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Straightforward Synthetic Approach to Aminoalcohols with 9-Oxabicyclo[3.3.1]nonane or Cyclooctane Core *via* Nucleophilic Ring-Opening of Spirocyclic Bis(oxiranes)

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Abstract

Nucleophilic ring-opening of bis(oxiranes), containing several reactive centers, can be used to elaborate straightforward atom-economy and stereoselective approaches to polyfunctionalized compounds. In the present work ring-opening of cis- and trans-diastereomers of a spirocyclic bis(oxirane), containing a cyclooctane core (namely, 1,8-dioxadispiro[2.3.2.3]dodecane), upon the treatment with various amines was studied. Trans-isomer afforded aminoalcohols with 9-oxabicyclo[3.3.1]nonane moiety, formed *via* domino-process, including opening of an oxirane ring followed by intramolecular cyclization. Ring-opening of cis-isomer gave aminosubstituted cis-cyclooctane-1,5-diols, derived from independent reaction of two oxirane moieties. Activation of oxirane rings by the addition of $LiClO_4$, acting as a Lewis acid, allowed involving a number of primary and secondary aliphatic amines as well as aniline derivatives into the reaction. Scope and limitations of the reaction were studied and a series of aminoalcohols with 9-oxabicyclo[3.3.1]nonane core and symmetric diaminodiols with cyclooctane core were obtained.

Keywords: oxiranes; amines; 9-oxabicyclo[3.3.1]nonanes; cyclooctanes; aminodiols; ring-opening; domino reaction; intramolecular cyclization

1. Introduction

Oxiranes represent versatile intermediates finding application in synthesis of medicinal drugs, natural compounds, polymers and other products with practicable properties [1–5]. Synthetically useful transformations of these strained rings are characterized with predictability, regio- and stereoselectivity, mild conditions and broad reaction scope [6–10]. Bis(oxiranes), containing several reactive centers, are the structures of particular interest. Generally they are used to elaborate straightforward approaches to polyfunctionalized compounds [11–13], though examples of formation of saturated O-heterocycles *via* intramolecular cyclization are reported as well [14,15]. An eight-membered ring present in the molecule opens additional synthetic opportunities due to transannular transformations leading to polycyclic structures [16,17].

Previously we have reported the first example of transannular reactions of spirocyclic bis(oxirane) **1a** as a nucleophile (Scheme 1) [18], which was later expanded for a tetrakis(oxirane) [19]. The reactivity of two diastereomers of bis(oxirane) **1a** and **1b** towards NaN_3 was investigated and it was shown to be determined by the configuration of oxirane moieties: while trans-isomer **1a** afforded 9-oxabicyclo[3.3.1]nonane **2**, formed *via* domino-process, including opening of one oxirane ring followed by intramolecular cyclization, cis-diastereomer **1b** gave the sole isomer of diazidodiol **3**, derived from independent ring-opening of two oxirane moieties.

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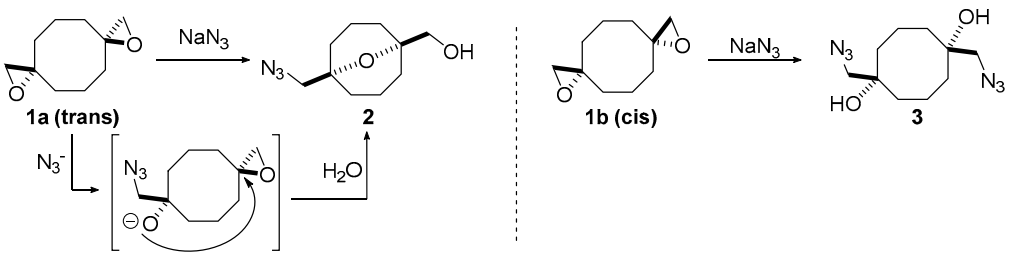

Scheme 1. Ring-opening of bis(oxiranes) **1a,b** with sodium azide [18].

It should be mentioned that molecules containing cleft-shaped frameworks such as bicyclo[3.3.1]nonanes and their aza-derivatives have found application as conformationally restricted molecules for the purposes of medicinal chemistry, metal complex catalysis, and detection of metal ions and small molecules [20]. Natural and synthetic derivatives of aza- and diazabicyclo[3.3.1]nonanes (granisetron, pentazocine, cytisine) are used as medicinal drugs (Figure 1) [21–23]. Numerous natural compounds containing fragments of bicyclo[3.3.1]nonane (for example, polycyclic polyprenylated acylphloroglucinols (PPAPs) [24,25]), 2-azabicyclo[3.3.1]nonane (morphine alkaloids [26]), 9-azabicyclo[3.3.1]nonane (granate [27] and bis(indole) alkaloids [28]), 3,7-diazabicyclo[3.3.1]nonane (bispidine-based alkaloids [29]), as well as synthetic bicyclo[3.3.1]nonanes, reveal a broad spectrum of biological activity, including anticancer properties [30–33].

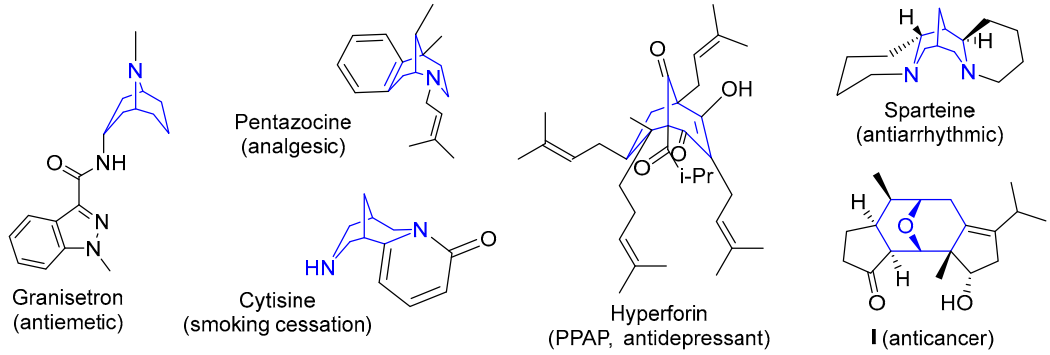

Figure 1. Examples of medicinal drugs and bioactive natural compounds containing bicyclo[3.3.1]nonane and related scaffolds.

