

# Regio- and Diastereoselective Synthesis of 2-Arylazetidines: Quantum Chemical Explanation of Baldwin's Rules for the Ring-Formation Reactions of Oxiranes<sup>†</sup>

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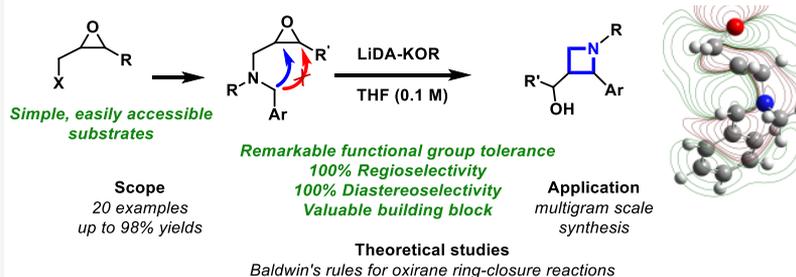


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## Transition Metal Free Regio- and Diastereoselective Intramolecular Ring Formation



**ABSTRACT:** A general, scalable two-step regio- and diastereoselective method has been described for the synthesis of versatile alkaloid-type azetidines from simple building blocks with excellent overall yields. In the kinetically controlled reaction, only the formation of the strained four-membered ring can be achieved instead of the thermodynamically favorable five-membered rings under appropriate conditions. Remarkable functional group tolerance has also been demonstrated. In this paper, we give a new scope of Baldwin's rules by density functional theory (DFT) calculations with an explicit solvent model, confirming the proposed reaction mechanisms and the role of kinetic controls in the stereochemical outcome of the reported transition-metal-free carbon–carbon bond formation reactions.

## INTRODUCTION

Despite the irrefutable importance of azetidines as bioactive compounds and pharmaceutical building blocks, they have received moderate attention compared to larger-ring-sized pyrrolidines and piperidines.<sup>1–3</sup> The most important strategy for the synthesis of saturated *N*-heterocycles relies on unimolecular cyclization reactions by nucleophilic substitution. This approach results in the efficient formation of three-, five-, and six-membered heterocycles but often fails to result in four-membered heterocycles. In general, azetidines are considered the most difficult of all to form.<sup>4</sup> Azetidines have excellent physicochemical properties, bioavailability and metabolic stability.<sup>5–8</sup> A wide variety of antibiotics,<sup>9–13</sup> numerous anticancer agents<sup>14,15</sup> containing azetidines, and other drug molecules have been developed over the last decade.<sup>13,16–21</sup> They have a significant role as synthetic building blocks of foldamers,<sup>22,23</sup> *N*-heterocycles,<sup>24–28</sup> and polymers.<sup>29</sup> It has also been demonstrated, that the introduction of these strained rings improves enormously the fluorescent properties of rhodamines<sup>30–32</sup> and coumarins<sup>33</sup> and the efficacy of homogenous catalysts as ligands,<sup>34,35</sup> which makes them an attractive and challenging synthetic topic for chemists nowadays. Compared to their widespread uses, there are

relatively few synthetic methods available, although they cover a wide range of structural variability.<sup>3,36–38</sup> In conclusion, there are no general methods for the synthesis of azetidines, with a wide variety of functional groups.<sup>39</sup> Only a few methods for the preparation of druglike azetidines have been reported.<sup>40–46</sup>

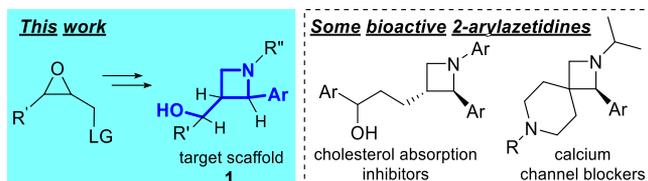
2-Arylazetidines also have a huge potential in synthetic and medicinal chemistry<sup>47–51</sup> (Scheme 1), even though no general synthetic method is known. Only a few approaches have been developed for the synthesis of 2-phenylazetidines. *N*-Protected 2-arylazetidines can be synthesized by stereospecific cross-coupling reactions,<sup>52</sup> by selective intermolecular sp<sup>3</sup>-C–H amination,<sup>53</sup> or by [2+2] photocycloaddition.<sup>1</sup> A few efficient synthetic methods of diversely substituted *N*-aryl-2-cyanoazetidines have also been published, based on an anionic ring-closure reaction, which requires the presence of an electron-withdrawing group (EWG) in the starting material.<sup>54</sup> A similar

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### Scheme 1. Chemical Skeleton of 2-Arylazetidines-3-ylmethanol Derivatives (1) and Selected Examples for Bioactive 2-Arylazetidines<sup>a</sup>



<sup>a</sup>(LG: leaving group.).

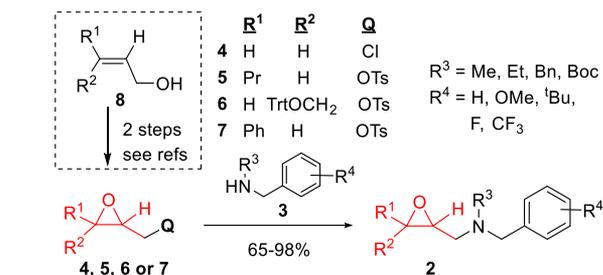
reaction promoted by an uncommonly used base has been reported by our group few years ago.<sup>55</sup>

Our goal was to enrich the available chemical library with *trans*-3-(hydroxymethyl)-2-arylazetidines (**1** in Scheme 1) for fragment-based drug discovery by a novel and versatile chemical synthesis from simple and readily available oxiranylmethyl-substituted benzylamines. This method is inspired by and designed according to Baldwin's rules.<sup>56</sup> While some theoretical explanation has been published in the last decade,<sup>57–59</sup> the quantum chemical background has not been established to date.

## RESULTS AND DISCUSSION

Our synthetic method to prepare 2-arylazetidines **1** consists of only two or four simple synthetic steps from commercially available starting materials (substituted oxiranes and *N*-alkylbenzylamines), providing a large range for functionalization. The key intermediates **2** were synthesized from *N*-substituted benzylamines (**3**) and epichlorohydrin (**4**) or readily prepared 2-substituted-(oxiran-2-yl)methyl 4-toluenesulfonates (**5–7**) (Scheme 2). As was demonstrated earlier, these versatile

### Scheme 2. Synthesis and isolated Yields of the Key Intermediate Oxiranylmethyl-benzylamine Derivatives (2) from Epichlorohydrin (4) or Tosylates (5–7)



epoxide intermediates could be synthesized easily in a two-step procedure from commercially available allyl alcohol derivatives (**8**).<sup>60,61</sup>

The key intermediates **2** (0.5 mmol) were treated with the mixture of lithium diisopropylamide and potassium *tert*-butoxide (LiDA-KOR superbases) in tetrahydrofuran at  $-78$  °C. The *four*-membered ring was formed regio- and diastereoselectively.<sup>55</sup> Noteworthy, compound **2** reacted exclusively on its benzylic position (Scheme 3), excluding the formation of alternative cyclic products. Spectroscopic investigations (*J* in <sup>1</sup>H NMR, ROESY, NOESY) of products confirmed that the substituents were situated in a *trans* geometry around the azetidines ring in positions 2 and 3. The application of other bases did not yield product **1**. To test the

feasibility of the reaction, the metalation of **2d** (in structure **2**  $R^1 = \text{Pr}$ ,  $R^2 = \text{H}$ ,  $R^3 = \text{Me}$ ,  $R^4 = \text{H}$ ) was investigated by different types of organometallic bases used in analogue cases under similar conditions.<sup>62</sup> Using 3 equiv of lithium diisopropyl amide (LDA) or lithium 2,2,6,6-tetramethyl piperidide (LiTMP) or KHMDS (potassium hexamethyldisilazide), only unreacted **2d** oxirane was isolated. When the reaction was performed by BuLi or LiC-KOR (a mixture of butyl lithium and potassium *tert*-butoxide), a complex mixture was obtained with low conversion and azetidines **1d** was detected only in traces.

This reaction was proved to be a scalable process as **1k** was prepared in 20 mmol scale with similar yields of the 0.5 mmol reaction.

In general, the isolated yields varied from moderate to good values with rather a good substituent tolerance, except a few examples. Compared to alternate literature protocols, this two-step synthetic procedure has significantly higher overall production and efficacy. In the cases when the  $R^1/R^2$  group was H, Pr, or Ph, the azetidines products were obtained in moderate to good yields without a significant appearance of any side product.

In contrast, the expected yields were slightly reduced for  $R^2 = \text{CH}_2\text{OTrt}$  products, as some unidentified side products were formed in small amounts.

Various  $R^3$  alkyl groups typically do not influence the good yields of the reactions. However, benzyl substitution allows the formation of certain byproducts through alternative deprotonation, lowering the overall yields. In the case of the product **1g**, two diastereomers formed in 5/1 ratio (liquid chromatography–mass spectrometry, LC–MS), which were separated by common column chromatography. The *N*-*boc* protection at the N atom allows the parallel deprotonation at the C atom in ca. 1/1 ratio and the formation of an allylic-type byproduct (**9**, Scheme 4), which competes with the main ring-opening mechanism.

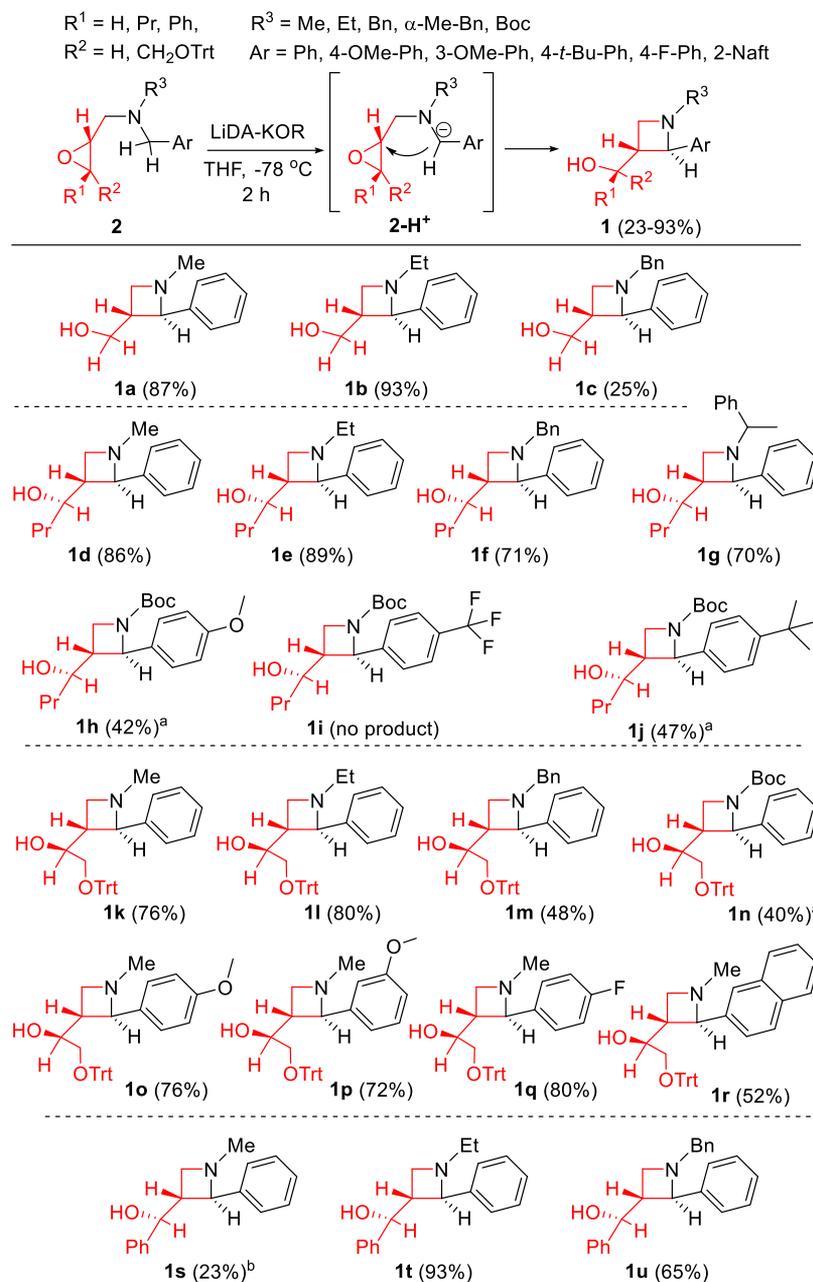
The electron donating group (EDG) substituents (*t*Bu, OMe) and F at the Ph ring ( $R^4$ ) had a beneficial effect on the yields of the reaction. In contrast, the strong EWG  $\text{CF}_3$  group at para and ortho positions (see Supporting Information (SI)) could stabilize the benzyl anion and decreased its nucleophilic character to inhibit the ring opening. Benzylamine moiety-containing bicyclic compounds were also tested. The *N*-oxiranylmethyl isoindole did not afford the desired fused heterocyclic product under the conditions applied. However, it should be emphasized that the reactions of the very similar tetrahydroisoquinoline derivatives have different routes, yielding completely different bridged heterocyclic systems.<sup>63</sup>

**Reaction Mechanism Study.** It is well known for ring-closure reactions that generally five-membered heterocycles are formed more commonly than four-membered products. In general, the relative reaction rate of cyclization steps can be 2 orders of magnitude larger for five-membered rings.<sup>4</sup>

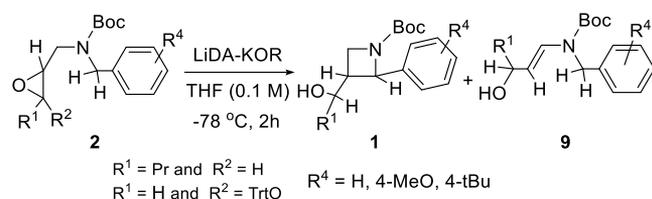
Theoretical calculations were performed at the M06-2X/6-31G(d,p) level of theory<sup>64</sup> with the implementation of an implicit-explicit solvation model<sup>65</sup> ( $\epsilon = 12.2$ ) by G16.<sup>66</sup> The explicit model<sup>67</sup> includes one  $\text{Li}^+$  ion and one  $\text{K}^+$  ion, bound to the  $\text{O}^-$  and the Ph ring, respectively, as shown in Figure 1. Moreover, both cations were solvated by two explicit THF molecules each, to mimic the surrounding media in the best way. The calculated values are given in the SI.

