (NCHPh), 59.1 (NCH*i*Pr), 31.3 (*C*H_2C=C), 31.1 (*C*HMe$_2$), 19.0 (Me), 18.4 (Me) ppm. $C_{15}H_{22}BrNO$ (312.25): calcd. C 57.70, H 7.10, N 4.49; found C 58.43, H 7.20, N 4.19.

(2*R*)-2-{[(1*R*,3*Z*)-4-Bromo-1-*tert*-butylbut-3-en-1-yl]amino}-2-phenylethanol (6d): Oil (36.4 mg, 86% yield). $[\alpha]_D^{20}$ = –99 (*c* = 0.9, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.30–7.16 (m, 5 H, Ar), 6.17 (q, *J* = 6.7 Hz, 1 H, CH=C*H*Br), 6.10 (d, *J* = 7.2 Hz, 1 H, C*H*=CHBr), 3.83 (dd, *J* = 4.5 and 8.5 Hz, 1 H, NCHPh), 3.60 (dd, *J* = 4.7 and 10.7 Hz, 1 H, C*H*HO), 3.46 (dd, *J* = 8.5 and 10.7 Hz, 1 H, CH*H*O), 2.43–2.25 (m, 2 H, CH_2C=C), 2.21 (t, *J* = 4.7 Hz, 1 H, NCH*t*Bu), 2.08 (br. s, 2 H, NH and OH), 0.79 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.1 (Ar), 134.2 (*C*H=CHBr), 128.7, 127.7 (Ar), 108.0 (CH=*C*HBr), 67.2 (NCHPh), 62.5 (N*C*H*t*Bu), 62.3 (CH_2O), 35.2 (*C*Me$_3$), 31.7 (*C*H_2C=C), 27.1 (C*Me$_3$*) ppm. $C_{16}H_{24}BrNO$ (326.27): calcd. C 58.90, H 7.41, N 4.29; found C 58.61, H 7.48, N 4.07.

[(1*R*,3*Z*)-4-Bromo-1-phenylbut-3-en-1-yl][(1*R*)-2-methoxy-1-phenylethyl]amine (7a): Oil (45.4 mg, 97% yield). $[\alpha]_D^{20}$ = –35 (*c* = 2.1, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.26–7.08 (m, 10 H, Ar), 6.06 (dt, *J* = 1.5 and 6.7 Hz, 1 H, CH=C*H*Br), 5.85 (q, *J* = 6.7 Hz, 1 H, C*H*=CHBr), 3.94 (dd, *J* = 5.0 and 6.5 Hz, 1 H, NCHPh), 3.69 (dd, *J* = 5.7 and 7.5 Hz, 1 H, NCHPh), 3.35–3.28 (m, 2 H, CH_2O), 3.26 (s, 3 H, OMe), 2.70–2.68 (m, 1 H, C*H*HC=C), 2.52–2.48 (m, 1 H, CH*H*C=C), 2.30 (br. s, 1 H, NH) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 143.4, 141.1 (Ar), 131.6 (*C*H=CHBr), 128.5, 127.8, 127.5, 127.4, 127.2 (Ar), 109.6 (CH=*C*HBr), 77.2 (CH_2O), 60.2 (N*C*HPh), 59.1 (N*C*HPh), 59.0 (OMe), 36.6 (*C*H_2C=C) ppm. $C_{19}H_{22}BrNO$ (360.29): calcd. C 63.34, H 6.15, N 3.89; found C 63.39, H 7.07, N 4.04.

[(1*S*,3*Z*)-4-Bromo-1-propylbut-3-en-1-yl][(1*R*)-2-methoxy-1-phenylethyl]amine (7b): Oil (39 mg, 92% yield). $[\alpha]_D^{20}$ = –83 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.33–7.18 (m, 5 H, Ar), 6.16 (dd, *J* = 1.2 and 6.2 Hz, 1 H, CH=C*H*Br), 6.06 (q, *J* = 6.2 Hz, 1 H, C*H*=CHBr), 4.01 (t, *J* = 6.2 Hz, 1 H, NCHPh), 3.38–3.31 (m, 2 H, CH_2O), 3.27 (s, 3 H, OMe), 2.46–2.39 (m, 1 H, NC*H*Pr), 2.27–2.23 (m, 3 H, CH_2C=C and NH), 1.36–1.18 (m, 4 H, CH_2CH_2CH$_3$), 0.72 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.1 (Ar), 131.7 (*C*H=CHBr), 128.5, 127.9, 127.5 (Ar), 109.5 (CH=*C*HBr), 78.0 (CH_2O), 59.5 (N*C*HPh), 58.9 (OMe), 52.9 (N*C*HPr), 37.6 (*C*H_2C=C), 33.5 (*C*H_2CH$_2$CH$_3$), 19.3 (CH_2*C*H_2CH$_3$), 14.2 (CH_3) ppm. $C_{16}H_{24}BrNO$ (326.27): calcd. C 58.90, H 7.41, N 4.29; found C 59.31, H 7.53, N 4.14.

