SYNTHETIC COMMUNICATIONS, 25(23), 3747-3763 (1995)

HETEROCYCLISATION OF UNSATURATED PHENYLSULFIDES. SYNTHESIS OF A NOVEL SERIES OF 2 SUBSTITUTED -2,3- DIHYDRO BENZOTHIAZOLES.

Ghislaine Martin*, Jean Sauleau, Michèle David and Armelle Sauleau

Laboratoire de Chimie Pharmaceutique, Faculté de Pharmacie, Avenue du Pr Léon Bernard, 35043 RENNES Cedex France.

Abstract: Aminoarylhydroxy thioalkenes react with tosyl derivatives to provide mainly N substituted -2 vinyl -2,3 dihydrobenzothiazoles. A different regiochemistry of cyclization depending on whether a methyl or a phenyl susbtituent was used, was observed. Formation of -2H- 3,4- dihydrobenzothiazines and dienes was observed.

The synthesis and pharmacological interest (antiinflamatory and antibacterial activity) of unsubstituted 3- alkyl or 3 -aryl benzothiazolines have been reported in several article[1a,1b]. However the examples with substituents

*to whom correspondence should be addressed

in the 2 position, were limited to simples ones (lower alkyl, allyl or halophenyl groups)[1a,2,3]

Following these observations, and as a continuation of our studies[4] about arylsulfides, we now report that, under acidic conditions, substituted *amino* arylthioalcenols undergo intramolecular cyclization leading to the synthesis of 2-vinyl -2,3-dihydro benzothiazole derivatives which has never been reported so far. The method we describ, is easy to perform with regard to the nature of the substitution in the 2- position of the bicyclic ring systems.

The aminoarylthioalcenols **2** can be prepared regioselectively from the reaction of ethylenic epoxides **1** with 2-amino thiophenol, in basic media . Formation of compounds **2** confirms the results of KERWIN and Col.[5] and INOUE and Col.[6] our ethylenic epoxides **1**, reacted with the 2-aminothiophenol anion, as ethylene oxide[5], styrene oxide[5] or glycidic esters to lead to uncyclized aminoalcohols. When heated with tosylchloride (TsCl), compounds **2** produced directly the corresponding N-tosyl derivatives **3** with good yields (90-95%). Compounds **3** were allowed to react in toluene, at 80°C, with toluneparasulphonic acid (TsOH). The reaction gave predominantly 2,3-dihydrobenzo-thiazoles **4** and, sometimes, a mixture of **4** with -2H-3,4-dihydro-1,4 benzothiazines **5** and dienes **6** (Table1). We verified that 1,4-benzothiazines **5** did not result from ring expansion of benzothiazolines **4** (the reaction of **4a** in toluene, at 80°C, was carried out in the presence of TsOH).

Scheme 1

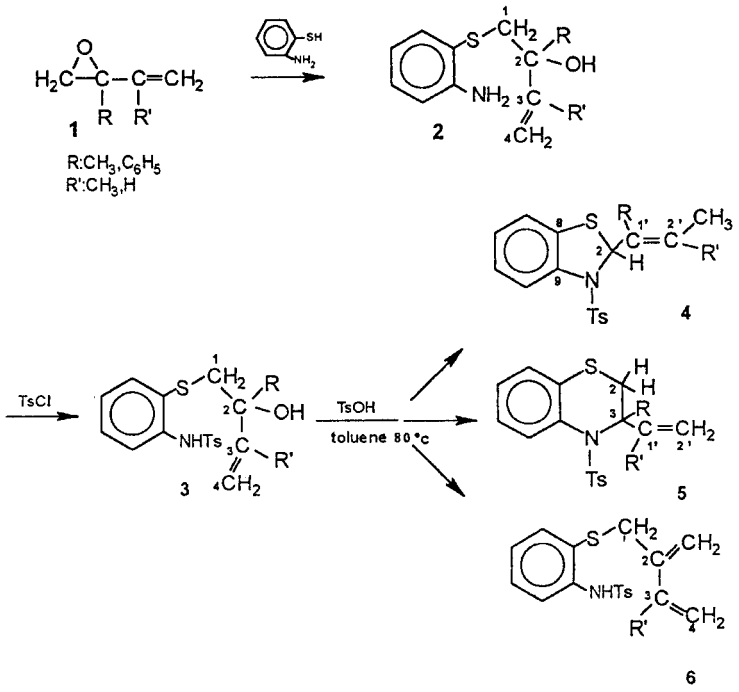


Table 1

Entry	R	R'	yields	Products (yields %)		
a	C_6H_5	CH_3	80	**4a** (100)	-	-
b	C_6H_5	H	50	**4b** (100)	-	-
c	CH_3	CH_3	70	**4c** (25)	**5c** (25)	**6c** (50)
d	CH_3	H	70	**4d** (33)	**5d** (33)	**6d** (33)

