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2-(1,3,5-DITHIAZINAN-5-YL)ETHANOL HETEROCYCLES, STRUCTURE AND REACTIVITY

Juan Carlos Gálvez-Ruiz, Javier C. Jaen-Gaspar, Indira G. Castellanos-Arzola, Rosalinda Contreras, and Angelina Flores-Parra*

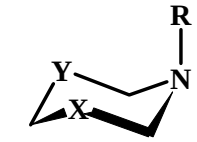
Chemistry Department, Centro de Investigación y de Estudios Avanzados del IPN. AP 14-740, CP 07000, Mexico D. F., Mexico
aflores@mail.cinvestav.mx

Abstract – Treatment of 2-(1,3,5-dithiazinan-5-yl)ethanol (**1**), 2-(1,3,5-dithiazinan-5-yl)-1-phenylethanol (**2**), 2-(1,3,5-dithiazinan-5-yl)-1-methylethanol (**3**) and 2-(1,3,5-dithiazinan-5-yl)-2-methyl-1-phenylethanol (**4**) with TsCl and NEt_3 in CH_2Cl_2 afforded the corresponding 3-tosyl-1,3-oxazolidine derivatives (**5-8**), whereas tosylation of **1-4** in the presence of $NHMe_3Cl$ gave the corresponding *O*-tosyl-2-(1,3,5-dithiazinan-5-yl)ethanol derivatives (**11-14**). The direct preparation of **5** and **7** from formaldehyde and *N*-tosylethanolamine (**9**) or *N*-tosyl-2-propanolamine was not successful. Reactions of **1** or **3** with benzylamine furnish 1,3,5-tribenzyl-1,3,5-triazinane. Heating of **1** and **2** affords the corresponding 1,3,5-tri(2-hydroxyethyl)-1,3,5-triazinanes. X-Ray diffraction studies of compounds (**1-9** and **11**) are reported.

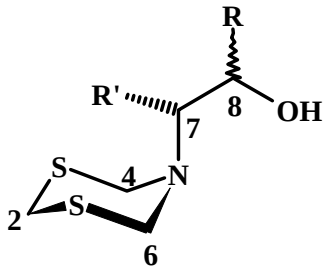
INTRODUCTION

We are interested in the synthesis and structure of nitrogenated 1,3-hetero-5-azinanes,[1] which are widely used as flavoring agents,[2a] antibiotics,[2b] enzymatic inhibitors,[2c] and organic reagents,[2d] and their aluminum,[3a,b] indium[3b] and boron[3b-g] coordination compounds.

We have reported compounds (**1-3**) (Scheme 1) which were synthesized from the corresponding primary amines and formaldehyde, compounds bearing sulfur atoms are obtained with the mentioned reagents and in the presence of NaSH.[3a] Herein, we report the tosylation reactions of compounds (**1-4**) which afford *N*-tosyl-1,3-oxazolidines and *O*-tosyl-2-(1,3,5-dithiazinan-5-yl)-1-ethanols and amination reactions which gives 1,3,5-triazinanes. Also thermic rearragement of **1-4** was observed, giving the corresponding 1,3-oxazolidines and 1,3,5-tri(2-hydroxyethyl)-1,3,5-triazinanes.



X, Y = O, NR or S



1 R= H, R'= H
2 R= Ph, R'= H
3 R= Me, R'= H
4 R= Ph, R'= Me

Scheme 1

RESULTS AND DISCUSSION

1,3,5-DITHIAZINANES (**1-4**)

Compounds (**1-4**) were prepared by reaction of formaldehyde, the corresponding β-ethanolamine and NaHS. Their ^{13}C NMR spectra present the characteristic chemical shifts for six membered ring compounds (δ for C4-C6 appears around 58.6 ppm and C2 at 33.7). ^{1}H NMR spectra show that **1-3** are in conformational equilibrium at room temperature, their ring inversion energy was calculated from variable temperature NMR experiments [$\Delta G^{\#}$ = 45.4, **1**; 49.3, **2**; and 49.5 kJmol^{-1}, **3**]. Found values were not far from those reported for *N*-methyl-1,3,5-dithiazinane[2f,g] [$\Delta G^{\#}$ = 46.0 kJmol^{-1}]. The preferred ring conformation of compound (**4**) was evidenced by its ^{1}H NMR spectrum at room temperature which show different resonances for axial and equatorial protons (H-4ax and H-6ax 4.66; H-4eq and H-6eq 4.53 ppm, their *geminal* coupling constants values are 14 Hz). Compound (**1**) has the exocyclic ethanol chain in conformational equilibrium, whereas **2-4** with alkyl or aryl substituent at the chain present a preferred staggered conformation deduced from the ^{1}H coupling pattern and originated by a hydrogen bond forming a “five membered ring”. The *anti* or *syn* position of hydrogen atoms in the molecule arm is deduced from

the values of the coupling constants ^{3}J(H7A,H8) = 9.9 Hz (*anti*) and ^{3}J(H7B,H8) = 2.9 Hz (*syn*). An interesting fact in the ^{1}H NMR spectra of **2** and **3** is the deshielding effect (≈ 0.68 ppm) for H-7A protons with respect to H-7B due to their position pointing at the sulfur atoms [for **2** H-7A δ = 3.08; H-7B δ = 2.40 and for **3** H-7A δ = 3.49; H-7B δ = 2.81 ppm] as it was confirmed by the X-Ray diffraction analyses (see below). In solution, the ^{15}N chemical shift and the O-H higher frequency signals indicate the strength of the hydrogen bond.[4] According to that, compound (**3**) has the strongest hydrogen bond (δ ^{15}N NMR data in $CDCl_3$: **1** -352.9 ppm; **2** -333.5; **3** -310.6; **4** -343.9; N-methyl-1,3,5-dithiazinane[2d] -360.5 ppm). The corresponding solid state structures of dithiazinanes (**1**-**4**) were obtained. (Figures 1-2)