[(1*R*,3*Z*)-4-Bromo-1-isopropylbut-3-en-1-yl][(1*R*)-2-methoxy-1-phenylethyl]amine (7c): Oil (21.2 mg, 50% yield). $[\alpha]_D^{20}$ = –87 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.33–7.15 (m, 5 H, Ar), 6.12 (td, *J* = 1.2 and 7.0 Hz, 1 H, CH=C*H*Br), 6.03 (q, *J* = 6.5 Hz, 1 H, C*H*=CHBr), 3.99 (t, *J* = 6.5 Hz, 1 H, NCHPh), 3.34 (d, *J* = 6.5 Hz, 2 H, CH_2O), 3.28 (s, 3 H, OMe), 2.35–2.18 (m, 3 H, CH_2C=C and NC*Hi*Pr), 1.56 (br. s, 1 H, NH), 1.54–1.47 (m, 1 H, C*H*Me$_2$), 0.82 (d, *J* = 6.7 Hz, 3 H, Me), 0.77 (d, *J* = 6.7 Hz, 3 H, Me) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.5 (Ar), 132.5 (*C*H=CHBr), 128.3, 128.1, 127.5 (Ar), 108.9 (CH=*C*HBr), 78.2 (CH_2O), 59.8 (N*C*HPh), 58.9 (N*C*H*i*Pr), 58.7 (OMe), 31.3 (*C*H_2C=C and *C*HMe$_2$), 19.7 (Me), 18.0 (Me) ppm. $C_{16}H_{24}BrNO$ (326.27): calcd. C 58.90, H 7.41, N 4.29; found C 58.49, H 7.64, N 3.77.

[(1*R*,3*Z*)-4-Bromo-1-*tert*-butylbut-3-en-1-yl][(1*R*)-2-methoxy-1-phenylethyl]amine (7d): Oil (42 mg, 95% yield). $[\alpha]_D^{20}$ = –100 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.36–7.19 (m, 5 H, Ar), 6.19 (q, *J* = 7.0 Hz, 1 H, CH=C*H*Br), 6.11 (d, *J* = 7.0 Hz, 1 H, C*H*=CHBr), 4.01 (dd, *J* = 4.7 and 8.0 Hz, 1 H, NCHPh), 3.41–3.37 (m, 2 H, CH_2O), 3.33 (s, 3 H, OMe), 2.51–2.41 (m, 1 H, C*H*HC=C), 2.38–2.25 (m, 1 H, CH*H*C=C), 2.13 (t, *J* = 5.0 Hz, 1 H, NC*H*t Bu), 1.68 (br. s, 1 H, NH), 0.84 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 141.2 (Ar), 134.5 (*C*H=CHBr),

128.4, 128.3, 127.5 (Ar), 107.5 (CH=*C*HBr), 78.2 (CH_2O), 61.9 (N*C*H*t*Bu), 60.1 (N*C*HPh), 58.9 (OMe), 35.5 (*C*Me_3), 31.6 (CH_2C=C), 27.2 (C*Me*$_3$) ppm.

(2*R*,4*S*)-2-*tert*-Butyl-4-[(trimethylsilyl)methyl]azetidine Hydrobromide (8): A solution of compound **3d** (0.13 mmol) in absolute ethanol (1.5 mL) was injected into a hydrogenation flask containing a suspension of palladium on charcoal (15 mg) in absolute ethanol (1 mL). The reaction was complete in 3 h. The mixture was filtered through Celite 545, and the residue was washed with ethanol. After evaporation of the solvent, the resulting solid was triturated with Et_2O and dried to afford the azetidine **8**. Solid (18.2 mg, 50% yield). M.p. 70 °C. $[\alpha]_D^{20}$ = –6 (*c* = 1.44, $CHCl_3$). ^{1}H NMR (250 MHz, CD_3OD): = 4.39–4.25 (m, 1 H, NC*H*CH_2TMS), 3.99 (t, *J* = 10 Hz, 1 H, NC*H*t*B*u), 2.43 (dt, *J* = 8.0 and 11.8 Hz, 1 H, CHC*H*HCH), 2.13–2.00 (m, 1 H, CHCH*H*CH), 1.19–1.04 (m, 2 H, C*H*$_2$TMS), 0.90 (s, 9 H, *t*Bu), 0.00 (s, 9 H, TMS) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 64.8 (N*C*H*t*Bu), 54.7 (N*C*HCH$_2$TMS), 32.5 (*C*Me_3), 29.5 (CH*C*H$_2$CH), 25.1 (C*Me*$_3$), 23.7 (*C*H_2TMS), –1.0 (TMS) ppm. $C_{11}H_{26}$BrNSi (280.32): calcd. C 47.13, H 9.35, N 5.00; found C 47.23, H 9.56, N 4.87.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of obtained compounds and AM1-calculated structures for bromonium and azetidinium ions.

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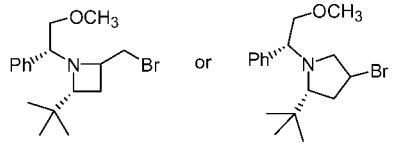

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