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Synthesis of 2,6-disubstituted morpholines through regioselective oxiranes ring opening by tosylamide under PTC conditions

Vittoria Lupi,[a,*] Domenico Albanese,[a] Dario Landini,[a] Davide Scaletti[a] and Michele Penso[b]

[a]*Dipartimento di Chimica Organica e Industriale, Università degli Studi di Milano, via Venezian 21, I-20133 Milano, Italy*
[b]*CNR-Istituto di Scienze e Tecnologie Molecolari (ISTM), via Golgi 19, I-20133 Milano, Italy*

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Abstract—Symmetric and non-symmetric 2,6-disubstituted morpholines were synthesized through regioselective nucleophilic ring opening of oxiranes with tosylamide under solid–liquid phase transfer catalysis (SL-PTC) conditions followed by cyclization of the tosylamido diols thus obtained and final deprotection of the corresponding *N*-tosyl morpholines. The morpholines prepared are interesting building blocks in the synthesis of pharmaceuticals and agrochemicals.

1. Introduction

Substituted morpholines have attracted considerable interest due to their presence in a number of therapeutically and biologically active compounds[1] or chiral reagents.[2] In particular, the 2,6-dimethylmorpholine skeleton is of paramount importance for the construction of a large class of agrochemical fungicides and bactericides.[3–11] Furthermore, the C_2-symmetric (2*R*,6*R*)-2,6-dimethylmorpholine has been prepared and then incorporated in Fisher-type aminocarbene complexes, behaving as an excellent chiral auxiliary.[12,13] Several 2,6-disubstituted morpholine derivatives are used as antitumor agents,[14] mild diuretics and anorectics.[15] This class of morpholines has been also employed as CO_2, H_2S, and COS adsorbents in the purification of liquids and gases,[16] and as fuel additives to provide fast-burning.[17] Finally, some morpholine derivatives have found applications as polymerization catalysts[18] and additives for inks.[19]

In spite of their industrial importance, few general preparations of 2,6-disubstituted morpholines are reported in the literature: (i) the dialkylation of a primary amine with an oxirane;[20] (ii) the reaction of a sulfonamide with excess chlorohydrin.[21,22] The amino or amido diols thus obtained have been cyclized to the corresponding morpholines in the presence of a base[23] or cyclodehydrated using concentrated sulfuric acid.[24] Alternatively, substituted morpholines have been prepared by a catalyzed vapor phase reaction of a dialkylene glycol with an aminating agent in the presence of hydrogen.[25]

This paper describes the synthesis of 2,6-disubstituted morpholines through the phase transfer (PT) catalyzed dialkylation of 4-toluenesulfonamide (**1**) by oxiranes **2** (Scheme 1), followed by cyclization of the tosylamido diols **4–7** thus obtained (Schemes 2 and 3), and final deprotection of the *N*-tosyl morpholines **10–13** to produce the target compounds **15** (Scheme 4). This procedure is regioselective and of general application, both for symmetric and non-symmetric morpholines.

2. Results and discussion

2.1. Oxirane ring opening by tosylamide

2.1.1. Preparation of symmetric tosylamido diols. In a previous paper,[26] we reported the preparation of β-tosylamido alcohols **3**, realized through ring opening of epoxides **2** with excess tosylamide (**1**), under solid–liquid PT catalysis (SL-PTC) conditions (Scheme 1, path a). As well as the mono-*N*-alkylation products **3**, small quantities of the *N*-dialkylated by-products **4**, **5** were isolated.

The direct dialkylation of **1** under analogous SL-PTC conditions with excess **2** (Scheme 1, path c), gave excellent yields (75–95%) (Table 1) of the (50:50) diastereoisomeric mixture **4**, **5** of the symmetric tosylamido diols, which could

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* Corresponding author. Tel.: +39 02 50314165; fax: +39 02 50314159; e-mail: vittoria.lupi@unimi.it

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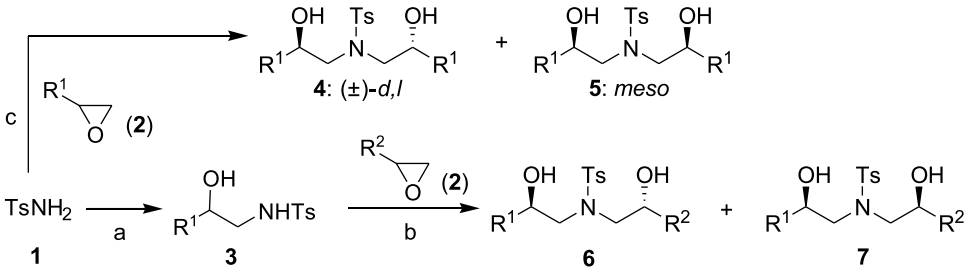


	2a	2b	2c	2d	2e	2f
R^1, R^2	C_6H_{13}	$PhOCH_2$	Ph	$AllylOCH_2$	$MeOCH_2$	t-$BuOCH_2$

	3a	3b	3c	3d
R^1	$PhOCH_2$	Ph	$AllylOCH_2$	$MeOCH_2$

	4,5a	4,5b	4,5c
R^1	C_6H_{13}	$PhOCH_2$	Ph

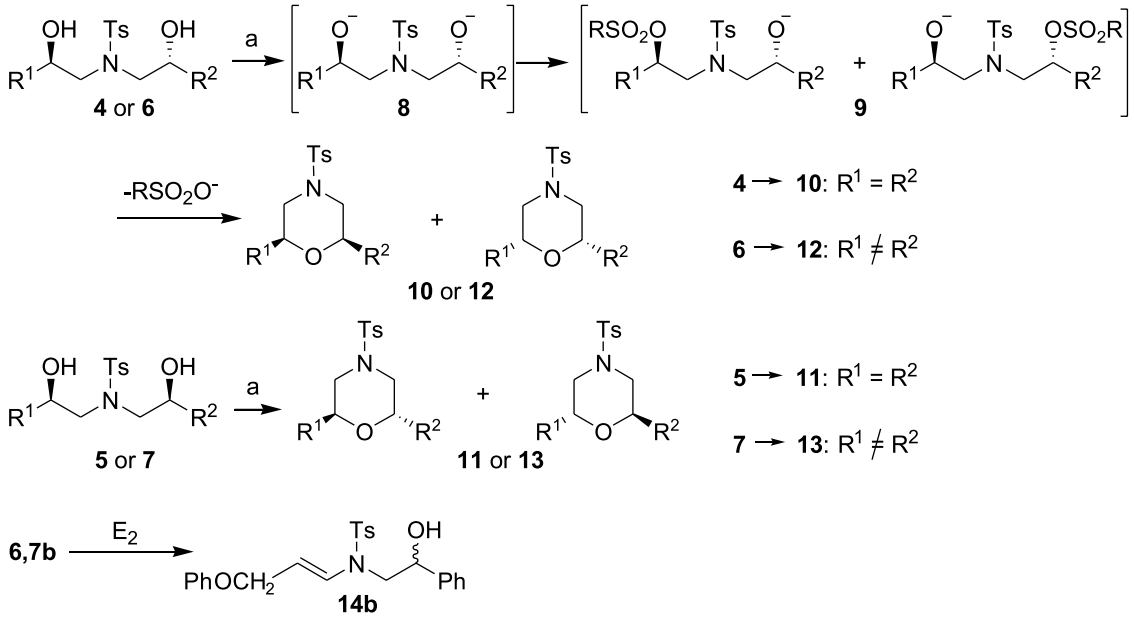
	6,7a	6,7b	6,7c	6,7d	6,7e
R^1	$PhOCH_2$	$PhOCH_2$	$PhOCH_2$	$AllylOCH_2$	$MeOCH_2$
R^2	C_6H_{13}	Ph	t-$BuOCH_2$	t-$BuOCH_2$	$PhOCH_2$

Scheme 1. (a) **1** (1 mol), **2** (0.5 mol), K_2CO_3 (0.05 mol), TEBA (0.05 mol), dioxane, 90 °C; (b) **2** (1.1 mol), **3** (1 mol), M_2CO_3 (0.1 mol), TEBA (0.1 mol), dioxane, 90 °C (or DME, 80 °C); (c) **1** (1 mol), **2** (3 mol), M_2CO_3 (0.1 mol), TEBA (0.1 mol), dioxane, 90 °C (or DME, 80 °C).

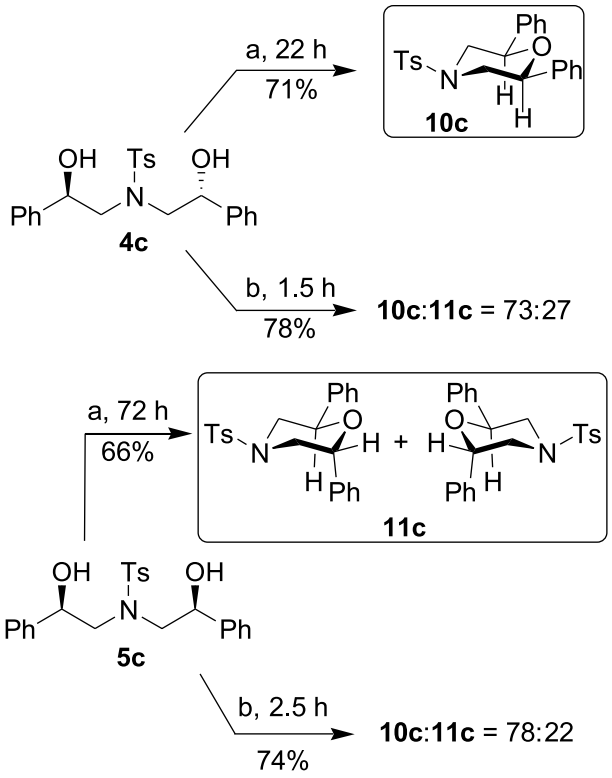
be easily separated by column chromatography to give the pure (±)-*d*,*l* **4** and *meso* **5** isomers.

