SYNTHESIS OF NEW N[1]TOSYL-1, 2, 4-TRIAZOLES FROM CONDENSATION OF ALDEHYDES WITH N[1]TOSYLAMIDRAZONES

Fatma Allouche,[a] Fakher Chabchoub,[b] Leila Chkir Ghdira,[c] Bechir Ben Hassine,[a] Mansour Salem,[b*]

[a]Laboratoire de Synthèse Organique Asymétrique et Catalyse Homogène, Faculté des Sciences de Monastir, 5019-Tunisie.

[b]Laboratoire de Chimie Appliquée : Hétérocycles, Corps Gras et Polymères, Faculté des Sciences de Sfax, 3018-Tunisie.

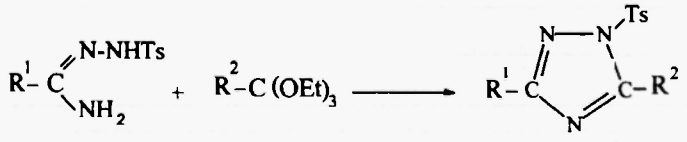
[c]Laboratoire de pharmagnosie-biologie, Institue Superieur de biotechnologie de Monastir, 5019 -Tunisie.

Abstract : The reaction of aldehydes with N[1]tosylamidrazones **1** in presence of a catalytic amount of para toluene sulfonic acid leads to the corresponding N[1]tosyl-1,2,4-triazoles **2a-h** in good yields. The structure of **2a** was ascertained by a crystal X-ray analysis.

Keywords : N[1]tosyl-1,2,4-triazole, aldehyde, N[1]tosylamidrazone, X-ray analysis.

Introduction

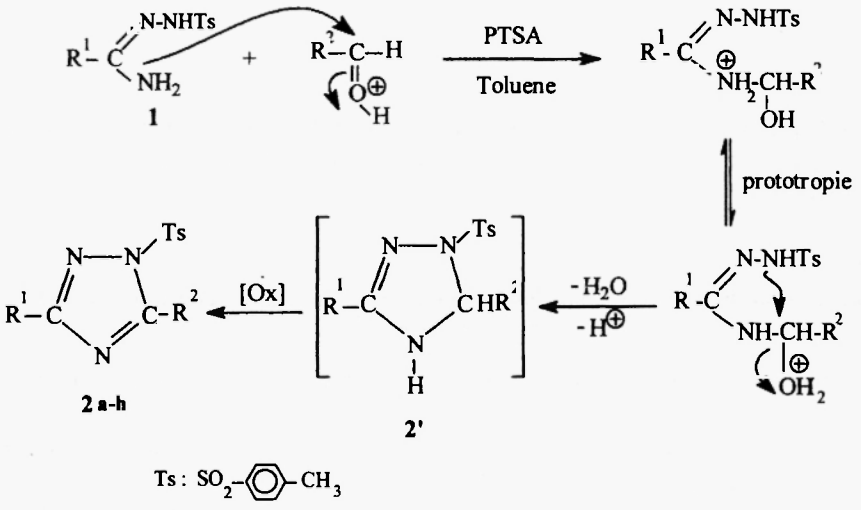
The 1,2,4-triazoles are crucial heterocyclic substances which have been used intensively in medicinal chemistry (1-4) and prepared by several ways (5-10). The N[1]tosyl-1,2,4-triazoles have been recently obtained from the action of orthoesters with amidrazones (11) . This study remained limited because of the very small number of orthoesters avaible (scheme 1) , which leads us to describe a simple synthesis of new N[1]tosyl-1,2,4-triazoles by the reaction of aldehydes with a variety of N[1] tosyl amidrazones **1**.



Scheme 1.

Results and discussion

In the search of routes to new N[1]tosyl-1,2,4-triazoles, we report here a simple preparation of compound **2** . We found that good yields were obtained when compound **1** and an aldehyde were heated under reflux of toluene with azeotropic removal of water. The use of a catalytic amount of p-toluenesulfonic acid gives satisfactory results. The reaction was completed within 3 hours (scheme 2).



Scheme 2 . synthesis of compounds **2a-h**

The structure of these compounds has been established by spectroscopic and analytical methods. In fact, in the IR spectrum, the absorption of –NH band is absent. This result was ascertained by the X ray analysis of the adduct **2a**, which was identified as 3-phenyl N¹tosyl-1,2,4-triazole (figure 1) .