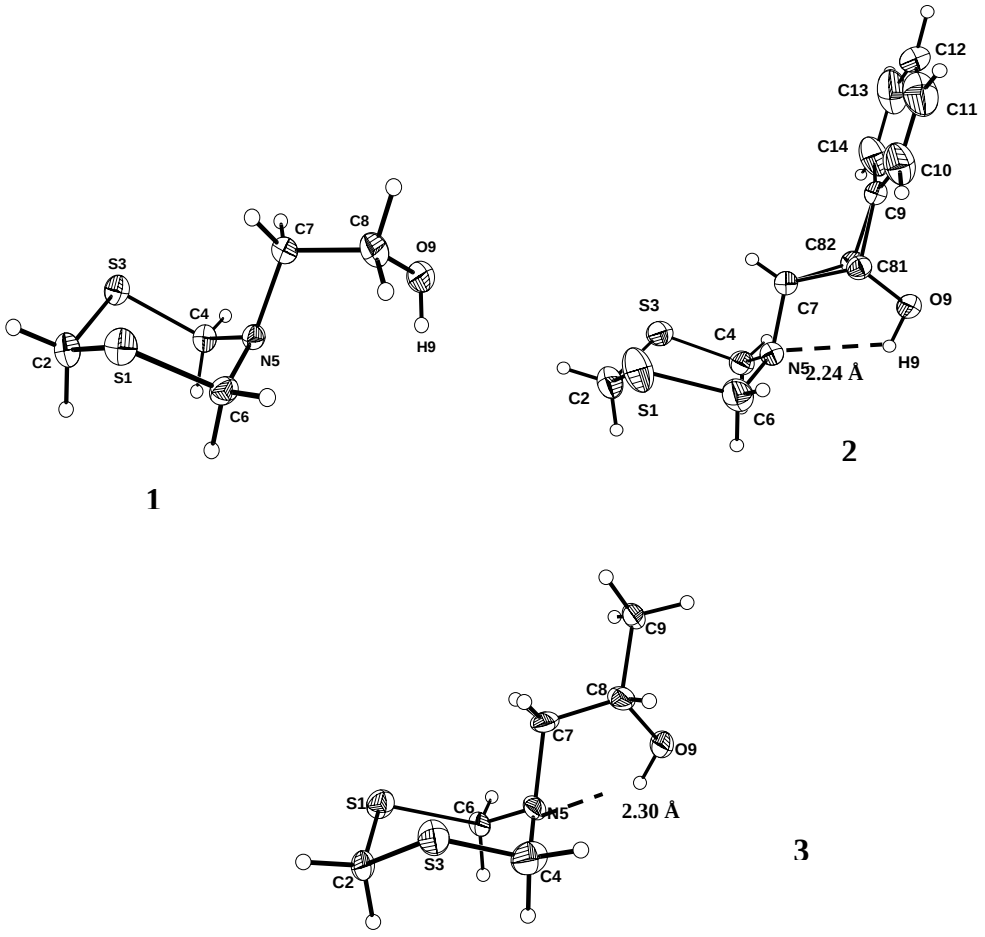
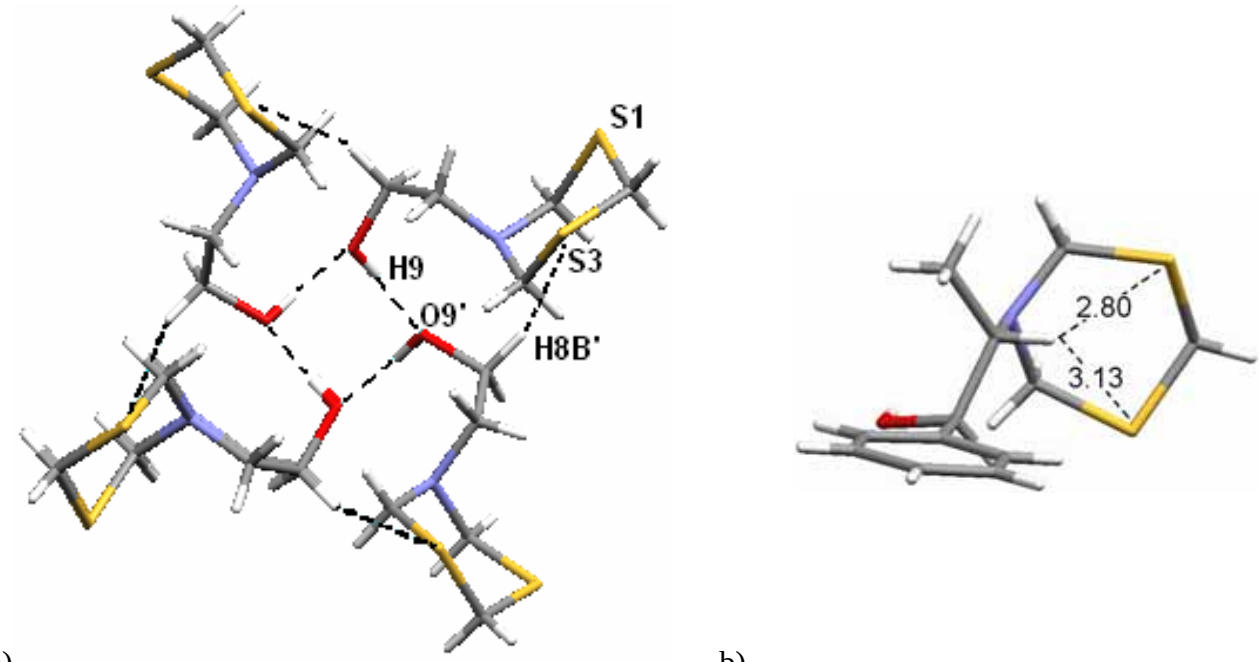


Figure 1 Molecular structures of compounds (**1**-**3**)

In all compounds the ring has a chair conformation with the N-R in axial position and the nitrogen atom presenting a 54% of sp^2 hybridation [Σ(C-N-C) angle values: **1** 342.4^{o}; **2** 342.9^{o}; **3** 342.3^{o}; **4** 340.5^{o}]. In **1**-**3**,

the O-H hydrogen is pointing to N-5 forming hydrogen bonds, distances N5···H9: **1** 2.93; **2** 2.24 and **3** 2.30 Å. The unit cell of **4** presents two molecules forming a dimer with two intermolecular hydrogen bonds [O-H···N 2.33 Å and C-H8···O 2.54 Å]. The macromolecular helix arrangement produced by intermolecular hydrogen bonds is shown in Figure 2a for compound (**1**) [H9···O9' (1.97 Å), S3···H8B"' (2.97 Å)]. In structures (**1**-**4**) short contacts between H7B and sulfur atoms (**1** 2.86; **2** 2.01 and 3.15; **3** 2.86; **4** 2.80 and 3.13 Å) were observed [(Σr_{VW}) H···S 3.25 Å], as it is represented in Figure 2b for **4**.



a) b)

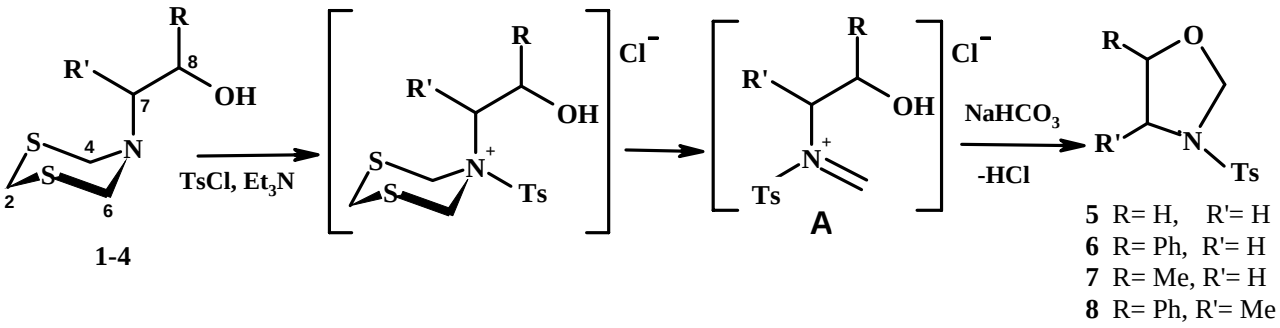
Figure 2 a) Macromolecular arrangement of **1**; b) short contacts between H7B and sulfur atoms in **4**

TOSYLATION REACTIONS

Tosylation products depend on the reaction conditions: for primary hydroxy groups it can be performed with tosyl chloride and Et_3N in CH_2Cl_2, while compounds (**1**-**4**) under these conditions did not afford the *O*-tosylated derivatives. In contrast, *N*-tosyl-1,3-oxazolidines (**5**-**8**) are obtained in good yields (90-95%) with a *N*-tosyl derivative and imines A as possible intermediates. (Scheme 2)

Structures of oxazolidines (**5**-**8**) were deduced from the NMR spectral data and by comparison with those of **1**-**4**. In the ^{13}C NMR spectra of **5**-**8**, the CH_2 signals of the dithiazinanyl cycle disappeared and those of

[OCH_2N] emerged at δ ≈ 81 ppm, the C-8 resonances were shifted to lower frequencies (Δδ ≈ 5.0). The ^{15}N signals for **5-8** appeared at -265 ppm, characteristic for *N*-tosyl groups.[4] Crystals of compounds (**5-8**) were studied by X-Ray diffraction. (Figures 3-5).