From a thermodynamic point of view, there are five deprotonation sites at compound **2**. However, the enthalpically

## Scheme 3. Scope of the LiDA-KOR-Induced Azetidine Formation



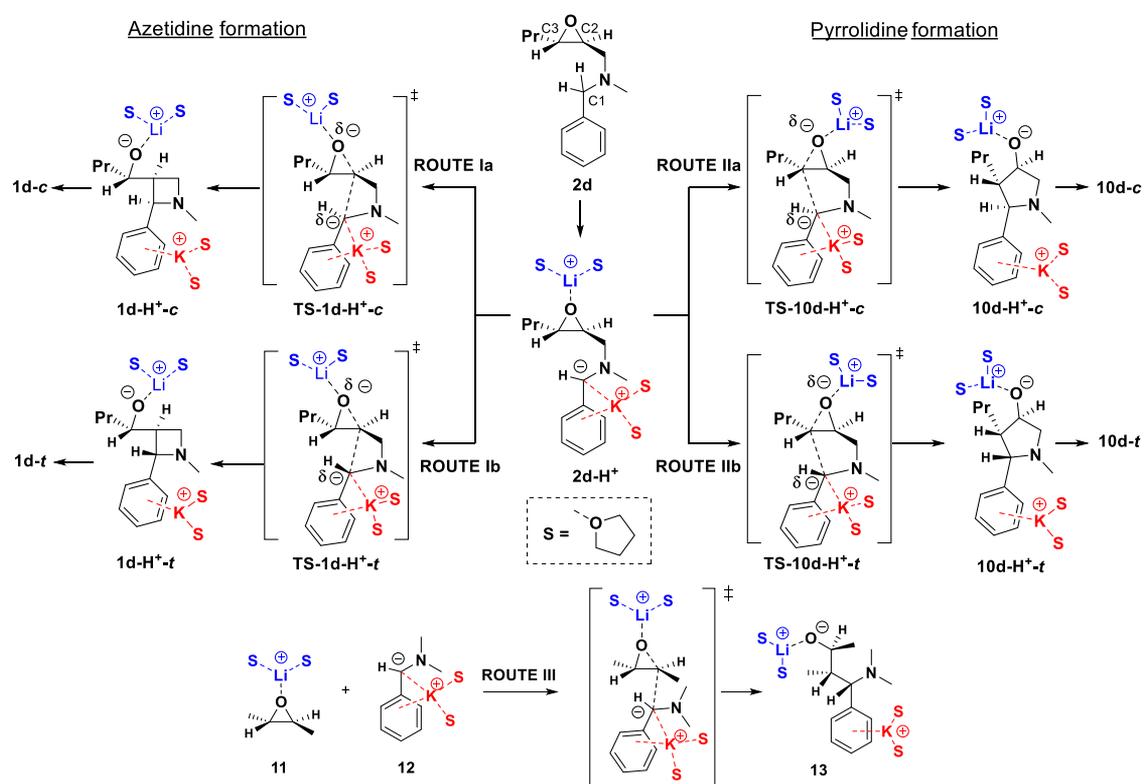
<sup>a</sup>Isolated yields of the products are also given. See Scheme 4. <sup>b</sup>Other products were also formed; see the Experimental Section.

Scheme 4. Formation of the Allylic Side Product (9) in the Case of *N*-Boc Protection of the Amine

and kinetically more favorable deprotonation was found at the benzylic position (C1), in agreement with the experiment. During these reaction mechanism studies, we focused only on the ring-closure steps from the metalation, leading to products for one selected molecule as an example (**2d**  $\rightarrow$  **1d**), including

all of the possible routes (Ia, Ib, IIa, and IIb, see Table 1 and Figure 1). The ring closure (Figure 1) of the metalated benzylaminomethyloxirane **2d-H<sup>+</sup>** may theoretically result in both pyrrolidine (**10d-H<sup>+</sup>-c**, **10d-H<sup>+</sup>-t**) and azetidine products (**1d-c**, **1d-t**), but in our experiments, the *trans* four-membered heterocycle was formed regio- (up to 90%) and diastereoselectively.

The resulting negatively charged nucleophilic carbon atom (C1) can react with both electrophilic carbon atoms in the oxirane (C2 and C3) from two faces (routes Ia, Ib, IIa, and IIb), as shown in Figure 1, leading to the two *cis-trans* product pairs (**1d-c/1d-t** and **10d-c/10d-t**), allowed by Baldwin's rules. In terms of the calculated thermodynamic stability of the resulting products, the two five-membered pyrrolidine derivatives are more stable than the more stressed four-



**Figure 1.** Conversion of the epoxide ( $2d-H^+$ ) into the four possible products ( $1d$  and  $10d$ ) via the four TSs (above), together with the bimolecular reaction (below). For the corresponding thermodynamic values, see Table 1.

**Table 1.** Conversion of the Epoxides ( $2d-H^+$ ) into the Four Possible Products ( $1d$  and  $10d$ ,  $t = trans$ ,  $c = cis$ ) and Their Reaction Enthalpy ( $\Delta H$ ), Gibbs Free Energy ( $\Delta G$ ) in  $\text{kJ mol}^{-1}$ , and Entropy ( $\Delta S$ ) in  $\text{J mol}^{-1} \text{K}^{-1}$ <sup>a</sup>

| $2d-H^+ \rightarrow$ | TS                  |                     |                     | product- $H^+$ |            |            |
|----------------------|---------------------|---------------------|---------------------|----------------|------------|------------|
|                      | $\Delta H^\ddagger$ | $\Delta G^\ddagger$ | $\Delta S^\ddagger$ | $\Delta H$     | $\Delta G$ | $\Delta S$ |
| $1d-H^+t$            | 50.5                | 58.0                | -25.2               | -160.2         | -152.4     | -26.1      |
| $1d-H^+c$            | 65.6                | 67.7                | -6.8                | -128.8         | -120.8     | -27.1      |
| $10d-H^+t$           | 70.8                | 79.4                | -28.7               | -267.1         | -245.1     | -73.6      |
| $10d-H^+c$           | 77.1                | 80.8                | -12.4               | -215.3         | -205.9     | -31.8      |
|                      |                     | TS-13               |                     | 13             |            |            |
| $11 \rightarrow 13$  | 60.2                | 70.8                | -72.1               | -197.0         | -167.4     | -99.3      |

<sup>a</sup>The thermodynamic values of the  $(11+12) \rightarrow \text{TS-13} \rightarrow 13$  process are also given. For details, see Figure 1.

membered azetidine derivatives, regardless of their *cis* ( $10d-c \rightarrow 1d-c$ :  $80.2 \text{ kJ mol}^{-1}$ ) or *trans* ( $10d-t \rightarrow 1d-t$ :  $63.0 \text{ kJ mol}^{-1}$ ) arrangements. In general, the *trans* geometries are always more stable than *cis* ( $1d-c \rightarrow 1d-t$ :  $25.3 \text{ kJ mol}^{-1}$ ;  $10d-c \rightarrow 10d-t$ :  $8.1 \text{ kJ mol}^{-1}$ ), which is due to the larger steric hindrance of the neighboring substituents (Table 1). Since the isolated products were azetidine derivatives in all of the cases, these thermodynamic data allowed us to conclude that the reaction was controlled kinetically.

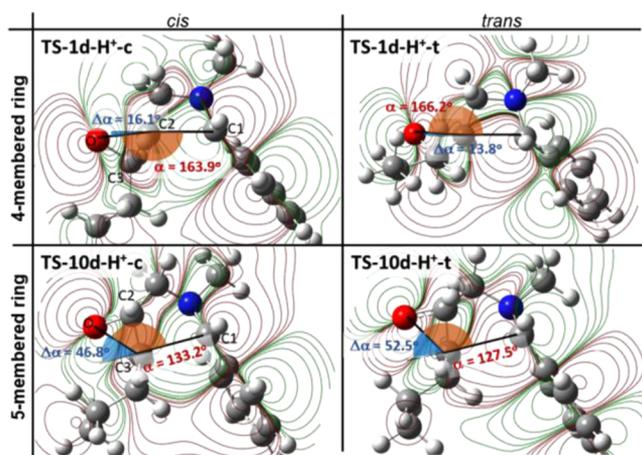
In the next section, we sought to answer the question of why the formation of the thermodynamically unfavorable four-membered azetidines is more advantageous, in agreement with Baldwin's rules. The two lowest TSs undoubtedly belong to the formation of the two azetidines  $1d-H^+t$  and  $1d-H^+c$ , preferring the formation of *trans* products, in contrast to the formation of pyrrolidines ( $10d-H^+c$ ,  $10d-H^+t$ ). The enthalpy ( $\Delta H^\ddagger$ ) and Gibbs free energy ( $\Delta G^\ddagger$ ) difference between the

two lowest gaps is only about  $10 \text{ kJ mol}^{-1}$ . Due to the low reaction temperature applied, this difference provides sufficient diastereoselectivity under kinetic control, in good agreement with the experiments.

Although the computed TS values confirm the experimental findings, they did not give a deep explanation for the exclusive formation of the azetidine derivatives. Moreover, Baldwin's rules also provide only a superficial and phenomenological interpretation. To reveal more details about the mechanism, a bimolecular model reaction ( $(11+12) \rightarrow \text{TS-13} \rightarrow 13$ , route III in Figure 1) was also carried out under the same condition as a concerted  $S_N2$ -type reaction, which mimics a nonrestricted alternative of the previous reaction (Figure 1). Here, the deprotonated dimethyl benzamide anion ( $12$ ) reacts with *trans* oxiranes ( $11$ ). Surprisingly, the computed activation parameters ( $\Delta H^\ddagger$  and  $\Delta G^\ddagger$ ) are significantly higher compared to those in the formation of the stretched four-membered product and somewhat lower than in the case of the five-membered product. On this basis, we suppose that the azetidine formation is superbeneficial.

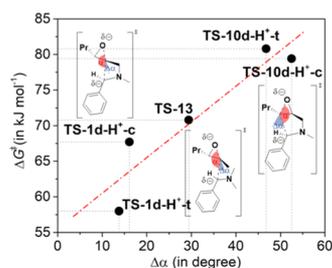
In the ideal transition state for  $S_N2$  reactions, the direction of the electrophile attack should be around  $180^\circ$  with the central atom and the leaving group, which provides the highest overlap between the nucleophilic highest occupied molecular orbital (HOMO) and the electrophilic lowest unoccupied molecular orbital (LUMO). In this ring-closure reaction, the central atom (C2 or C3), the attacking carbanion (C1), and the leaving oxygen atom (O) cannot be in this optimal linear arrangement in either case due to the bent bond angles in the oxirane-ring.

Analyzing the geometries of the transition states leading to the five- (TS- $10d-H^+c$  and TS- $10d-H^+t$ ) and four-membered rings (TS- $1d-H^+c$ , TS- $1d-H^+t$ ; Figure 2), as well as the TS-13, we found that the angle of the attack enclosed by the C1–



**Figure 2.** Transition states (TS-1d-H<sup>+</sup> and TS-10d-H<sup>+</sup>) of the four- and five-membered rings (without explicit ions and molecules), representing their HOMOs leading to the azetidines (1d) and pyrrolidine derivatives (10d) derived from the oxirane derivative 2d-H<sup>+</sup>. Black lines show the bond angles between the C1–C2–O and C1–C3–O atoms, corresponding to  $\alpha$  (orange).  $\Delta\alpha = 180^\circ - \alpha$  (blue). The carbon, hydrogen, nitrogen, and oxygen atoms are marked in gray, white, blue, and red, respectively.

C2–O atoms is most favorable for the formation of the four-membered *trans* and *cis* isomers (*trans*: 166.2° and *cis*: 163.9°) than five-membered cases (C–C3–O, *trans*: 133.2°, *cis*: 127.5°). Moreover, the nonrestricted model also exhibits lower angles than TS-1d-H<sup>+</sup> (150.6°). The special preferred arrangement of the C1–C2–O in the TS-1d-H<sup>+</sup> is due to the stretched double bicyclic transition structure, which provides the optimal arrangement for the orbital overlap and can be illustrated by the  $\Delta\alpha$  value ( $=180^\circ - \alpha$ , blue angles in Figures 2 and 3). In the case of route II, pyrrolidine is already distorted in the opposite direction, thereby significantly reducing the overlap.



**Figure 3.** Correlation between the  $\Delta\alpha$  ( $\Delta\alpha = 180^\circ - \alpha$ ) (blue) of TS-1d-H<sup>+</sup>, TS-10d-H<sup>+</sup>, and TS-13 and the related  $\Delta G^\ddagger$  values.

This overlap between the HOMO of 12 and the LUMO of 13 is significantly less than that of the TS-1-H<sup>+</sup>, thanks to the dominance of the steric hindrance in the absence of the supporting ring stretch. Consequently, this may be the reason for the lowest activation  $\Delta G^\ddagger$  of the four-membered *trans* azetidines derivative.

## CONCLUSIONS

In summary, an efficient, scalable, and stereo- and diastereo-specific method was developed for the preparation of 2-arylazetidines (1), using strong alkali amide-type bases. The results of the quantum chemical investigation of the

mechanism are consistent with the experimental findings and shed light on the details of the regio- and stereoselectivity of the azetidines formation reaction. Thus, we were able to find the quantum mechanical and structural explanation of Baldwin's rules for the ring opening of oxiranes, controlled by the balance between the ring stretch and overlap.

## EXPERIMENTAL SECTION

**General Remarks.** All commercial starting materials were purchased from Sigma-Aldrich Kft., Hungary, and were used without further purification. All organometallic reactions were conducted under a dry nitrogen atmosphere using the Schlenk-technique. Solvents were freshly distilled and dried over molecular sieves.

<sup>1</sup>H NMR and <sup>13</sup>C {<sup>1</sup>H} NMR spectra were recorded at 500/300 and 126/75 MHz on Bruker Avance 500 or 300 spectrometers. All <sup>1</sup>H NMR and <sup>13</sup>C chemical shifts were referenced to the tetramethylsilane (TMS). All chemical shifts are quoted in parts per million (ppm), measured from the center of the signal, except in the case of multiplets, which are quoted as a range. Coupling constants are quoted to the nearest 0.1 Hz. Splitting patterns are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sxt), multiplet (m), broad singlet (br. s), and combinations thereof. The assignment of spectra was aided by DEPT 135 and 1D (NOESY) and 2D NMR spectroscopy (NOESY, ROESY, HSQC). For the assignment, see SI NMR spectra.