The efficiency of the different alkaline metal carbonates M_2CO_3, used in catalytic amounts,[24] is related to the nature of the substituent on the oxirane ring: sodium carbonate is the most active base in the case of 1,2-epoxyoctane (**2a**) and 1,2-epoxy-3-phenoxypropane (**2b**), while cesium carbonate is more effective with styrene oxide (**2c**) (Table 1). Most probably, as confirmed by the results concerning the preparation of non-symmetric amido diols **6**, **7** described later, the base–epoxide relationship is the determinant factor for the in situ alkylation of the intermediate amido alcohol **3**.

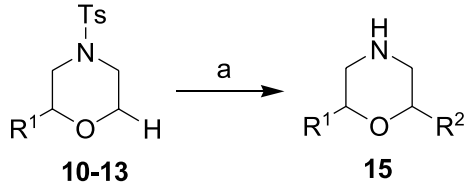
2.1.2. Preparation of non-symmetric tosylamido diols. The synthesis of non-symmetric tosylamido diols **6** and **7** involves a two-step alkylation protocol. After the preparation of the β-tosylamido alcohol **3** (Table 2, Step 1), this intermediate was reacted under SL-PTC conditions with a second epoxide **2** ($R^2 \neq R^1$) (Scheme 1, path b; Table 2, step 2). From the (1:1) diastereoisomeric mixture **6**, **7** formed under these conditions, the pure tosylamido diols **6** and **7**



Scheme 2. (a) **4**–**7** (1 mol), NaH (2.1 mol), RSO_2X (Tf_2O or TsCl, 1 mol), solvent, 0–25 °C. R^1 and R^2 substituents are described in Scheme 1.



Scheme 3. (a) NaH (2.1 mol), TsCl (1 mol), DCM, 40 °C; (b) NaH (2.1 mol), Tf_2O (1 mol), DCM, 25 °C.



Scheme 4. (a) 40% HBr–AcOH (PhOH), 25–80 °C.

Table 1. Preparation of symmetric tosylamido diols **4**, **5** under SL-PTC conditions[a]

	R^1	*t* (h)	Products			
				(%)[b]		(%)[b]
2a	C_6H_{13}[c]	10	**4a**	47	**5a**	48
2b	$PhOCH_2$[c]	6	**4b**	45	**5b**	45
2c	Ph[d]	6	**4c**	38	**5c**	37

[a] Scheme 1, path c. Reaction conditions: $TsNH_2$ (**1**) (1 mol), oxirane **2** (3 mol), TEBA (0.1 mol), Na_2CO_3 (0.1 mol).
[b] Isolated yields, after column chromatography.
[c] In DME at 80 °C.
[d] In the presence of Cs_2CO_3 (0.1 mol), in dioxane at 90 °C.

were separated by column chromatography. As found in the synthesis of symmetric amido diols **4**, **5**, in the alkylation of **3** the choice of the base is crucial (Table 2). As expected, in an attempt to prepare **6**, **7** by using equimolar amounts of oxiranes **2b** and **2c**, by operating in a one-pot reaction conditions, a complex mixture of the possible symmetric and non-symmetric amido diols was obtained.

2.2. Cyclization of tosylamido diols to 2,6-dialkyl-*N*-tosyl-morpholines

Poor results were obtained in the cyclization of diols **4**–**7** to *N*-tosyl-morpholines **10**–**13** by using literature methods of direct dehydration,[23,24] therefore, a detailed study for the best cyclization conditions of the isolated stereoisomers **4**–**7** was undertaken (Scheme 2).

The best results were obtained by generating the oxydianion **8** in the presence of excess NaH in dichloromethane (DCM) or 1,2-dimethoxyethane (DME), and promoting the cyclization through the in situ formation of the two possible mono-triflates **9** with (trifluoromethane)sulfonic anhydride (Tf_2O). Cyclization of the intermediate **9** proceeds through an intramolecular nucleophilic displacemement with stereoselective inversion of configuration at the reactive center. Furthermore, the *O*-triflation of **8** was not a regioselective process and, as a result, racemic morpholines were formed.

In the cyclization of symmetric tosylamido diols **4a**,**b** and **5b** (Table 3), the use of tosyl chloride (entries 1, 4, 6) instead of Tf_2O resulted in longer reaction times and lower yields of *N*-tosyl morpholines **10a**,**b** and **11b**. In the case of symmetric diols derived from 2-phenyl-oxirane (**2c**), it was found that the formation of *meso* morpholine **10c**, the less hindered isomer, bearing equatorial phenyl groups, proceeded with a higher reaction rate than the formation of *d*,*l* isomer **11c** (Table 3, entries 8–11).

In particular, starting from **4c**, in the presence of TsCl, **10c** was isolated as a sole product in 71% yield (entry 8), whilst by using Tf_2O a mixture of **10c**:**11c** (entry 9), which consisted mainly of *meso* **10c**, was produced (Scheme 3). In the same way, the activation of **5c** with tosyl chloride afforded the corresponding *d*,*l* **11c** (entry 10), whereas with Tf_2O an analogous mixture of **10c**:**11c** (entry 11) was obtained. When the mono-*O*-tosylate **9** (Scheme 2, R = Tol) is the intermediate, the nucleophilic substitution proceeds through a bimolecular mechanism, with complete inversion of the carbon atom, while in the case of the mono-*O*-triflate **9** (Scheme 2, R = CF_3), which bears a better leaving group, a unimolecular mechanism, via a carbocation, is responsible for the major formation of **10c**.

A similar behavior was found in the cyclization reactions of non-symmetric tosylamido diols **6**, **7** (Table 4) and TsCl was used as an activating agent when a phenyl group is present, as in diols **6**, **7b** (entries 3, 4).

2.3. *N*-Detosylation of *N*-tosyl-morpholines to 2,6-dialkyl-morpholines

The 2,6-disubstituted morpholines **15** (Scheme 4) can be obtained by deprotection of the corresponding *N*-tosyl morpholines **10**–**13** by reaction with 40% HBr–AcOH (Table 5).[27] In the case of the morpholines **10b**,**c**, **11b** and **12**, **13c** (entries 3–7), that contain phenyl and phenoxymethyl groups, the reactions were conducted in the presence of phenol as bromine scavenger, to avoid aromatic bromination of the products.

Table 2. Preparation of non-symmetric tosylamido diols **6**, **7** under SL-PTC conditions

Step 1[a]		*t* (h)	Product		Step 2[b]		Base	*t* (h)	Products			
Epoxide	R^1		**3**	(%)[c]	Epoxide	R^2			**6**, **7**	(%)[c]		(%)[c]
2b	$PhOCH_2$	2	**3a**	91	**2a**	C_6H_{13}	K_2CO_3	11	**6a**	35	**7a**	35
2b	$PhOCH_2$	2	**3a**	91	**2c**	Ph	Cs_2CO_3	22	**6b**	36	**7b**	36
2c	Ph	6	**3b**	93	**2b**	$PhOCH_2$	Na_2CO_3	6	**6b**	33	**7b**	32
2b	$PhOCH_2$	2	**3a**	91	**2f**	*t*-$BuOCH_2$	Na_2CO_3	48	**6**, **7c**	70[d]	—	—
2d	$AllylOCH_2$	2	**3c**	79	**2f**	*t*-$BuOCH_2$	Na_2CO_3	20	**6**, **7d**	70[d]	—	—
2e	$MeOCH_2$	2	**3d**	83	**2b**	$PhOCH_2$	Na_2CO_3	20	**6**, **7e**	82[d]	—	—

[a] Scheme 1, path a. Reaction conditions: $TsNH_2$ (**1**) (1 mol), epoxide **2** (0.5 mol), TEBA (0.05 mol), K_2CO_3 (0.05 mol), dioxane, 90 °C.
[b] Scheme 1, path b. Reaction conditions: epoxide **2** (1.1 mol), tosylamido alcohol **3** (1 mol), TEBA (0.1 mol), M_2CO_3 (0.1 mol), dioxane, 90 °C.
[c] Isolated yields.
[d] Isolated as (50:50) inseparable mixture of the diastereoisomers **6** and **7**.

Table 3. Cyclization of symmetric tosylamido diols **4** and **5** to *N*-tosyl morpholines **10** and **11**[a]

Entry		Method[b]	*t* (h)	Product	(%)[c]
1	**4a**	A	13	**10a**	55
2	**4a**	B	6	**10a**	78
3	**5a**	C	6	**11a**	80
4	**4b**	A	48	**10b**	72
5	**4b**	B	13	**10b**	77
6	**5b**	A[d]	23	**11b**	75
7	**5b**	B[d]	6	**11b**	80
8	**4c**	D[d]	22	**10c**	71
9	**4c**	B[d]	1.5	**10c**	57
				11c	21
10	**5c**	D[d]	72	**11c**	66
11	**5c**	B[d]	2.5	**10c**	58
				11c	16

[a] Reaction conditions: tosylamido diol **4**, **5** (1 mol), NaH (2.1 mol), RSO_2X (1 mol)—solvent, 0–25 °C.
[b] A: TsCl–DME; B: Tf_2O–DCM; C: Tf_2O–DME; D: TsCl–DCM, 25 °C.
[c] Isolated yields.
[d] At 40 °C.

Table 4. Cyclization of non-symmetric tosylamido diols **6**, **7** to *N*-tosyl morpholines **12** and **13**[a]

Entry		Method[b]	*t* (h)	Product	(%)[c]
1	**6a**	B	2	**12a**	85
2	**7a**	B	7	**13a**	77
3	**6b**	D	54	**12b**	46[d]
4	**7b**	D	28	**13b**	65[e]
5	**7b**	B	5	**13b**	54[f]
6	**6c**, **7c**[g]	B	5	**12c**	74[h]
				13c	64[i]
7	**6d**, **7d**[g]	D	28	**12d**	70[h]
				13d	59[i]
8	**6e**, **7e**[g]	B	5	**12e**	57[h]
				13e	53[i]

[a] Reaction conditions: tosylamido diol **6**, **7** (1 mol), NaH (2.1 mol), RSO_2X (1 mol)—solvent, 25 °C.
[b] B: Tf_2O–DCM; D: TsCl–DCM.
[c] Isolated yields.
[d] Together with **13b** (7%).
[e] Together with **12b** (3%) and **14b** (14%).
[f] Together with **12b** (25%).
[g] Starting from the corresponding (50:50) diastereoisomeric mixture **6**, **7**.
[h] Isolated yield calculated from the molar amount of the corresponding tosylamido diol **6**.
[i] Isolated yield calculated from the molar amount of the corresponding tosylamido diol **7**.