Scheme 2 Possible reaction path to 1,3-oxazolidines in tosylation reactions

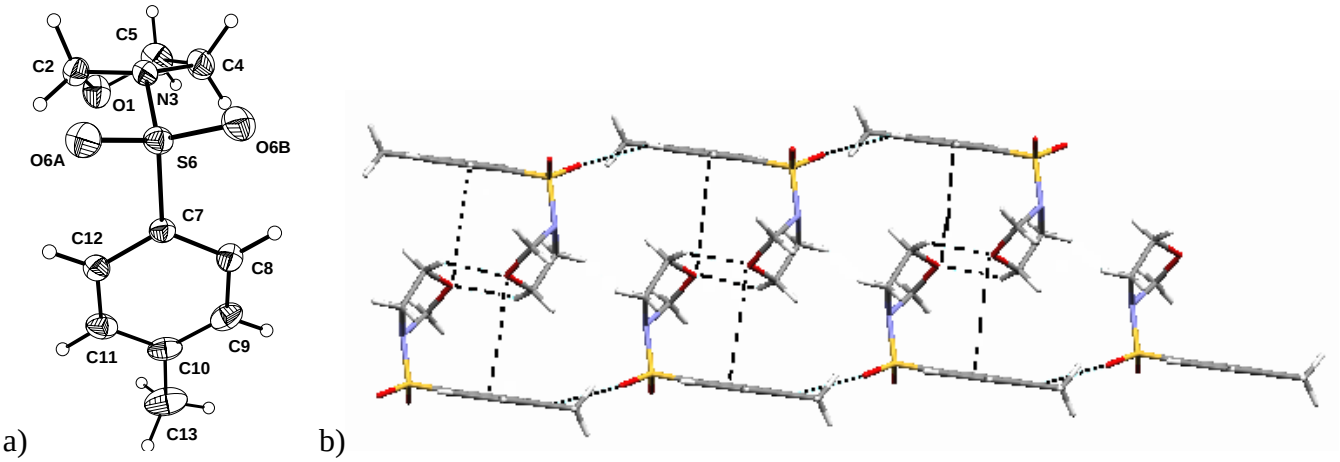
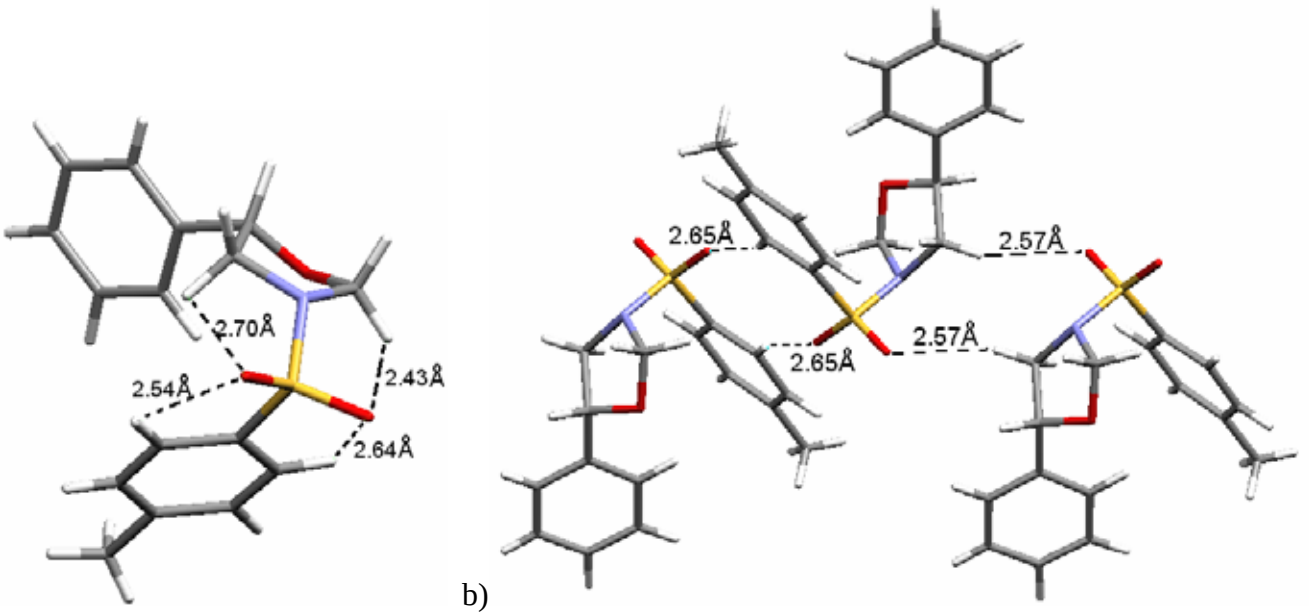


Figure 3 a) ORTEP representation of compound (**5**) and b) macromolecular arrangement of (**5**)

The oxazolidine ring in **5-8** has an envelop conformation with the oxygen atom out of the molecular plane [O3-C4-C5-N1, 25.39°]. Intramolecular hydrogen bonds between oxygen atoms of the tosyl group and the neighboring hydrogen atoms were found, as shown in Figure 4 for compound (**6**). Oxygen atoms of the tosyl groups show intermolecular interactions, giving different macromolecular arrangements in the unit cell, as well as the formation of polymers by intermolecular hydrogen bonds.



a) b)

Figure 4 Compound (**6**) a) intramolecular hydrogen bonds and b) intermolecular hydrogen bonds

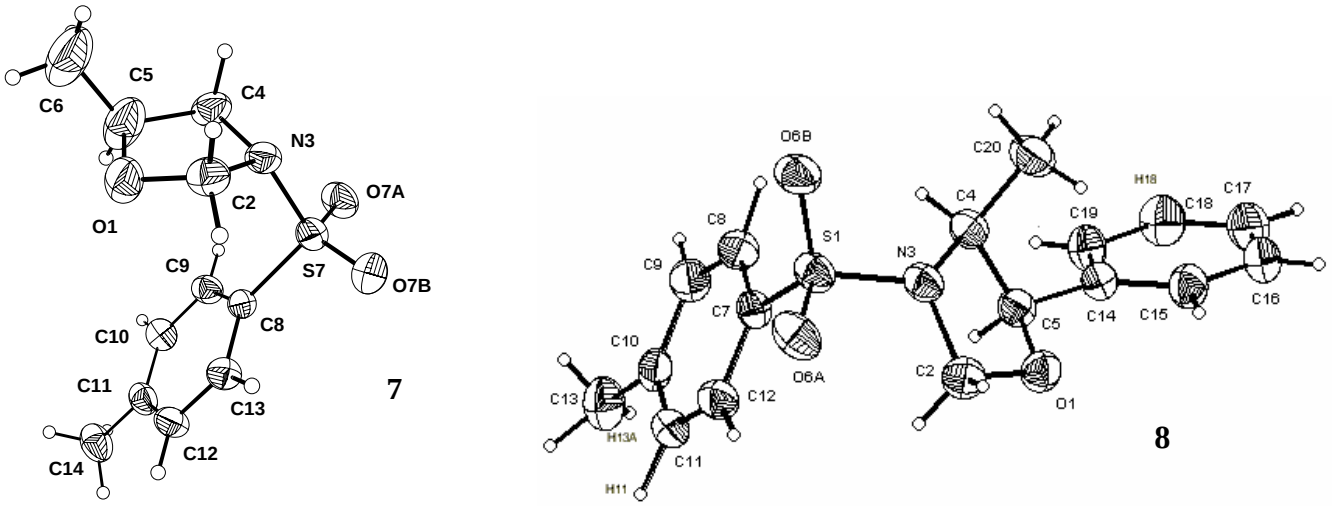
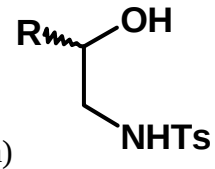


Figure 5 Molecular structures of compounds (**7** and **8**)

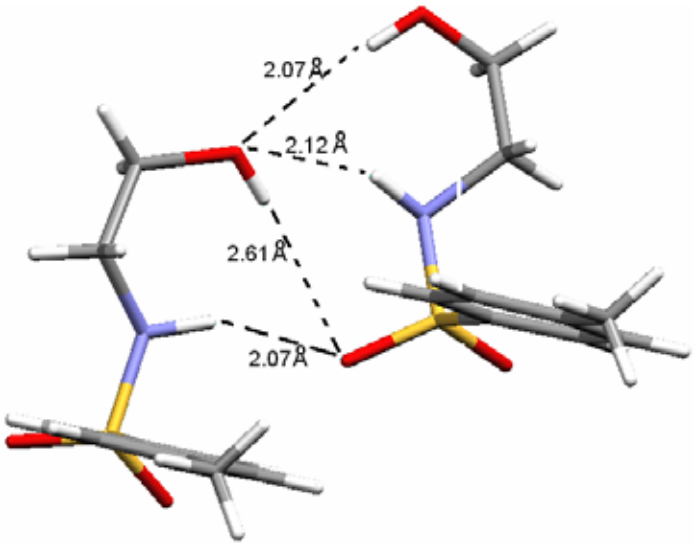
N-Tosylethanolamines (**9** and **10**) were prepared in order to probe if the *N*-tosyl-1,3-oxazolidines could be directly prepared from them. (Scheme 3) Ethanolamine and 2-propanolamine were treated with tosyl chloride in the presence of $NHMe_3Cl$. Two compounds were obtained from the ethanolamine, they were separated through a chromatographic column: *N*-tosylethanolamine (**9**, 50%) and the *N*-tosylaziridine (50%), both were identified by NMR and MS spectra and in the case of **9** also by X-Ray diffraction analysis.