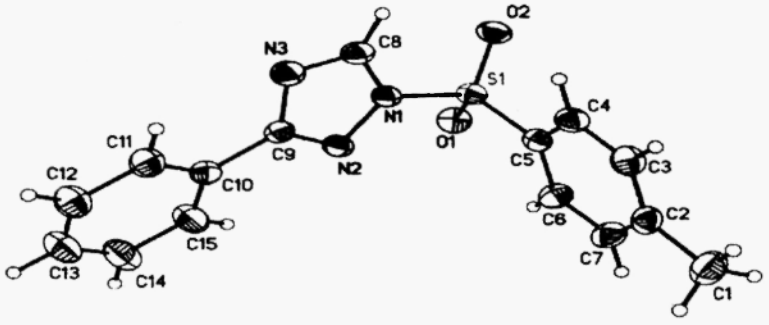


Figure 1. X-Ray structure of **2a**

Table I . Synthesis of new N¹tosyl-1,2,4-triazoles **2a-h**

Entry	Product	R¹	R²	Yields (%)	Mp (°C)
1	**2a**	Ph	H	81	174-176
2	**2b**	4 -CH_3 -C_6H_4	H	83	159-161
3	**2c**	4 -CH_3 -C_6H_4	Ph	75	157-159
4	**2d**	Isopropyl	4 -Cl C_6H_4	74	184-186
5	**2e**	4 -CH_3 -C_6H_4	4 -CH_3 -C_6H_4	77	249-251
6	**2f**	4 -CH_3 -C_6H_4	4 -Cl C_6H_4	79	227-229
7	**2g**	Ph	4 -Cl C_6H_4	76	172-174
8	**2h**	4 -CH_3 -C_6H_4	3,4 -$C_6H_3Cl_2$	78	179-181

Conclusion

To conclude, the condensation of N^1 tosylamidrazone with various aldehydes afforded a new class of N^1 tosyl-1,2,4-triazoles in good yield (table I). This method is general and these new compounds may display a biological proprities, in particularity compound **2a** have an antimutagenic activitie .

Experimental section

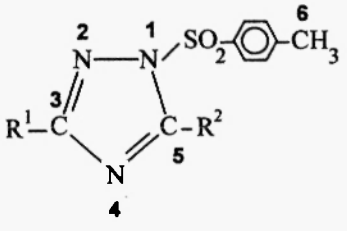
Melting points were taken on a Buchi-510 capillary melting point apparatus. Infrared spectra (potassium bromide) were run on a JASCO FT-IR-420 infrared spectrometer. The mass spectra were measured using an AEI MS-50 mass spectrometer operating in electron impact mode at 70 eV. The ^1H and ^{13}C NMR spectra were recorded on a BRUKER spectrometer AC-300 in DMSO-d with internal Me_4Si. Column chromatographie used silica gel 60 (220-440mesh ASTM).

The N^1tosyl amidrazone **1** were prepared according to litterature by the reaction of tosyl hydrazine with imidates (11).

Typical procedure for the synthesis of compounds **2a-h**.

N^1tosyl amidrazone **1** (5mmol) was suspended in 100ml of toluene and aldehyde (5mmol) [with paraformaldheyde (15mmol) : **2a-b**] and PTSA (100mg) were added. The mixture was heated for 3h with azeotropic removal water . The solvent was removed in a rotory evaporator. The solution was cooled , washed with IN aqueous $NaHCO_3$ and extracted with $CHCl_3$ (3X40ml). The extracts were dried ($MgSO_4$), the solvent was removed in a rotory evaporator and the crud product was purified on a silica column and eluted with chloroform.

Characteristics of compounds **2a-h** :



R^1 = Ph , 4-$CH_3C_6H_4$, $(CH_3)_2$-CH (7, 8, 9)

R^2 = Ph , H , 4-ClC_6H_4 , $CH_3C_6H_4$ (10)

Compound **2a** : ^1H NMR : δ(ppm) : 2.44 (s,3H), 7.36-8.12 (m, 9H), 8.74 (s, 1H) ; ^{13}C NMR : δ(ppm) : C_6 = 21.93, C_{arom} = 128.23-144.16 , C_5 = 145.47 , C_3 = 161.85 ; IR (cm^{-1}) 1592; MS (70 eV): $M^{+\cdot}$ =299 ; Anal. cald for $C_{15}H_{13}N_3O_2S$: C, 60.20 ; H, 4.34 ; N,14.04 . found: C, 60.34; H, 4.19; N, 13.86%.

Compound **2b** : ^1H NMR :δ(ppm): 2.28(s,3H); 2.36(s,3H); 7.10-7.91(m,8H); 8.85(s,1H); ^{13}C NMR: δ(ppm):C_7 = 22.08 ; C_6 = 22.25 ; C_{arom} = 128.05-146.46 ; C_5 = 147.35 ; C_3 = 161.65; IR (cm^{-1})1595 ; MS(70 eV): $M^{+\cdot}$ = 313 .

Compound **2c** : ^1H NMR: δ(ppm):2.28(s, 3H);2.31(s, 3H); 7.23-7.83(m,13H);^{13}C NMR: δ (ppm):C_7 = 21.54; C_6 = 21.75 ; C_{arom} = 125.89-145.80; C_5 = 155.60; C_3 = 158.82 ; IR (cm^{-1})1605 ; MS (70 eV): $M^{+\cdot}$ = 389.