9-Oxabicyclo[3.3.1]nonane moiety, as well as similar frameworks, represents a conformationally restricted 3D-scaffold attractive for the drug-design and occurring in bioactive compound. For example, diterpenoid **I** (Figure 1) exhibits antiproliferative activity towards cancer cells with good selectivity comparing to normal cell lines [34]. At the same time, in contrast to above-mentioned bicyclononane derivatives, 9-oxabicyclo[3.3.1]nonanes are rather hard to synthesize and much less examples of them are described, that makes the search for straightforward approaches to these compounds a challenging task.

As for diazidodiol **3**, it represented an attractive structure to be used as a linker moiety for construction of conjugates for biomedical applications using azide-alkyne cycloaddition strategies [35,36]. It was successfully used to obtain bis(triazoles) [37] and bis(steroid) derivatives with anticancer activity [38].

In the present work we aimed to elaborate preparative approaches to other types of products of nucleophilic ring-opening of bis(oxiranes) **1a** and **2b**. Amines were chosen as nucleophiles because the expected products of ring-opening – aminoalcohols and diaminodiols – are of interest as scaffolds occurring in a number of bioactive and natural compounds. For instance, adrenalin represents a β-aminoalcohol, as well as a number of adrenergic drugs, such as a short-acting bronchodilator albuterol [39]; 2-deoxystreptamine (2-DOS) is the aminocyclitol core of clinically important

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aminoglycoside antibiotics (gentamicin, neomycin, etc.) [40]; linear aminodi- or polyol moieties are present in natural antibiotics such as amicoumacin A [41] and zwittermicin A [42] (Figure 2).

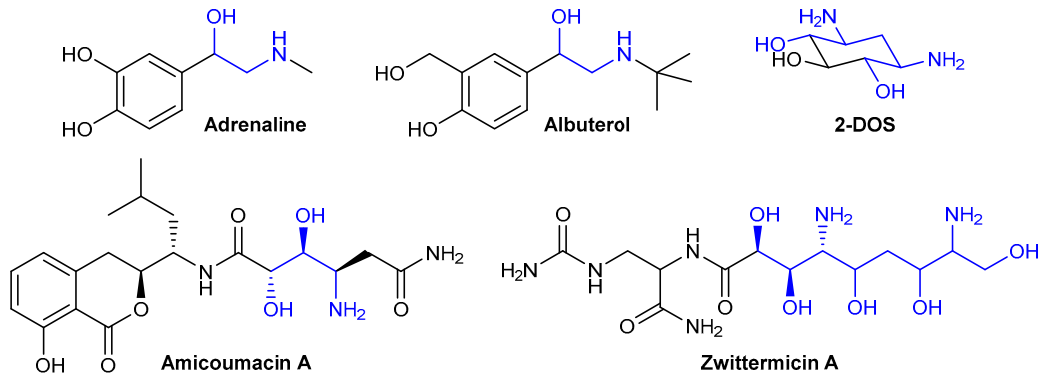
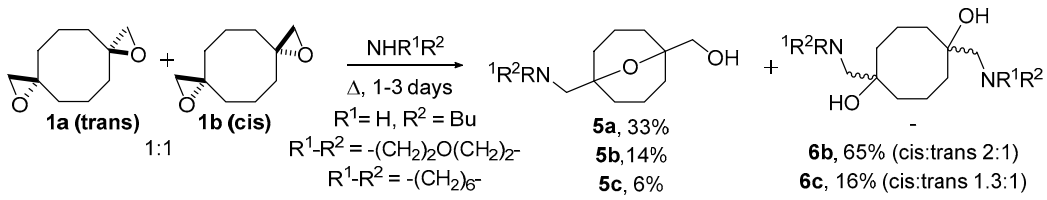


Figure 2. Examples of bioactive and natural compounds containing aminoalcohol scaffolds.

2. Results and Discussion

A diastereomeric mixture of bis(oxiranes) **1a**,**b** was studied upon the treatment with *n*-butylamine, morpholine, azepane and aniline (Scheme 2). The reactions were performed under reflux in the medium of an amine without a solvent. In the case of *n*-butylamine 9-oxabicyclo[3.3.1]nonane **5a**, derived from transannular reaction of trans-isomer **1a**, was the only product. Cis-bis(oxirane) **1b** did not interact with butylamine. Reaction of **1a,b** with more nucleophilic morpholine and azepane besides oxabicyclononane derivatives **5c,d** afforded symmetric diaminodiols **6c,d**, the products of independent ring-opening. Diaminodiols **6b,c** were obtained as diastereomeric mixtures where cis-isomers prevailed. The configuration of isomers **6b,c** was established basing on different symmetry of molecules as it has been previously done for the starting bis(oxiranes) [18]. Aniline, containing less nucleophilic amino group, did not interact with bis(oxiranes) **1a**,**b** in this conditions.



Scheme 2. Ring-opening of bis(oxiranes) **1a,b** with *n*-butylamine, morpholine and azepane; amines used as solvent.

In order to involve a broader scope of amines into the reaction and to improve its yield and selectivity, the conditions of nucleophilic opening were optimized on the examples of morpholine and butylamine. The solvent, temperature, time and reagents ratios were varied, but the reaction proceeded slowly until the additive of $LiClO_4$ was used (see Table S1). $LiClO_4$ was chosen because of its ability to promote oxiranes ring-opening by acting as Lewis acid with non-nucleophilic anion [43]. Optimal conditions were found to be reflux in acetonitrile for 5 h in the presence of $LiClO_4$. Various quantities of $LiClO_4$ were required, depending on the structure of amine: reactions with butylamine required 10-fold excess per oxirane ring, while for more nucleophilic morpholine 1.2-fold excess per oxirane ring was enough for complete conversion of starting bis(oxiranes). It should be mentioned that in optimized conditions only cis-isomers of diaminodiols **6** were formed, *i.e.*, only transannular reaction proceeded for trans-bis(oxirane) **1a**.