Table 5. Deprotection of *N*-tosyl morpholines **10–13**

Entry	Substrate	Method[a]	*t* (h)	Product	(%)[b]
1	**10a**	A	2	**15a**	65
2	**11a**	B	4	**15b**	63
3	**10b**	C	4	**15c**	75
4	**11b**	C	4	**15d**	75
5	**10c**	D	9	**15e**	61
6	**12a**	D	24	**15f**	74
7	**13a**	D	24	**15g**	67

[a] **10–13** (1 mol); A: 40% HBr–AcOH (30 mol), 60 °C; B: 40% HBr–AcOH (30 mol), 80 °C; C: 40% HBr–AcOH (30 mol), PhOH (3 mol), 60 °C; D: 40% HBr–AcOH (30 mol), PhOH (3 mol), 25 °C.
[b] Isolated yields.

3. Conclusions

In conclusion, in this work we have outlined a viable synthesis of 2,6-disubstituted morpholines **15** through the regioselective ring opening of a pair of easily accessible, appropriately substituted epoxides **2** with $TsNH_2$ **1**, employing SL-PTC conditions. The strategy described here, involving the cyclization of the tosyl amido diols **4–7** thus obtained, followed by deprotection of the corresponding *N*-tosyl morpholines **10–13**, enabled us to prepare a variety of 2,6-disubstituted morpholines **15**, which are tools of great interest as building blocks in the synthesis of pharmaceuticals and agrochemicals. Moreover, the inexpensive, readily available and environmentally friendly reagents add attractiveness to this method.

4. Experimental

4.1. General informations

Melting points were determined on a Büchi 535 apparatus and are corrected. ^1H NMR spectra were recorded on a Bruker AC 300 spectrometer operating at 300.133 MHz; TMS was used as an external reference; δ values are in ppm and *J* values are in Hz. Reagent-grade commercially available reagents and solvents were used and dried, when required, before use. Petroleum ether (PE) having a boiling range of 40–60 °C was used in the chromatographic purifications. Epoxides **2a–f** are commercially available. Alkaline metal carbonates were dried by heating at 140 °C

under vacuum (0.05 mmHg) for 6 h. Analytical TLC was performed using Merck pre-coated silica gel F_{254} plates.

4.2. General method for the preparation of β-tosylamido alcohols 3

A heterogeneous mixture of $TsNH_2$ (**1**) (342 mg, 2 mmol), TEBA (23 mg, 0.1 mmol) and epoxide **2** (1 mmol) solution in anhydrous dioxane (0.5 mL) and anhydrous K_2CO_3 (14 mg, 0.1 mmol), was magnetically stirred at 90 °C until no starting material **1** was detectable (TLC analysis). After cooling, the crude product was diluted with DCM (10 mL), filtered through celite, the solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (230–400 mesh). Starting epoxide **2**, reaction time, chromatographic eluant, yield and physical, spectroscopic and analytical data of amido alcohols **3a**–**d** are as follows.

4.2.1. *N*-(2-Hydroxy-3-phenoxy-propyl)-4-methyl-benzenesulfonamide (3a). 2-Phenoxymethyl-oxirane (**2b**); 2 h; AcOEt–PE 1:1. **3a**, 292.5 mg, 91%; white solid, mp 63 °C (lit.,[26] 64–66 °C); ν_{max} (Nujol) 3479, 3245, 1599, 1586, 1499, 1417, 1332, 1310, 1253, 1154, 1078, 1046, 1023, 952, 813, 750 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.75 (2H, d, $J=8.3$ Hz, *Ts*), 7.32–7.25 (4H, m, *Ar*), 6.97 (1H, t, $J=7.4$ Hz, *Ph*), 6.85 (2H, d, $J=8.1$ Hz, *Ph*), 5.12 (1H, t, $J=6.3$ Hz, N*H*), 4.11–4.07 (1H, m, C*H*OH), 3.96–3.91 (2H, m, CH_2OPh), 3.25 (1H, ddd, $J=3.9$, 7.0, 13.2 Hz, CH_aH_bN), 3.13–3.05 (1H, m, CH_aH_bN), 2.64 (1H, d, $J=4.6$ Hz, O*H*), 2.43 (3H, s, Ar*Me*). Anal. calcd for $C_{16}H_{19}NO_4S$: C, 59.79; H, 5.96; N, 4.36. Found: C, 59.80; H, 5.93; N, 4.39.

4.2.2. *N*-(2-Hydroxy-2-phenyl-ethyl)-4-methyl-benzenesulfonamide (3b). 2-Phenyl-oxirane (**2c**); 6 h; Et_2O–PE 1:1. **3b**, 271.0 mg, 93%; white solid, mp 105–106 °C (lit.,[26] 107–108 °C); ν_{max} (Nujol) 3401, 3149, 1918, 1662, 1598, 1318, 1148, 1098, 1088, 1065 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.72 (2H, d, $J=8.3$ Hz, *Ts*), 7.34–7.23 (8H, m, *Ar*+N*H*), 5.01–4.99 (1H, m, C*H*OH), 3.05 (1H, dd, $J=3.6$, 8.6 Hz, CH_aH_bN), 3.01 (1H, dd, $J=4.6$, 8.5 Hz, CH_aH_bN), 2.42 (3H, s, Ar*Me*), 2.31 (1H, d, $J=3.5$ Hz, O*H*). Anal. calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N 4.81. Found: C, 61.91; H, 5.92; N, 4.78.

4.2.3. *N*-(3-Allyloxy-2-hydroxy-propyl)-4-methyl-benzenesulfonamide (3c). 2-Allyloxymethyl-oxirane (**2f**); 2 h; AcOEt–PE 1:2. **3c**, 225.4 mg, 79%; wax; ν_{max} (Nujol) 3470, 3280, 2974, 1728, 1599, 1340, 1160, 1090, 994 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.71 (2H, d, $J=8.1$ Hz, *Ts*), 7.27 (2H, d, $J=8.1$ Hz, *Ts*), 5.88–5.75 (1H, m, =C*H*CH_2O), 5.37 (1H, t, $J=6.0$ Hz, N*H*), 5.24–5.13 (2H, m, CH_2=), 3.93 (2H, d, $J=5.2$ Hz, =CHCH_2O), 3.88–3.81 (1H, m, C*H*OH), 3.44–3.34 (2H, m, CH_2OAll), 3.12–3.04 (1H, m, CH_aH_bNH), 2.95–2.87 (1H, m, CH_aH_bNH), 2.90 (1H, bs, O*H*) 2.39 (3H, s, Ar*Me*). Anal. calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91. Found: C, 54.81; H, 6.67; N, 4.81.

4.2.4. *N*-(2-Hydroxy-3-methoxy-propyl)-4-methyl-benzenesulfonamide (3d). 2-Methoxymethyl-oxirane (**2e**); 2 h; AcOEt–PE 1:1. **3d**, 215.2 mg, 83%; wax; ν_{max} (Nujol) 3392, 3284, 1926, 1662, 1598, 1332, 1162, 1222, 1055, 952, 901, 862, 816, 708, 662 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.73 (2H, d, $J=8.1$ Hz, *Ts*), 7.29 (2H, d, $J=8.1$ Hz, *Ts*), 5.11 (1H, t, $J=5.9$ Hz, N*H*), 3.87–3.80 (1H, m, C*H*OH), 3.42–3.35 (2H, m, CH_2OMe), 3.33 (3H, s, O*Me*), 3.14–3.06 (1H, m, CH_aH_bNH), 2.96–2.88 (1H, m, CH_aH_b-NH), 2.70 (1H, bs, O*H*), 2.41 (3H, s, Ar*Me*). Anal. calcd for $C_{11}H_{17}NO_4S$: C, 50.95; H, 6.61; N, 5.40. Found: C, 50.89; H, 6.60; N, 5.46.

4.3. General method for the preparation of symmetric tosylamido diols 4 and 5

A heterogeneous mixture of $TsNH_2$ (**1**) (171 mg, 1 mmol), TEBA (23 mg, 0.1 mmol), epoxide **2** (3 mmol) solution in anhydrous dimethoxyethane or dioxane (0.75 mL) and anhydrous alkaline carbonate (0.1 mmol), was magnetically stirred at 80–90 °C until no starting material **1** was detectable (TLC analysis). After the usual workup, as described for the preparation of tosylamido alcohols **3**, the residue was purified by flash column chromatography on silica gel (230–400 mesh). Starting epoxide **2**, solvent, temperature, base, reaction time, chromatographic eluant, yield and physical, spectroscopic and analytical data of amido diols **4** and **5** are as follows.

4.3.1. Tosylamido diols 4a and 5a. 2-Hexyl-oxirane (**2a**); dimethoxyethane; 80 °C; Na_2CO_3; 10 h; Et_2O–PE 1:3. **4a**, 201.0 mg, 47%; white solid, mp 61–62 °C; ν_{max} (Nujol) 3392, 1909, 1737, 1600, 1494, 1343, 1158, 1099, 848, 764, 666 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.68 (2H, d, $J=8.2$ Hz, *Ts*), 7.32 (2H, d, $J=8.2$ Hz, *Ts*), 3.93–3.89 (2H, m, 2C*H*OH), 3.23 (2H, bs, 2O*H*), 3.02–2.99 (4H, m, 2CH_2N), 2.42 (3H, s, Ar*Me*), 1.43–1.27 (20H, m, 2C_5H_{10}), 0.86 (6H, t, $J=6.9$ Hz, 2*Me*). Anal. calcd for $C_{23}H_{41}NO_4S$: C, 64.60; H, 9.66; N, 3.28. Found: C, 64.71; H, 9.70, N, 3.26. **5a**, 205.3 mg, 48%; white solid, mp 86–87 °C; ν_{max} (Nujol) 3400–3200 (br), 1934, 1820, 1734, 1660, 1597, 1494, 1340, 1162, 1088, 848, 818, 726, 648 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.68 (2H, d, $J=8.2$ Hz, *Ts*), 7.33 (2H, d, $J=8.2$ Hz, *Ts*), 4.02–3.98 (2H, m, 2C*H*OH), 3.68 (2H, bs, 2O*H*), 3.37 (2H, dd, $J=14.7$, 2.4 Hz, 2CH_aCH_bN), 2.76 (2H, dd, $J=14.7$, 9.8 Hz, 2CH_aCH_bN), 2.43 (3H, s, Ar*Me*), 1.37–1.27 (20H, m, 2C_5H_{10}), 0.87 (6H, t, $J=6.9$ Hz, 2*Me*). Anal. calcd for $C_{23}H_{41}NO_4S$: C, 64.60; H, 9.66; N, 3.28. Found: C, 64.68; H, 9.72; N, 3.20.