HRMS-EI<sup>+</sup> data were obtained using either electrospray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI analyses were performed on an Agilent 6230 TOF LC/MS spectrometer (ion trap; analyzed using Excalibur). High-resolution EI analysis was performed on an Autospec spectrometer (magnetic sector; analyzed using MassLynx).

Thin-layer chromatography (TLC) was performed on commercially available precoated TLC plates (Merck Silica gel 60 F<sub>254</sub> aluminum sheets or Merck aluminum oxide 60 F<sub>254</sub> plates). Visualization was achieved either under UV light at 254 nm or by exposure to iodine or the aqueous solution of (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·Ce(SO<sub>4</sub>)<sub>2</sub> and sulfuric acid.

Flash column chromatography was performed by a CombiFlash R<sub>f</sub> 150 (Teledyne ISCO) apparatus using gradient elution in normal (silica column; hexane–ethyl acetate as the eluent) phase mode. Gradient elution preparative high-performance liquid chromatography (HPLC) was performed (HPLC Gilson 333 instrument, UV detector 220 nm) on a Phenomenex Gemini C18 (250 mm × 50.00 mm; 10 μm, 110 Å) column using 0.4 g of NH<sub>4</sub>HCO<sub>3</sub> in 1 L of water and acetonitrile (A/B) or 10 mL of trifluoroacetic acid in 1 L of water and acetonitrile (C/B) as the two solvents.

**General Procedures.** *General Procedure A for the Preparation of Trialkyl Amines from Epichlorohydrin.* To a solution of amines (30.0 mmol, 1.0 equiv) in EtOH (4 mL) and water (2 mL) was added epichlorohydrin (30.0 mmol, 2.35 mL, 1.0 equiv) at 0 °C using an ice bath. The mixture was stirred for 5 h at room temperature and then cooled to 0 °C in an ice bath. Toluene (3 mL) and NaOH (0.054 mmol, 2.16 g) were added and then stirred at 25 °C for 16 h. The mixture was concentrated under reduced pressure, and then water (20.0 mL) was added to it. The organic compounds were extracted with dichloromethane (4 × 30 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by column chromatography.

*General Procedure B for the Preparation of Trialkyl Amines from Tosylates.* Tosylate (10.0 mmol, 1.0 equiv) was dissolved in dry *N,N*-dimethylformamide (DMF, 10 mL) under a dry nitrogen atmosphere, and potassium iodide (5.00 mmol, 0.5 equiv) was added into it. The solution was cooled to 0 °C in an ice bath, and the secondary amine (HNRR', 21.00 mmol, 2.1 equiv) was added into the solution. The reaction mixture was stirred for 24 h at 40 °C and heated by an oil bath, and then it was poured into a mixture of ice (100 g), saturated sodium hydrogen carbonate solution (200 mL), and diethyl ether (50 mL). Then, the phases were separated and the aqueous mixture was

extracted with diethyl ether (4 × 60 mL). The combined organic layers were washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by column chromatography.

**General Procedure C for the Preparation of *N*-Boc-Amino-methyloxiranes.** Sodium hydride (55% in mineral oil, 1.8 mmol, 72.2 mg, 1.5 equiv) was washed with dry hexane (3 × 3 mL) under a dry nitrogen atmosphere. Then, it was dried in vacuo followed by the addition of dry DMF (2 mL) and cooled (0 °C in an ice bath). A dimethylformamide solution (7 mL) of *N*-boc-benzylamine derivative<sup>68</sup> (1.20 mmol, 1.0 equiv) was added dropwise to the cold (0 °C) suspension of sodium hydride and DMF, and the mixture was stirred for 2 h at room temperature. The obtained yellowish solution was slowly added into a dry DMF solution (7 mL) of tosylate (1.2 mmol, 1.0 equiv) at 5 °C and cooled in an ice bath under a nitrogen atmosphere. The reaction mixture was stirred for 24 h, and then it was poured into a mixture of ice (15 g) and saturated sodium hydrogen carbonate solution (10 mL). The aqueous mixture was extracted with diethyl ether (5 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by column chromatography.

**General Procedure D for the Preparation of Azetidines via Superbase-Induced Reactions.** Potassium *tert*-butoxide in tetrahydrofuran (THF, 1.0 mmol, 1 mL in 1 M THF solution) was cooled to -78 °C in a cold bath, using dry ice in acetone, in a Schlenk tube under a nitrogen atmosphere and diluted with 1 mL of absolute THF. Diisopropylamine (1.0 mmol, 0.10 g, 0.14 mL, 2.0 equiv) and a 1.59 M hexane solution of butyllithium (1.5 mmol, 0.94 mL, 3.0 equiv) were added dropwise into the solution. The reaction mixture was stirred for 20 min at -78 °C. Oxirane (2, 0.5 mmol, 1.0 equiv) in absolute THF (2 mL) was added dropwise, and the mixture was stirred at -78 °C for 2 h. Water (10.0 mL) and diethyl ether (5 mL) were added to the cold mixture, and then it was allowed to warm up to room temperature. The phases were separated, and the aqueous phase was extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with brine (1 × 10 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude mixture was purified by column chromatography or in some cases by preparative HPLC.

**Synthesis of Benzylaminomethyl-oxiranes.** *N*-Benzyl-*N*-methyl-1-(oxiran-2-yl)methanamine (**2a**). It was prepared according to general procedure A using *N*-methylbenzylamine (30.0 mmol, 3.64 g, 3.87 mL) and epichlorohydrin (30.0 mmol, 2.35 mL). Purification by column chromatography on silica gel (10–40% EtOAc in hexane) afforded the title compound as a yellowish oil (**2a**, 3.16 g, 18.0 mmol, 60%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.37–7.21 (5H, m, C[7,8,9]-H), 3.64 (1H, AB d, *J* = 13.1 Hz, C[5]-H), 3.50 (1H, AB d, *J* = 13.1 Hz, C[5]-H), 3.15–3.07 (1H, m, C[2]-H), 2.81–2.68 (2H, m, 2 × C[1]-H), 2.49–2.41 (1H, m, C[3]-H), 2.38–2.32 (4H, m, C[3]-H, 3 × C[4]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 138.7 (C[6]), 129.0 (C[7]), 128.3 (C[8]), 127.1 (C[9]), 62.6 (C[5]), 59.7 (C[3]), 50.8 (C[2]), 45.0 (C[1]), 42.9 (C[4]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>16</sub>NO 178.1226; found 178.1219.

*N*-Benzyl-*N*-ethyl-1-(oxiran-2-yl)methanamine (**2b**). It was prepared according to general procedure A using *N*-ethylbenzylamine (30.0 mmol, 4.06 g, 4.46 mL) and epichlorohydrin (30.0 mmol, 2.35 mL). Purification by column chromatography on silica gel (0–30% EtOAc in hexane) afforded **2b** as a yellowish oil (3.10 g, 16.2 mmol, 54%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.37–7.21 (5H, m, C[8,9,10]-H), 3.76 (1H, AB d, *J* = 13.7 Hz, C[6]-H), 3.57 (1H, AB d, *J* = 13.7 Hz, C[6]-H), 3.09–3.00 (1H, m, C[2]-H), 2.81–2.52 (4H, m, 2 × C[1]-H, 2 × C[4]-H), 2.52–2.37 (2H, m, C[3]-H), 1.08 (3H, t, *J* = 7.1 Hz, 3 × C[5]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 139.5 (C[7]), 128.9 (C[8]), 128.2 (C[9]), 126.9 (C[10]), 58.5 (C[6]), 55.8 (C[3]), 51.1 (C[2]), 48.2 (C[4]), 45.2 (C[1]), 11.9 (C[5]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>NO 192.1383; found 192.1382.

*N,N*-Dibenzyl-1-(oxiran-2-yl)methanamine (**2c**). It was prepared according to general procedure A using dibenzylamine (30.0 mmol,

5.92 g, 5.77 mL) and epichlorohydrin (30.0 mmol, 2.35 mL). Purification by column chromatography on silica gel (0–15% EtOAc in hexane) afforded **2c** as a yellowish oil (1.98 g, 7.80 mmol, 26%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.38 (4H, d, *J* = 7.2 Hz, 4 × C[6]-H), 7.30 (4H, t, *J* = 7.2 Hz, 4 × C[7]-H), 7.26–7.20 (2H, m, Hz, 2 × C[8]-H), 3.80 (2H, AB d, *J* = 13.7 Hz, 2 × C[4]-H), 3.56 (1H, AB d, *J* = 13.7 Hz, 2 × C[4]-H), 3.06 (1H, td, *J* = 6.2 Hz, 3.4 Hz, C[2]-H), 2.76 (1H, dd, *J* = 13.8 Hz, 3.4 Hz, C[3]-H) 2.65 (1H, t, *J* = 4.5 Hz, C[1]-H), 2.46–2.37 (2H, m, C[1]-H, C[3]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 139.3 (C[5]), 128.8 (C[6]), 128.2 (C[7]), 126.9 (C[8]), 58.9 (C[4]), 55.8 (C[3]), 51.0 (C[2]), 45.0 (C[1]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539; found 254.1539.

*N*-Benzyl-*N*-methyl-1-(3-propyloxiran-2-yl)methanamine (**2d**). It was prepared according to general procedure B using *N*-methylbenzylamine (16.6 mmol, 2.01 g, 2.15 mL) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (6.67 mmol, 1.80 g). Purification by column chromatography on silica gel (0–25% EtOAc in hexane) afforded the title compound (**2d**) as a yellowish oil (1.26 g, 5.75 mmol, 86%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.34–7.24 (5H, m, C[7,8,9]-H), 3.63 (1H, AB d, *J* = 13.0 Hz, C[5]-H), 3.50 (1H, d, *J* = 13.0 Hz, C[5]-H), 2.91–2.85 (1H, m, C[2]-H), 2.71–2.64 (2H, m, C[1]-H, C[3]-H), 2.40 (1H, AB dd, *J* = 13.2 Hz, 6.2 Hz, C[3]-H) 2.30 (3H, s, 3 × C[4]-H), 1.53–1.44 (4H, m, 2 × C[10]-H, 2 × C[11]-H), 0.95 (3H, t, *J* = 6.9 Hz, 3 × C[12]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 138.7 (C[6]), 129.0 (C[7]), 128.3 (C[8]), 127.1 (C[9]), 62.6 (C[5]), 59.3 (C[3]), 57.0 (C[1/2]), 56.8 (C[1/2]), 42.9 (C[4]), 33.9 (C[10]), 19.3 (C[11]), 13.9 (C[12]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>22</sub>NO 220.1701; found 220.1703.

*N*-Benzyl-*N*-ethyl-1-(3-propyloxiran-2-yl)methanamine (**2e**). It was prepared according to general procedure B using *N*-ethylbenzylamine (3.88 mmol, 0.525 g, 0.57 mL) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.85 mmol, 0.500 g). Purification by column chromatography on silica gel (0–30% EtOAc in hexane) afforded the title compound as a yellowish oil (**2e**, 0.363 g, 1.55 mmol, 84%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.36–7.22 (5H, m, C[8,9,10]-H), 3.73 (1H, AB d, *J* = 13.6 Hz, C[6]-H), 3.73 (1H, AB d, *J* = 13.6 Hz, C[6]-H), 2.86–2.80 (1H, m, C[2]-H), 2.72–2.46 (5H, m, C[1]-H, 2 × C[4]-H, 2 × C[6]-H) 1.52–1.39 (4H, m, 2 × C[11]-H, 2 × C[12]-H) 1.07 (3H, t, *J* = 7.2 Hz, 3 × C[5]-H), 0.94 (3H, t, *J* = 6.8 Hz, 2 × C[13]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 139.6 (C[7]), 128.9 (C[8]), 128.2 (C[9]), 126.9 (C[10]), 58.5 (C[6]), 57.3 (C[1/2]), 57.0 (C[1/2]), 55.4 (C[3]), 48.1 (C[4]), 33.9 (C[12]), 19.3 (C[13]), 13.9 (C[14]), 11.8 (C[5]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>24</sub>NO 234.1852; found 234.1861.

*N,N*-Dibenzyl-1-(3-propyloxiran-2-yl)methanamine (**2f**). It was prepared according to general procedure B using dibenzylamine (3.88 mmol, 0.765 g, 0.745 mL) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.85 mmol, 0.500 g). Purification by column chromatography on silica gel (0–12% EtOAc in hexane) afforded the title compound as a yellowish oil (0.535 g, 1.81 mmol, 93%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.38 (4H, d, *J* = 7.2 Hz, 4 × C[6]-H), 7.31 (4H, t, *J* = 7.2 Hz, 4 × C[7]-H), 7.26–7.19 (2H, m, Hz, 2 × C[8]-H), 3.76 (2H, AB d, *J* = 13.5 Hz, 2 × C[4]-H), 3.56 (2H, AB d, *J* = 13.5 Hz, 2 × C[4]-H), 2.86–2.84 (1H, m, C[1]-H), 2.68 (1H, dd, *J* = 13.5 Hz, 4.1 Hz, C[3]-H), 2.62 (1H, m, C[2]-H), 2.49 (1H, dd, *J* = 13.5 Hz, 5.7 Hz, C[3]-H), 1.44–1.42 (4H, m, 2 × C[9]-H, 2 × C[10]-H) 0.92 (3H, t, *J* = 7.2 Hz, 3 × C[11]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 139.4 (C[5]), 128.8 (C[6]), 128.2 (C[7]), 126.9 (C[8]), 58.9 (C[4]), 57.2 (C[1/2]), 56.8 (C[1/2]), 55.5 (C[3]), 33.8 (C[9]), 19.3 (C[10]), 13.9 (C[11]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>26</sub>NO 296.2009; found 296.2021.