Bis(oxiranes) **1a** and **1b** were treated with various amines in optimized conditions (Table 1). In most cases diastereomeric mixture of starting bis(oxiranes) was involved into reaction, ratio of starting diastereomers **1a**:**1b** varying from 1:0.8 to 1:0.9; in some cases when the products were hard

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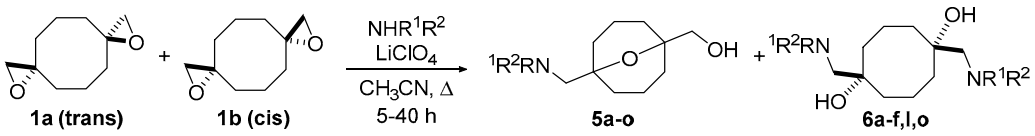
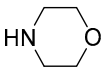
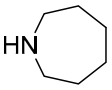
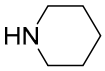
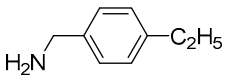
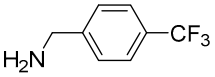
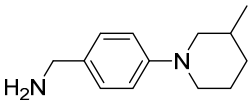
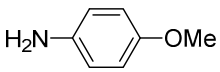
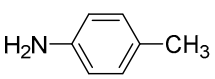
to separate, individual diastereomers **1a** or **1b** were used as starting material. Bis(oxirane) **1a** smoothly reacted with primary and secondary amines, affording aminoalcohols **5a-k** of 9-oxabicyclo[3.3.1]nonane series. Aniline, as well as EDG-substituted *p*-toluidine and *p*-anisidine, afforded the products of transannular reaction **5l-n** after reflux for 5–10 h, while the reaction with *p*-bromoaniline gave the product **5o** only after reflux for 30 h. Bis(oxirane) **1b** also interacted with the abovementioned amines, yet, unfortunately, resulting diaminodiols **6** were hard to isolate due to low chromatographic mobility and tendency to form salts. Nevertheless, diaminodiols **6a-f** could be isolated *via* column chromatography in moderate to high yields. Reaction of **1b** with *p*-bromoaniline even after 40 h afforded an equimolar mixture of diaminodiol **6o** and 7-{[(4-bromophenyl)amino]methyl}-1-oxaspiro[2.7]decan-7-ol (**7o**), the product of ring-opening of one oxirane moiety. Amines with stronger electron-acceptor substituents, namely, *p*-nitroaniline, sulfanilamide and methanesulfonamide did not act as nucleophiles towards bis(oxiranes) **1a,b** in the described conditions.

Table 1. Ring-opening of bis(oxiranes) **1a,b** with various amines.



NHR^1R^2	product	Yield,%[1]	product	Yield,%[1]
NH_2Bu	**5a**	81	**6a**	65[2]
	**5b**	88	**6b**	97
	**5c**	54	**6c**	19
	**5d**	83	**6d**	97[2]
	**5e**	83	**6e**	61[2]
$NHBu_2$	**5f**	83[2]	**6f**	65[2]
$NH_2CH_2C{\equiv}CH$	**5g**	70	**6g**	–
NH_2CH_2Ph	**5h**	80	**6h**	–
	**5i**	65	**6i**	–
	**5j**	40[2]	**6j**	–[3]
	**5k**	16	**6k**	–
NH_2Ph	**5l**	36	**6l**	6
	**5m**	95	**6m**	–
	**5n**	26	**6n**	–

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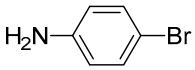	**5o**	17	**6o**	$2^{2,3}$

[1] Isolated yields, taking in account ratio of starting diastereomers **1a,b**. [2]Obtained from individual diastereomer **1a** or **1b**. [3]The products of opening of one oxirane ring **7j,o** (see section 3.2) were obtained.

To summarize, a preparative method of ring-opening of spirocyclic bis(oxiranes) **1a,b** upon the treatment with various amines in presence of $LiClO_4$ was elaborated to yield a series of aminoalcohols with 9-oxabicyclo[3.3.1]nonane core and substituted cis-cyclooctane-1,5-diols, containing two fragments of amine. The products of the ring-opening of trans-bis(oxirane) **1a**, functionalized 9-oxabicyclo[3.3.1]nonanes, represent a valuable conformationally restricted scaffold for drug-design, while the ring-opening of cis-bis(oxirane) **1b** with bioactive amines may be used as a stereoselective approach to bivalent ligands with a hydrophobic linker.

3. Materials and Methods

3.1. General

^1H and ^{13}C NMR spectra were recorded on a 400 MHz spectrometer Agilent 400-MR (Agilent Technologies, Santa Clara, CA, USA; 400.0, 100.6 or 376.3 MHz for ^1H, ^{13}C or ^{19}F, respectively) at r.t. in $CDCl_3$, if not stated otherwise; chemical shifts δ were measured with reference to $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.16 ppm) or to $CFCl_3$. When necessary, assignments of signals in NMR spectra were made using 2D techniques. Accurate mass measurements (HRMS) were obtained on Bruker micrOTOF II (Bruker Daltonik GmbH, Bremen, Germany) or G3 QTof quadrupole-time-of-flight (Waters, Milford MA, USA) with electrospray ionization (ESI). Analytical thin layer chromatography was carried out with silica gel plates supported on aluminum (ALUGRAM® Xtra SIL G/UV_{254}, Macherey-Nagel, Duren, Germany); the detection was done by UV lamp (254 nm). Column chromatography was performed on silica gel (Silica 60, 0.015–0.04 mm, Macherey-Nagel, Duren, Germany). Bis(oxiranes) **1a,b**[18] were obtained *via* described method. All other starting materials were commercially available. All reagents except commercial products of satisfactory quality were purified according to literature procedures prior to use.

3.2. Reaction of Bis(oxiranes) 1a,b with Amines (General Method)

To a solution of bis(oxirane) (0.1 mmol, 17 mg) in dry CH_3CN (3 mL) $LiClO_4$ (0.5–2 mmol) and corresponding amine (0.22 mmol) were added. The mixture was stirred at 80°C for 5–40 h. The solvent was evaporated under reduced pressure. The product was isolated *via* preparative column chromatography (SiO_2).

{5-[(Butylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5a). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 81% (20 mg), yellow oil, R_f 0.20 (light petrol : EtOAc : MeOH 3:1:0.1). ^1H NMR (δ, ppm, J, Hz): 0.91 (t, 3H, ^3J =7.3, CH_3), 1.27-1.39 (m, 4H, $2CH_2$, cy-Oct + CH_2, Bu), 1.39-1.57 (m, 4H, $2CH_2$, cy-Oct + CH_2, Bu), 1.58-1.75 (m, 6H, $6CH_2$, cy-Oct), 1.91-2.08 (m, 2H, $2CH_2$, cy-Oct), 2.54 (s, 2H, CH_2N), 2.61-2.69 (m, 2H, CH_2N, Bu), 3.11 (br.s, 2H, OH + NH), 3.31 (s, 2H, $\underline{CH_2}OH$). ^{13}C NMR (δ, ppm): 14.1 (CH_3), 18.5 ($2CH_2$, cy-Oct), 20.6 (CH_2, Bu), 29.8 ($2CH_2$, cy-Oct), 31.4 (CH_2, Bu), 31.8 ($2CH_2$, cy-Oct), 50.2 (CH_2N, Bu), 61.2 (CH_2N), 71.4 (CH_2OH), 71.7 ($\underline{C}$-CH_2N), 72.5 ($\underline{C}$-CH_2O). HRMS (ESI^+, m/z): calculated for $C_{14}H_{27}NO_2$ $[M+H]^+$: 242.2115, found: 242.2122.