The products were isolated by column chromatography on silica gel and identified by their analytical and spectral data. All compounds were investigated by ^{1}H, ^{13}C NMR, IR and mass spectrometry.The X-ray analysis of compounds **4d** and **5d** was also carried out using cristals obtained from absolute ethanol.

In IR spectra, the structures of **4** and **5** were attested by the absence of hydroxyl and NH between (3300 and 3500 cm^{-1}) absorptions; for **6**, conjugated -CH=CH_2 (990 and 905 cm^{-1}) and -C=CH_2 (900 cm^{-1}) were noted. In NMR spectra, the assignments were made on the basis of the multiplicity and intensity of the signals (Experimental part). The structures were assigned on the basis of the following 500 MHz ^{1}H NMR observations:

1- in **4,** the absence of the vinylic proton(-C=CH_2) and the downfield chemical shift of the proton on carbon 2, which resonates for **4a**,**4b** and **4c** ar around 6.5 ppm.In **4d**,CH_2 is in the upper field (6.0 ppm) owing to its proximity to the phenyl group of NH-Ts.

2- the two nonequivalent protons of the S-CH_2 in compounds **5** and **6** are in the positions expected for Ar-S-CH_2 protons [8]. Their chemical shifts for **5d** and **6d** are compared with those of compound **3d** in Table 2.

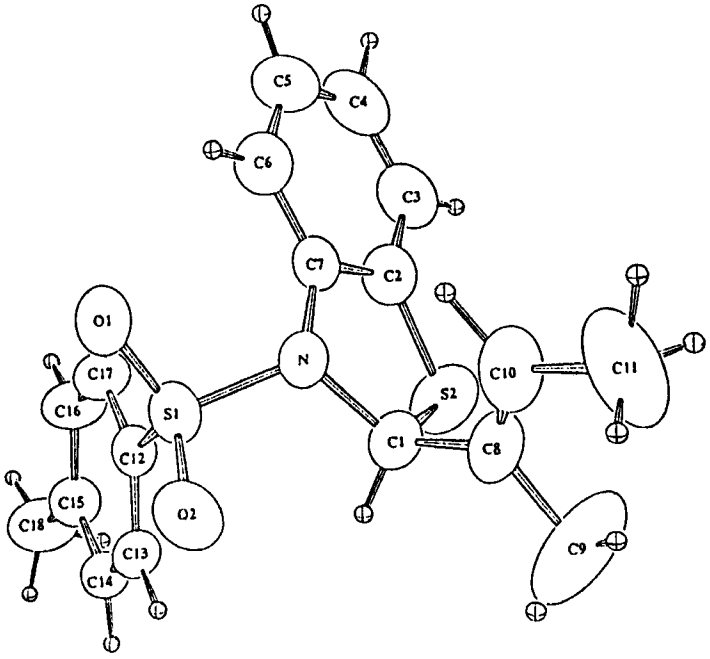
The ^{13}C NMR spectra confirm the structure of these compounds; the chemical shifts and ^{1}J values are assigned in Experimental part. The comparison of compound uncyclized **3** with cyclized products **5** (table 2), shows that the signal for S-CH_2 in the side chain of **3**, is consistently the furthest downfield around 49 ppm (in **5** it is around 35 ppm).

Table 2

S-CH_2 (δ ppm) ^{1}H and ^{13} C NMR of compounds **3d**, **5d** and **6d**.

Compound	**3d**	**5d**	**6d**
^{1}H	2.69 to 2.79(AB) J=13.2Hz	2.96 to 3.04(AB) J=12.2Hz	3.28 (s)
^{13}C	49.5 ^{1}J=141.1Hz	34.4 ^{1}J=142.2Hz	38.1 ^{1}J=141.6Hz.