a)



9 R= H
10 R= Me

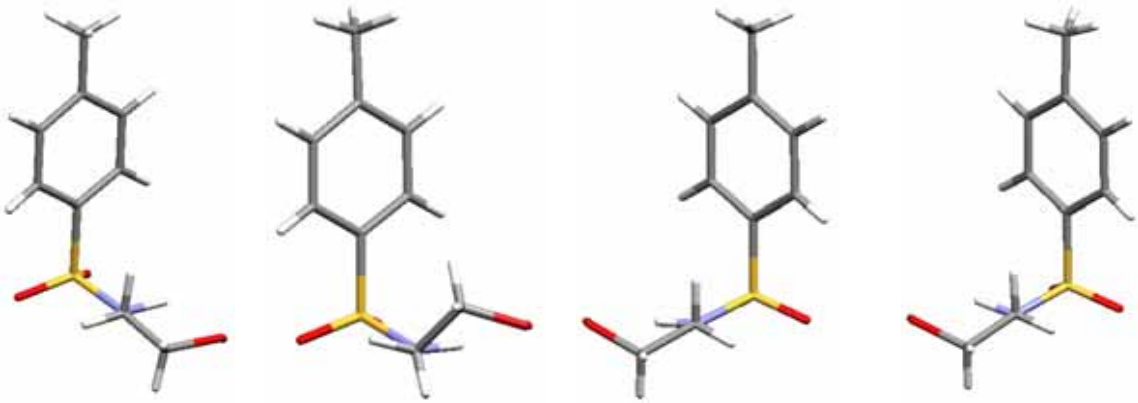
b)



Scheme 3 a) Compounds (**9**-**10**) and b) intermolecular hydrogen bonds in the cell of compound (**9**)

2-Propanolamine gave *N*-tosyl-2-propanolamine (**10**, 90%) and the corresponding *N*-tosyl-2-methyl-aziridine (10%). Syntheses of *N*-tosylated oxazolidines from **9** or **10** with formaldehyde failed.

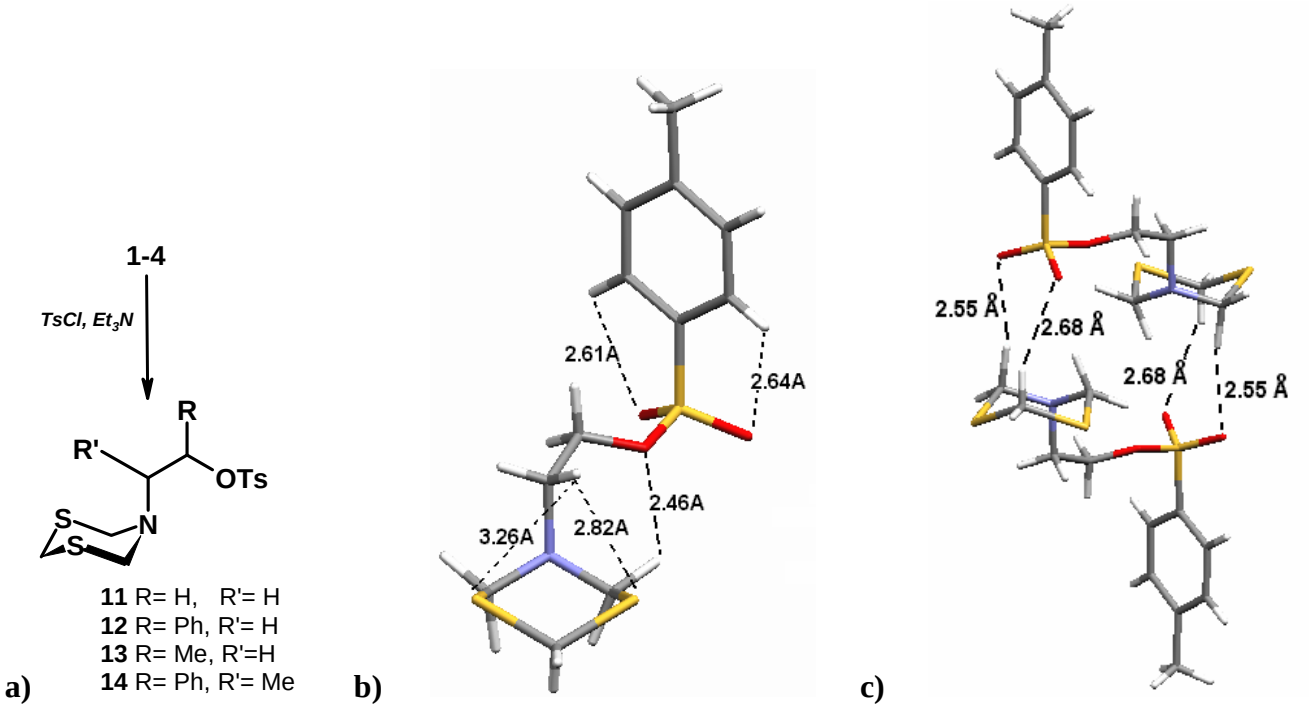
Crystals of compound (**9**) were analyzed, four different conformers were observed in the unit cell (A-D), Scheme 4. Conformer A is enantiomer of C and D, conformer B has the sharper dihedral angle S-N-C-C. All of them have *cis* OH and N-H groups without forming intramolecular hydrogen bonds, they present strong intermolecular hydrogen bonds as is represented in Scheme 3b.



angles	**A**	**B**	**C**	**D**
[S-N-C-C]	174.91	104.83	178.14	175.47
[O-C-C-N]	56.29	63.30	65.28	65.37
[H-N-S]	116.99	113.89	123.79	114.83
[C-N-S]	116.42	121.22	119.10	118.43
[H-N-C]	103.19	114.61	108.24	104.21

Scheme 4 View of the four conformers (A-D) of **9** in the unit cell, the N-C bond is eclipsed

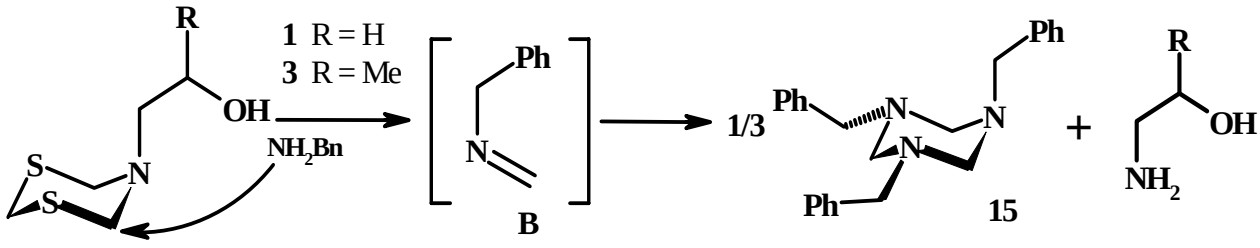
O-Tosylated compounds (**11-14**) were obtained by treatment of **1-4** with TsCl in presence of $NHMe_3Cl$ and Et_3N.[5] (Scheme 5). The ^{13}C NMR signal for C-8 in compounds (**11-14**) was shifted to higher frequencies ($\Delta\delta$ = 8.7, 8,2, 14.1 and 0.1 ppm, respectively). Crystalline structure of **11** was obtained; it is represented in Schemes 5b and 5c, showing the intra- and intermolecular hydrogen bonds.



Scheme 5 a) Synthesis of compounds (**11-14**), b) solid state structure of compound (**11**), hydrogen bonds are represented, c) a dimer is formed for **11** by collaborative intermolecular hydrogen bonds.

REACTION OF DITHIAZINANES (**1**) AND (**3**) WITH BENZYLAMINE.