4.3.2. Tosylamido diols 4b and 5b. 2-Phenoxymethyl-oxirane (**2b**); dimethoxyethane; 80 °C; Na_2CO_3; 6 h; Et_2O–PE 1:1. **4b**, 212.2 mg, 45%; white solid, mp 75 °C; ν_{max} (Nujol) 3369 (br), 1598, 1587, 1335, 1248, 1146, 1087, 942, 917, 809, 751 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.72 (2H, d, $J=8.2$ Hz, *Ts*), 7.35–7.24 (6H, m, *Ar*), 6.97 (2H, t, $J=7.4$ Hz, *Ph*), 6.89 (4H, d, $J=8.1$ Hz, *Ph*), 4.38–4.31 (2H, m, 2C*H*OH), 4.02 (4H, d, $J=5.2$ Hz, 2CH_2OPh), 3.48 (2H, d, $J=4.5$ Hz, 2O*H*), 3.36 (4H, d, $J=5.7$ Hz, 2CH_2N), 2.42 (3H, s, Ar*Me*). Anal. calcd for $C_{25}H_{29}NO_6S$: C, 63.67; H, 6.20; N, 2.97. Found: C, 63.60; H, 6.26; N, 3.00. **5b**, 212.2 mg, 45%; white solid, mp 112 °C; ν_{max} (Nujol) 3233 (br), 1597, 1587, 1494, 1342, 1249, 1161, 1040, 993, 922, 813, 751 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.72 (2H, d, $J=8.2$ Hz, *Ts*), 7.33–7.24 (6H, m, *Ar*), 6.96 (2H, t, $J=7.3$ Hz, *Ph*), 6.89 (4H, d, $J=8.2$ Hz, *Ph*), 4.43–4.37 (2H, m, 2C*H*OH), 4.00 (4H, d, $J=5.2$ Hz, 2CH_2OPh), 3.66 (2H,

bs, 2O*H*), 3.60 (2H, dd, $J=15.0$, 2.9 Hz, 2CH_aH_bN), 3.20 (2H, dd, $J=15.0$, 8.6 Hz, 2CH_aH$_b$N), 2.42 (3H, s, Ar*Me*). Anal. calcd for $C_{25}H_{29}NO_6S$: C, 63.67; H, 6.20; N, 2.97. Found: C, 63.56; H, 6.25; N, 2.93.

4.3.3. Tosylamido diols 4c and 5c. 2-Phenyl-oxirane (**2c**); dioxane; 90 °C; Cs_2CO_3; 6 h; Et_2O–PE 2:3. **4c**, 156.4 mg, 38%; white solid, mp 82–83 °C; ν_{max} (Nujol) 3294 (br), 1730, 1599, 1343, 1158, 1065, 952, 844, 811 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.68 (2H, d, $J=8.3$ Hz, *Ts*), 7.43–7.25 (12H, m, *Ar*), 5.13 (2H, dd, $J=10.0$, 3.0 Hz, 2C*H*OH), 3.44 (2H, d, $J=3.0$ Hz, 2O*H*), 3.33 (2H, dd, $J=14.7$, 10.0 Hz, 2C$H_a$$H_b$N), 3.17 (2H, dd, $J=14.7$, 3.0 Hz, 2CH_aH$_b$N), 2.38 (3H, s, Ar*Me*). Anal. calcd for $C_{23}H_{25}NO_4S$: C, 67.13; H, 6.12; N, 3.40. Found: C, 67.18; H, 6.18; N, 3.33. **5c**, 152.2 mg, 37%; white solid, mp 166–168 °C; ν_{max} (Nujol) 3310, 3196, 1733, 1599, 1344, 1154, 1088, 1056, 991, 869, 814 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.67 (2H, d, $J=8.3$ Hz, *Ts*), 7.44–7.25 (12H, m, *Ar*), 5.24 (2H, dd, $J=9.8$, 2.5 Hz, 2C*H*OH), 3.60 (2H, dd, $J=15.0$, 2.5 Hz, 2C$H_a$$H_b$-N), 4.16 (2H, bs, 2O*H*), 2.99 (2H, dd, $J=15.0$, 9.8 Hz, 2CH_aH$_b$N), 2.38 (3H, s, Ar*Me*). Anal. calcd for $C_{23}H_{25}NO_4S$: C, 67.13; H, 6.12; N, 3.40. Found: C, 67.20, H, 6.08; N, 3.46.

4.4. General method for the preparation of non-symmetric tosylamido diols 6 and 7

A heterogeneous mixture of tosylamido alcohol **3** (1 mmol), TEBA (23 mg, 0.1 mmol), epoxide **2** (1.1 mmol) solution in anhydrous dioxane (1.5 mL) and anhydrous alkaline carbonate (0.1 mmol), was magnetically stirred at 90 °C until no starting material **1** was detectable (TLC analysis). After the usual workup, the residue was purified by flash column chromatography on silica gel (230–400 mesh). Starting oxirane **2**, tosylamido alcohol **3**, base, reaction time, chromatographic eluant, yield and physical, spectroscopic and analytical data of non-symmetric tosylamido diols **6** and **7** are as follows.

4.4.1. Tosylamido diols 6a and 7a. 2-Hexyl-oxirane (**2a**), **3a**; K_2CO_3; 11 h; AcOEt–PE 1:6. **6a**, 157.4 mg, 35%; white solid, mp 67–69 °C; ν_{max} (Nujol) 3316, 3258, 1918, 1733, 1602, 1589, 1500, 1343, 1247, 1158, 1042, 980, 911, 816, 752, 655 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.70 (2H, d, $J=$ 8.2 Hz, *Ts*), 7.35–7.25 (4H, m, *Ar*), 6.95 (1H, t, $J=7.3$ Hz, *Ph*), 6.89 (2H, d, $J=8.1$ Hz, *Ph*), 4.36–4.29 (1H, m, C$H_{c'}$OH), 4.05–4.00 (2H, m, CH_2OPh), 3.95 (1H, m, CH_cOH), 3.62 (1H, bs, O*H*), 3.35 (1H, dd, $J=14.7$, 8.0 Hz, C$H_{a'}H_{b'}$N), 3.26 (1H, dd, $J=14.7$, 3.4 Hz, C$H_{a'}$H$_{b'}$-N), 3.19 (1H, bs, O*H*), 3.12 (1H, dd, $J=14.4$, 3.7 Hz, C$H_a$$H_b$N), 3.05 (1H, dd, $J=14.4$, 8.2 Hz, CH_aH$_b$N), 2.43 (3H, s, Ar*Me*), 1.43–1.25 (10H, m, C_5H_{10}), 0.88 (3H, t, $J=$ 6.9 Hz, *Me*). Anal. calcd for $C_{24}H_{35}NO_5S$: C, 64.11; H, 7.85; N, 3.12. Found: C, 63.10; H, 7.90; N, 3.07. **7a**, 157.4 mg, 35%; white solid, mp 88–89 °C; ν_{max} (Nujol) 3320, 3272, 1912, 1730, 1600, 1590, 1504, 1350, 1252, 1156, 988, 912, 756 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.69 (2H, d, $J=8.3$ Hz, *Ts*), 7.32–7.24 (4H, m, *Ar*), 6.95 (1H, t, $J=$ 7.3 Hz, *Ph*), 6.88 (2H, d, $J=8.0$ Hz, *Ph*), 4.38–4.23 (1H, m, C$H_{c'}$OH), 4.20 (1H, bs, O*H*), 4.03–3.99 (1H, m, CH_cOH), 3.99–3.92 (2H, m, CH_2OPh), 3.65 (1H, bs, O*H*), 3.62 (1H, dd, $J=14.9$, 2.7 Hz, C$H_{a'}H_{b'}$N), 3.38 (1H, dd, $J=14.7$, 2.3 Hz, C$H_a$$H_b$N), 3.08 (1H, dd, $J=14.9$, 8.8 Hz, C$H_{a'}$H$_{b'}$-N), 2.87 (1H, dd, $J=14.7$, 9.6 Hz, CH_aH$_b$N), 2.42 (3H, s, Ar*Me*), 1.41–1.26 (10H, m, C_5H_{10}), 0.87 (3H, t, $J=6.9$ Hz, *Me*). Anal. calcd for $C_{24}H_{35}NO_5S$: C, 64.11; H, 7.85; N, 3.12. Found: C, 64.22; H, 7.90; N, 3.16.