[5-(Morpholin-4-ylmethyl)-9-oxabicyclo[3.3.1]nonan-1-yl]methanol (5b). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 88% (22 mg), orange oil, R_f 0.20 (light petrol : EtOAc : MeOH 3:1:0.1). ^1H NMR (δ, ppm): 1.28-1.46 (m, 4H, $4CH_2$, cy-Oct), 1.57-1.78 (m, 6H, $6CH_2$, cy-Oct), 1.94-2.11 (m, 2H, $2CH_2$, cy-Oct), 2.23 (s, 2H, CH_2N), 2.37 (br.s, 1H, OH), 2.51-2.62 (m, 4H, $2CH_2N$, morpholine), 3.28 (s, 2H, $\underline{CH_2}OH$), 3.64-3.73 (m, 4H, $2CH_2O$, morpholine). ^{13}C NMR (δ, ppm): 18.8 ($2CH_2$, cy-Oct), 29.8 ($2CH_2$, cy-Oct), 31.9 ($2CH_2$, cy-Oct), 55.7 ($2CH_2N$, morpholine), 67.2

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($2CH_2O$, morpholine), 70.0 (CH_2N), 71.6 (CH_2OH), 72.1 (C-CH_2O), 73.7 (C-CH_2N). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{14}H_{25}NO_3$ $[M+H]^+$: 256.1907, found: 256.1906.

[5-(Azepan-1-ylmethyl)-9-oxabicyclo[3.3.1]nonan-1-yl]methanol (5c). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 54% (15 mg), yellow oil, R_f 0.26 (light petrol : DCM : MeOH 1:3:1). ^{1}H NMR (*δ*, ppm): 1.31-1.47 (m, 4H, $4CH_2$, cy-Oct), 1.51-1.73 (m, 14H, $6CH_2$, cy-Oct + $4CH_2$, azepane), 1.93-2.09 (m, 2H, $2CH_2$, cy-Oct), 2.41 (s, 2H, CH_2N), 2.73-2.83 (m, 4H, $2CH_2N$, azepane), 3.29 (s, 2H, CH_2OH), 4.62 (br.s, 1H, OH). ^{13}C NMR (*δ*, ppm): 18.9 ($2CH_2$, cy-Oct), 27.5 ($2CH_2$, azepane), 29.1 ($2CH_2$, azepane), 30.0 ($2CH_2$, cy-Oct), 31.7 ($2CH_2$, cy-Oct), 57.9 ($2CH_2N$, azepane), 69.2 (CH_2N), 71.79 (CH_2OH), 71.83 (C-CH_2OH), 74.4 (C-CH_2N). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{16}H_{29}NO_2$ $[M+H]^+$: 268.2271, found: 268.2272.

[5-(Piperidin-1-ylmethyl)-9-oxabicyclo[3.3.1]nonan-1-yl]methanol (5d). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 78% (13 mg), yellow oil, R_f 0.14 (light petrol: DCM : MeOH 1:3:0.5). ^{1}H NMR (*δ*, ppm): 1.29-1.48 (m, 4H, $4CH_2$, cy-Oct + 2H, CH_2, piperidine), 1.49-1.81 (m, 6H, $6CH_2$, cy-Oct + 4H, $2CH_2$, piperidine), 1.95-2.11 (m, 2H, $2CH_2$, cy-Oct), 2.14-2.34 (m, 2H, CH_2N), 2.54 (br.s, 4H, $2CH_2N$, piperidine), 3.29 (s, 2H, CH_2O). ^{13}C NMR (*δ*, ppm): 18.9 ($2CH_2$, cy-Oct), 24.1 (CH_2, piperidine), 26.1 ($2CH_2$, piperidine), 29.9 ($2CH_2$, cy-Oct), 32.0 ($2CH_2$, cy-Oct), 56.8 ($2CH_2N$, piperidine), 70.2 (CH_2N), 71.7 (CH_2OH), 72.0 (C-CH_2OH), 73.6 (C-CH_2N). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{15}H_{27}NO_2$ $[M+H]^+$: 254.2115, found: 254.2119.

[5-(Pyrrolidin-1-ylmethyl)-9-oxabicyclo[3.3.1]nonan-1-yl]methanol (5e). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 83% (20 mg), yellow oil, R_f 0.24 (light petrol : DCM : MeOH 1:4:1). ^{1}H NMR (*δ*, ppm): 1.32-1.40 (m, 2H, $2CH_2$, cy-Oct), 1.44 -1.52 (m, 2H, $2CH_2$, cy-Oct), 1.58-1.76 (m, 6H, $6CH_2$, cy-Oct), 1.78-1.92 (m, 4H, $2CH_2$, pyrrolidine), 1.96-2.13 (m, 2H, $2CH_2$, cy-Oct), 2.56 (br.s, 2H, CH_2N), 2.82 (br.s, 4H, $2CH_2N$, pyrrolidine), 3.32 (br.s, 2H, $2CH_2OH$, pyrrolidine). ^{13}C NMR (*δ*, ppm): 18.8 ($2CH_2$, cy-Oct), 23.8 ($2CH_2$, pyrrolidine), 29.6 ($2CH_2$, cy-Oct), 32.1 ($2CH_2$, cy-Oct), 56.5 ($2CH_2$, pyrrolidine), 68.1 (CH_2N), 71.5 (CH_2OH), 72.3 (C-CH_2N), 72.8 (C-CH_2OH). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{14}H_{25}NO_2$ $[M+H]^+$: 240.1958, found: 240.1961.

1,5-Bis[(dibutylamino)methyl]cyclooctane-1,5-diol (5f). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 83% (25 mg), yellow oil, R_f 0.16 (EtOAc). ^{1}H NMR (*δ*, ppm, *J*, Hz): 0.89 (t, ^3J = 7.2, 6H, $2CH_3$, Bu), 1.20-1.31 (m, 4H, $2CH_2$, Bu), 1.31-1.45 (m, 8H, $4CH_2$, cy-Oct + $2CH_2$, Bu), 1.56-1.77 (m, 6H, $6CH_2$, cy-Oct), 1.95-2.08 (m, 2H, $2CH_2$, cy-Oct), 2.30 (s, 2H, CH_2N), 2.44-2.57 (m, 4H, $2CH_2N$, Bu), 3.28 (s, 2H, CH_2O). ^{13}C NMR (*δ*, ppm): 14.3 ($2CH_3$, Bu), 18.9 ($2CH_2$, cy-Oct), 20.8 ($2CH_2$, Bu), 29.5 ($2CH_2$, Bu), 29.8 ($2CH_2$, cy-Oct), 31.8 ($2CH_2$, cy-Oct), 56.1 ($2CH_2N$, Bu), 66.3 (CH_2N), 71.7 (CH_2O), 72.1 (C-CH_2O), 73.8 (C-CH_2N). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{18}H_{35}NO_2$ $[M+H]^+$: 298.2741, found: 298.2725.