Compounds (**1** and **3**) undergo in THF, at room temperature, a benzylamine nucleophilic attack at the endocyclic methylene groups to give the imine B intermediate which by trimerization affords the triazinane (**15**) in 95%. Heterocycle (**15**) was identified by comparison with the reported structure.[6] The direct preparation of triazinane from primary amines and formaldehyde is also known.[2c] (Scheme 6)

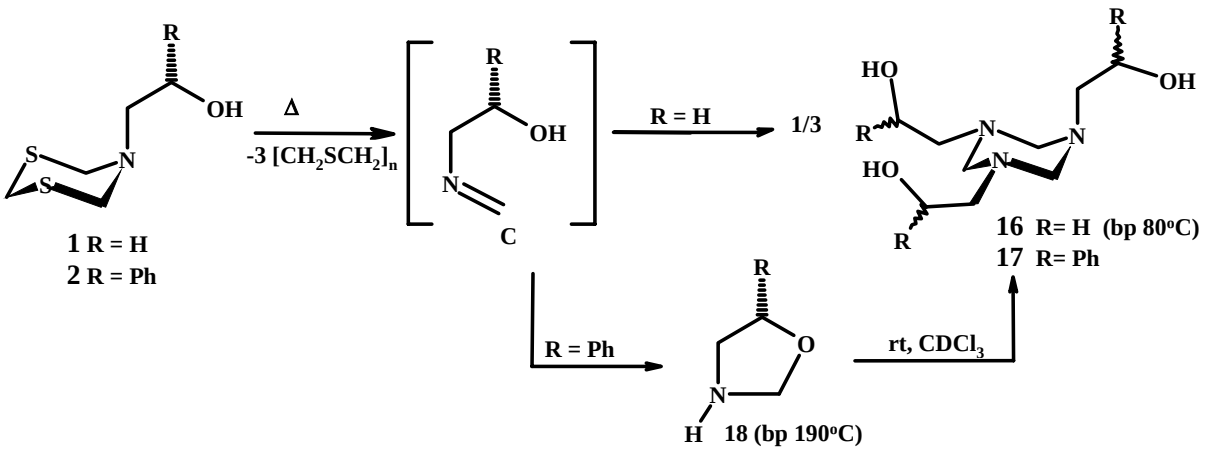


Scheme 6

THERMIC TREATMENT OF DITHIAZINANES (**1**) AND (**2**)

Compound (**1**) was heated without solvent at 100 ^{o}C (0.125 mmHg) and distilled at 80 ^{o}C (0.125 mmHg), to quantitatively afford the 1,3,5-triazinane (**16**) (Scheme 7). Compound (**16**) presents only one broad signal at 4.67 ppm (^{1}H) and 73.8 ppm (^{13}C) for the NCH_2N protons.[2c] Heating compound (**2**) at 200 ^{o}C [0.5 mmHg] yields the 5-phenyl-1,3-oxazolidine (**18**, 90%) which is a liquid, that can be distilled (bp 190 ^{o}C, 0.5 mmHg), ^{13}C NMR spectrum presents a signal at 82 ppm characteristic for the [NCH_2O] oxazolidine group.

At room temperature, after two days in $CHCl_3$ or without solvent, compound (**18**) was transformed into triazinane (**17**, 80%). Under the same heating conditions, compound (**3**) only sublimated. Reactions between corresponding ethanolamines and formaldehyde did not afford triazinanes (**16** and **17**), but other heterocycles.[7] Therefore heating of 2-(1,3,5-dithiazinan-5-yl)ethanols (**1** and **2**) is a good synthetic method for preparation of 1,3,5-tris(2-hydroxyethyl)-1,3,5-triazinanes (**16** and **17**). It seems clear that imine C is an intermediate for these reactions. Compound (**16**) is already known as metal atoms ligand.[8]



Scheme 7 Thermic rearrangement of compounds (**1** and **3**)

CONCLUSIONS

Our study confirms the versatility in the synthesis of dithiazinanols, which can be converted into different compounds depending on the reaction conditions and substitutents. Herein, we reported the synthesis of *N*-tosyloxazolidines (**5**-**8**) *via* opening of 2-(1,3,5-dithiazinan-5-yl)alkylethanols. The direct synthesis

through of tosylation of the N-H oxazolidine or cyclization of *N*-tosyl hydroxyamine does not work. *O*-Ts derivatives (**11**-**14**) can be obtained modifying the tosylation reaction conditions. We found that dithiazinanols (**1**-**3**) are also starting materials for substituted triazines. The X-Ray analyses of dithiazinanols (**1**-**4**), the *N*-tosyloxazolidines (**5**-**8**) and *N*-tosylhydroxyamine (**9**) and *O*-tosyldithiazinanol (**11**) allowed us to confirm the structures and to study their preferred conformations derived in part from the hydrogen bonding.

EXPERIMENTAL

All solvents were freshly distilled. ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded with a JEOL GXS- 270 (^{1}H 270 MHz) or a JEOL Eclipse (^{1}H 400 MHz). ^{1}H and ^{13}C δ are referenced to TMS, and ^{15}N to CH_3NO_2. ^{15}N spectra were obtained at 27.25 MHz (JEOL GXS-270) by the refocused INEPT pulse sequence with $^{2}J(^{15}N\text{-}^{1}H)$ =2.5 Hz. Variable temperature experiments were performed with a temperature controller to keep the temperature constant within 0.3^{o}C. Samples were dissolved in THF-d_8. Melting points were measured on a Gallenkamp apparatus and are uncorrected. Elemental analyses were performed by Oneida Research Services, Whitesboro, New York. The MS spectra were obtained to 20 eV in a HP 5989 spectrometer.

Crystal data were obtained with an Enraf-Nonius Kappa CCD or a Siemens-P4 diffractometer both equipped with area-detectors. Relevant data are reported in the complementary information. Computation for compounds (**1**-**4**, **5**-**8**) were performed by SHELXS-97 (Sheldrick 1990) and SHELXL-97 programs (Sheldrick 1997). Atomic form factors for neutral C, N, O and H were taken from ref. 9. Hydrogen atoms were found on difference electron density maps. Crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Bank CCDC 236636 (**1**), 236637 (**2**), 236638 (**3**), 236639 (**4**), 236640 (**5**), 236641 (**6**), 236642 (**7**), 237220 (**8**), 241303 (**9**) and 236643 (**11**). Copies of the data can be obtained free of charge on application to, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. Code + 44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

***2-(1,3,5-Dithiazinan-5-yl)ethanol (*1**). General procedure for compounds (**1-4**). To a cool (5^{o}C) solution of ethanolamine (10 mL, 0.166 mol) in water (50 mL), another aqueous solution (5 ^{o}C) of NaHS (27.9 g, 0.5 mol) and aqueous formaldehyde (37%, 62.3 mL, 0.83 mol) were slowly added. The reaction mixture was stirred for 30 min at 5 ^{o}C and 24 h at rt. Then, the white solids were washed with water and dissolved in $CHCl_3$ (30 mL). The chloroformic solution was dried with anhydrous Na_2SO_4 and concentrated under vacuum. Crystals were obtained from $CHCl_3$ (24.6 g, 90%). Mp 39 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 4.32 (s, 4H, 2H-4 and 2H-6), 3.99 (s, 2H, H-2), 3.54 (t, ^{3}J 5.2 Hz, 2H, H-8), 3.08 (t, ^{3}J 5.2 Hz, 2H, H-7), 2.67 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ 58.8 (C8), 58.4 (C4 and C6), 51.3 (C7), 33.8 (C2). ^{15}N NMR ($CHCl_3$): δ -352.9. Anal. Calcd for $C_5H_{11}NOS_2$: C, 36.34; H, 6.71; N, 8.47. Found: C, 36.24; H, 6.94; N, 8.44.

***2-(1,3,5-Dithiazinan-5-yl)-1-phenylethanol* (2)**. To 2-phenylethanolamine (10 g, 72.9 mmol) in water (75 mL) and THF (5 mL) were added NaHS (12.2 g, 219 mmol) and aqueous formaldehyde (37%, 27.4 mL, 365 mmol). Yellow crystals were obtained (12.3 g, 70%). Mp 56-59 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 7.4-7.2 (br s, 5H, Ph), 4.60 (dd, ^{3}J 13.5, 2.9 Hz, 1H, H-8), 4.31 (br s, 4H, 2H-4 and 2H-6), 4.00 (br s, 2H, H-2), 3.63 (s, 1H, OH), 3.49 (dd, ^{2}J 13.5, ^{3}J 2.9 Hz, 1H, H-7A), 2.81 (dd, ^{2}J 13.5, ^{3}J 9.9 Hz, 1H, H-7B). ^{13}C NMR ($CDCl_3$): δ 141.8 (C*i*), 128.2 (2C*m*), 127.2 (C*p*), 125.6 (2C*o*), 69.5 (C8), 58.8 (br s, C4 and C6), 57.1 (C7), 33.4 (C2). ^{15}N NMR ($CDCl_3$): δ -333.5. Anal. Calcd for $C_{11}H_{15}NOS_2$: C, 54.74; H, 6.26; N, 5.80. Found: C, 54.39; H, 6.23; N, 5.92.