4.4.2. Tosylamido diols 6b and 7b. Phenyl-oxirane (**2c**), **3a**; Cs_2CO_3; 22 h; methyl-*tert*-butyl ether–PE 2:3. **6b**, 159.0 mg, 36%; white solid, mp 104–106 °C; ν_{max} (Nujol) 3552, 3320, 1733, 1599, 1590, 1344, 1246, 1154, 963, 812, 754, 660 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.69 (2H, d, $J=$ 8.2 Hz, *Ts*), 7.40–7.25 (9H, m, *Ar*), 6.97 (1H, t, $J=7.3$ Hz, *Ph*), 6.91 (2H, d, $J=8.0$ Hz, *Ph*), 5.15 (1H, dd, $J=2.9$, 9.6 Hz, C*H*Ph), 4.36–4.32 (1H, m, C*H*CH$_2$OPh), 4.06 (2H, d, $J=5.2$ Hz, CH_2OPh), 3.48 (1H, dd, $J=8.1$, 14.0 Hz, C$H_a$$H_b$N), 3.44 (2H, bs, 2O*H*), 3.34–3.25 (2H, m, CH_2N), 3.21–3.17 (1H, m, CH_aH$_b$N), 2.40 (3H, s, Ar*Me*). Anal. calcd for $C_{24}H_{27}NO_5S$: C, 65.28; H, 6.16; N, 3.17. Found: C, 63.80; H, 6.70; N, 3.06. **7b**, 159.0 mg, 36%; white solid, mp 93.5–95.5 °C; ν_{max} (Nujol) 3540, 3332, 1730, 1602, 1594, 1350, 1260, 1156, 964, 820, 758, 662 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.70 (2H, d, $J=8.2$ Hz, *Ts*), 7.40–7.24 (9H, m, *Ar*), 7.00–6.89 (3H, m, *Ph*), 5.21 (1H, dd, $J=9.7$, 2.5 Hz, C*H*Ph), 4.52–4.42 (1H, m, C*H*CH$_2$OPh), 4.00 (2H, d, $J=5.3$ Hz, CH_2OPh), 3.66 (1H, dd, $J=15.0$, 2.7 Hz, C$H_{a'}H_{b'}$N), 3.53 (1H, dd, $J=14.7$, 2.5 Hz, CH_aH$_b$N), 3.12 (1H, dd, $J=14.7$, 8.7 Hz, C$H_{a'}$H$_{b'}$N), 3.10 (1H, dd, $J=14.7$, 9.7 Hz, CH_aH$_b$N), 2.62 (2H, bs, 2O*H*), 2.41 (3H, s, Ar*Me*). Anal. calcd for $C_{24}H_{27}NO_5S$: C, 65.28; H, 6.16; N, 3.17. Found: C, 64.90; H, 6.40; N, 3.12.

4.4.3. Tosylamido diols 6c, 7c. 2-*tert*-Butoxymethyl-oxirane (**2f**), **3a**; Na_2CO_3; 48 h; AcOEt–PE 1:3. **6c**, **7c** (50:50), 316.1 mg, 70%; colourless oil; ν_{max} (neat) 3391 (br), 3064, 3041, 2975, 2926, 2877, 1928, 1736, 1599, 1494, 1456, 1390, 1348, 1305, 1246, 1168, 1089, 974, 816, 755, 692, 665 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.70 (2H-**6c**+2H-**7c**, d, $J=8.8$ Hz, *Ts*), 7.31–7.23 (4H-**6c**+4H-**7c**, m, *Ar*), 6.94 (1H-**6c**+1H-**7c**, t, $J=7.3$ Hz, *Ph*), 6.88 (2H-**6c**+2H-**7c**, d, $J=7.3$ Hz, *Ph*), 4.39–4.32 (1H-**7c**, m, C*H*CH$_2$OPh), 4.30–4.25 (1H-**6c**, m, C*H*CH$_2$OPh), 4.16–3.92 (3H-**6c**+ 3H-**7c**, m, 2CH_2OPh+2C*H*CH$_2$OBu^t), 3.76 (2H-**6c**+2H-**7c**, bs, 4O*H*), 3.62 (2H-**7c**, dd, $J=14.7$, 2.9 Hz, 2C$H_a$$H_b$N), 3.47 (2H-**6c**, dd, $J=14.7$, 2.9 Hz, 2CH_aH$_b$N), 3.44–3.14 (2H-**6c**+2H-**7c**, m, 2CH_2OBu^t), 3.10 (2H-**6c**, dd, $J=14.7$, 8.8 Hz, 2CH_aH$_b$N), 3.03 (2H-**7c**, dd, $J=14.7$, 8.8 Hz, 2CH_aH$_b$N), 2.41 (3H-**6c**+3H-**7c**, s, 2Ar*Me*), 1.17 (9H, s, CMe_3), 1.16 (9H, s, CMe_3). Anal. calcd for $C_{23}H_{33}NO_6S$: C, 61.17; H, 7.37; N, 3.10. Found: C, 60.98; H, 7.21; N, 3.12.

4.4.4. Tosylamido diols 6d, 7d. 2-*tert*-Butoxymethyl-oxirane (**2f**), **3c**; Na_2CO_3; 20 h; AcOEt–PE 1:8. **6d**, **7d** (45:55); 290.9 mg, 70%, wax; ν_{max} (Nujol) 3402 (br), 2975, 1727, 1646, 1599, 1494, 1391, 1342, 1290, 1195, 1163, 1089, 996, 925, 816, 753, 659 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.70 (2H-**6d**+2H-**7d**, d, $J=8.1$ Hz, 2*Ts*), 7.31 (2H-**6d**+ 2H-**7d**, d, $J=8.1$ Hz, 2*Ts*), 5.95–5.82 (1H-**6d**+1H-**7d**, m, 2C*H*=CH$_2$), 5.29–5.16 (2H-**6d**+2H-**7d**, m, 2CH_2=), 4.17–4.14 (1H-**7d**, m, C*H*CH$_2$OAll), 4.09–4.06 (1H-**6d**, m, C*H*CH$_2$OAll), 4.01 (2H-**6d**+2H-**7d**, dd, $J=2.9$, 15.4 Hz, 2OCH_2CH=CH$_2$), 3.84 (2H, bs, 2O*H*), 3.70 (2H, bs, 2O*H*), 3.47 (2H-**6d**+2H-**7d**, d, $J=5.1$ Hz, 2CH_2-OAll), 3.21 (2H-**6d**+2H-**7d**, d, $J=5.5$ Hz, 2CH_2OBu^t),

3.53–3.12 (5H-**6d**+3H-**7d**, m, (C*H*CH$_2$OBu^t+2C*H*$_2$N)+(CH$_a$*H*$_b$N+CH$_{a'}$*H*$_{b'}$N+C*H*CH$_2$OBu^t), 3.05–2.97 (1H-**7d**, m, C*H*$_{a'}$H$_{b'}$N), 3.04–2.96 (1H-**7d**, m, C*H*$_a$H$_b$N), 2.42 (3H-**6d**+3H-**7d**, s, 2Ar*Me*), 1.18 (9H, s, C*Me*$_3$), 1.17 (9H, s, C*Me*$_3$). Anal. calcd for $C_{20}H_{33}NO_6S$: C, 57.81; H, 8.00; N, 3.37. Found: C, 57.67; H, 8.09; N, 3.31.

4.4.5. Tosylamido diols 6e, 7e. 2-Phenoxymethyl-oxirane (**2b**), **3d**; Na_2CO_3; 20 h; AcOEt–PE 2:3. **6e**, **7e** (50:50), 335.8 mg, 82%; colourless oil; ν_{max} (neat) 3392 (br), 3064, 2925, 1599, 1588, 1494, 1455, 1338, 1246, 1160, 1089, 995, 816, 757, 693, 658 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.71 (2H-**6e**+2H-**7e**, d, J=8.3 Hz, *Ts*), 7.34–7.24 (4H-**6e**+4H-**7e**, m, *Ar*), 6.96 (1H-**6e**+1H-**7e**, t, J=7.3 Hz, *Ph*), 6.89 (2H-**6e**+2H-**7e**, d, J=7.9 Hz, *Ph*), 4.54 (2H-**6e**+2H-**7e**, bs, 4O*H*), 4.43–4.25 (1H-**6e**+1H-**7e**, m, 2C*H*OH), 4.22–4.03 (1H-**6e**+1H-**7e**, m, 2C*H*OH), 4.02–3.96 (2H-**6e**+2H-**7e**, m, 2C*H*$_2$OPh), 3.63–3.51 (2H-**7e**, m, CH$_a$*H*$_b$N+CH$_{a'}$*H*$_{b'}$N), 3.48–3.42 (2H-**6e**+2H-**7e**, m, 2C*H*$_2$OMe), 3.38 (3H, s, O*Me*), 3.37 (3H, s, O*Me*), 3.34–3.22 (4H-**6e**, m, 2C*H*$_2$N), 3.19–2.98 (2H-**7e**, m, C*H*$_a$H$_b$N+C*H*$_{a'}$H$_{b'}$N), 2.43 (3H-**6e**+3H-**7e**, s, 2Ar*Me*). Anal. calcd for $C_{20}H_{27}NO_6S$: C, 58.66; H, 6.65; N, 3.42. Found: C, 58.72; H, 6.44; N, 3.32.

4.5. General method for the preparation of 2,6-dialkyl-4-(toluene-4-sulfonyl)-morpholines 10–13

In a flame-dried round bottomed flask, 60% sodium hydride (84 mg, 2.1 mmol) was rinsed with anhydrous *n*-pentane (3×0.5 mL). A tosylamido diol **4–7** (1 mmol) solution in anhydrous dichloromethane or dimethoxyethane (5 mL) was cooled at 0 °C and then added to the NaH by syringe, under nitrogen atmosphere. The reaction mixture was stirred at 0 °C until hydrogen evolution ended. A solution of tosyl chloride (TsCl, 1 mmol) or trifuoromethanesulfonic anhydride (Tf_2O, 1 mmol) in dichloromethane (DCM, 5 mL) or dimethoxyethane (DME, 5 mL) was added to the reaction mixture and the stirring was continued at 25–40 °C until disappearance of the starting diol **4–7** (TLC analysis). After cooling, H_2O (2 mL) was added, DCM was evaporated under reduced pressure and the residue was extracted with AcOEt (4×10 mL). The organic phase was dried over sodium sulfate, the solvent was evaporated to dryness under vacuum and the crude was purified by flash column chromatography on silica gel (230–400 mesh). Starting tosylamido diol **4–7**, cyclization agent (TsCl or Tf_2O), solvent, temperature, reaction time, chromatographic eluant, yield and physical, spectroscopic and analytical data are as follows.

4.5.1. Morpholine 10a. Tosylamido diol **4a**; Tf_2O; DCM; 25 °C; 6 h; Et_2O–PE 1:18. **10a**, 319.5 mg, 78%; white solid, mp 56 °C; ν_{max} (Nujol) 1922, 1666, 1600, 1493, 1348, 1170, 1128, 1094, 1000, 956, 816, 784, 663, 619 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.61 (2H, d, J=8.2 Hz, *Ts*), 7.32 (2H, d, J=8.2 Hz, *Ts*), 3.54 (2H, d, J=10.8 Hz, 2CH$_a$*H*$_b$N), 3.50–3.44 (2H, m, 2C*H*O), 2.43 (3H, s, Ar*Me*), 1.92 (2H, dd, J=10.8, 10.8 Hz, 2C*H*$_a$H$_b$N), 1.54–1.25 (20H, m, 2C$_5$*H*$_{10}$), 0.87 (6H, t, J=6.9 Hz, 2*Me*). Anal. calcd for $C_{23}H_{39}NO_3S$: C, 67.44; H, 9.60; N, 3.42. Found: C, 67.20; H, 9.68; N, 3.41.