{5-[(Propargylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5g). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 70% (16 mg), yellow oil, R*f* 0.32 (light petrol : EtOAc : MeOH 1:1:1). ^{1}H NMR (*δ*, ppm, *J*, Hz): 1.30-1.40 (m, 2H, $2CH_2$, cy-Oct), 1.41-1.52 (m, 2H, $2CH_2$, cy-Oct), 1.57-1.74 (m, 6H, $6CH_2$, cy-Oct), 1.95-2.10 (m, 2H, $2CH_2$, cy-Oct), 2.28 (t, ^4J = 2.4, 1H, CH, propargyl), 2.67 (s, 2H, CH_2N), 3.06 (br.s, 2H, NH, OH), 3.35 (s, 2H, CH_2O), 3.54 (d, ^4J = 2.4 Hz, CH_2, propargyl). ^{13}C NMR (*δ*, ppm): 18.4 ($2CH_2$, cy-Oct), 29.7 ($2CH_2$, cy-Oct), 31.6 ($2CH_2$, cy-Oct), 38.5 (CH_2, propargyl), 59.8 (CH_2N), 71.3 (CH_2OH), 71.7 (C-CH_2N), 72.6 (C-CH_2O), 72.8 (CH, propargyl), 80.9 (C, propargyl). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{13}H_{21}NO_2$ $[M+H]^+$: 224.1645, found: 224.1649.

{5-[(Benzylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5h). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 80% (22 mg), yellow oil, R*f* 0.39 (light petrol : EtOAc : MeOH 1:1:0.5). ^{1}H NMR (*δ*, ppm): 1.27–1.36 (m, 2H, $2CH_2$, cy-Oct), 1.37–1.50 (m, 2H, $2CH_2$, cy-Oct), 1.54–1.71 (m, 6H, $4CH_2$, cy-Oct), 1.89–2.03 (m, 2H, $2CH_2$, cy-Oct), 2.57 (s, 2H, CH_2N), 3.31 (s, 2H, CH_2O), 4.00 (s, 2H, $PhCH_2N$), 4.10 (br.s, 2H, NH+OH), 7.28–7.41 (m, 5H, 5CH, Ph). ^{13}C NMR (*δ*, ppm): 18.5 ($2CH_2$, cy-Oct), 29.7 ($2CH_2$, cy-Oct), 31.7 ($2CH_2$, cy-Oct), 53.7 ($PhCH_2N$), 60.0 (CH_2N), 71.5 (CH_2OH), 71.8 (C), 72.6 (C), 127.5 (CH, Ph), 128.7 (4CH, Ph), 138.7 (C, Ph). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{17}H_{25}NO_2$ $[M+H]^+$: 276.1958, found: 276.1965.

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(5-{[(4-Ethylbenzyl)amino]methyl}-9-oxabicyclo[3.3.1]nonan-1-yl)methanol (5i). Reaction time –5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 65% (20 mg), yellow oil, R_f 0.78 (light petrol : DCM : MeOH 1:1:0.5). ^{1}H NMR (δ, ppm, *J*, Hz): 1.23 (t, 3H, ^3J 7.6, CH_3), 1.25–1.34 (m, 2H, $2CH_2$, cy-Oct), 1.38–1.49 (m, 2H, $2CH_2$, cy-Oct), 1.56–1.74 (m, 6H, $6CH_2$, cy-Oct), 1.91–2.06 (m, 2H, $2CH_2$, cy-Oct), 2.55 (s, 2H, CH_2N), 2.64 (q, 2H, ^3J 7.6, CH_2, Et), 3.26 (s, 2H, CH_2O), 3.77 (br.s, 2H, NH+OH), 3.93 (s, 2H, $ArCH_2N$), 7.15–7.20 (m, 2H, 2CH, Ar), 7.30–7.36 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm): 15.7 (CH_3), 18.4 ($2CH_2$, cy-Oct), 28.7 (CH_2, Et), 29.6 ($2CH_2$, cy-Oct), 31.7 ($2CH_2$, cy-Oct), 53.3 ($ArCH_2N$), 59.5 (CH_2N), 71.2 (CH_2OH), 71.3 (C-CH_2N), 72.8 (C-CH_2OH), 128.3 (2CH, Ar), 129.0 (2CH, Ar), 134.4 (C, Ar), 143.9 (C, Ar). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{19}H_{29}NO_2$ $[M+H]^+$: 304.2271, found: 304.2272.

[5-({[4-(Trifluoromethyl)benzyl])amino}methyl)-9-oxabicyclo[3.3.1]nonan-1-yl]methanol (5j). Reaction time – 10 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 40% (13 mg), yellow oil, R_f 0.24 (light petrol : EtOAc 1:1). ^{1}H NMR (δ, ppm, *J*, Hz): 1.31–1.46 (m, 4H, $4CH_2$, cy-Oct), 1.55–1.78 (m, 6H, $6CH_2$, cy-Oct), 1.93–2.09 (m, 2H, $2CH_2$, cy-Oct), 2.47 (s, 2H, CH_2N), 3.31 (s, 2H, CH_2O), 3.87 (s, 2H, $ArCH_2N$), 7.41–7.50 (m, 2H, 2CH, Ar), 7.54–7.60 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm, *J*, Hz): 18.6 ($2CH_2$, cy-Oct), 29.9 ($2CH_2$, cy-Oct), 31.8 ($2CH_2$, cy-Oct), 53.7 ($ArCH_2N$), 61.0 (CH_2N), 71.6 (CH_2OH), 72.3 (C), 72.4 (C), 124.5 (q, $^1J_{CF}$ 272), 125.4 (q, $^3J_{CF}$ 4, 2CH, Ar), 128.3 (2CH, Ar), 129.3 (q, $^2J_{CF}$ 32, C, Ar), 145.0 (C, Ar). ^{19}F NMR (δ, ppm): -62.37 (s, 3F). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{18}H_{24}F_3NO_2$ $[M+H]^+$: 344.1832, found: 344.1836.