***2-(1,3,5-Dithiazinan-5-yl)-1-methylethanol* (3)**. To *iso*propanolamine (40 mL, 0.51 mol) in water (75 mL) were added NaHS (85.8 g, 1.53 mol) and aqueous formaldehyde (37%, 191.7 mL, 2.55 mol). Crystals were obtained from $CHCl_3$ (69 g, 75%). Mp 70 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 4.32 (s, 4H, 2H-4 and 2H-6), 3.99 (s, 2H, H-2), 3.54 (qdd, ^{3}J 6.2, 9.9, 2.9 Hz, 1H, H-8), 3.08 (dd, ^{2}J 13.5, ^{3}J 2.9 Hz, 1H, H-7A), 2.67 (s, 1H, OH), 2.4 (dd, ^{2}J 13.5, ^{3}J 9.9 Hz, 1H, H-7B), 1.15 (d, ^{3}J 6.2 Hz, 3H, CH_3-9). ^{13}C NMR ($CDCl_3$): δ 63.6 (C8), 58.7 (br s, C4 and C6), 57.2 (C7), 33.7 (C2), 20.1 (C9). ^{15}N NMR ($CHCl_3$): δ -310.6. Anal. Calcd for $C_6H_{13}NOS_2$: C, 40.19; H, 7.31; N, 7.81. Found: C, 40.07; H, 7.79; N, 7.83.

***(-)-(1R,2S)-2-(1,3,5-Dithiazinan-5-yl)-2-methyl-1-phenylethanol* (4)**. To (-)-(1*R*,2*S*)-*nor*ephedrine (0.5 g,

3.30 mmol) in CH_3OH (20 mL), a solution of NaHS (0.55 g, 9.91 mmol) and aqueous formaldehyde (37%, 1.24 mL, 16.53 mmol) were added. A viscous yellow solid was crystallized from $CHCl_3/CH_3OH$ (70/30) (0.79 g, 94%). Mp 73-75 ^oC. ^1H NMR ($CDCl_3$): δ 7.4 (m, 5H, Ph), 5.2 (d, ^3J 3.0 Hz, 1H, H-8), 4.66 (d, ^2J 14.0 Hz, 2H, H-4eq and H-6eq), 4.53 (d, ^2J 14.0 Hz, 2H, H-4ax and H-6ax), 4.10 (s, 2H, H-2), 3.83 (dq, ^3J 6.0, 3.0 Hz, 1H, H-7), 0.93 (d, ^3J 6.0 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 141.1 (C*i*), 129.9 (C*p*), 128.1 (2C*m*), 125.7 (2C*o*), 70.9 (C8), 57.3 (C7), 56.2 (C4 and C6), 33.8 (C2), 10.0 (CH_3). ^{15}N NMR ($CDCl_3$): δ -343.9. Anal. Calcd for $C_{12}H_{17}OS_2N$: C, 56.46; N, 5.48; H, 6.66. Found: C, 56.58; N, 5.27; H, 6.64. $[\alpha]_D$ = -35.8^o (C 0.1, CH_3OH).

3-Tosyl-1,3-oxazolidine **(5)**. General procedure for the preparation of 3-tosylated oxazolidines. To an aqueous solution of 1,3,5-dithiazinane (**1**) (7.7 g, 46.6 mmol) $NaHCO_3$ (4.2 g, 50 mmol) and TsCl (8.89 g, 46.6 mmol) in dry $CHCl_3$ (30 mL) were added. The reaction mixture was stirred for 12 h at rt and filtered. Then, 10 mL of H_2O was added and the product extracted with $CHCl_3$ (2x30 mL). The organic solutions were dried with $NaSO_4$ and concentrated under vacuum. The white solid was crystallized from $CHCl_3$ (10.0 g, 95%). Mp. 100-101 ^oC. ^1H NMR ($CDCl_3$): δ 7.67 (d, ^3J 8.4 Hz, 2H, H*o*-Ts), 7.27 (d, ^3J 8.4 Hz, 2H, H*m*-Ts), 4.77 (s, 2H, H-2), 3.58 (t, ^3J 6.7 Hz, 2H, H-5), 3.36 (t, ^3J 6.7 Hz, 2H, H-4), 2.36 (s, 3H, CH_3-Ts). ^{13}C NMR ($CDCl_3$): δ 145.4 (C*i*-Ts), 134 (C*p*-Ts), 129.9 (C*o*-Ts), 127.7 (C*m*-Ts), 80.67 (C2), 66.1 (C5), 46.1 (C4), 21.6 (CH_3-Ts). ^{15}N NMR ($CDCl_3$): δ -267.2. Anal. Calcd for $C_{10}H_{13}NO_3S$: C, 52.86; H, 5.72; N, 6.16. Found: C, 52.45; H, 5.68; N, 6.06.

5-Phenyl-3-tosyl-1,3-oxazolidine **(6)** was prepared following the general procedure from dithiazinane (**2**) (1.24 g, 5.1 mmol), $NaHCO_3$ (1.7 g, 20.4 mmol) and TsCl (7.0 g, 5.1 mmol). Compound (**6**) is a pale yellow liquid (1.4 g, 90%). ^1H NMR ($CDCl_3$): δ 7.68 (d, ^3J 7.0 Hz, 2H, H*o*-Ts), 7.53 (m, 5H, Ph) 7.28 (d, ^3J 7.0 Hz, 2H, H*m*-Ts), 4.91 (d, ^2J 5.8 Hz, 1H, H-2A), 4.68 (d, ^2J 5.8 Hz, 1H, H-2B), 3.80 (dd, ^3J 6.4, 9.5 Hz, 1H, H-5), 3.51 (dd, ^2J 10.0, ^3J 6.4 Hz, 1H, H-4A), 2.80 (dd, ^2J 10.0, ^3J 9.5 Hz, 1H, H-4B), 2.42 (s, 3H, CH_3-Ts). ^{13}C NMR ($CDCl_3$): δ 144.0 (C*i*-Ts), 141.6 (C*i*), 133.7 (C*p*-Ts), 129.7 (2C*m*-Ts), 128.1 (2C*m*), 128.0 (2C*o*-Ts), 127.6 (2C*o*-Ts), 127.0 (C*p*), 127.0(C*p*), 125.5 (2C*o*), 80.1 (C2), 74.1 (C5), 52.2 (C4), 21.4

(C16). ^{15}N NMR ($CDCl_3$): δ -265.4. Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.35; H, 5.65; N, 4.62. Found: C, 63.32; H, 6.13; N, 4.56.

5-Methyl-3-tosyl-1,3-oxazolidine **(7)** was prepared from dithiazinane (**3**) (1.74 g, 9.7 mmol), compound (**7**) was crystallized from $CHCl_3$ (2.1 g, 90%). Mp 82-84 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 7.69 (d, ^{3}J 8.0 Hz, 2H, H*o*-Ts), 7.21 (d, ^{3}J 8.0 Hz, 2H, H*m*-Ts), 5.92 (q br, ^{3}J 6.2 Hz, 1H, H-5), 3.81 (br s, 1H, H-2A), 3.50 (br s, 1H, H-2B), 2.89 (dd, ^{2}J 13.2, ^{3}J 3.3 Hz, 1H, H-4A), 2.71 (t, ^{2}J 13.2, ^{3}J Hz, 1H, H-4B), 2.32 (s, 3H, CH_3-Ts), 1.04 (d, ^{3}J 6.2 Hz, 3H, CH_3-6). ^{13}C NMR ($CDCl_3$): δ 144.0 (C*i*-Ts), 143.4 (C*i*), 133.5 (C*p*-Ts), 129.7 (2C*m*-Ts), 128.0 (2C*o*-Ts), 127.4 (C*p*), 126.9 (2C*o*), 66.5 (C2), 50.0 (C3), 21.4 (CH_3-Ts), 20.4 (CH_3). ^{15}N NMR ($CDCl_3$): δ -265.4. Anal. Calcd for $C_{11}H_{17}NOS_2$: C, 54.30; H, 7.04; N, 5.76. Found: C, 54.39; H, 7.13; N, 5.64.