4.5.2. Morpholine 11a. Tosylamido diol **5a**; Tf_2O; DME; 25 °C; 6 h; AcOEt–PE 1:20. **11a**, 327.7 mg, 80%; white solid, mp 40–41 °C; ν_{max} (Nujol) 1600, 1364, 1170, 1092, 949, 814, 677 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.60 (2H, d, J=8.2 Hz, *Ts*), 7.32 (2H, d, J=8.2 Hz, *Ts*), 3.79–3.73 (2H, m, 2C*H*O), 2.98 (2H, dd, J=11.2, 3.3 Hz, 2CH$_a$*H*$_b$N), 2.67 (2H, dd, J=11.2, 5.8 Hz, 2C*H*$_a$H$_b$N), 2.43 (3H, s, Ar*Me*), 1.65–1.27 (20H, m, 2C$_5$*H*$_{10}$), 0.87 (6H, t, J=6.9 Hz, 2*Me*). Anal. calcd for $C_{23}H_{39}NO_3S$: C, 67.44; H, 9.60; N, 3.42. Found: C, 67.12; H, 9.52; N, 3.40.

4.5.3. Morpholine 10b. Tosylamido diol **4b**; Tf_2O; DCM; 25 °C; 13 h; AcOEt–PE 1:10. **10b**, 349.2 mg, 77%; white solid, 125–127 °C; ν_{max} (Nujol) 1599, 1586, 1494, 1341, 1254, 1211, 1160, 1119, 1052, 1036, 999, 814, 753, 692, 666 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.66 (2H, d, J=8.2 Hz, *Ts*), 7.36–7.25 (6H, m, *Ar*), 6.96 (2H, t, J=7.3 Hz, *Ph*), 6.87 (4H, d, J=8.1 Hz, *Ph*), 4.08–4.04 (4H, m, 2C*H*O+C*H*$_2$OPh), 3.92–3.87 (4H, m, 2CH$_a$*H*$_b$N+C*H*$_2$OPh), 2.44 (3H, s, Ar*Me*), 2.26 (2H, dd, J=10.8, 10.8 Hz, 2C*H*$_a$H$_b$N). Anal. calcd for $C_{25}H_{27}NO_5S$: C, 66.20; H, 6.00; N, 3.09. Found: C, 66.11; H, 5.98; N, 3.06.

4.5.4. Morpholine 11b. Tosylamido diol **5b**; Tf_2O; DCM; 40 °C; 6 h; AcOEt–PE 1:8. **11b**, 362.8 mg, 80%; white solid, mp 143–145 °C; ν_{max} (Nujol) 1601, 1582, 1492, 1341, 1252, 1160, 1120, 1050, 998, 814, 754, 690, 666 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.65 (2H, d, J=8.2 Hz, *Ts*), 7.34–7.27 (6H, m, *Ar*), 6.97 (2H, t, J=7.3 Hz, *Ph*), 6.89 (4H, d, J=8.0 Hz, *Ph*), 4.28–4.25 (2H, m, 2C*H*O), 4.13 (2H, dd, J=9.6, 5.4 Hz, CH$_{a'}$*H*$_{b'}$OPh), 4.11 (2H, dd, J=9.6, 6.4 Hz, C*H*$_{a'}$H$_{b'}$OPh), 3.25 (2H, dd, J=11.6, 3.3 Hz, 2CH$_a$*H*$_b$N), 3.04 (2H, dd, J=11.6, 5.7 Hz, 2C*H*$_a$H$_b$N), 2.43 (3H, s, Ar*Me*). Anal. calcd for $C_{25}H_{27}NO_5S$: C, 66.20; H, 6.00; N, 3.09. Found: C, 66.31; H, 6.07; N, 3.05.

4.5.5. Morpholine 10c. Tosylamido diol **4c**; TsCl; DCM; 40 °C; 22 h; Et_2O–PE 1:3. **10c**, 279.4 mg, 71%; white solid, mp 128–130 °C; ν_{max} (Nujol) 1960, 1821, 1732, 1597, 1494, 1341, 1228, 1166, 1068, 962, 814, 776, cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.59 (2H, d, J=8.2 Hz, *Ts*), 7.47–7.27 (12H, m, *Ar*), 4.85 (2H, dd, J=10.6, 2.5 Hz, 2C*H*O), 3.89 (2H, dd, J=10.6, 2.5 Hz, 2CH$_a$*H*$_b$N), 2.41 (3H, s, Ar*Me*), 2.28 (2H, dd, J=10.6, 10.6 Hz, 2C*H*$_a$H$_b$N). Anal. calcd for $C_{23}H_{23}NO_3S$: C, 70.20; H, 5.89; N, 3.56. Found: C, 70.09; H, 5.60; N, 3.61.

4.5.6. Morpholine 11c. Tosylamido diol **5c**; TsCl; DCM; 40 °C; 72 h; Et_2O–PE 1:3. **11c**, 259.7 mg, 66%; wax; ν_{max} (Nujol) 1962, 1823, 1732, 1596, 1495, 1342, 1306, 1230, 1167, 1089, 1065, 961, 926, 815, 774, 702, 692, 651 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.65 (2H, d, J=8.2 Hz, *Ts*), 7.46–7.30 (12H, m, *Ar*), 4.90 (2H, dd, J=5.7, 3.7 Hz, 2C*H*O), 3.35 (2H, dd, J=11.6, 5.7 Hz, 2CH$_a$*H*$_b$N), 3.27 (2H, dd, J=11.6, 3.7 Hz, 2C*H*$_a$H$_b$N), 2.45 (3H, s, Ar*Me*). Anal. calcd for $C_{23}H_{23}NO_3S$: C, 70.20; H, 5.89; N, 3.56. Found: C, 70.33; H, 5.90; N, 3.60.

4.5.7. Morpholine 12a. Tosylamido diol **6a**; Tf_2O; DCM; 25 °C; 2 h; Et_2O–PE 1:1. **12a**, 366.8 mg, 85%; colourless oil; ν_{max} (neat) 1661, 1600, 1496, 1378, 1302, 1245, 1169, 1121, 1094, 815, 754, 692 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.64 (2H, d, J=8.2 Hz, *Ts*), 7.33 (2H, d, J=8.2 Hz, *Ts*), 7.30–7.24 (2H, m, *Ph*), 6.95 (1H, t, J=7.3 Hz, *Ph*), 6.87 (2H, d, J=8.2 Hz, *Ph*), 4.05–4.00 (1H, m, C*H*O), 4.00–3.92

(1H, m, C*H*O), 3.86–3.81 (2H, m, CH_2OPh), 3.63–3.57 (2H, m, CH$_a$$H_b$N+CH$_{a'}$$H_{b'}$N), 2.43 (3H, s, Ar*Me*), 2.16 (1H, dd, *J*=10.8, 10.4 Hz, C$H_{a'}$H$_{b'}$N), 2.00 (1H, dd, *J*=11.2, 11.2 Hz, CH_aH$_b$N), 1.49–1.25 (10H, m, C_5H_{10}), 0.87 (3H, t, *J*=7.0 Hz, *Me*). Anal. calcd for $C_{24}H_{33}NO_4S$: C, 66.79; H, 7.71; N, 3.25. Found: C, 66.64; H, 7.78; N, 3.20.

4.5.8. Morpholine 13a. Tosylamido diol **7a**; Tf_2O; DCM; 25 °C; 7 h; AcOEt–PE 1:9. **13a**, 332.3 mg, 77%; colourless oil; ν_{max} (neat) 1662, 1598, 1588, 1496, 1376, 1300, 1244, 1168, 1120, 1093, 812, 754, 690 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.62 (2H, d, *J*=8.2 Hz, *Ts*), 7.33–7.24 (4H, m, *Ar*), 6.96 (1H, t, *J*=7.3 Hz, *Ph*), 6.87 (2H, d, *J*=8.2 Hz, *Ph*), 4.20–4.17 (1H, m, C*H*CH$_2$OPh), 4.12 (1H, dd, *J*=9.4, 5.4 Hz, CH$_a$$H_b$OPh), 4.02 (1H, dd, *J*=9.4, 6.4 Hz, CH_aH$_b$-OPh), 3.84–3.81 (1H, m, C*H*C_6H_{13}), 3.15 (1H, dd, *J*=11.4, 3.3 Hz, CH$_{a'}$$H_{b'}$N), 3.08 (1H, dd, *J*=11.4, 3.3 Hz, CH$_a$$H_b$-N), 2.98 (1H, dd, *J*=11.4, 5.5 Hz, C$H_{a'}$H$_{b'}$N), 2.73 (1H, dd, *J*=11.4, 6.0 Hz, CH_aH$_b$N), 2.42 (3H, s, Ar*Me*), 1.70–1.66 (2H, m, CHCH_2), 1.37–1.22 (8H, m, C_4H_8), 0.87 (3H, t, *J*=6.9 Hz, *Me*). Anal. calcd for $C_{24}H_{33}NO_4S$: C, 66.79; H, 7.71; N, 3.25. Found: C, 66.90; H, 7.78; N, 3.20.