Scheme 2



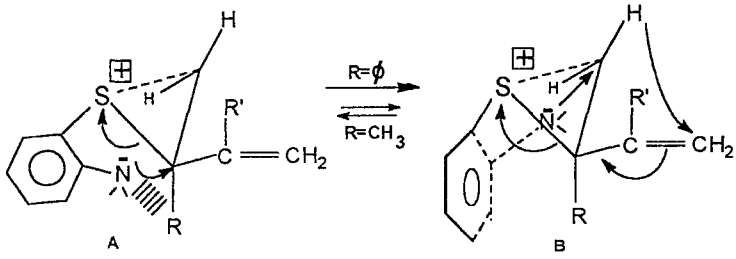
The cis arrangement of the CH_3 groups attached to the double bond in the side chain of **4d** (geometry Z), is based upon NMR ^{13}C spectral evidence; the additional shielding of the 1' methyl carbon (11.7 ppm) is caused by the cis oriented 2' methyl carbon (13.7 ppm) (gamma gauche effect) [9]. This observation is confirmed by X-ray data spectra (scheme 2).

Finally, for products **4**, the low intensity signal for C-8 appears upfield (around 133 ppm) compared to the low intensity signal for C-9 (around 144 ppm), which is consistent with the differences in shielding of sulfur and nitrogen atoms[10].

Table 1 shows the clear substituent effect on the reactivity of **3** in cyclization. The cyclization seems to depend on the nature of R. An electron donating group ($R=CH_3$) -entries c and d in Table 1, facilitates the elimination reaction and leads to the formation of dienes **6**, but cyclization still occurs. With R=phenyl, the reaction appears to be more selective:only dihydrobenzothiazole **4** is obtained. Apparently, the reaction proceeds via an episulfonium intermediate which undergoes a nucleophilic opening by the adjacent NH-Ts group via a SN2-type mechanism. Moreover it is known[11]that episulfonium ions reveal the reactivity patterns quite typical of cationoid systems.

The regioselectivity of this opening is not subject to charge control but we think that it is affected principally by steric hindrance. We suggest that the compounds are produced according to scheme 2 where the episulfonium ion is drawn in its two mains conformations A and B; the relative amounts of **4** and **5** reflect a preference for A or B.

Scheme 3



The conformer of type A shows steric hindrance between the R and NH-Ts groups (N in the scheme 3) and thus, the equilibrium can be displaced towards the conformer of type B where minimal steric effects are normally expected.

When R is a phenyl, the conformation B is favoured by minimization of the steric interactions, the nucleophilic attack can only take place on the methylene site: only compounds **4** are obtained .

If R=CH_3, the two paths via A and B are plausible: a mixture of products **4** and **5** are formed.

In conclusion, this work shows that N-tosylation is a good way to have access to 2-vinyl dihydrobenzothiazoles. The presence of a tosyl group induces a specific reactivity: the episulfonium intermediate formed is stable enough to favour substitution and cyclization rather than elimination.Extension to the synthesis of many substituted dihydrobenzothiazole systems should be possible and their structure - activity relationship will be studied.

EXPERIMENTAL

Melting points were determined on a kofler stage and are uncorected. ^1H NMR spectra were recorded on a 500 MHZ Brucker DMX and 300 MHZ Brucker AM

300 WB spectrometers .^{13}C NMR spectra were realised on a 125 MHz Brucker DMX and a 75 MHz Brucker AM 300 WB spectrometers . For all the spectra, $CDCl_3$ is utilized as solvent and chemical shifts are in ppm. Mass spectral data were obtained on a Varian 311 high resolution spectrometer.I.R. spectra were recorded on a Perkin Elmer 16PC F.T. spectrometer.

General procedure for synthesis of (2-aminophenylthio)-3-butene 2a to 2d.

Freshly distilled 2 amino thiophenol (0.031M) was added to a solution of KOH (0.031 M)in éthanol and stirred for 5 minutes. Then the solution was cooled to room temperature and the époxyde(0.031M) was added. The reaction occured at room temperature when R= phenyl and was heated at 50°C when R=CH_3. After two hours, water was added to the mixture. After extraction with ether, the organic layer was dried with Na_2SO_4 and evaporated. When R=phenyl, the product was chromatographied on a silica gel column with CH_2Cl_2/ethyl acetate (80/20) as eluent. When R=CH_3,the product was distilled under high vacuum .