(1*R*)-*N*-Benzyl-1-phenyl-*N*-(3-propyloxiran-2-yl)methyl)ethan-1-amine (**2g**). It was prepared according to general procedure B using (1*R*)-*N*-benzyl-1-phenylethan-1-amine (3.89 mmol, 0.822 g) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.85 mmol, 500 mg). Purification by column chromatography on silica gel (0–10% EtOAc in hexane) afforded **2g** as a yellowish oil (0.430 g, 1.39 mmol, 75%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.45–7.18 (10H, m, C[6-8, 12-14]-H), 4.00 (1H, td, *J* = 17.9 Hz, 67 Hz, C[9]-H NHCH<sub>3</sub>),

3.79–3.71 (1H, m, C[4]-H), 3.60–3.46 (1H, m, C[4]-H), 2.77–2.49 (4H, m, C[1]-H, C[2]-H, 2 × C[3]-H), 1.43–1.31 (7H, m, 3 × C[9]-H, 2 × C[15]-H, 2 × C[16]-H), 0.90 (3H, m, 3 × C[17]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 143.7, 142.9, 140.5, 140.4, 128.6, 128.2, 128.1, 127.9, 127.8, 126.8, 126.8, 126.7, 59.0, 58.4, 57.9, 57.7, 57.6, 57.1, 55.2, 55.2, 51.9, 51.7, 33.9, 19.3, 19.23, 16.0, 14.1, 13.9. HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{14}\text{H}_{22}\text{NO}$  310.2165; found 310.2159.

**tert-Butyl (4-Methoxybenzyl)((3-propyloxiran-2-yl)methyl)carbamate (2h)**. It was prepared according to general procedure C using *tert*-butyl (4-methoxybenzyl)carbamate (1.85 mmol, 440 mg) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.85 mmol, 500 mg). Purification by column chromatography on Florisil (0–20% EtOAc in hexane) afforded the title compound as a yellowish oil (436 mg, 1.30 mmol, 70%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.17 (2H, d,  $J = 7.2$  Hz, 2 × C[9]-H), 6.85 (2H, d,  $J = 7.2$  Hz, 2 × C[10]-H), 4.53 (1H, AB d,  $J = 15.0$  Hz, C[7]-H), 4.37 (1H, d,  $J = 15.0$  Hz, C[7]-H), 3.78 (3H, s, 3 × C[12]-H), 3.63–2.65 (4H, m, C[1]-H, C[2]-H, 2 × C[3]-H), 1.60–1.35 (13H, m, 9 × C[6]-H, 2 × C[13]-H, 2 × C[14]-H), 0.94 (3H, t,  $J = 6.8$  Hz, 3 × C[15]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 158.9 (C[11]), 155.6 (C[4]), 130.3 (C[9]), 129.3 (C[8]), 128.8 (C[9]), 113.9 (C[10]), 80.0 (C[5]), 57.4 (C[1]), 56.8 (C[2]), 55.2 (C[12]), 50.8 (C[7]), 50.3 (C[7]), 47.8 (C[3]), 33.7 (C[13]), 28.5 (C[6]), 19.2 (C[14]), 13.9 (C[15]). HRMS (ESI $^+$ ) for  $\text{C}_{19}\text{H}_{29}\text{NNaO}_4$  ( $[\text{M} + \text{Na}]^+$ ): calcd for 358.1989; found 358.1982. HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{22}\text{NO}_4$  280.1543; found 280.1533.

**tert-Butyl (4-Trifluoromethylbenzyl)((3-propyloxiran-2-yl)methyl)carbamate (2i)**. It was prepared according to general procedure C using *tert*-butyl (4-(trifluoromethyl)benzyl)carbamate (1.85 mmol, 510 mg) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.85 mmol, 500 mg). Purification by column chromatography on Florisil (0–10% EtOAc in hexane) afforded the title compound **2i** as a yellowish oil (520 mg, 1.39 mmol, 76%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ :  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.58 (2H, d,  $J = 7.8$  Hz, 2 × C[9]-H), 7.41–7.30 (2H, m, 2 × C[10]-H), 4.66 (1H, AB d,  $J = 15.0$  Hz, C[7]-H), 4.49 (1H, AB d,  $J = 15.0$  Hz, C[7]-H), 3.82–2.66 (4H, m, C[1]-H, C[2]-H, 2 × C[3]-H), 1.55–1.40 (13H, m, 9 × C[6]-H, 2 × C[13]-H, 2 × C[14]-H), 0.94 (3H, t,  $J = 6.8$  Hz, 3 × C[15]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 155.5 (C[4]), 142.6 (q,  $J = 1.8$  Hz, C[9]), 130.0 (C[8]), 127.7 (q,  $J = 31$  Hz, C[11]), 127.3, 125.5 (q,  $J = 3.6$  Hz, C[10]), 129.9 (q,  $J = 27.3$  Hz, C[12]), 80.6 (C[5]), 56.9 (C[1]), 56.7 (C[2]), 51.2 (C[7]), 50.7 (C[7]), 48.5 (C[3]), 33.6 (C[13]), 28.4 (C[6]), 19.2 (C[14]), 13.9 (C[15]). HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{15}\text{H}_{19}\text{F}_3\text{NO}_3$  318.1312; found 318.1327.

**tert-Butyl (4-tert-Butyl Benzyl)((3-propyloxiran-2-yl)methyl)carbamate (2j)**. It was prepared according to general procedure C using *tert*-butyl (4-(*tert*-butyl)benzyl)carbamate (1.85 mmol, 490 mg) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.85 mmol, 500 mg). Purification by column chromatography on Florisil (0–20% EtOAc in hexane) afforded the title compound as a yellowish oil (540 mg, 1.49 mmol, 81%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ :  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.33 (2H, d,  $J = 7.8$  Hz, 2 × C[10]-H), 7.17 (2H, d,  $J = 7.5$  Hz, 2 × C[9]-H), 4.59 (1H, AB d,  $J = 15.3$  Hz, C[7]-H), 4.38 (1H, AB d,  $J = 15.3$  Hz, C[7]-H), 3.56–2.63 (4H, m, C[1]-H, C[2]-H, 2 × C[3]-H), 1.53–1.38 (13H, m, 9 × C[13]-H, 2 × C[14]-H, 2 × C[15]-H), 1.31 (9H, s, 9 × C[6]-H), 0.93 (3H, t,  $J = 6.3$  Hz, C[16]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 155.7 (C[4]), 150.2 (C[11]), 135.2 (C[8]), 127.6 (C[9]), 127.3 (C[9]), 125.4 (C[10]), 80.1 (C[5]), 57.6 (C[2]), 56.8 (C[1]), 57.0 (C[2]), 51.0 (C[7]), 50.6 (C[7]), 48.0 (C[3]), 34.5 (C[12]), 33.7 (C[14]), 31.4 (C[6]), 28.5 (C[13]), 19.2 (C[15]), 13.9 (C[16]). HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{28}\text{NO}_3$  306.2064; found 306.2077.

**N-Benzyl-N-methyl-1-(3-((trityloxy)methyl)oxiran-2-yl)methanamine (2k)**. It was prepared according to general procedure B using *N*-benzylmethylamine (4.2 mmol, 0.509 g, 0.542 mL) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (2.0 mmol, 1.00 g). Purification by column chromatography on silica gel

(0–30% EtOAc in hexane) afforded the title compound as a yellowish oil (0.867 g, 1.93 mmol, 96%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.44 (6H, d,  $J = 7.8$  Hz, 6 × C[13]-H), 7.30–7.21 (14H, m, Ar-H), 3.55 (1H, AB d,  $J = 13.0$  Hz, C[5]-H), 3.41 (1H, d,  $J = 13.0$  Hz, C[5]-H), 3.32 (1H, dd,  $J = 10.5$  Hz, 6.0 Hz, C[10]-H), 3.18 (2H, m, C[1]-H, C[2]-H), 3.10 (1H, dd,  $J = 10.5$ , 4.5 Hz, C[10]-H), 2.57 (1H, dd,  $J = 13.5$ , 3.5 Hz, C[3]-H), 2.21 (3H, s, 3 × C[4]-H), 2.18 (1H, dd,  $J = 13.5$ , 6.0 Hz, C[3]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 143.7 (C[12]), 138.5 (C[6]), 129.0 (C[13]), 128.6 (C[14]), 128.2 (C[7]), 127.9 (C[8]), 127.1 (C[15]), 127.1 (C[9]), 86.9 (C[11]), 62.4 (C[10]), 62.2 (C[5]), 55.4 (C[3]), 55.1 (C[1]), 54.2 (C[2]), 42.7 (C[4]). HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{31}\text{H}_{32}\text{NO}_2$  450.2433; found 450.2443.

**N-Benzyl-N-ethyl-1-(3-((trityloxy)methyl)oxiran-2-yl)methanamine (2l)**. It was prepared according to general procedure B using *N*-ethylbenzylamine (4.2 mmol, 0.568 g, 0.625 mL) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (2.0 mmol, 1.00 g). Purification by column chromatography on silica gel (0–20% EtOAc in hexane) afforded the title compound as a yellowish oil (0.713 g, 1.54 mmol, 77%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.44 (6H, d,  $J = 7.8$  Hz, 6 × C[14]-H), 7.30–7.20 (14H, m, Ar-H), 3.67 (1H, AB d,  $J = 13.0$  Hz, C[6]-H), 3.49 (1H, d,  $J = 13.0$  Hz, C[6]-H), 3.29 (1H, dd,  $J = 10.5$  Hz, 6.0 Hz, C[11]-H), 3.18–3.10 (2H, m, C[1]-H, C[2]-H), 3.08 (1H, dd,  $J = 10.5$ , 4.5 Hz, C[11]-H), 2.61–2.54 (2H, m, C[3]-H, C[4]-H), 2.52–2.45 (1H, m, C[4]-H), 2.30 (1H, dd,  $J = 13.5$ , 6.0 Hz, C[3]-H), 0.98 (3H, t,  $J = 7.2$  Hz, 3 × C[5]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 143.8 (C[13]), 139.4 (C[7]), 128.8 (C[9]), 128.7 (C[14]), 128.2 (C[8]), 127.9 (C[15]), 127.1 (C[16]), 126.9 (C[10]), 86.9 (C[12]), 62.3 (C[11]), 58.3 (C[6]), 55.3 (C[3]), 54.3 (C[1]), 51.5 (C[2]), 47.9 (C[4]), 11.8 (C[5]). HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{32}\text{H}_{34}\text{NO}_2$  464.2590; found 464.2596.

**N,N-Dibenzyl-1-(3-((trityloxy)methyl)oxiran-2-yl)methanamine (2m)**. It was prepared according to general procedure B using dibenzylamine (4.2 mmol, 0.828 g, 0.808 mL) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (2.0 mmol, 1.00 g). Purification by column chromatography on silica gel (0–10% EtOAc in hexane) afforded the title compound as a yellowish oil (894 mg, 1.70 mmol, 85%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ :  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.41 (6H, d,  $J = 7.5$  Hz, 6 × C[12]-H), 7.33–7.20 (19H, m, Ar-H), 3.71 (2H, AB d,  $J = 13.7$  Hz, 2 × C[4]-H), 3.47 (2H, d,  $J = 13.7$  Hz, 2 × C[4]-H), 3.24 (1H, dd,  $J = 9.9$  Hz, 5.5 Hz, C[9]-H), 3.20–3.11 (2H, m, C[1]-H, C[2]-H), 3.05 (1H, dd,  $J = 9.9$  Hz, 3.9 Hz, C[9]-H), 2.59 (1H, dd,  $J = 13.7$ , 3.1 Hz, C[3]-H), 2.18 (1H, dd,  $J = 13.7$  Hz, 6.2 Hz, C[3]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 143.7 (C[11]), 139.1 (C[5]), 128.8 (C[6]), 128.6 (C[13]), 128.2 (C[7]), 127.8 (C[12]), 127.1 (C[14]), 126.9 (C[8]), 86.9 (C[10]), 62.2 (C[9]), 58.6 (C[4]), 55.3 (C[1]), 54.2 (C[1]), 51.6 (C[2]). HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{37}\text{H}_{36}\text{NO}_2$  526.2746; found 526.2733.

**tert-Butyl Benzyl((3-((trityloxy)methyl)oxiran-2-yl)methyl)carbamate (2n)**. It was prepared according to general procedure C using *tert*-butyl (benzyl)carbamate (1.2 mmol, 316 mg) and (3-propyloxiran-2-yl)methyl (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (1.2 mmol, 601 mg). Purification by column chromatography on Florisil (0–20% EtOAc in hexane) afforded the title compound as a yellowish oil (372 mg, 0.70 mmol, 58%).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta_{\text{H}}$ : 7.41 (6H, d,  $J = 7.8$  Hz, 6 × C[15]-H), 7.30–7.18 (12H, m, Ar-H), 7.11–7.05 (2H, m, Ar-H), 4.59 (1H, AB d,  $J = 15.5$  Hz, C[7]-H), 4.32–4.26 (1H, m, C[7]-H), 3.68–2.78 (6H, m, C[1]-H, C[2]-H, 2 × C[3]-H, 2 × C[12]-H), 1.44 (9H, s, 2 × C[6]-H).  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta_{\text{C}}$ : 155.6 (C[4]), 143.6 (C[14]), 138.9 (C[8]), 138.1 (C[8]), 128.6 (C[15]), 128.4 (C[10]), 127.9 (C[9]), 127.9 (C[16]), 127.3 (C[11]), 127.1 (C[17]), 87.0 (C[13]), 80.2 (C[5]), 62.3 (C[12]), 54.9 (C[1]), 54.3 (C[2]), 50.9 (C[7]), 45.0 (C[3]), 28.4 (C[6]). HRMS (ESI)  $m/z$ :  $[\text{M} + \text{H}]^+$  calcd for  $\text{C}_{35}\text{H}_{38}\text{NO}_4$  536.2801; found 536.2816.

**N-(4-Methoxybenzyl)-N-methyl-1-(3-((trityloxy)methyl)oxiran-2-yl)methanamine (2o)**. It was prepared according to general procedure B using 1-(4-methoxyphenyl)-*N*-methylmethanamine (2.1

mmol, 0.318 g) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (1.0 mmol, 0.50 g). Purification by column chromatography on silica gel (10–40% EtOAc in hexane) afforded the title compound as a yellowish oil (0.363 g, 0.76 mmol, 76%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ<sub>H</sub>: 7.44 (6H, d, J = 7.4 Hz, 6 × C[14]-H), 7.32–7.19 (9H, m, Ar-H), 7.16 (2H, d, J = 5.1 Hz, 2 × C[7]-H), 6.81 (2H, d, J = 5.1 Hz, 2 × C[8]-H), 3.79 (1H, s, 3 × C[10]-H), 3.49 (1H, AB d, J = 12.9 Hz, C[5]-H), 3.38–3.26 (2H, m, C[5]-H, C[11]-H), 3.21–3.14 (2H, m, C[1]-H, C[2]-H), 3.10 (1H, dd, J = 6.3 Hz, 2.7 Hz, C[11]-H), 2.55 (1H, dd, J = 13.2 Hz, 3.3 Hz, C[3]-H), 2.20 (3H, s, 3 × C[4]-H), 2.20–2.10 (1H, m, C[3]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 158.7 (C[9]), 143.7 (C[13]), 130.5 (C[6]), 130.2 (C[7]), 128.6 (C[14]), 127.9 (C[15]), 127.1 (C[16]), 113.6 (C[8]), 86.9 (C[12]), 62.2 (C[11]), 61.7 (C[5]), 55.2 (C[3]), 55.2 (C[10]), 55.1 (C[1]), 54.2 (C[2]), 42.6 (C[4]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>32</sub>H<sub>34</sub>NO<sub>3</sub> 480.2533; found 480.2523.