4.5.9. Morpholine 12b. Tosylamido diol **6b**; TsCl; DCM; 25 °C; 54 h; AcOEt–PE 1:7. **12b**, 194.8 mg, 46%; white solid, mp 124–126 °C; ν_{max} (Nujol) 1598, 1586, 1492, 1344, 1238, 1166, 1122, 1066, 1052, 966, 774, 756 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.62 (2H, d, *J*=8.2 Hz, *Ts*), 7.37–7.25 (9H, m, *Ar*), 6.97 (1H, t, *J*=7.3 Hz, *Ph*), 6.89 (2H, d, *J*=8.2 Hz, *Ph*), 4.73 (1H, dd, *J*=10.5, 2.4 Hz, C*H*Ph), 4.20–4.12 (1H+1H, m, C*H*CH$_2$OPh+CH$_a$$H_b$N), 3.99–3.93 (2H, m, C$H_2$OPh), 3.82 (1H, d, *J*=11.0 Hz, CH$_{a'}$$H_{b'}$N), 2.43 (3H, s, Ar*Me*), 2.32 (1H, dd, *J*=10.5, 10.5 Hz, CH_aH$_b$N), 2.22 (1H, dd, *J*=11.0, 11.0 Hz, C$H_{a'}$H$_{b'}$N). Anal. calcd for $C_{24}H_{25}NO_4S$: C, 68.06; H, 5.95; N, 3.31. Found: C, 67.92; H, 5.91; N, 3.23. Together with **13b** (29.6 mg, 7%).

4.5.10. Morpholine 13b. Tosylamido diol **7b**; TsCl; DCM; 25 °C; 28 h; AcOEt–PE 1:7. **13b**, 275.3 mg, 65%; white solid, mp 146–148 °C; ν_{max} (Nujol) 1598, 1587, 1493, 1345, 1236, 1167, 1131, 1122, 1065, 1051, 968, 813, 776, 757, 682 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.64 (2H, d, *J*=8.2 Hz, *Ts*), 7.44–7.24 (9H, m, *Ar*), 6.96 (1H, t, *J*=7.3 Hz, *Ph*), 6.90 (2H, d, *J*=8.2 Hz, *Ph*), 4.95 (1H, dd, *J*=6.9, 3.2 Hz, C*H*Ph), 4.24–4.18 (1H, m, C*H*CH$_2$OPh), 4.21–4.18 (2H, m, CH_2OPh), 3.41 (1H, dd, *J*=11.8, 3.2 Hz, CH$_a$$H_b$N), 3.29 (1H, dd, *J*=11.5, 3.9 Hz, CH$_{a'}$$H_{b'}$N), 3.10 (1H, dd, *J*=11.5, 2.6 Hz, C$H_{a'}$H$_{b'}$N), 3.06 (1H, dd, *J*=11.8, 6.9 Hz, CH_aH$_b$-N), 2.43 (3H, s, Ar*Me*). Anal. calcd for $C_{24}H_{25}NO_4S$: C, 68.06; H, 5.95; N, 3.31. Found: C, 68.20; H, 5.92; N, 3.42. Together with **12b** (12.7 mg, 3%) and **14b** (59.3 mg, 14%). Vinyl tosylamide **14b**; wax; ν_{max} (Nujol) 3320, 3040, 1734, 1600, 1588, 1345, 1246, 1156, 964, 814, 756, 660 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.64 (2H, d, *J*=8.2 Hz, *Ts*), 7.44–7.24 (9H, m, *Ar*), 6.96 (1H, t, *J*=7.3 Hz, *Ph*), 6.90 (2H, d, *J*=8.2 Hz, *Ph*), 5.97 (1H, dt, *J*=6.2, 6.2 Hz, C*H*=CHN), 5.48 (1H, d, *J*=7.7 Hz, CH=C*H*N), 4.88–4.73 (3H, m, CH_2-OPh+C*H*Ph), 3.42–3.34 (1H+1H, m, OH+CH$_a$$H_b$N), 3.15–3.07 (1H, m, C$H_aH_b$N), 2.40 (3H, s, Ar*Me*). Anal. calcd for $C_{24}H_{25}NO_4S$: C, 68.06; H, 5.95; N, 3.31. Found: C, 68.21; H, 5.89; N, 3.08.

4.5.11. Morpholines 12c and 13c. Tosylamido diols **6c**, **7c** (50:50); Tf_2O; DCM; 25 °C; 5 h; AcOEt–PE 1:10. **12c**, 320.8 mg, 74%; wax; ν_{max} (Nujol) 1599, 1580, 1346, 1247, 1167, 1120, 1087, 814, 756 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.65 (2H, d, *J*=8.4 Hz, *Ts*), 7.35–7.24 (4H, m, *Ar*), 6.95 (1H, t, *J*=7.4 Hz, *Ph*), 6.86 (2H, d, *J*=7.7 Hz, *Ph*), 4.10–3.96 (1H+1H, m, 2C*H*O), 3.86–3.73 (4H, m, CH_2OPh+CH_2OBu^t), 3.47 (1H, dd, *J*=11.0, 4.8 Hz, CH$_a$$H_b$N), 3.23 (1H, dd, *J*=11.0, 7.0 Hz, CH$_{a'}$$H_{b'}$N), 2.44 (3H, s, Ar*Me*), 2.20 (1H, dd, *J*=11.0, 11.0 Hz, C$H_{a'}$H$_{b'}$N), 2.09 (1H, dd, *J*=11.0, 11.0 Hz, CH_aH$_b$N), 1.15 (9H, s, CMe_3). Anal. calcd for $C_{23}H_{31}NO_5S$: C, 63.72; H, 7.21; N, 3.23. Found: C, 63.42; H, 7.18; N, 3.20.

Compound **13c**. 277.5 mg, 64%; wax; ν_{max} (Nujol) 1600, 1576, 1346, 1246, 1168, 1120, 1086, 816, 758 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.63 (2H, d, *J*=8.1 Hz, *Ts*), 7.34–7.25 (4H, m, *Ar*), 6.96 (1H, t, *J*=7.4 Hz, *Ph*), 6.88 (2H, d, *J*=7.7 Hz, *Ph*), 4.22–4.17 (1H, m, C*H*CH$_2$OPh), 4.14–4.08 (1H, m, C*H*CH$_2$OBu^t), 4.00–3.89 (2H, m, CH_2OPh), 3.54 (2H, d, *J*=6.2 Hz, CH_2OBu^t), 3.31 (1H, dd, *J*=11.4, 2.9 Hz, CH$_{a'}$$H_{b'}$N), 3.07 (1H, dd, *J*=11.4, 4.8 Hz, CH$_a$$H_b$-N), 2.99 (1H, dd, *J*=11.4, 3.6 Hz, CH_aH$_b$N), 2.83 (1H, dd, *J*=11.4, 6.2 Hz, C$H_{a'}$H$_{b'}$N), 2.43 (3H, s, Ar*Me*), 1.19 (9H, s, CMe_3). Anal. calcd for $C_{23}H_{31}NO_5S$: C, 63.72; H, 7.21; N, 3.23. Found: C, 63.82; H, 7.24; N, 3.18.

4.5.12. Morpholines 12d and 13d. Tosylamido diols **6d**, **7d** (45:55); TsCl; DCM; 25 °C; 28 h; AcOEt–PE 1:8. **12d**, 278.3 mg, 70%; colourless oil; ν_{max} (neat), 3066, 2975, 2922, 2872, 1730, 1646, 1598, 1494, 1455, 1348, 1195, 1168, 1088, 996, 816, 787, 664 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.64 (2H, d, *J*=8.1 Hz, *Ts*), 7.33 (2H, d, *J*=8.1 Hz, *Ts*), 5.91–5.78 (1H, m, C*H*=CH$_2$), 5.26–5.16 (2H, m, CH_2=), 3.96 (2H, d, *J*=5.5 Hz, OCH_2CH=CH$_2$), 3.78–3.64 (4H, m, 2CH_2O), 3.53–3.43 (2H, m, C*H*O), 3.39 (1H, dd, *J*=11.0, 5.2 Hz, CH$_a$$H_b$N), 3.18 (1H, dd, *J*=11.0, 7.4 Hz, CH$_{a'}$$H_{b'}$N), 2.43 (3H, s, Ar*Me*), 2.14 (1H, dd, *J*=11.0, 11.0 Hz, C$H_{a'}$H$_{b'}$N), 2.03 (1H, dd, *J*=10.7, 10.7 Hz, CH_aH$_b$N), 1.14 (9H, s, CMe_3). Anal. calcd for $C_{20}H_{31}NO_5S$: C, 60.43; H, 7.86; N, 3.52. Found: C, 60.56; H, 7.78; N, 3.53.

Compound **13d**. 234.5 mg, 59%; colourless oil; ν_{max} (neat) 3526 (br), 3068, 2972, 2923, 2870, 1726, 1646, 1594, 1494, 1456, 1344, 1170, 1094, 994, 814, 785, 664 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.62 (2H, d, *J*=8.1 Hz, *Ts*), 7.33 (2H, d, *J*=8.1 Hz, *Ts*), 5.93–5.78 (1H, m, C*H*=CH$_2$), 5.28–5.17 (2H, m, CH_2=), 3.98 (2H, d, *J*=5.9 Hz, OCH_2CH=CH$_2$), 3.89–3.87 (1H, m, C*H*O), 3.58–3.43 (5H, m, C*H*O+2CH_2O), 3.15 (1H, dd, *J*=11.4, 2.9 Hz, CH$_a$$H_b$N), 3.03 (1H, dd, *J*=11.4, 4.8 Hz, CH$_{a'}$$H_{b'}$N), 2.94 (1H, dd, *J*=11.4, 3.7 Hz, C$H_{a'}$H$_{b'}$N), 2.74 (1H, dd, *J*=11.4, 7.0 Hz, CH_aH$_b$-N), 2.43 (3H, s, Ar*Me*), 1.15 (9H, s, CMe_3). Anal. calcd for $C_{20}H_{31}NO_5S$: C, 60.43; H, 7.86; N, 3.52. Found: C, 60.60; H, 7.81; N, 3.44.