2a (R=C_6H_5 , R'=CH_3): **2-hydroxy-2-phenyl-3methyl-1- (2-aminophenylthio) -3-butene.**

Brown solid F:64°C, (90%).^1H nmr δ ppm: 6.64-7.46(9H,m,phenyl); 5.01-5.19 (2H,m,=CH_2); 3,33-3.58(2H, AB; J=13,3Hz, S-CH_2). 1.61(3H,s,CH_3);^{13}C nmr δ ppm: 111.9 (txq , ^1J=156.6 Hz,C(4)); 78.5(s,C(2));47.5 (t , ^1J= 141.6Hz, C(1)); 19.2 (qxm,^1J=127.2Hz,CH_3).ir ν, cm^{-1} :3348-3440(NH_2)(OH),904(CH_2), 750-698 (mono and 1-2 disubstitution phenyl)

2b(R=C_6H_5, R'=H) : **2-hydroxy-2- phenyl-1- (2-aminophenythio)- 3-butene.**

Oil (90%).^1H nmr δ ppm: 6.67-7.43(9H,m,phenyl); 5.36-6.14 (3H,m, CH=CH_2) ;

3.27- 3.35 (2H,AB, J= 13.5Hz ,S-CH_2). .^{13}C nmr δ ppm: 114.1 (t,^{1}J=157.0Hz) C(4));76.5(s,C(2));48.9(t, ^{1}J=141.6Hz, C(2)H_2).ir ν, cm^{-1} 3352-3470(NH2)(OH); 1606(NH),992-926(CH);750-760(mono and 1-2 disubstitution phenyl).

2c(R=R'=CH_3): 2-hydroxy-2-methyl-3- méthyl-1- (2-aminophenylthio)- 3-butene.

Yellow oil (80%) bp:155°C/2 mmHg .^{1}H nmr δppm: 6.65-7.50 (4H,m, phenyl); 5.07-5.92 (3H,m, =CH_2); 2.89-3.06 (2H,AB,J=13.3 Hz,S-CH_2); 1.33 (3H,s, CH_3).^{13}C nmr δ ppm : 110.9 (t, ^{1}J=156.5Hz, C(4));74.9(s,C(2)); 47.2(txq; ^{1}J= 140.8Hz,C(1)),26.8(q, ^{1}J=127.3H Hz, CH_3(2));19.4 (qxdxd , ^{1}J= 126.4 Hz, CH_3(3)) .ir ν,cm^{-1} 3344(OH)(NH_2),902 (=CH_2), 748 (1.2 disubstitution phenyl). ms(m/z): calculated :223.1030, found: 223. 1034; 223(17.69), 139(76.29), 125 (100), 124(71.44),80(38.61).

2d (R=CH_3,R'=H): 2-hydroxy-2-methyl-1- (2-aminophenylthio)-3-butene.

Yellow oil (90%)bp: 141°C/10.5 mmHg. ^{1}H nmr δ ppm: 6.69-7.49 (4H,m,phenyl); 5.07-5.92 (3H,m, CH=CH_2) 2.89-3.06(2H,AB,J=13.3Hz, S-CH_2);1.33(3H,s, CH_3). ^{13}C nmr δ ppm: 113.1(t,^{1}J= 155.3 Hz,C4); 67.6(s,C(2)); 48.8(txm,^{1}J= 140.5Hz, C(1));27.2 (q,^{1}J=127.2Hz,CH_3). ir ν,cm^{-1}:3346(NH_2)(OH), 994-924 (=CH), 748 (1-2disubstitution phenyl).

General procedure for synthesis of (2-tosylaminophenylthio)-3-butene 3a to 3d.

Tosylchloride ($4.5x10^{-2}$M) was added to a solution of compound **2** (4.5×10^{-3}M) in pyridine (25 ml). The mixture was stirred at room temperature for 5 hours. After extraction with ether, the organic layer was dried (Na_2SO_4) and the residu was

chromatographied on a silica gel column with CH_2Cl_2/Ethyl acetate (90/10) as eluent, to give compounds **3** .