*N*-(3-Methoxybenzyl)-*N*-methyl-1-(3-((trityloxy)methyl)oxiran-2-yl)methanamine (2p). It was prepared according to general procedure B using 1-(3-methoxyphenyl)-*N*-methylmethanamine (2.1 mmol, 0.318 g) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (1.0 mmol, 0.50 g). Purification by column chromatography on silica gel (10–40% EtOAc in hexane) afforded the title compound as a yellowish oil (0.424 g, 0.88 mmol, 88%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.46 (6H, d, J = 7.4 Hz, 6 × C[16]-H), 7.31–7.15 (10H, m, Ar-H), 6.86–6.75 (3H, m, Ar-H), 3.78 (3H, s, 3 × C[12]-H), 3.54 (1H, AB d, J = 13.2 Hz, C[5]-H), 3.38 (1H, AB d, J = 13.2 Hz, C[5]-H), 3.32 (1H, dd, J = 10.1 Hz, 5.6 Hz, C[13]-H), 3.23–3.07 (3H, m, C[1]-H, C[2]-H, C[13]-H), 2.60 (1H, dd, J = 13.5 Hz, 3.3 Hz, C[3]-H), 2.22 (3H, s, 3 × C[4]-H), 2.16 (1H, dd, J = 13.5 Hz, 6.4 Hz, C[3]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 159.6 (C[8]), 143.7 (C[15]), 140.3 (C[6]), 129.2 (C[10]), 128.6 (C[16]), 127.9 (C[17]), 127.1 (C[18]), 121.3 (C[11]), 114.3 (C[7]), 112.6 (C[9]), 86.9 (C[14]), 62.4 (C[5]), 62.1 (C[13]), 55.4 (C[3]), 55.2 (C[12]), 55.2 (C[1]), 54.1 (C[2]), 42.8 (C[4]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>32</sub>H<sub>34</sub>NO<sub>3</sub> 480.2533; found 480.2535.

*N*-(4-Fluorobenzyl)-*N*-methyl-1-(3-((trityloxy)methyl)oxiran-2-yl)methanamine (2q). It was prepared according to general procedure B using 1-(4-fluorophenyl)-*N*-methylmethanamine (2.1 mmol, 0.292 g) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (1.0 mmol, 0.50 g). Purification by column chromatography on silica gel (10–45% EtOAc in hexane) afforded the title compound as a yellowish oil (0.365 g, 0.78 mmol, 78%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.44 (6H, d, J = 7.4 Hz, 6 × C[13]-H), 7.32–7.19 (11H, m, Ar-H), 6.95 (2H, t, J = 8.5 Hz, 2 × C[8]-H), 3.51 (1H, AB d, J = 13.0 Hz, C[5]-H), 3.38 (1H, d, J = 13.0 Hz, C[5]-H), 3.32 (1H, dd, J = 10.3 Hz, 6.0 Hz, C[10]-H), 3.15–3.12 (2H, m, C[1]-H, C[2]-H), 3.08 (1H, dd, J = 10.0 Hz, 4.7 Hz, C[10]-H), 2.55 (1H, dd, J = 13.5, 3.4 Hz, C[3]-H), 2.20 (3H, s, 3 × C[4]-H), 2.20–2.10 (1H, m, C[3]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 161.9 (d, J = 243 Hz, C[9]), 143.7 (C[12]), 134.3 (d, J = 2.8 Hz, C[6]), 130.4 (d, J = 7.9 Hz, C[7]), 128.6 (C[13]), 127.9 (C[14]), 127.1 (C[15]), 115.0 (d, J = 21.1 Hz, C[8]), 86.9 (C[11]), 62.2 (C[10]), 61.5 (C[5]), 55.3 (C[3]), 55.0 (C[1]), 54.1 (C[2]), 42.6 (C[4]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>31</sub>H<sub>31</sub>FNO<sub>2</sub> 468.2333; found 468.2325.

*N*-Methyl-1-(naphthalen-2-yl)-*N*-(3-((trityloxy)methyl)oxiran-2-yl)methylmethanamine (2r). It was prepared according to general procedure B using *N*-methyl-1-(naphthalen-2-yl)methanamine (2.1 mmol, 0.360 g) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (1.0 mmol, 0.500 g). Purification by column chromatography on silica gel (0–5% MeOH in DCM) afforded the title compound as a yellowish oil (0.332 g, 0.67 mmol, 67%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 8.25–8.22 (1H, m, C[9]-H), 7.84–7.79 (1H, m, C[12]-H), 7.79–7.72 (1H, m, C[14]-H), 7.49–7.42 (8H, m, Ar-H), 7.37–7.33 (2H, m, Ar-H), 7.32–7.18 (9H, m, Ar-H), 3.98 (1H, dd, J = 13.2 Hz, C[5]-H), 3.78 (1H, dd, J = 13.2 Hz, C[5]-H), 3.33 (1H, dd, J = 9.9 Hz, 4.8 Hz C[16]-H), 3.25–3.15 (2H, m, C[1]-H, C[2]-H), 3.33 (1H, dd, J = 9.9 Hz, 3.5 Hz C[16]-H), 2.71–2.59 (1H, m, C[3]-H), 2.29–2.25 (4H, C[3]-H, 3 × C[4]-H).

<sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>C</sub>: 143.7 (C[18]), 134.4 (C[6]), 133.8 (C[8]), 132.4 (C[13]), 128.6 (C[19]), 128.4 (C[20]), 128.0 (C[15]), 127.9 (C[12]), 127.4 (C[9]), 127.1 (C[21]), 125.8 (C[14]), 125.6 (C[7]), 125.1 (C[10]), 124.6 (C[11]), 86.9 (C[17]), 62.1 (C[16]), 60.7 (C[5]), 55.7 (C[3]), 55.2 (C[1]), 55.1 (C[2]), 42.9 (C[4]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>35</sub>H<sub>34</sub>NO<sub>2</sub> 500.2584; found 500.2576.

*N*-Benzyl-*N*-methyl-1-(3-phenyloxiran-2-yl)methanamine (2s). It was prepared according to general procedure B using *N*-methylbenzylamine (2.76 mmol, 0.335 g, 0.356 mL) and (3-phenyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.31 mmol, 0.40 g). Purification by column chromatography on silica gel (10–30% EtOAc in hexane) afforded the title compound as a yellowish oil (0.205 g, 0.81 mmol, 62%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.37–7.21 (10H, m, C[7-9, 11-13]-H), 3.66 (1H, AB d, J = 13.0 Hz, C[5]-H), 3.63–3.60 (1H, m, C[1]-H), 3.55 (1H, AB d, J = 13.0 Hz, C[5]-H), 3.20–3.12 (1H, m, C[2]-H), 2.80 (1H, dd, J = 13.3 Hz, 3.9 Hz, C[3]-H), 2.58 (1H, dd, J = 13.3 Hz, 6.2 Hz, C[3]-H), 2.35 (3H, s, 3 × C[4]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 138.6 (C[6]), 137.3 (C[10]), 129.0 (C[7]), 128.5 (C[11]), 128.3 (C[8]), 128.1 (C[13]), 127.1 (C[9]), 125.6 (C[12]), 62.6 (C[5]), 61.4 (C[1]), 59.0 (C[2]), 56.9 (C[3]), 43.0 (C[4]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539; found 254.1536.

*N*-Benzyl-*N*-ethyl-1-(3-phenyloxiran-2-yl)methanamine (2t). It was prepared according to general procedure B using *N*-benzylethylamine (2.76 mmol, 0.373 g, 0.411 mL) and (3-phenyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.31 mmol, 0.40 g). Purification by column chromatography on silica gel (15–30% EtOAc in hexane) afforded the title compound 2t as a yellowish oil (0.260 g, 0.97 mmol, 74%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.38–7.20 (10H, m, C[7-9, 12-14]-H), 3.75 (1H, AB d, J = 13.8 Hz, C[5]-H), 3.67–3.57 (2H, m, C[1]-H, C[5]-H), 3.12 (1H, m, C[2]-H), 2.43 (1H, dd, J = 13.8 Hz, 3.9 Hz, C[3]-H), 2.70–2.59 (3H, m, C[2]-H, 2 × C[4]-H), 1.10 (3H, t, J = 6.9 Hz, 3 × C[5]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 139.4 (C[7]), 137.4 (C[11]), 128.8 (C[8]), 128.4 (C[12]), 128.2 (C[9]), 128.1 (C[14]), 126.9 (C[10]), 125.6 (C[13]), 61.6 (C[1]), 58.6 (C[2]), 57.0 (C[6]), 55.1 (C[3]), 48.2 (C[4]), 11.9 (C[5]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>22</sub>NO 268.1696; found 268.1703.

*N,N*-Dibenzyl-1-(3-phenyloxiran-2-yl)methanamine (2u). It was prepared according to general procedure B using dibenzylamine (2.76 mmol, 0.544 g, 0.531 mL) and (3-phenyloxiran-2-yl)methyl 4-methylbenzenesulfonate (1.31 mmol, 0.400 g). Purification by column chromatography on silica gel (0–20% EtOAc in hexane) afforded 2u as a yellowish oil (0.313 g, 95 mmol, 72%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.44–7.18 (15H, m, C[6-8, 10-12]-H), 3.81 (2H, AB d, J = 13.7 Hz, 2 × C[4]-H), 3.63 (2H, AB d, J = 13.7, 2 × C[4]-H), 3.58–3.53 (1H, m, C[1]-H), 3.20–3.10 (1H, m, C[2]-H), 2.87 (1H, dd, J = 13.8 Hz, 3.7 Hz, C[3]-H), 2.63 (1H, dd, J = 5.8 Hz, 14.1 Hz C[3]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 139.2 (C[5]), 137.3 (C[9]), 128.8 (C[6]), 128.4 (C[10]), 128.3 (C[7]), 128.1 (C[12]), 127.0 (C[8]), 125.6 (C[11]), 61.6 (C[1]), 58.9 (C[4]), 56.7 (C[2]), 55.2 (C[3]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>23</sub>H<sub>24</sub>NO 330.1852; found 330.1852.

*N*-Methyl-1-(3-propyloxiran-2-yl)-*N*-(2-(trifluoromethyl)benzyl)methanamine (2v). It was prepared according to general procedure B using *N*-methyl-1-(2-(trifluoromethyl)phenyl)methanamine (4.27 mmol, 0.845 g) and (3-propyloxiran-2-yl)methyl 4-methylbenzenesulfonate (2.03 mmol, 0.550 g). Purification by column chromatography on silica gel (0–30% EtOAc in hexane) afforded the title compound as a yellowish oil (0.517 g, 1.80 mmol, 89%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.83 (1H, J = 7.8 Hz, C[8]-H), 7.61 (1H, d, J = 7.8 Hz, C[11]-H), 7.52 (1H, t, J = 7.6 Hz, C[10]-H), 7.32 (1H, t, J = 7.6 Hz, C[11]-H), 3.76 (1H, AB d, J = 14.7 Hz, C[5]-H), 3.68 (1H, d, J = 14.7 Hz, C[5]-H), 2.95–2.81 (1H, m, C[2]-H), 2.76–2.62 (2H, m, C[1]-H, C[3]-H), 2.47 (1H, AB dd, J = 13.2 Hz, 6.2 Hz, C[3]-H), 2.32 (3H, s, 3 × C[4]-H), 1.56–1.39 (4H, m, 2 × C[13]-H, 2 × C[14]-H), 0.96 (3H, t, J = 6.9 Hz, 3 × C[15]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (75 MHz, CDCl<sub>3</sub>) δ<sub>C</sub>: 138.4 (q, J = 1.5 Hz, C[6]), 131.8 (C[9]), 130.4 (C[11]), 128.5 (q, J = 30 Hz, C[7]), 126.8 (C[10]), 125.7 (q, J = 6

H<sub>z</sub>, C[8]), 124.5 (q, *J* = 273 Hz, C[12]), 59.7 (C[3]), 58.0 (q, *J* = 1.7 Hz, C[5]), 57.9, 57.1 (C[2]), 56.8 (C[1]), 43.1 (C[4]), 33.9 (C[13]), 19.3 (C[14]), 13.9 (C[15]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>22</sub>NO 288.1564; found 288.1572.

2-((3-((Trityloxy)methyl)oxiran-2-yl)methyl)isoindoline (**2w**). It was prepared according to general procedure B using isoindoline (4.2 mmol, 0.500 g) and (3-((trityloxy)methyl)oxiran-2-yl)methyl 4-methylbenzenesulfonate (2.0 mmol, 1.00 g). Purification by column chromatography on Florisil (0–40% EtOAc in hexane) afforded **2w** as a yellowish oil (0.780 g, 1.74 mmol, 87%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.49–7.46 (6H, d, *J* = 7.8 Hz, 6 × C[11]-H), 7.33–7.17 (13H, m, Ar-H), 3.98–3.90 (4H, m, 4 × C[4]-H), 3.43 (1H, dd, *J* = 10.2 Hz, 5.7 Hz, C[8]-H), 3.30–3.21 (2H, m, C[1]-H, C[2]-H), 3.15 (1H, dd, *J* = 10.2 Hz, 4.5 Hz, C[8]-H), 2.91 (1H, dd, *J* = 12.9 Hz, 3.6 Hz, C[3]-H), 2.51 (1H, dd, *J* = 12.9 Hz, 6.6 Hz, C[3]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 143.7 (C[10]), 139.9 (C[5]), 128.6 (C[12]), 127.9 (C[11]), 127.2 (C[6]), 126.8 (C[7]), 122.3 (C[13]), 87.0 (C[9]), 62.1 (C[4]), 59.3 (C[8]), 55.4 (C[1]), 54.4 (C[2]), 53.8 (C[3]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>31</sub>H<sub>30</sub>NO<sub>2</sub> 448.2271; found 448.2293.