[5-({[4-(3-Methylpiperidin-1-yl)benzyl]amino}methyl)-9-oxabicyclo[3.3.1]non-1-yl]methanol (5k). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 16% (6 mg), yellow oil, R_f 0.78 (light petrol : DCM : MeOH 1:1:0.5). ^{1}H NMR (δ, ppm, *J*, Hz): 0.94 (d, 3H, ^3J 6.6, CH_3), 0.99-1.13 (m, 1H, CH_2, piperidine), 1.19–1.35 (m, 2H, cy-Oct), 1.40–1.51 (m, 2H, $2CH_2$, cy-Oct), 1.50–1.87 (m, 10H, $6CH_2$, cy-Oct + $2CH_2$ piperidine + CH, piperidine), 1.88–2.09 (m, 2H, $2CH_2$, cy-Oct), 2.31– 2.41 (m, 1H, CH_2N, piperidine), 2.60–2.73 (m, 1H, CH_2N, piperidine), 2.76 (s, 2H, CH_2N), 3.34 (s, 2H, CH_2O), 3.54–3.69 (m, 2H, $2CH_2N$, piperidine), 4.26 (s, 2H, $ArCH_2N$), 6.86–6.96 (m, 2H, 2CH, Ar), 7.36–7.38 (d, 2H, 2CH, Ar), 7.89 (br.s, 2H, NH+OH). ^{13}C NMR (δ, ppm): 18.1 ($2CH_2$, cy-Oct), 19.6 (CH_3), 25.2 (CH_2, piperidine), 28.9 ($2CH_2$, cy-Oct), 30.9 (CH, piperidine), 31.3 ($2CH_2$, cy-Oct), 33.0 (CH_2, piperidine), 49.2 (CH_2, piperidine), 51.7 ($ArCH_2N$), 55.7 (CH_2N), 56.9 (CH_2, piperidine), 69.4 (C-CH_2N), 70.7 (CH_2OH), 73.8 (C-CH_2OH), 116.1 (2CH, Ar), 118.9 (C, Ar), 131.6 (2CH, Ar), 152.5 (C, Ar). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{23}H_{36}N_2O_2$ $[M+H]^+$: 373.2850, found: 373.2852.

{5-[(Phenylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5l). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 36% (9 mg), yellow oil, R_f 0.77 (light petrol : EtOAc 1:2). ^{1}H NMR (δ, ppm): 1.35–1.43 (m, 2H, $2CH_2$, cy-Oct), 1.44–1.53 (m, 2H, $2CH_2$, cy-Oct), 1.59–1.79 (m, 6H, $4CH_2$, cy-Oct), 1.97–2.11 (m, 2H, $2CH_2$, cy-Oct), 3.03 (s, 2H, CH_2N), 3.35 (s, 2H, CH_2O), 6.58-6.73 (m, 3H, 3CH, Ph), 7.12–7.19 (m, 2H, 2CH, Ph). ^{13}C NMR (101 MHz, $CDCl_3$) δ, ppm: 18.5 ($2CH_2$, cy-Oct), 29.8 ($2CH_2$, cy-Oct), 31.6 ($2CH_2$, cy-Oct), 55.4 (CH_2N), 71.5 (CH_2OH), 72.4 (C), 72.5 (C), 113.0 (2CH, Ph), 117.3 (CH, Ph), 129.3 (2CH, Ph), 148.9 (C, Ph). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{16}H_{23}NO_2$ $[M+H]^+$: 262.1802, found: 262.1806.

{5-[(4-Methoxyphenylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5m). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 95% (27 mg), yellow oil, R_f 0.32 (EtOAc : DCM 1:5). ^{1}H NMR (δ, ppm): 1.34-1.42 (m, 2H, $2CH_2$, cy-Oct), 1.43-1.53 (m, 2H, $2CH_2$, cy-Oct), 1.59-1.81 (m, 6H, $6CH_2$, cy-Oct), 1.96-2.10 (m, 2H, $2CH_2$, cy-Oct), 2.97 (s, 2H, CH_2N), 3.35 (s, 2H, CH_2O), 3.74 (s, 3H, OMe), 6.56-6.64 (m, 2H, 2CH, Ar), 6.74-6.80 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm): 18.5 ($2CH_2$, cy-Oct), 29.9 ($2CH_2$, cy-Oct), 31.7 ($2CH_2$, cy-Oct), 56.0 (OMe), 56.5 (CH_2N), 71.6 (CH_2O), 72.4 (C-CH_2NH), 72.5 (C-CH_2OH), 114.3 (2CH, Ar), 115.1 (2CH, Ar), 143.3 (C-NH, Ar), 152.1 (C-O, Ar). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{17}H_{25}NO_3$ $[M+H]^+$: 292.1907, found: 292.1911.

{5-[(4-Methylphenylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5n). Reaction time – 10 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 26% (7 mg), yellow oil, R_f 0.67 (light petrol : EtOAc 1:1). ^{1}H NMR (δ, ppm): 1.32–1.42 (m, 2H, $2CH_2$, cy-Oct), 1.43–1.53 (m, 2H, $2CH_2$, cy-Oct), 1.57–1.82 (m, 6H, $4CH_2$, cy-Oct), 1.95–2.11 (m, 2H, $2CH_2$, cy-Oct), 2.23 (s, 3H, CH_3), 3.00

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(s, 2H, CH_2N), 3.35 (s, 2H, CH_2O), 6.52-6.58 (m, 2H, 2CH, Ar), 6.93–7.01 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm): 18.5 ($2CH_2$, cy-Oct), 20.5 (CH_3), 29.8 ($2CH_2$, cy-Oct), 31.6 ($2CH_2$, cy-Oct), 55.7 (CH_2N), 71.6 (CH_2OH), 72.4 (C), 72.5 (C), 113.1 (2CH, Ar), 126.4 (C, Ar), 129.8 (2CH, Ar), 146.7 (C, Ar). HRMS (ESI^+, *m*/*z*): calculated for $C_{17}H_{25}NO_2$ $[M+H]^+$: 276.1958, found: 276.1966.