4.5.13. Morpholines 12e and 13e. Tosylamido diols **6e**, **7e** (50:50); Tf_2O; DCM; 25 °C; 5 h; AcOEt–PE 1:15. **12e**, 223.1 mg, 57%; colourless oil; ν_{max} (neat) 3063, 3040, 2917, 2850, 2057, 1929, 1746, 1599, 1494, 1456, 1347, 1245, 1168, 1000, 816, 757, 687 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.64 (2H, d, *J*=8.1 Hz, *Ts*), 7.35–7.24 (4H, m, *Ar*), 6.95 (1H, t, *J*=7.4 Hz, *Ph*), 6.86 (2H, d, *J*=8.1 Hz, *Ph*),

4.08–4.01 (1H, m, C*H*CH_2OPh), 4.00–3.98 (1H, m, C*H*CH_2OMe), 3.87–3.85 (2H, m, CH_2OPh), 3.84–3.82 (1H, m, CH_aH_bN), 3.68 (1H, dd, J=11.0, 1.0 Hz, $CH_{a'}H_{b'}$N), 3.43 (2H, dd, J=4.4, 1.5 Hz, CH_2OMe), 3.34 (3H, s, O*Me*), 2.44 (3H, s, Ar*Me*), 2.23 (1H, dd, J=11.0, 11.0 Hz, $CH_{a'}H_{b'}$N), 2.21 (1H, dd, J=11.0, 11.0 Hz, CH_aH_bN). Anal. calcd for $C_{20}H_{25}NO_5S$: C, 61.36; H, 6.44; N, 3.58. Found: C, 61.42; H, 6.32; N, 3.53.

Compound **13e**. 207.5 mg, 53%; colourless oil; ν_{max} (neat) 3064, 3042, 2918, 2848, 2058, 1927, 1746, 1600, 1496, 1456, 1350, 1244, 1169, 1000, 814, 758, 686 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.63 (2H, d, J=8.1 Hz, *Ts*), 7.34–7.25 (4H, m, *Ar*), 6.96 (1H, t, J=7.4 Hz, *Ph*), 6.89 (2H, d, J=8.1 Hz, *Ph*), 4.25–4.20 (1H, m, C*H*CH_2OMe), 4.18–4.15 (1H, m, C*H*CH_2OPh), 4.07–4.02 (2H, m, CH_2OPh), 3.60 (1H, dd, J=10.3, 5.1 Hz, $CH_{a'}H_{b'}$N), 3.51 (1H, dd, J=10.3, 5.1 Hz, $CH_{a'}H_{b'}$N), 3.37 (3H, s, O*Me*), 3.15 (2H, d, J=11.7 Hz, CH_2OMe), 3.06 (1H, dd, J=11.7, 5.1 Hz, CH_aH_bN), 2.88 (1H, dd, J=11.7, 6.6 Hz, CH_aH_bN), 2.43 (3H, s, Ar*Me*). Anal. calcd for $C_{20}H_{25}NO_5S$: C, 61.36; H, 6.44; N, 3.58. Found: C, 61.28; H, 6.52; N, 3.52.

4.6. General method for the preparation of 2,6-dialkylmorpholines 15

A mixture of *N*-tosyl morpholine **10–13** (1 mmol), 30% HBr–AcOH (6 mL, 30 mmol) and, if it is the case, phenol (0.28 g, 3 mmol) was magnetically stirred at 25–80 °C until no starting material was detectable (TLC analysis). After cooling, the reaction mixture was poured into ice (20 g), NaOH pellets were added until pH 8 was reached and the aqueous phase was extracted with AcOEt (4×10 mL); the organic phase was dried over sodium sulfate, evaporated under vacuum and purified by flash column chromatography on silica gel (230–400 mesh). Starting *N*-tosyl morpholine **10–13**, reaction time, chromatographic eluant, yield and physical, spectroscopic and analytical data of morpholines **15** are as follows.

4.6.1. Morpholine 15a. *N*-tosyl morpholine **10a**; 60 °C; 2 h; MeOH–CH_2Cl_2 1:20. **15a**, 166.0 mg, 65%; wax; ν_{max} (Nujol) 3350, 1920, 1668, 1600, 1497, 1168, 1096, 1000, 816, 784, 663, 619 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 5.82 (1H, bs, N*H*), 3.71–3.66 (2H, m, 2C*H*O), 3.14 (2H, dd, J=11.4, 1.2 Hz, 2CH_aH_bN), 2.56 (2H, dd, J=11.4, 11.4 Hz, 2CH_aH_bN), 1.45–1.26 (20H, m, 2C_5H_{10}), 0.87 (6H, t, J=6.9 Hz, 2*Me*). Anal. calcd for $C_{16}H_{33}NO$: C, 75.23; H, 13.02; N, 5.48. Found: C, 75.11; H, 13.00; N, 5.51.

4.6.2. Morpholine 15b. *N*-tosyl morpholine **11a**; 80 °C; 4 h; MeOH–CH_2Cl 1:30. **15b**, 160.9 mg, 63%; wax; ν_{max} (Nujol) 3320, 1602, 1168, 1090, 949, 810, 678 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.82 (1H, bs, N*H*), 3.94–3.87 (2H, m, 2C*H*O), 3.17 (2H, dd, J=12.6, 3.6 Hz, 2CH_aH_bN), 2.86 (2H, dd, J=12.6, 6.1 Hz, 2CH_aH_bN), 1.86–1.77 (2H, m, CH_2CH), 1.51–1.39 (2H, m, $CHCH_2CH_2$), 1.36–1.27 (16H, m, 2C_2H_4), 0.86 (6H, t, J=6.9 Hz, 2*Me*). Anal. calcd for $C_{16}H_{33}NO$: C, 75.23; H, 13.02; N, 5.48. Found: C, 75.34; H, 13.10; N, 5.40.

4.6.3. Morpholine 15c. *N*-tosyl morpholine **10b**; 60 °C; 4 h; MeOH–CH_2Cl_2 1:30. **15c**, 224.5 mg, 75%; wax; ν_{max} (Nujol) 3340, 1600, 1586, 1494, 1250, 1162, 1119, 1054, 1036, 813, 755, 694 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.37–6.76 (10H, m, *Ph*), 4.09–3.85 (6H, m, 2CH_2OPh+2C*H*O), 3.14–3.06 (2H, m, 2CH_aH_bN), 2.75–2.66 (2H, m, 2CH_aH_bN), 1.80 (1H, bs, N*H*). Anal. calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.33; H, 7.04; N, 4.72.

4.6.4. Morpholine 15d. *N*-tosyl morpholine **11b**; 60 °C; 4 h; MeOH–CH_2Cl_2 1:20. **15d**, 224.5 mg, 75%; white solid, mp 75–77 °C; ν_{max} (Nujol) 3348, 1600, 1584, 1491, 1252, 1160, 1120, 1050, 816, 756, 692 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.31–7.25 (4H, m, *Ph*), 6.98–6.91 (6H, m, *Ph*), 4.18–4.16 (2H, m, 2C*H*O), 4.20–4.10 (4H, m, 2CH_2OPh), 3.12 (2H, dd, J=12.2, 3.0 Hz, 2CH_aH_bN), 2.93 (2H, dd, J=12.2, 4.5 Hz, 2CH_aH_bN), 2.21 (1H, bs, N*H*). Anal. calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.10; H, 7.04; N, 4.63.

4.6.5. Morpholine 15e. *N*-tosyl morpholine **10c**; 25 °C; 9 h; MeOH–CH_2Cl_2 1:30. **15e**, 146.0 mg, 61%; wax; ν_{max} (Nujol) 3344, 1962, 1820, 1734, 1597, 1496, 1226, 1164, 1068, 964, 812, 774, cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.46–7.25 (10H, m, *Ph*), 4.71 (2H, dd, J=10.5, 2.4 Hz, 2C*H*O), 3.13 (2H, dd, J=12.7, 2.4 Hz, 2CH_aH_bN), 2.80 (2H, dd, J=12.7, 10.5 Hz, 2CH_aH_bN), 2.00 (1H, bs, N*H*). Anal. calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.06; N, 5.85. Found: C, 80.42; H, 7.02; N, 5.78.

4.6.6. Morpholine 15f. *N*-tosyl morpholine **12a**; 25 °C; 24 h; MeOH–CH_2Cl_2 1:14. **15f**, 205.3 mg, 74%; colourless oil; ν_{max} (neat) 3342, 1662, 1599, 1586, 1498, 1300, 1244, 1166, 1122, 814, 754 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.29–7.24 (2H, m, *Ph*), 6.94–6.87 (3H, m, *Ph*), 4.04 (1H, dd, J=8.6, 4.2 Hz, CH_aH_bOPh), 4.00–3.91 (1H, m, C*H*CH_2OPh), 3.89 (1H, dd, J=8.6, 5.3 Hz, CH_aH_bOPh), 3.62–3.50 (1H, m, C*H*C_6H_{13}), 3.19 (1H, dd, J=11.4, 11.4 Hz, CH_aH_bN), 2.99 (1H, dd, J=11.2, 11.2 Hz, $CH_{a'}H_{b'}$N), 2.95 (1H, bs, N*H*), 2.72 (1H, dd, J=11.2, 11.2 Hz, $CH_{a'}H_{b'}$N), 2.55 (1H, dd, J=11.4, 11.4 Hz, CH_aH_bN), 1.49–1.25 (10H, m, C_5H_{10}), 0.87 (3H, t, J=6.9 Hz, *Me*). Anal. calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.72; H, 9.76; N 5.12.

4.6.7. Morpholine 15g. *N*-tosyl morpholine **13a**; 25 °C; 24 h; MeOH–CH_2Cl_2 1:36. **15g**, 185.9 mg, 67%; colourless oil; ν_{max} (neat) 3338, 1660, 1599, 1588, 1494, 1302, 1245, 1166, 1118, 1095, 813, 756, 692 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.28–7.23 (2H, m, *Ph*), 6.95–6.90 (3H, m, *Ph*), 4.13 (2H, d, J=5.7 Hz, CH_2OPh), 4.09–4.02 (1H, m, C*H*CH_2OPh), 3.76–3.69 (1H, m, C*H*C_6H_{13}), 3.04 (1H, dd, J=12.4, 3.5 Hz, $CH_{a'}H_{b'}$N), 2.96 (1H, dd, J=12.2, 3.3 Hz, CH_aH_bN), 2.87 (1H, dd, J=12.4, 4.9 Hz, $CH_{a'}H_{b'}$N), 2.61 (1H, dd, J=12.2, 6.4 Hz, CH_aH_bN), 2.01 (1H, bs, N*H*), 1.70–1.25 (10H, m, C_5H_{10}), 0.87 (3H, t, J=6.9 Hz, *Me*). Anal. calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.72; H, 9.75; N, 5.02.

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