**Synthesis of 2-Phenylazetidines.** (1-Methyl-2-phenylazetid-3-yl)methanol (**1a**). It was prepared according to general procedure D using **2a** (1.39 mmol, 300 mg). Purification by column chromatography on silica gel (0–20% MeOH in DCM) afforded the title compound (**1a**) as a yellowish oil (261 mg, 1.47 mmol, 87%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ<sub>H</sub>: 7.38 (2H, d, *J* = 7.8 Hz, Ar-H), 7.32 (2H, t, *J* = 7.5 Hz, Ar-H), 7.24 (1H, t, *J* = 7.3 Hz, Ar-H), 3.74 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.70 (2H, t, *J* = 4.5 Hz, 2 × C[9]-H), 3.57 (1H, t, *J* = 6.8 Hz, C[3]-H), 2.75 (1H, t, *J* = 7.5 Hz, C[3]-H), 2.59 (1H, td, *J* = 7.0 Hz, 5.9 Hz, C[2]-H), 2.34 (3H, s, 3 × C[8]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 141.9 (C[4]), 128.4 (C[5]), 127.4 (C[7]), 126.7 (C[6]), 73.3 (C[1]), 63.2 (C[9]), 55.6 (C[3]), 44.4 (C[8]), 42.5 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>16</sub>NO 178.1264; found 178.1239.

(1-Ethyl-2-phenylazetid-3-yl)methanol (**1b**). It was prepared according to general procedure D using **2b** (1.70 mmol, 325 mg). Purification by column chromatography on silica gel (0–10% MeOH in DCM) afforded the title compound (**1b**) as a yellowish oil (302 mg, 1.58 mmol, 93%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.38 (2H, d, *J* = 7.1 Hz, 2 × C[5]-H), 7.28 (2H, t, *J* = 7.1 Hz, 2 × C[6]-H), 7.23–7.19 (1H, m, C[7]-H), 3.78–3.70 (2H, d + bs, *J* = 7.8 Hz, C[1]-H, OH), 3.62–3.52 (2H, m, 2 × C[10]-H), 3.50 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.69–2.59 (2H, m, C[3]-H, C[8]-H), 2.54–2.40 (2H, m, C[2]-H, C[8]-H), 0.90 (3H, t, *J* = 7.8 Hz, C[9]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 142.5 (C[4]), 128.3 (C[5]), 127.2 (C[7]), 126.7 (C[6]), 71.7 (C[1]), 62.8 (C[10]), 53.5 (C[3]), 52.8 (C[8]), 42.2 (C[2]), 12.5 (C[9]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>17</sub>NO 192.1383; found 192.1389.

(1-Benzyl-2-phenylazetid-3-yl)methanol (**1c**). It was prepared according to general procedure D using **2c** (1.70 mmol, 431 mg). Purification by column chromatography on silica gel (40–80% EtOAc in hexane) afforded the title compound (**1c**) as a yellowish oil (105 mg, 0.29 mmol, 25%). Pure TFA salt of **1c** can be isolated by preparative HPLC (using 0.1% TFA in 1 L of water and acetonitrile). <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 500 MHz) δ<sub>H</sub>: 10.27 (1H, bs, NH), 7.47–7.41 (4H, m, Ar-H), 7.41–7.35 (6H, m, Ar-H), 5.29 (1H, bs, C[1]-H), 5.17 (1H, bs, OH), 4.46 (2H, bs, 2 × C[8]-H), 3.92 (2H, bs, 2 × C[3]-H), 3.60–3.55 (2H, m, 2 × C[13]-H), 3.25 (1H, bs, C[2]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (DMSO-*d*<sub>6</sub>, 126 MHz) δ<sub>C</sub>: 142.4 (C[4]), 138.2 (C[9]), 128.8 (C[10]), 128.3 (C[5]), 128.2 (C[11]), 127.2 (C[7]), 126.9 (C[12]), 126.7 (C[6]), 71.0 (C[1]), 63.4 (C[13]), 61.9 (C[8]), 53.5 (C[3]), 43.2 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>19</sub>NO 254.1539; found 254.1530.

(1-Methyl-2-phenylazetid-3-yl)butan-1-ol (**1d**). It was prepared according to general procedure D using **2d** (0.91 mmol, 200 mg). Purification by column chromatography on silica gel (40–100% EtOAc in hexane) afforded the title compound (**1d**) as a yellowish oil (172 mg, 0.78 mmol, 86%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.40 (2H, d, *J* = 7.2 Hz, 2 × C[5]-H), 7.33 (2H, t, *J* = 7.3 Hz, 2 × C[6]-H), 7.29–7.22 (1H, m, C[7]-H), 3.75 (1H, d, *J* = 8.1 Hz, C[1]-H),

3.70–3.62 (1H, m, C[9]-H), 3.55 (1H, t, *J* = 6.6 Hz, C[3]-H), 2.83 (1H, dd, *J* = 8.7 Hz, 6.8 Hz, C[3]-H), 2.55–2.44 (2H, m, C[2]-H, OH), 2.33 (3H, s, 3 × C[8]-H), 1.40–1.20 (4H, m, 2 × C[10]-H, 2 × C[11]-H), 0.84 (3H, t, *J* = 6.6 Hz, 3 × C[12]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 141.8 (C[4]), 128.4 (C[5]), 127.5 (C[7]), 127.2 (C[6]), 72.8 (C[1]), 71.3 (C[9]), 54.4 (C[3]), 46.0 (C[2]), 44.2 (C[8]), 37.4 (C[10]), 18.6 (C[11]), 14.0 (C[12]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>22</sub>NO 220.1701; found 220.1696.

(1-Ethyl-2-phenylazetid-3-yl)butan-1-ol (**1e**). It was prepared according to general procedure D using **2e** (0.89 mmol, 200 mg). Purification by column chromatography on silica gel (40–100% EtOAc in hexane) afforded the title compound (**1e**) as a yellowish oil (178 mg, 0.76 mmol, 89%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.42 (2H, d, *J* = 7.3 Hz, 2 × C[5]-H), 7.33 (2H, t, *J* = 7.3 Hz, 2 × C[6]-H), 7.29–7.22 (1H, m, C[7]-H), 3.80 (1H, d, *J* = 8.1 Hz, C[1]-H), 3.75–3.65 (1H, m, C[10]-H), 3.53 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.76 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.67–2.54 (1H, m, C[2]-H), 2.54–2.37 (2H, m, 2 × C[8]-H), 1.63 (1H, bs, OH), 1.35–1.26 (4H, m, 2 × C[11]-H, 2 × C[12]-H), 0.93–0.83 (6H, m, 3 × C[9]-H, 3 × C[13]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 142.9 (C[4]), 128.3 (C[5]), 127.2 (C[7]), 127.1 (C[6]), 71.4 (C[1]), 71.2 (C[10]), 52.7 (C[3]), 52.1 (C[8]), 46.1 (C[2]), 37.4 (C[11]), 18.6 (C[12]), 14.0 (C[9]), 12.7 (C[13]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>24</sub>NO 234.1852; found 234.1862.

(1-Benzyl-2-phenylazetid-3-yl)butan-1-ol (**1f**). It was prepared according to general procedure D using **2f** (0.97 mmol, 286 mg). Purification by column chromatography on silica gel (0–10% MeOH in DCM) afforded the title compound (**1f**) as a yellowish oil (203 mg, 0.71 mmol, 71%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.45 (2H, d, *J* = 6.9 Hz, 2 × C[5]-H), 7.38–7.15 (8H, m, Ar-H), 4.00 (1H, d, *J* = 7.9 Hz, C[1]-H), 3.81 (1H, AB d, *J* = 12.9 Hz, C[8]-H), 3.74–3.64 (1H, m, C[14]-H), 3.44 (1H, AB d, *J* = 12.9 Hz, C[8]-H), 3.42–3.35 (1H, m, C[3]-H), 2.85 (1H, t, *J* = 7.8 Hz, C[3]-H), 2.50–2.35 (1H, m, C[2]-H), 1.61 (1H, bs, OH), 1.38–1.20 (4H, m, 2 × C[15]-H, 2 × C[16]-H), 0.84 (3H, t, *J* = 6.9 Hz, 3 × C[17]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 142.4 (C[4]), 138.3 (C[9]), 128.8 (C[10]), 128.3 (C[5]), 128.1 (C[11]), 127.3 (C[7]), 127.1 (C[12]), 126.9 (C[6]), 71.2 (C[1]), 70.3 (C[13]), 61.7 (C[8]), 52.2 (C[3]), 46.8 (C[2]), 37.4 (C[14]), 18.6 (C[15]), 14.0 (C[16]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>26</sub>NO 296.2009; found 296.2008.

1-(2-Phenyl-1-(1-phenylethyl)azetid-3-yl)butan-1-ol (**1g**). It was prepared according to general procedure D using **2g** (0.97 mmol, 300 mg). Purification by column chromatography on silica gel (10–100% EtOAc in hexane) afforded the title compound (**1g diastereomer I**; 139 mg, 0.45 mmol, 46%) and (**1g diastereomer II**; 85 mg, 0.28 mmol) as a yellowish oil (in overall 70% yield). **1g diastereomer I**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.58 (2H, d, *J* = 7.4 Hz, C[5]-H), 7.42–7.20 (8H, m, Ar-H), 4.03 (1H, d, *J* = 7.7 Hz, C[1]-H), 3.72–3.60 (1H, m, C[15]-H), 3.46 (1H, q, *J* = 6.5 Hz, C[8]-H), 3.19 (1H, t, *J* = 7.5 Hz, C[3]-H), 2.66 (1H, t, *J* = 7.5 Hz, C[3]-H), 2.35–2.20 (1H, m, C[2]-H), 1.44 (1H, bs, OH), 1.32–1.15 (4H, m, 2 × C[16]-H, 2 × C[17]-H), 0.94 (3H, d, *J* = 6.5 Hz, 3 × C[14]-H), 0.82 (3H, t, *J* = 6.4 Hz, 3 × C[18]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>C</sub>: 144.7 (C[9]), 144.3 (C[4]), 128.3 (C[11]), 128.2 (C[6]), 127.4 (C[12]), 127.0 (C[13]), 127.0 (C[5]), 126.9 (C[7]), 71.0 (C[15]), 69.8 (C[1]), 68.4 (C[8]), 51.0 (C[3]), 46.4 (C[2]), 37.3 (C[16]), 22.1 (C[12]), 18.6 (C[17]), 14.0 (C[18]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>27</sub>NO 310.2165; found 310.2174.

**1g diastereomer II**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.12–6.98 (7H, m, Ar-H), 6.98–6.90 (3H, m, Ar-H), 3.74 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.70–3.55 (2H, m, C[3]-H, C[15]-H), 3.41 (1H, q, *J* = 6.5 Hz, C[8]-H), 2.93 (1H, t, *J* = 7.2 Hz, C[3]-H), 2.54–2.38 (1H, m, C[2]-H), 1.55 (1H, bs, OH), 1.35–1.15 (7H, m, 3 × C[14]-H, 2 × C[16]-H, 2 × C[17]-H), 0.81 (1H, t, *J* = 6.8 Hz, 3 × C[18]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>C</sub>: 142.6 (C[4/9]), 142.4 (C[4/9]), 128.0 (C[11]), 127.5 (C[6/C12/C13]), 127.5 (C[6/C12/C13]), 126.7 (C[5]), 126.5 (C[7]), 71.9 (C[15]), 70.4 (C[1]), 68.3 (C[8]), 52.0 (C[3]), 45.4 (C[2]), 37.3 (C[16]), 20.4 (C[12]), 18.5

(C[17]), 13.9 (C[18]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{14}H_{22}NO$  310.2165; found 310.2169.

**tert-Butyl 3-(1-Hydroxybutyl)-2-(4-methoxyphenyl)azetidine-1-carboxylate (1h).** It was prepared according to general procedure D using **2h** (0.60 mmol, 200 mg). Purification by preparative HPLC (using 0.4 g of  $NH_4HCO_3$  in 1 L of water and acetonitrile) afforded the title compound (**1h**, 84 mg, 0.25 mmol, 42%) as a yellowish oil and **9h** (72 mg, 0.21 mmol, 36%) as a yellowish oil.

**tert-Butyl 3-(1-Hydroxybutyl)-2-(4-methoxyphenyl)azetidine-1-carboxylate (1h).**  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ (ppm):  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta_H$ : 7.28 (2H, d,  $J = 8.2$  Hz,  $2 \times C[6]$ -H), 6.88 (2H, d,  $J = 8.2$  Hz,  $2 \times C[5]$ -H), 4.87 (1H, d,  $J = 5.7$  Hz, C[1]-H), 3.99 (1H, t,  $J = 8.4$  Hz, C[3]-H), 3.88 (t,  $J = 7.4$  Hz, C[3]-H), 3.81 (4H, s,  $3 \times C[8]$ -H, C[12]-H), 2.48–2.35 (1H, m, C[2]-H), 1.81 (1H, bs, OH), 1.55–1.16 (13H, m,  $9 \times C[11]$ -H,  $2 \times C[13]$ -H,  $2 \times C[14]$ -H), 0.90 (t,  $J = 6.0$  Hz,  $3 \times C[15]$ -H).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 75 MHz)  $\delta_C$ : 159.0 (C[7]), 156.7 (C[9]), 133.9 (C[4]), 127.5 (C[5]), 113.9 (C[6]), 79.5 (C[10]), 71.8 (C[12]), 66.0 (C[1]), 55.3 (C[8]), 48.0 (C[3]), 44.9 (C[2]), 37.0 (C[13]), 28.3 (C[11]), 18.7 (C[14]), 14.0 (C[15]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{19}H_{30}NO_4$  336.2169; found 336.2175.