{5-[(4-Bromophenylamino)methyl]-9-oxabicyclo[3.3.1]nonan-1-yl}methanol (5o). Reaction time – 30 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 17% (6 mg), yellow oil, R_f 0.58 (light petrol : EtOAc 1:1). ^1H NMR (δ, ppm): 1.34–1.43 (m, 2H, $2CH_2$, cy-Oct), 1.43–1.52 (m, 2H, $2CH_2$, cy-Oct), 1.58–1.75 (m, 6H, $4CH_2$, cy-Oct), 1.97–2.12 (m, 2H, $2CH_2$, cy-Oct), 2.98 (s, 2H, CH_2N), 3.35 (s, 2H, CH_2O), 6.45-6.54 (m, 2H, 2CH, Ar), 7.19–7.26 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm): 18.5 ($2CH_2$, cy-Oct), 29.8 ($2CH_2$, cy-Oct), 31.6 ($2CH_2$, cy-Oct), 55.3 (CH_2N), 71.6 (CH_2OH), 72.4 (C), 72.6 (C), 108.7 (C, Ar), 114.5 (2CH, Ar), 132.0 (2CH, Ar), 148.0 (C, Ar). HRMS (ESI^+, *m*/*z*): calculated for $C_{16}H_{22}BrNO_2$ $[M+H]^+$: 340.0907, found: 340.0916.

1,5-Bis[(butylamino)methyl]cyclooctane-1,5-diol (6a). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 56% (19 mg), yellow oil, R_f 0.05 (CH_3CN). ^1H NMR (δ, ppm, *J*, Hz): 0.90 (t, 6H, ^3J 7.2, $2CH_3$), 1.29-1.38 (m, 4H, $2CH_2$, Bu), 1.39-1.50 (m, 10H, $6CH_2$, cy-Oct + $2CH_2$, Bu), 1.77-1.90 (m, 6H, $6CH_2$, cy-Oct), 2.46 (s, 4H, $2CH_2N$), 2.62 (t, 4H, ^3J 7.1, $2CH_2N$, Bu). ^{13}C NMR (δ, ppm): 14.1 ($2CH_3$, Bu), 18.8 ($2CH_2$, cy-Oct), 20.5 ($2CH_2$, Bu), 32.6 ($2CH_2$, Bu), 37.5 ($4CH_2$, cy-Oct), 50.5 ($2CH_2N$, Bu), 60.5 ($2CH_2N$), 72.8 (2C). HRMS (ESI^+, *m*/*z*): calculated for $C_{18}H_{38}N_2O_2$ $[M+H]^+$: 315.3006, found: 315.3015.

1,5-Bis(morpholin-4-ylmethyl)cyclooctane-1,5-diol (6b). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 97% (33 mg), yellow oil, R_f = 0.61 (light petrol : EtOAc : MeOH 3:1:1). ^1H NMR (δ, ppm): 1.37-1.54 (m, 6H, $6CH_2$, cy-Oct), 1.79-1.95 (m, 6H, $6CH_2$, cy-Oct), 2.26 (s, 4H, $2CH_2N$), 2.60-2.63 (m, 8H, $4CH_2N$, morpholine), 2.99 (br.s, 2H, 2OH), 3.68-3.71 (m, 8H, $4CH_2O$, morpholine). ^{13}C NMR (δ, ppm): 18.4 ($2CH_2$, cy-Oct), 37.9 ($4CH_2$, cy-Oct), 56.3 ($4CH_2N$, morpholine), 67.5 ($4CH_2O$, morpholine), 69.0 ($2CH_2N$), 74.0 (2C). HRMS (ESI^+, *m*/*z*): calculated for $C_{18}H_{34}N_2O_4$ $[M+H]^+$: 343.2591, found: 343.2596

1,5-Bis(azepan-4-ylmethyl)cyclooctane-1,5-diol (6c). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 19% (7 mg), yellow oil, R_f 0.08 (light petrol : DCM : MeOH 1:3:1). ^1H NMR (δ, ppm): 1.38-1.52 (m, 6H, $6CH_2$, cy-Oct), 1.53-1.71 (m, 16H, $8CH_2$, azepane), 1.78-1.96 (m, 6H, $6CH_2$, cy-Oct), 2.43 (s, 4H, $2CH_2N$), 2.74-2.86 (m, 8H, $4CH_2N$, azepane). ^{13}C NMR (δ, ppm): 18.7 ($2CH_2$, cy-Oct), 27.1 ($4CH_2$, azepane), 29.1 ($4CH_2$, azepane), 37.8 ($4CH_2$, cy-Oct), 59.2 ($4CH_2N$, azepane), 68.8 ($2CH_2N$), 73.7 (2C). HRMS (ESI^+, *m*/*z*): calculated for $C_{22}H_{42}N_2O_2$ $[M+H]^+$: 367.3319, found: 367.3319.

1,5-Bis(piperidin-4-ylmethyl)cyclooctane-1,5-diol (6d). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 97% (30 mg), yellow oil, R_f 0.09 (light petrol : DCM : MeOH 1:3:2). ^1H NMR (δ, ppm): 1.35-1.53 (m, 6H, $6CH_2$, cy-Oct + 4H, $2CH_2$, piperidine), 1.53-1.65 (m, 8H, $4CH_2$, piperidine), 1.79-1.95 (m, 6H, $6CH_2$, cy-Oct), 2.29 (s, 4H, $2CH_2N$), 2.61 (br.s, 8H, $4CH_2N$, piperidine). ^{13}C NMR (δ, ppm): 18.5 ($2CH_2$, cy-Oct), 23.9 ($2CH_2$, piperidine), 26.3 ($4CH_2$, piperidine), 38.0 ($4CH_2$, cy-Oct), 57.4 ($4CH_2N$, piperidine), 68.6 ($2CH_2N$), 73.3 (2C). HRMS (ESI^+, *m*/*z*): calculated for $C_{20}H_{38}N_2O_2$ $[M+H]^+$: 339.3006, found 339.3003.

1,5-Bis(pyrrolidin-4-ylmethyl)cyclooctane-1,5-diol (6e). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 61% (23 mg), yellow oil, R_f 0.1 (light petrol : DCM : MeOH 1:1:1). ^1H NMR (δ, ppm): 1.40-1.57 (m, 6H, $6CH_2$, cy-Oct), 1.68-1.79 (m, 8H, $4CH_2$, pyrrolidine), 1.80-1.94 (m, 6H, $6CH_2$, cy-Oct), 2.45 (s, 4H, $2CH_2N$), 2.62-2.74 (m, 8H, $4CH_2N$, pyrrolidine). ^{13}C NMR (δ, ppm): 18.6 ($2CH_2$, cy-Oct), 24.3 ($4CH_2$, pyrrolidine), 38.0 ($4CH_2$, cy-Oct), 57.0 ($4CH_2$, pyrrolidine), 67.2 ($2CH_2N$), 73.4 (2C). HRMS (ESI^+, *m*/*z*): calculated forc