(4S,5R)-4-Methyl-5-phenyl-3-tosyl-1,3-oxazolidine **(8)** was prepared from compound (**4**) (0.36 g, 1.42 mmol). The white solid was recrystallized from $CHCl_3$/CH_3OH (70/30) (0.41 g, 90%). Mp 102-104 $^{\circ}$C. IR (KBr): υ (cm^{-1}) 2988, 1594. ^{1}H NMR ($CDCl_3$): δ 7.82(d, ^{3}J 7.2, 2H, 2H*o*). 7.36 (d, ^{3}J 7.0, 2H, 2H*o*-Ts), 7.35 (m, 3H, 2H*m* and H*p*), 7.13 (d, ^{3}J 7.0, 2H, 2H*m*-Ts), 4.37 (d, ^{3}J 5.0, 1H, H-5), 4.06 (dq, ^{3}J 5.0 and 7.0, 1H, H-4), 3.44 (s, 2H, 2H-2), 2.44 (s, 3H, Ts-CH_3), 0.83 (d, ^{3}J 7.0, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 144.2 (C*i*-Ts), 135.8 (C*p*-Ts), 134.6 (C*i*), 130.0 (C*o*-Ts), 128.3 (C*o*), 127.8 (C*p*), 127.6 (C*m*), 125.9 (C*m*-Ts), 81.7 (C2), 79.4 (C5), 57.5 (C4), 21.5 (CH_3-Ts), 16.3 (CH_3). MS: *m/z* (%) 317.2 [M^{+}]. Anal. Calcd for $C_{17}H_{19}NO_3S$: C, 64.36; H, 5.98; N, 4.41. Found: C, 64.08; H, 5.99; N, 4.41.

N-Tosylethanolamine **(9).** General procedure for tosylation. Ethanolamine (1.0 g, 16.3 mmol), $NHMe_3Cl$ (0.15 g, 1.6 mmol) and NEt_3 (4.54 mL, 32.7 mmol) were dissolved in a mixture of toluene/CH_2Cl_2 (1:1, 10 mL), at 0 ^{o}C. TsCl (4.68 g, 24.5 mmol) was dissolved in 10 mL of a mixture of the same solvents, added to the reaction mixture and stirred for 1 h at 0 ^{o}C. Then, the solids were filtered and water (5 mL) was added to the filtrate and it was extracted with $CHCl_3$. The solution was dried with Na_2SO_4 and the solvent evaporated under vacuum. A colorless liquid (3.5 g) was obtained as a mixture of compound (**9**, 50%) and *N*-tosylaziridine (50%). Compound (**9**) crystallized from $CHCl_3$. The reaction mixture was directly

analyzed by NMR and by MS spectra previous separation a the chromatographic column. Compound (**9**): ^{1}H NMR ($CDCl_3$): δ 7.70 (d, ^{3}J 8.0, 2H, H*o*-Ts), 7.33 (d, ^{3}J 8.0, 2H, H*m*-Ts), 5.39 (br s, 1H, OH), 4.04 (t, ^{3}J 5.0 Hz, 2H, H-1), 3.66 (t, ^{3}J 5.0 Hz, 2H, H-2), 2.45 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 145.5 (C*i*-Ts), 132.3 (C*p*-Ts), 130.2 (C*m*-Ts), 128.1 (C*o*), 68.9 (C1), 61.3 (C2), 21.8 (CH_3-Ts). MS: *m/z* (%) 215(2) [M^+], 184(77), 155(100), 91(83).

N-Tosylaziridine: ^{1}H NMR ($CDCl_3$): δ 7.75 (d, ^{3}J 8.0, 2H, H*o*-Ts), 7.28 (d, ^{3}J 8.0, 2H, H*m*-Ts), 3.20(t, ^{3}J 4.9 Hz, 4H, 2H-1 and 2H-2), 2.41 (s, 3H, CH_3-Ts). ^{13}C NMR ($CDCl_3$): δ 143.9 (C*i*-Ts), 136.8 (C*p*-Ts), 130.0 (C*m*-Ts), 127.2 (C*o*), 45.4 (C1 and C2), 21.7 (CH_3). MS: *m/z* (%) 197(11) [M^+], 91(60), 42(100).

N-Tosyl-2-propanolamine **(10)** was prepared as compound (**9**) from 1-aminopropan-2-ol (1.0 g, 13 mmol), $NHMe_3Cl$ (0.12 g, 1.3 mmol) NEt_3 (3.61 mL, 26 mmol) and TsCl (3.81 g, 20 mmol). Compound (**10**) is a viscous liquid (2.8 g, 90%). ^{1}H NMR ($CDCl_3$): δ 7.74 (d, ^{3}J 8.2, 2H, H*o*-Ts), 7.25 (d, ^{3}J 8.2, 2H, H*m*-Ts), 6.00 (dd, ^{3}J 8.02, 3.1, 1H, NH), 3.53 (br s, 1H, OH), 3.16 (qdd, ^{3}J 6.3, 7.0, 5.4, 1H, H-1), 2.96 (ddd, ^{2}J 12.8, ^{3}J 7.0, 3.1, 1H, H-2A), 2.74 (ddd, ^{2}J 12.8, ^{3}J 8.0, 5.4, 1H, H-2B), 2.38 (s, 3H, CH_3), 1.08 (d, ^{3}J 6.3, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 143.3 (C*i*-Ts), 136.8 (C*p*-Ts), 129.7 (C*m*-Ts), 127.0 (C*o*-Ts), 66.4 (C2), 50.1 (C3), 21.5 (CH_3), 20.4 (CH_3-Ts). MS: *m/z* (%) 230(3) [M^++1], 200(38), 184(33), 155(100), 91(90).

O-Tosyl-2-(1,3,5-dithiazinan-5-yl)ethanol **(11)** was prepared as compound (**9**) from **1** (1.0 g, 6.0 mmol), $NHMe_3Cl$ (58 mg, 6.0 mmol), TsCl (1.72 g, 9.0 mmol). Compound (**11**) is a yellow solid (1.8 g, 98%). IR (KBr): ν (cm^{-1}) 3051 [C-H], 1261.78 [N-C]. ^{1}H NMR ($CDCl_3$): δ 7.47 (d, ^{3}J 8.1 Hz, 2H, H*o*-Ts), 7.25 (d, ^{3}J8.1 Hz, 2H, H*m*-Ts), 4.27 (br s, 4H, 2H-4 and 2H-6), 4.04 (t, ^{3}J 5.4 Hz, 2H, H-8), 4.02 (s, 2H, H-2), 3.24 (t, ^{3}J 5.4 Hz, 2H, H-8), 2.46 (s, 3H, CH_3-Ts). ^{13}C NMR ($CDCl_3$): δ 145.0 (C*i*-Ts), 142.9 (C*p*-Ts), 129.9 (2C*o*-Ts), 127.9 (2C*m*-Ts), 33.7 (C2), 58.5 (C4 and C6), 48.0 (C7), 67.6 (C8), 21.7 (CH_3-Ts). Anal. Calcd for $C_5H_{11}NOS_2$: C, 46.20; H, 5.44; N, 4.28. Found: C, 46.37; H, 5.46; N, 4.38.

O-Tosyl-2-(1,3,5-dithiazinan-5-yl)-1-phenylethanol **(12)** was prepared as compound (**9**) from **2** (1.0 g, 5.0 mmol), $NHMe_3Cl$ (47 mg, 0.5 mmol) NEt_3 (1.39 mL, 10 mmol) and TsCl (1.42 g, 7.5 mmol).