**tert-Butyl (E)-(3-Hydroxyhex-1-en-1-yl)(4-methoxybenzyl)carbamate (9h).**  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ :  $^1H$  NMR (300 MHz,  $CDCl_3$ )  $\delta_H$ : 7.30–7.02 (1H, bs, C[6]-H), 7.12 (2H, d,  $J = 8.1$  Hz,  $2 \times C[12]$ -H), 6.83 (2H, d,  $J = 8.4$  Hz,  $2 \times C[13]$ -H), 4.82 (1H, bs, C[5]-H), 4.64 (2H, bs,  $2 \times C[10]$ -H), 4.05 (1H, bs, C[4]-H), 3.79 (3H, s,  $3 \times C[15]$ -H), 1.61–1.17 (13H, m,  $2 \times C[2]$ -H,  $2 \times C[3]$ -H,  $9 \times C[9]$ -H), 0.87 (3H, t,  $J = 7.2$  Hz,  $3 \times C[1]$ -H).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 75 MHz)  $\delta_C$ : 158.6 (C[14]), 129.3 (C[6]), 128.9 (C[11]), 127.8 (C[12]), 113.9 (C[13]), 112.2 (C[5]), 81.6 (C[8]), 72.1 (C[4]), 55.3 (C[15]), 47.0 (C[10]), 39.9 (C[3]), 28.2 (C[9]), 18.8 (C[2]), 13.9 (C[1]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{19}H_{30}NO_4$  336.2169; found 336.2178.

**tert-Butyl 3-(1-Hydroxybutyl)-2-(4-tert-butylphenyl)azetidine-1-carboxylate (1j).** It was prepared according to general procedure D using **2j** (1.25 mmol, 450 mg). Purification by preparative HPLC (using 0.4 g of  $NH_4HCO_3$  in 1 L of water and acetonitrile) afforded the title compound (**1j**, 198 mg, 0.55 mmol, 47%) as a yellowish oil and **9j** (143 mg, 0.43 mmol, 34%) as a yellowish oil.

**tert-Butyl 3-(1-Hydroxybutyl)-2-(4-tert-butylphenyl)azetidine-1-carboxylate (1j).**  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta_H$ : 7.35 (2H, d,  $J = 8.3$  Hz,  $2 \times C[6]$ -H), 7.27 (2H, d,  $J = 6.9$  Hz,  $2 \times C[5]$ -H), 4.92 (1H, bs, C[1]-H), 3.99 (1H, t,  $J = 8.3$  Hz, C[3]-H), 3.92 (1H, dd,  $J = 8.3$  Hz, 6.4 Hz, C[3]-H), 3.79 (1H, s, C[13]-H), 2.43 (1H, bs, C[2]-H), 2.38–2.22 (1H, bs, OH), 1.53–1.08 (22H, m,  $9 \times C[9]$ -H,  $9 \times C[12]$ -H,  $2 \times C[14]$ -H,  $2 \times C[15]$ -H), 0.92 (3H, t,  $J = 6.9$  Hz,  $3 \times C[16]$ -H).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 126 MHz)  $\delta_C$ : 156.8 (C[10]), 150.3 (C[7]), 138.7 (C[4]), 125.8 (C[5]), 125.3 (C[6]), 79.5 (C[11]), 71.5 (C[13]), 66.1 (C[1]), 48.9 (C[3]), 44.6 (C[2]), 36.9 (C[14]), 34.5 (C[8]), 31.4 (C[9]), 28.3 (C[12]), 18.8 (C[15]), 14.0 (C[16]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{22}H_{32}NO_4$  362.2690; found 362.2687.

**tert-Butyl (E)-(3-Hydroxyhex-1-en-1-yl)(4-tert-butyl)carbamate (9j).**  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ : 7.32 (2H, d,  $J = 8.5$  Hz,  $2 \times C[13]$ -H), 7.11 (2H, d,  $J = 8.5$  Hz,  $2 \times C[12]$ -H), 7.18+7.03 (0.5 + 0.5 H, bs, C[6]-H), 4.81 (1H, bs, C[5]-H), 4.66 (2H, bs,  $2 \times C[10]$ -H), 4.05 (1H, bs, C[4]-H), 1.67 (1H, bs, OH), 1.52–1.22 (22H, m,  $2 \times C[2]$ -H,  $2 \times C[3]$ -H,  $9 \times C[9]$ -H,  $9 \times C[19]$ -H), 0.84 (3H, t,  $J = 7.5$  Hz,  $3 \times C[1]$ -H).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 75 MHz)  $\delta_C$ : 149.9 (C[9]), 138.6 (C[11]), 134.2 (C[14]), 129.3 (C[6]), 126.3 (C[14]), 125.4 (C[13]), 112.3 (C[5]), 81.6 (C[8]), 72.1 (C[4]), 47.4 (C[10]), 39.8 (C[3]), 34.4 (C[15]), 31.4 (C[9]), 28.2 (C[16]), 18.7 (C[2]), 14.0 (C[1]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{22}H_{32}NO_4$  362.2690; found 362.2683.

**1-(1-Methyl-2-phenylazetidin-3-yl)-2-(trityloxy)ethan-1-ol (1k).** **1.0 mmol Scale Synthesis.** It was prepared according to general procedure D using **2k** (1.0 mmol, 449 mg). Purification by column chromatography on silica gel (40–100% EtOAc in hexane) afforded the title compound (**1k**) as a yellowish solid (341 mg, 0.76 mmol, 76%).

**Scale-up Synthesis.** Potassium *tert*-butoxide (40 mmol, 4.49 g, 2.0 equiv) was dissolved in dry THF (50 mL) and cooled to  $-78$  °C, using dry ice in acetone, in a Schlenk flask (200 mL) under a nitrogen atmosphere. Diisopropylamine (40 mmol, 4.05 g, 5.65 mL, 2.0 equiv) and a 1.59 M hexane solution of BuLi (46 mmol, 29 mL, 2.3 equiv) were added dropwise into the solution (yellowish). The reaction mixture was stirred for 20 min at  $-78$  °C. Oxirane (**2k**, 8.98 g, 20 mmol, 1.0 equiv) in dry THF (100 mL) was added dropwise, the dark red mixture was stirred at  $-78$  °C for 2 h. The cold reaction mixture was poured carefully into the mixture of diethyl ether (100 mL) and water (50.0 mL), and then it was allowed to warm up to room temperature. The phases were separated, and the aqueous phase was extracted with diethyl ether ( $3 \times 100$  mL). The combined organic layers were washed with brine ( $1 \times 200$  mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude mixture (8.4 g) was purified by flash chromatography on silica gel (50–100% EtOAc in hexane), affording **1k** as an off-white solid (7.01 g, 15.7 mmol, 78%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ : 7.34 (8H, t,  $J = 9.2$  Hz, Ar-H), 7.34 (8H, t,  $J = 7.8$  Hz, Ar-H), 7.24–7.19 (4H, m, Ar-H), 3.92 (1H, td,  $J = 7.2$  Hz, 3.8 Hz, C[9]-H), 3.84 (1H, d,  $J = 7.8$  Hz, C[1]-H), 3.42 (1H, t,  $J = 7.0$  Hz, C[3]-H), 3.00 (1H, dd,  $J = 9.2$  Hz, 3.6 Hz, C[10]-H), 2.90 (1H, dd,  $J = 9.2$  Hz, 8.5 Hz, C[10]-H), 2.71 (1H, t,  $J = 7.4$  Hz, C[3]-H), 2.53–2.47 (1H, m, C[2]-H), 2.29 (3H, s,  $3 \times C[8]$ -H).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 75 MHz)  $\delta_C$ : 143.7 (C[12]), 142.3 (C[4]), 128.6 (C[13]), 128.3 (C[5]), 127.9 (C[14]), 127.2 (C[7]), 127.1 (C[15]), 127.0 (C[6]), 86.8 (C[11]), 73.5 (C[9]), 72.6 (C[1]), 65.7 (C[10]), 54.5 (C[3]), 44.2 (C[8]), 43.1 (C[2]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{31}H_{32}NO_2$  450.2433; found 450.2424.

**1-(1-Ethyl-2-phenylazetidin-3-yl)-2-(trityloxy)ethan-1-ol (1l).** It was prepared according to general procedure D using **2l** (1.0 mmol, 463 mg). Purification by column chromatography on silica gel (20–60% EtOAc in hexane) afforded the title compound (**1l**) as a yellowish solid (371 mg, 0.80 mmol, 80%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ : 7.39–7.32 (8H, m, Ar-H), 7.32–7.18 (12H, m, Ar-H), 3.93 (1H, td,  $J = 6.9$  Hz, 3.2 Hz, C[10]-H), 3.85 (1H, d,  $J = 7.8$  Hz, C[1]-H), 3.39 (1H, d,  $J = 7.0$  Hz, C[3]-H), 3.02 (1H, dd,  $J = 9.2$  Hz, 3.5 Hz, C[11]-H), 2.90 (1H, dd,  $J = 9.2$  Hz, 7.7 Hz, C[11]-H), 2.64–2.51 (2H, m, C[3]-H, C[8]-H), 2.48–2.35 (2H, m, C[2]-H, C[8]-H), 2.17 (1H, bs, OH), 0.87 (3H, t,  $J = 7.2$  Hz,  $3 \times C[9]$ -H).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 75 MHz)  $\delta_C$ : 143.7 (C[13]), 143.1 (C[4]), 128.6 (C[14]), 128.2 (C[5]), 127.9 (C[15]), 127.9 (C[7]), 127.1 (C[16]), 127.0 (C[6]), 86.8 (C[12]), 72.7 (C[10]), 71.9 (C[1]), 65.6 (C[11]), 52.7 (C[3]), 52.3 (C[8]), 42.9 (C[2]), 12.7 (C[9]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{32}H_{34}NO_2$  464.2590; found 464.2586.

**1-(1-Benzyl-2-phenylazetidin-3-yl)-2-(trityloxy)ethan-1-ol (1m).** It was prepared according to general procedure D using **2m** (1.0 mmol, 525 mg). Purification by column chromatography on silica gel (0–25% EtOAc in hexane) afforded the title compound (**1m**) as a yellowish solid (252 mg, 0.80 mmol, 48%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ : 7.41–7.32 (8H, m, Ar-H), 7.32–7.18 (17H, m, Ar-H), 4.03 (1H, d,  $J = 7.6$  Hz, C[1]-H), 3.99–3.89 (1H, m, C[13]-H), 3.79 (1H, AB d,  $J = 13.0$  Hz, C[8]-H), 3.38 (2H, d,  $J = 13.0$  Hz, C[8]-H), 3.26 (1H, t,  $J = 7.0$  Hz, C[3]-H), 3.01 (1H, dd,  $J = 9.4$  Hz, 7.0 Hz, C[14]-H), 2.90 (1H, dd,  $J = 9.4$  Hz, 7.5 Hz, C[14]-H), 2.68 (1H, dd,  $J = 8.3$  Hz, 7.0 Hz, C[3]-H), 2.50–2.38 (1H, m, C[2]-H), 2.27 (1H, bs, OH).  $^{13}C\{^1H\}$  NMR ( $CDCl_3$ , 75 MHz)  $\delta_C$ : 143.7 (C[16]), 142.6 (C[4]), 138.3 (C[9]), 128.7 (C[10]), 128.6 (C[17]), 128.2 (C[6]), 128.2 (C[11]), 127.9 (C[18]), 127.9 (C[7]), 127.1 (C[19]), 127.1 (C[5]), 126.9 (C[12]), 86.8 (C[15]), 72.8 (C[13]), 71.2 (C[1]), 65.6 (C[14]), 61.7 (C[8]), 52.6 (C[3]), 43.6 (C[2]). HRMS (ESI)  $m/z$ :  $[M + H]^+$  calcd for  $C_{37}H_{36}NO_2$  526.2746; found 526.2744.

**tert-Butyl 3-(1-Hydroxy-2-(trityloxy)ethyl)-2-phenylazetidine-1-carboxylate (1n).** It was prepared according to general procedure D using **2n** (1.0 mmol, 535 mg). Purification by column chromatography on silica gel (0–20% EtOAc in hexane) afforded the title compound (**1n**) as a yellowish solid (215 mg, 0.40 mmol, 40%).  $^1H$  NMR ( $CDCl_3$ , 300 MHz)  $\delta_H$ : 7.41–7.35 (6H, m, Ar-H), 7.32–7.20 (14H, m, Ar-H), 5.06 (1H, m, C[1]-H), 4.05–3.95 (1H, m, C[11]-H), 3.89 (1H,  $J = 8.4$  Hz, C[3]-H), 3.68 (1H, dd,  $J = 8.4$

H<sub>z</sub>, 6.2 Hz C[3]-H), 3.12 (1H, dd, *J* = 9.4 Hz, 3.6 Hz C[12]-H), 3.00 (1H, dd, *J* = 9.4 Hz, 7.4 Hz C[12]-H), 2.55–2.25 (1H, m, C[2]-H), 1.30 (9H, bs, 9 × C[10]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 126 MHz) δ<sub>c</sub>: 156.5 (C[8]), 143.5 (C[14]), 141.8 (C[4]), 128.5 (C[15]), 128.3 (C[5]), 127.9 (C[16]), 127.2 (C[17]), 127.1 (C[7]), 125.9 (C[6]), 87.0 (C[13]), 79.5 (C[9]), 72.0 (C[11]), 65.3 (C[12]), 60.4 (C[1]), 53.8 (C[3]), 41.6 (C[2]), 28.3 (C[10]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>35</sub>H<sub>38</sub>NO<sub>4</sub> 536.2801; found 536.2805.

**1-(2-(4-Methoxyphenyl)-1-methylazetid-3-yl)-2-(trityloxy)ethan-1-ol (1o).** It was prepared according to general procedure D using **2o** (0.63 mmol, 300 mg). Purification by column chromatography on silica gel (0–20% MeOH in DCM) afforded the title compound (**1o**) as a yellowish solid (260 mg, 0.54 mmol, 76%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.45–7.36 (6H, m, 6 × C[14]-H), 7.33–7.24 (11H, m, Ar-H), 6.80 (2H, d, *J* = 8.6 Hz, 2 × C[6]-H), 3.96–3.88 (1H, m, C[10]-H), 3.77 (3H, s, 3 × C[8]-H), 3.72 (1H, d, *J* = 7.5 Hz, C[1]-H), 3.37 (1H, t, *J* = 6.9 Hz, C[3]-H), 3.00 (1H, dd, *J* = 9.6 Hz, 3.6 Hz, C[11]-H), 2.88 (1H, dd, *J* = 9.6 Hz, 7.2 Hz, C[11]-H), 2.63 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.50–2.38 (1H, m, C[2]-H), 2.26 (3H, s, 3 × C[9]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>c</sub>: 158.9 (C[7]), 143.7 (C[13]), 134.4 (C[4]), 128.6 (C[14]), 128.2 (C[5]), 127.9 (C[15]), 127.1 (C[16]), 113.7 (C[6]), 86.8 (C[12]), 73.1 (C[1]), 72.5 (C[10]), 65.7 (C[11]), 55.3 (C[8]), 54.4 (C[3]), 44.0 (C[9]), 43.3 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>32</sub>H<sub>34</sub>NO<sub>3</sub> 480.2533; found 480.2538.