1,5-Bis[(dibutylamino)methyl]cyclooctane-1,5-diol (6f). Reaction time – 20 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:5. Yield 65% (28 mg), yellow oil, R_f 0.24 (light petrol : DCM : MeOH 1:4:1). ^1H NMR (CD_3OD; δ, ppm, *J*, Hz): 0.96 (t, ^3J = 7.3, 12H, $4CH_3$, Bu), 1.25-1.42 (m, 8H, $4CH_2$, Bu), 1.46-1.64 (m, 14H, $6CH_2$, cy-Oct + $4CH_2$, Bu), 1.85-1.98 (m, 6H, $6CH_2$, cy-Oct), 2.64 (br.s, 4H, $2CH_2N$), 2.79 (br.s, 8H, $4CH_2N$, Bu). ^{13}C NMR (CD_3OD; δ, ppm): 14.3 ($4CH_3$, Bu), 18.8 ($2CH_2$, cy-Oct),

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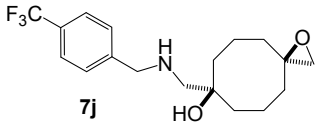
21.4 ($4CH_2$, Bu), 29.0 ($4CH_2$, Bu), 38.4 ($4CH_2$, cy-Oct), 57.2 ($4CH_2N$, Bu), 66.5 ($2CH_2N$), 74.6 (2C). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{26}H_{54}N_2O_2$ [M+H]$^+$: 427.4258, found: 427.4282.

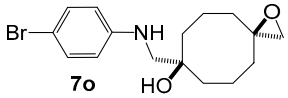
1,5-Bis[(phenylamino)methyl]cyclooctane-1,5-diol (6l). Reaction time – 5 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 6% (2 mg), yellow oil, R_f 0.58 (light petrol : EtOAc 2:1). ^{1}H NMR (δ, ppm): 1.56–1.71 (m, 6H, $6CH_2$, cy-Oct), 1.83–1.93 (m, 2H, $2CH_2$, cy-Oct), 1.93–2.04 (m, 4H, $4CH_2$, cy-Oct), 3.05 (s, 4H, $2CH_2N$), 6.59-6.77 (m, 6H, 6CH, Ph), 7.12–7.20 (m, 4H, 4CH, Ph). ^{13}C NMR (δ, ppm): 18.5 ($2CH_2$, cy-Oct), 37.3 ($4CH_2$, cy-Oct), 55.9 ($2CH_2$, CH_2N), 74.2 (2C), 113.4 (4CH, Ar), 118.0 (2CH, Ar), 129.4 (4CH, Ar), 148.9 (2C, Ar). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{22}H_{30}N_2O_2$ [M+H]$^+$: 355.2380, found: 355.2388.

1,5-Bis[(4-bromophenylamino)methyl]cyclooctane-1,5-diol (6o). Reaction time – 40 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 4% (2 mg), yellow oil, R_f 0.32 (light petrol : EtOAc 1:2). ^{1}H NMR (δ, ppm): 1.50–1.69 (m, 6H, $6CH_2$, cy-Oct), 1.79–1.91 (m, 2H, $2CH_2$, cy-Oct), 1.91–2.02 (m, 4H, $4CH_2$, cy-Oct), 3.00 (s, 4H, $2CH_2N$), 6.49-6.59 (m, 4H, 4CH, Ar), 7.20–7.29 (m, 4H, 4CH, Ph). ^{13}C NMR (δ, ppm): 18.4 ($2CH_2$, cy-Oct), 37.3 ($4CH_2$, cy-Oct), 55.8 ($2CH_2$, CH_2N), 74.2 (2C), 109.4 (2C, Ar), 114.9 (4CH, Ar), 132.1 (4CH, Ar), 147.9 (C, Ar). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{22}H_{28}Br_2N_2O_2$ [M+H]$^+$: 511.0590, found: 511.0587.



7j

7-({[(4-Trifluoromethyl)benzyl]amino}methyl)-1-oxaspiro[2.7]decan-7-ol (7j). Reaction time – 10 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 7% (2 mg), yellow oil, R_f 0.16 (EtOAc). ^{1}H NMR (δ, ppm): 1.38-1.49 (m, 4H, $2CH_2$, cy-Oct), 1.56-1.87 (m, 8H, $6CH_2$, cy-Oct), 2.55 (s, 2H, CH_2O), 2.60 (s, 2H, CH_2N), 3.90 (s, 2H, $ArCH_2N$), 7.37–7.48 (m, 2H, 2CH, Ar), 7.54–7.64 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm): 19.3 ($2CH_2$, cy-Oct), 34.9 ($2CH_2$, cy-Oct), 35.9 ($2CH_2$, cy-Oct), 54.1 (CH_2N), 55.3 (CH_2O), 58.1 ($ArCH_2N$), 59.1 (C, epoxy), 73.8 (C-OH), 125.5 (q, $^3J_{CF}$ 4, 2CH, Ar), 128.4 (2CH, Ar). Signals of CF_3-group and quaternary carbon atoms were not observed due to low concentration of the compound. ^{19}F NMR (δ, ppm): -62.44 (c, 3F). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{18}H_{24}F_3NO_2$ [M+H]$^+$: 344.1832, found: 344.1827.



7o

7-{[(4-Bromophenyl)amino]methyl}-1-oxaspiro[2.7]decan-7-ol (7o). Reaction time – 40 h. Reagents ratio (bis(oxirane) : amine : $LiClO_4$) – 1:2.2:20. Yield 6% (2 mg), yellow oil, R_f 0.39 (light petrol : EtOAc 1:1). ^{1}H NMR (δ, ppm): 1.47-1.92 (m, 12H, $6CH_2$, cy-Oct), 2.63 (s, 2H, CH_2O), 3.04 (s, 2H, CH_2N), 7.48–7.58 (m, 2H, 2CH, Ar), 7.19–7.26 (m, 2H, 2CH, Ar). ^{13}C NMR (δ, ppm): 19.4 ($2CH_2$, cy-Oct), 34.9 ($2CH_2$, cy-Oct), 35.8 ($2CH_2$, cy-Oct), 53.5 (CH_2N), 55.5 (CH_2O), 59.0 (C, epoxy), 75.1 (C-OH), 109.2 (C, Ar), 114.8 (2CH, Ar), 132.1 (2CH, Ar), 147.9 (C, Ar). HRMS (ESI$^+$, *m*/*z*): calculated for $C_{16}H_{22}BrNO_2$ [M+H]$^+$: 340.0907, found: 340.0915.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Table S1: Optimization of ring-opening conditions; copies of NMR spectra of the obtained compounds.

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Conflicts of Interest: The authors declare no conflicts of interest.

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