Compound **2d** : ^1H NMR δ(ppm): 1.29(d,6H); 2.48 (s,3H); 3.17(m,1H) ; 6.9-7.98 (m,8H); ^{13}C NMR:δ (ppm):C_8 = 14.35; C_6 = 21.53; C_9 = 27.55 ; C_{arom} = 126.83-144.53; C_5 = 159.87; C_3 = 161.89; IR(cm^{-1})1589; MS(70 eV): $M^{+\cdot}$ = 377.5.

Compound **2e** : ^{1}H NMR: δ(ppm): 2.31(s,3H); 2.37(s,3H); 2.49(s, 3H);7.29-7.97(m,12H); ^{13}C NMR:δ(ppm):C_7 = 21.64 ; C_6 = 21.92 ; C_{10} = 22.32 ; C_{arom} = 126.07-143.44 ; C_5 = 156.44 ; C_3 = 161.04 ; IR (cm^{-1})1585; MS(70 eV): $M^{+\cdot}$ = 403 ; Anal. Cald for $C_{23}H_{21}N_3O_2S$: C, 68.48; H, 5.21; N,10.42. found: C, 68.37; H, 5.39; N,10.61 %

Compound **2f** : ^{1}H NMR :δ (ppm):2.34(s, 3H) ; 2.36 (s, 3H) ; 7.20-8.08 (m, 12H) ; ^{13}C NMR : δ (ppm): C_7 = 21.32 ; C_6 = 22.11 ; C_{arom} = 125.84-141.93; C_5 =154.54 ; C_3 = 157.45; IR (cm^{-1})1602 ; MS (70 eV): $M^{+\cdot}$ = 423.5 .

Compound **2g** : ^{1}H NMR : δ (ppm): 2.31 (s, 3H); 7.35-8.4 (m, 13H) ; ^{13}C NMR : δ (ppm): C_6 = 21.49 ; C_{arom} = 126.48-142.61; C_5 =155.66; C_3 = 158.57; IR(cm^{-1})1600 ; MS(70 eV): $M^{+\cdot}$ = 409 ; Anal. cald for $C_{21}H_{16}ClN_3O_2S$: C, 61.53 ; H, 3.90; N,10.25. found: C, 61.42; H, 3.86; N, 10.06%.

Compound **2h** : ^{1}H NMR : δ (ppm): 2.33 (s, 3H) ; 2.38(s,3H); 7.03-7.79(m,11H) ; ^{13}C NMR : δ (ppm): C_7 = 21.29; C_6 = 21.59 ; C_{arom} = 126.99-141.09 ; C_5 = 154.20; C_3 = 157.22; IR (cm^{-1})1602; MS (70 eV): $M^{+\cdot}$ = 458 .

Crystal data for **2a** : $C_{15}H_{13}N_3O_2$, M=299; crystal system monoclinic, space group P2(1)/c, a=6.2790(10), b=9.4880 (10) c=24.382 (2) Å, β=95.44 (2), V=1446.0(3) $Å^3$, Z=4 , d_{calc} =1.375, T=293(2) K, Kα Mo(λ=0.71073 Å), μ = 0.231mm^{-1}, of 40741 measured data , 4321 were independent (R_{int} = 0.0950),R_1[I>2σ(I)]=0.0497, wR_2 = 0.1432 and GOOF=1.038.

Aknowledgement

The X-ray analysis has been realized in « Laboratoire de Cristallographie et Modelisation des Matériaux Minéraux et Biologiques » UMR-CNRS , thus we are grateful to professor Slimane Dahaoui for the facilities provided.

References

1 Y. Naito, F. Akahoshi, S. Takeda, T. Okada , M. Kajii, *J. Med. Chem.*, **39**, 3019, (1996) .

2 O.G. Todoulou , A. E. Papadaki-Valiraki ,E. C.Filippatos, S. Ikeda , E. De. Clercq, *Eur. J. Med. Chem. Chim. Ther.*, **29**, 127, (1994).

3 A. A. Ikizler, C. B. Johansson , O. Bekircan, C. Celik, *Acta. Pol. Pharm.*, **56**, 283, (1999).

4 I.A.Shehata, M.N.Nasr, H.I. El-Subbagh, M.M.Gineinah, S.M.Kheira, *Scien Pharm.*, **64**, 133, (1996).

5 M. Regitz, B. Eistert, *Chem. Ber.*, **96**, 3121, (1963).

6 B. Baccar, J. Barrans, *C. R.. Acad. Sci. Paris.*, **259**, 1340, (1964).

7 Hueein, F.A.; Kadir, A. A. *J. Indian. Chem. Soc.*, **45**, 729, (1968) .

8 M. Chihaoui, B. Baccar, R. Mathis, *C. R.. Acad. Sci. Paris.*, **293**, 573, (1981).

9 M.L. Benkhould, B. Baccar, *J. Soc. Chim. Tunisie.*, **3**, 3, (1991).

10 F. Chabchoub, M. Trabelsi, M. Salem, *J. Soc. Chim. Tunisie.*, **3**, 171, (1998).

11 M. Kossentini, F. Chabchoub, Y. LeBigot, M. Salem, *J. Soc. Chim. Tunisie.*, 4, 1233, (2001).

Received on March 30, 2003