**1-(2-(3-Methoxyphenyl)-1-methylazetid-3-yl)-2-(trityloxy)ethan-1-ol (1p).** It was prepared according to general procedure D using **2p** (0.83 mmol, 400 mg). Purification by column chromatography on silica gel (0–20% MeOH in DCM) afforded the title compound (**1p**) as a yellowish solid (290 mg, 0.60 mmol, 72%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.40–7.32 (6H, m, 6 × C[14]-H), 7.31–7.12 (11H, m, Ar-H), 6.98 (1H, s, C[5]-H), 6.88 (1H, d, *J* = 7.5 Hz, C[8]-H), 6.76 (1H, dd, *J* = 7.5 Hz, 1.8 Hz C[7]-H), 3.92 (1H, td, *J* = 6.6 Hz, 3.6 Hz, C[12]-H), 3.80–3.75 (4H, m, C[1]-H, 3 × C[10]-H), 3.38 (1H, t, *J* = 6.9 Hz, C[3]-H), 3.02 (1H, dd, *J* = 9.3 Hz, 3.6 Hz, C[13]-H), 2.92 (1H, dd, *J* = 9.0 Hz, 7.2 Hz, C[13]-H), 2.64 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.51–2.42 (1H, m, C[2]-H), 2.29 (3H, s, 3 × C[11]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>c</sub>: 159.7 (C[6]), 143.9 (C[4]), 143.7 (C[15]), 129.2 (C[8]), 128.6 (C[16]), 127.8 (C[17]), 127.1 (C[18]), 119.4 (C[9]), 113.1 (C[7]), 112.1 (C[5]), 86.8 (C[14]), 73.5 (C[1]), 72.7 (C[12]), 65.7 (C[13]), 55.2 (C[10]), 54.5 (C[3]), 44.2 (C[11]), 43.1 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>32</sub>H<sub>34</sub>NO<sub>3</sub> 480.2533; found 480.2521.

**1-(2-(4-Fluorophenyl)-1-methylazetid-3-yl)-2-(trityloxy)ethan-1-ol (1q).** It was prepared according to general procedure D using **2q** (0.43 mmol, 200 mg). Purification by column chromatography on silica gel (40–100% EtOAc in hexane) afforded the title compound (**1q**) as a yellowish solid (160 mg, 0.35 mmol, 80%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.38–7.21 (17H, m, aromatic H), 6.92 (2H, t, *J* = 8.8 Hz, 2 × C[6]-H), 3.97–3.85 (1H, m, C[9]-H), 3.77 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.37 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.98 (1H, dd, *J* = 9.6 Hz, 3.9 Hz, C[10]-H), 2.88 (1H, dd, *J* = 9.3 Hz, 7.5 Hz, C[10]-H), 2.66 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.46–2.36 (1H, m, C[2]-H), 2.26 (3H, s, 3 × C[8]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>c</sub>: 162.1 (d, *J* = 243.3 Hz, C[7]), 143.7 (C[12]), 138.1 (d, *J* = 2.9 Hz, C[4]), 128.8 (C[5]), 128.6 (C[13]), 127.9 (C[14]), 127.2 (C[15]), 115.1 (d, *J* = 21.0 Hz, C[6]), 86.9 (C[10]), 72.7 (C[1]), 72.4 (C[9]), 65.8 (C[10]), 54.4 (C[3]), 44.1 (C[8]), 43.3 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>31</sub>H<sub>31</sub>FNO<sub>2</sub> 468.2333; found 468.2322.

**1-(1-Methyl-2-(naphthalen-2-yl)azetid-3-yl)-2-(trityloxy)ethan-1-ol (1r).** It was prepared according to general procedure D using **2r** (0.4 mmol, 200 mg). Purification by column chromatography on silica gel (40–100% EtOAc in hexane) afforded the title compound (**1r**) as a yellowish solid (104 mg, 0.21 mmol, 52%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 8.28 (1H, d, *J* = 8.1 Hz, C[7]-H), 7.84 (2H, t, *J* = 6.9 Hz, C[10]-H, C[12]-H), 7.73 (1H, d, *J* = 8.1 Hz, C[13]-H), 7.46–7.34 (18H, m, aromatic H), 4.59 (1H, d, *J* = 7.5 Hz, C[1]-H), 4.00 (1H, q, *J* = 5.1 Hz, C[15]-H), 3.46 (1H, t, *J* = 6.6 Hz, C[3]-H), 2.98–2.84 (2H, m, C[3]-H, C[16]-H), 2.80–2.72 (1H, m, C[16]-H), 2.66–2.54 (1H, m, C[2]-H), 2.29 (3H, s, 3 × C[14]-H). <sup>13</sup>C{<sup>1</sup>H} NMR

(CDCl<sub>3</sub>, 300 MHz) δ<sub>c</sub>: 143.6 (C[18]), 137.8 (C[4]), 133.8 (C[6]), 131.2 (C[11]), 128.6 (C[13]), 128.5 (C[19]), 127.8 (C[20]), 127.7 (C[10]), 127.1 (C[21]), 125.7 (C[7]), 125.6 (C[12]), 125.4 (C[85]), 125.2 (C[9]), 123.4 (C[5]), 86.7 (C[17]), 72.3 (C[15]), 69.7 (C[1]), 66.8 (C[16]), 54.4 (C[3]), 44.6 (C[14]), 44.3 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>35</sub>H<sub>34</sub>NO<sub>2</sub> 500.2584; found 500.2560.

**1-Methyl-2-phenylazetid-3-yl(phenyl)methanol (1s\_trans).** It was prepared according to general procedure D using **2s** (0.87 mmol, 220 mg). Purification by preparative HPLC (using 0.4 g of NH<sub>4</sub>HCO<sub>3</sub> in 1 L of water and acetonitrile) afforded the title compounds **1s\_trans** (51 mg, 0.20 mmol, 23%), **1s\_cis** (15 mg, 0.06 mmol, 7%), **1o\_trans** (48 mg, 0.23 mmol, 19%), and **1o\_cis** (30 mg, 0.23 mmol, 12%) as yellowish oils. Crude product: LC–MS area%: **1s\_trans**: 31%, **1s\_cis**: 11%, **1o\_trans**: 33%, **1o\_cis**: 25%

**trans-1-Methyl-2-phenylazetid-3-yl(phenyl)methanol (1s\_trans).** <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 500 MHz) δ<sub>H</sub>: 7.25–7.09 (10H, m, aromatic H), 5.44 (1H, bs, OH), 4.60 (1H, d, *J* = 5.9 Hz, C[9]-H), 3.82 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.29 (1H, t, *J* = 6.8 Hz, C[3]-H), 2.91 (1H, dd, *J* = 8.4 Hz, 6.4 Hz, C[3]-H), 2.45 – (1H, m, C[2]-H), 2.22 (3H, s, 3 × C[8]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (DMSO-*d*<sub>6</sub>, 126 MHz) δ<sub>c</sub>: 143.9 (C[10]), 142.5 (C[4]), 127.9 (C[11/C5]), 127.9 (C[11/C5]), 126.9 (C[13]), 126.7 (C[7]), 126.5 (C[12]), 126.2 (C[6]), 72.6 (C[9]), 71.2 (C[1]), 54.4 (C[3]), 47.8 (C[2]), 44.0 (C[8]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539; found 254.1544.

**cis-1-Methyl-2-phenylazetid-3-yl(phenyl)methanol (1s\_cis).** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ<sub>H</sub>: 7.28–7.18 (8H, m, aromatic H), 7.08–7.04 (2H, m, aromatic H), 4.36 (1H, dd, *J* = 5.1 Hz, 3.5 Hz, C[9]-H), 3.34 (1H, d, *J* = 10.7 Hz, C[3]-H), 3.13 (1H, d, *J* = 9.2 Hz, C[2]-H), 3.09 (1H, dd, *J* = 9.2 Hz, 3.2 Hz, C[1]-H), 2.81 (1H, dd, *J* = 10.7 Hz, 5.9 Hz, C[3]-H), 2.50 (1H, bs, OH), 2.20 (3H, s, 3 × C[8]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 126 MHz) δ<sub>c</sub>: 141.1, 140.4, 128.6, 128.5, 128.1, 127.7, 127.6, 126.7, 79.9 (C[1]), 77.9 (C[9]), 66.1 (C[2]), 65.7 (C[3]), 40.4 (C[8]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539; found 254.1529.

**trans-1-Methyl-4,5-diphenylpyrrolidin-3-ol (10s\_trans).** <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 500 MHz) δ<sub>H</sub>: 7.30–7.15 (8H, m, aromatic H), 7.09–7.06 (2H, m, aromatic H), 5.15 (1H, d, *J* = 5.5 Hz, OH), 4.23–4.17 (1H, m, C[3]-H), 3.84 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.15 (1H, dd, *J* = 12.0 Hz, 10.1 Hz, C[4]-H), 2.94 (1H, dd, *J* = 10.1 Hz, 5.3 Hz, C[2]-H), 2.72 (1H, dd, *J* = 10.1 Hz, 7.4 Hz, C[4]-H), 2.03 (3H, s, 3 × C[9]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (DMSO-*d*<sub>6</sub>, 126 MHz) δ<sub>c</sub>: 141.2, 141.2, 128.2, 128.2, 128.1, 127.6, 127.2, 126.3, 78.1 (C[1]), 76.3 (C[3]), 64.9 (C[2]), 64.9 (C[4]), 40.1 (C[9]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539; found 254.1549.

**cis-1-Methyl-4,5-diphenylpyrrolidin-3-ol (10s\_cis).** <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 500 MHz) δ<sub>H</sub>: 7.02–6.98 (4H, m, aromatic H), 6.97–6.90 (4H, m, aromatic H), 6.87–6.84 (2H, m, aromatic H), 5.22 (1H, d, *J* = 4.5 Hz, OH), 4.36–4.31 (1H, m, C[3]-H), 3.84 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.66 (1H, dd, *J* = 9.8 Hz, 6.4 Hz, C[4]-H), 3.22 (1H, dd, *J* = 7.8 Hz, 3.0 Hz, C[2]-H), 2.35 (1H, dd, *J* = 9.8 Hz, 5.6 Hz, C[4]-H), 2.15 (3H, s, 3 × C[9]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (DMSO-*d*<sub>6</sub>, 125 MHz) δ<sub>c</sub>: 141.0, 139.3, 129.1, 127.9, 127.3, 127.2, 126.1, 125.5, 75.2 (C[3]), 72.9 (C[1]), 64.7 (C[4]), 60.6 (C[2]), 40.7 (C[9]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO 254.1539; found 254.1542.

**1-Ethyl-2-phenylazetid-3-yl(phenyl)methanol (1t).** It was prepared according to general procedure D using **2t** (0.75 mmol, 200 mg). Purification by column chromatography on silica gel (0–20% MeOH in DCM) afforded the title compound (**1t**) as a white solid (187 mg, 0.70 mmol, 93%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.31–7.13 (10H, m, Ar-H), 4.67 (1H, d, *J* = 5.4 Hz, C[10]-H) 3.90 (1H, d, *J* = 8.1 Hz, C[1]-H), 3.45 (1H, t, *J* = 6.9 Hz, C[3]-H) 2.94 (1H, t, *J* = 6.9 Hz, C[3]-H) 2.68–2.40 (3H, m, C[2]-H, 2 × C[8]-H), 0.91 (3H, t, *J* = 7.2 Hz, 3 × C[9]-H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>c</sub>: 142.6 (C[11]), 142.5 (C[4]), 128.4 (C[5]), 128.0 (C[12]), 127.7 (C[14]), 126.9 (C[7]), 126.8 (C[6]), 126.1 (C[13]), 74.0 (C[10]), 70.6 (C[1]), 52.7 (C[3]), 52.3 (C[8]), 47.0 (C[2]), 12.6 (C[9]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>22</sub>NO 268.1696; found 268.1702.

(1-Benzyl-2-phenylazetididin-3-yl)(phenyl)methanol (**1u**). It was prepared according to general procedure D using **2u** (0.68 mmol, 225 mg). Purification by column chromatography on silica gel (0–10% MeOH in DCM) afforded the title compound (**1u**) as a white solid (146 mg, 0.44 mmol, 65%). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ<sub>H</sub>: 7.31–7.19 (15H, m, Ar-H), 4.72 (1H, d, *J* = 7.8 Hz, C[14]-H), 4.10 (1H, d, *J* = 7.8 Hz, C[1]-H), 3.83 (1H, AB d, *J* = 12.9 Hz, C[8]-H), 3.45 (1H, AB d, *J* = 12.9 Hz, C[8]-H), 3.36 (1H, t, *J* = 6.9, Hz, C[3]-H), 3.03 (1H, t, *J* = 6.9 Hz, C[3]-H), 2.70–2.59 (1H, m, C[2]-H), 2.09 (1H, bs, OH). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>, 75 MHz) δ<sub>C</sub>: 142.7 (C[14]), 142.3 (C[4]), 138.6 (C[9]), 128.9 (C[10]), 128.6 (C[15]), 128.4 (C[5]), 128.3 (C[11]), 128.0 (C[17]), 127.2 (C[7]), 127.1 (C[12]), 127.0 (C[6]), 126.3 (C[17]), 74.2 (C[13]), 70.0 (C[1]), 61.9 (C[8]), 52.7 (C[3]), 48.0 (C[2]). HRMS (ESI) *m/z*: [M + H]<sup>+</sup> calcd for C<sub>23</sub>H<sub>24</sub>NO 330.1852; found 330.1866.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.0c01310>.

NMR spectra of compounds **1**, **2**, and **9** and data of quantum chemical calculations (PDF)

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E.K. performed experiments and spectroscopic characterization and provided technical assistance. Theoretical calculations were carried out by Z.M. This manuscript was written by E.K., F.F., and Z.M. with comments from all authors.

### Notes

The authors declare no competing financial interest.

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## ■ DEDICATION

<sup>†</sup>This research paper is dedicated to the memory of Professor Sir Jack Edward Baldwin, who pioneered the selectivity of the ring-closure reactions of alicyclic compounds.

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