Compound (**12**) is as a brown liquid (1.5 g, 84%). ^{1}H NMR ($CDCl_3$): δ 7.57 (d, ^{3}J 8.0, 2H, H*o*-Ts), 7.20 (m, 5H, Ph), 7.12 (d, ^{3}J 8.0, 2H, H*m*-Ts), 4.02 (s, 2H-2), 4.56 (dd, ^{3}J 7.8, 3.9, 1H, H-8), 4.07 (br s, 4H, 2H-4 and 2H-6), 3.43(dd, ^{2}J 14.7 Hz, ^{3}J 3.9 Hz, 1H, H-7A), 2.83 (dd, ^{2}J 14.7 Hz, ^{3}J 7.8 Hz, 1H, H-7B), 2.39 (s, 3H-16). ^{13}C NMR ($CDCl_3$): δ 144.5 (C*i*-Ts), 141.6 (C*i*), 134.3(C*p*-Ts), 129.6(2C*o*-Ts), 128.0 (2C*m*), 127.7 (2C*m*-Ts), 127.1 (C*p*), 125.7 (C*o*), 77.7 (C8), 59.0 (C4 and C6), 54.3 (C7), 33.5 (C2), 21.6 (CH_3-Ts). Anal. Calcd for $C_{18}H_{21}NO_3S_3$: C, 54.96; H, 5.83; N, 4.50. Found: C, 54.87; H, 6.04; N, 4.64.

O-Tosyl-2-(1,3,5-dithiazinan-5-yl)-1-methylethanol **(13)** was prepared as compound (**9**) from **3** (1.0 g, 5.0 mmol), $HNMe_3Cl$ (47 mg, 0.5 mmol) NEt_3 (1.39 mL, 0.01 mol) and TsCl (1.42 g, 7.5 mmol). Compound (**13**) is a brown liquid (1.5 g, 84%). ^{1}H NMR ($CDCl_3$): δ 7.57 (d, ^{3}J 8.0, 2H, H*o*-Ts), 7.02 (d, ^{3}J 8.0, 2H, H*m*-Ts), 4.02 (s, 2H, H-2), 4.07 (br s, 4H, 2H-4 and 2H-6), 3.13 (dd, ^{2}J 14.7, ^{3}J 3.9, 1H, H-7A), 2.83 (dd, ^{2}J 14.7, ^{3}J 7.8, 1H, H-7B), 4.56 (qdd, ^{3}J 6.4, 7.8, 3.9, 1H, H-8), 2.39 (s, 3H, CH_3-Ts), 1.25 (d, ^{3}J 6.4 Hz, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 144.5 (C*i*-Ts), 134.6 (C*p*-Ts), 130.0 (2C*m*-Ts), 129.6 (2C*o*-Ts), 77.7 (C8), 59.0 (C4 and C6), 54.3 (C7), 33.5 (C2), 21.6 (CH_3-Ts), 19.0 (CH_3). Anal. Calc. for $C_{13}H_{19}NO_3S_3$: C, 48.22; H, 6.27; N, 4.75. Found: C, 48.34; H, 6.60; N, 4.58.

O-Tosyl-2-(1,3,5-dithiazinan-5-yl)-2-methyl-1-phenylethanol **(14)** was prepared as compound (**9**) from (**4**) (1.0 g, 3.9 mmol), $NHMe_3Cl$ (37 mg, 0.4 mmol) NEt_3 (1.08 mL, 7.8 mmol) and TsCl (1.11 g, 5.87 mmol). Compound (**14**) is a colorless liquid (1.5 g, 98%). ^{1}H NMR ($CDCl_3$): δ 7.57 (d, ^{3}J 8.0, 2H, H*o*-Ts), 7.21 (m, 5H, Ph), 7.02 (d, ^{3}J 8.0, 2H, H*m*-Ts), 4.98 (d, ^{3}J 1.0, 1H, H-8), 4.52 (d, ^{2}J 13.9, 2H, H-4ax, H-6ax), 4.37 (d, ^{2}J 13.9, 2H, H-4eq and H-6eq), 4.02 (br s, 2H, H-2), 3.67 (m, 1H, H-7), 2.21 (s, 3H, CH_3-Ts), 0.79 (d, ^{3}J 6.8, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 143.1 (C*i*-Ts), 142.2 (*Ci*), 140.2 (C*p*-Ts), 129.1 (2C*m*-Ts), 128.3 (2C*m*), 127.1 (C*p*), 126.2 (2C*o*), 126.1 (2C*o*-Ts), 77.1 (C8), 57.6 (C7), 56.6 (C4 and C6), 34.0 (C2), 21.6 (CH_3-Ts), 10.4 (CH_3). Anal. Calcd for $C_{19}H_{23}NO_3S_3$: C, 55.72; H, 5.66; N, 3.42. Found: C, 55.74; H, 5.60; N, 3.58.

1,3,5-Tribenzyl-1,3,5-triazinane **(15)**. To compound (**1**) (0.34 g, 3 mmol), benzylamine (2.0 mL, 30 mmol) was added and the mixture was stirred 24 h at rt, then the reaction mixture was dissolved in $CHCl_3$

(30 mL) and washed with water (3 x 20 mL) and the chloroformic solution dried with Na_2SO_4 and evaporated. The 1,3,5-triazinane was obtained as a yellow liquid, it crystallized after one day at rt (1.0 g, 95%). mp 41-43 ^oC. ^1H NMR ($CDCl_3$): δ 7.33 (br s, 15H, Ph), 3.56 (br s, 6H, 2H-2, 2H-4 and 2H-6), 3.80(s, 2H, CH_2-Ph). ^{13}C NMR ($CDCl_3$): δ 138.6 (3C*i*), 129.0 (6C*o*), 128.4 (6C*m*), 127.1 (3C*p*), 74.1 (C2, C4 and C6), 57.2 (3CH_2-Ph).

1,3,5-Tri(2-hydroxyethyl)-1,3,5-triazinane **(16)**. Compound (**1**) (10 g, 60.7 mmol) was distilled at 100 ^oC, 0.12 mmHg and transformed into triazinane (**16**), viscous liquid (3.8 g, 85%). ^1H NMR ($CDCl_3$): δ 4.67 (br s, 6H, CH_2-O), 3.51 (t, ^3J 5.2 Hz, 6H, CH_2-N), 2.47 (t, ^3J 5.2 Hz, 6H, 2H-2, 2H-4 and 2H-6), 3.31 (br s, 3H, OH). ^{13}C NMR ($CDCl_3$): δ 73.8 (3CH_2-O), 59.20 (C2, C4 and C6), 55.01 (3CH_2-N). Anal. Calcd for $C_9H_{21}N_3O_3 \cdot 1/2[H_2O]$: C, 47.35; H, 9.71, N, 18.41. Found: C, 47.33; H, 9.74; N, 18.45.

5-Phenyl-1,3-oxazolidine **(18)** was obtained from **3** by distillation at 190 ^oC and 0.5 mmHg. Oxazolidine (**18**) is a colorless liquid (2.8 g, 90%). ^1H NMR ($CDCl_3$): δ 7.3-7.23 (br s, 5H, Ph), 4.80 (br s, 1H, H-2A), 4.71 (br s, 1H, H-5), 4.50 (br s, 1H, H-2B), 3.46 (br s, 1H, H-4A), 2.85 (br s, 1H, H-4B). ^{13}C NMR ($CDCl_3$): δ 142.6 (C*i*), 128.6 (C*m*), 127.4 (C*p*), 125.4 (C*o*), 83.2 (C2), 76.9 (C5), 55.9 (C4). Anal. Calcd for $C_{27}H_{33}N_3O_3$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.31; H, 7.49; N, 9.50.

1,3,5-Tri(2-phenyl-2-hydroxyethyl)-1,3,5-triazinane **(17)**. Compound (**18**) in $CHCl_3$ (or without solvent) was transformed after 45 h at rt into a colorless liquid which is a mixture in a 80/20 ratio of compounds **17**/**18**. ^1H NMR ($CDCl_3$): δ 7.4-7.2 (br s, 15H, Ph), 4.78 (d, ^3J 8.4 Hz, 3H, H-8), 3.53 (br s, 6H, 2H-2, 2H-4 and 2H-6), 2.70 (d, ^2J 10.6 Hz, 3H, H-7A), 2.55 (dd, ^2J 10.6, ^3J 8.4 Hz, 3H, H-7B), 2.4 (s, 3H, OH). ^{13}C NMR ($CDCl_3$): δ 142.5 (3C*i*), 128.5 (6C*m*), 127.6 (3C*p*), 126.1 (6C*o*), 74.0 (C2, C4 and C6), 70.8 (3C8), 61.3 (3C7). Anal. Calcd for $C_{27}H_{33}N_3O_3 \cdot H_2O$: C, 71.50; H, 7.48; N, 9.26. Found: C, 71.27; H, 7.41; N, 8.89.

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