3a(R=C_6H_5, R'=CH_3) : **2-hydroxy-2-phenyl-3- méthyl-1- (2-tosylaminophenyl-thio)-3-butene.**

^{1}H nmr δ ppm: 6.92-7.69(13H,m,phenyl); 5.07-5.17 (2H ,m,=CH_2); 3.06- 3.34 (2H, AB, J=13.1Hz,S-CH_2); 2.30(3H,s,CH_3Ts);1.59(3H,s,CH_3(3)).^{13}C nmr δ ppm: 112.7 (txq, ^{1}J=156.8Hz ,C(4)); 78.5(s,C(2)); 48.5(t,^{1}J,=142.0 Hz, C(1)); 21.5 (qxt, ^{1}J=126.9Hz, CH_3Ts); 19.1(qxdxd, ^{1}J= 126.7 Hz; CH_3(3)).ir ν,cm^{-1}: 3498(OH), 3250(NH), 1334 and 1158 (SO_2),758+698(mono and 1.2 disubstitution phenyl).

3b (R=C_6H_5,R'=H): **2-hydroxy-2-phenyl-1- (2-tosylaminophenylthio)- 3-butene.**

^{1}H nmr δ ppm:6.92-7.68 (13H,m,phenyl); 5.25- 6.15(3H,m, CH=CH_2); 3.05-3.11 (2H,AB, J=13.3 Hz,S-CH_2); 2.30 (s, CH_3Ts).^{13}C nmr δppm:115.9(t,^{1}J=156.2Hz, C(4));76.5(s,C(2)); 49.7 (t, ^{1}J=142.5Hz,C(1));21.5(qxt,^{1}J=127.4,CH_3Ts).ir ν,cm^{-1} : 3486(OH),3248(NH), 1334-1158(502), 990-924 (-CH=CH_2) , 814(1-4 disubs-titution phenyl),758-700 (mono and 1-2 disubstitution phenyl) .

3c (R=R'=CH_3) : **2-hydroxy-2, 3-dimethyl-1- (2-tosylaminophenylthio)- 3-butene.**

^{1}H nmr δppm : 6.96-7.71(8H,m,phenyl); 4.94-5.13(2H,m,=CH_2); 2.67-2.93 (2H, AB,J=13.2 Hz,S-CH_2); 2.35 (3H,s,CH_3Ts);1.34(3H,s, CH_3(2)); 1.67(3H,s,CH_3 (3) ^{13}C nmr δppm: 111.6 (txq, ^{1}J=156.7Hz,C(4)),74.8(s,C(2));48.2 (txq, ^{1}J= 141.1Hz, C(2)H_2); 26.8(q,^{1}J=127.3Hz, CH_3-C(2)); 21.5 (qxt, ^{1}J=127.3 ,CH_3Ts); 19.3(qxm,

^{1}J=126.6Hz,CH_3-C(3)).ir ν, cm^{-1}:3494(OH), 3254(NH), 1334-1158(SO_2), 908 (C=CH).

3d(R=CH_3,R'=H): **2-hydroxy-2-methyl-1- (2-tosylaminophenylthio)- 3- butene.** ^{1}H nmr δ ppm:6.96-7.71(8H,m,phenyl); 5.11- 5.86 (3H,m, CH=CH_2) ; 2.69- 2.79 (2H,AB, J=13.2Hz,S=CH_2); 2.35 (3H,s, CH_3Ts);1.32(3H,s,CH_3(2). ^{13}C nmr δ ppm 113.9(t,^{1}J= 155.1Hz , C(4));72. 8(s, C (2));49.5 (t,^{1}J=141.1Hz ,C(1));27.2 (q, ^{1}J= 127.4 Hz,CH_3(2)) ; 21.5(qxt, ^{1}J=126.9 CH_3Ts). ir ν, cm^{-1}: 3492 (OH), 3248(NH) , 1332,1160 ($S0_2$).

General procedure for synthesis of -2,3-dihydrobenzothiazoles 4 and 2H-3,4-dihydro-1,4- benzothiazines 5.

Compounds **3** (2.5 mM)in toluene was heated at 90°C and then TsOH (2.5 mM) was added. After 2 hours (**3c,3d**) or one day (**3a,3b**), the mixture was cooled and poored on a cold solution 10% of sodium hydroxyde, washed with water, extracted with ether and dried (Na_2SO_4). After evaporation, compound **4,5** and **6** were separated by chromatography on silica gel column, eluted with toluene.

4a (R=C_6H_5, R'=CH_3) : **2-[(1-phenyl-2-methyl)-1-propene]-3-tosylamino -2, 3 - dihydrobenzothiazole.**

M.p.:102°C.^{1}H nmr δ ppm: 6.67-7.48 (13H,m,phenyl); 6.81 (1H,s,C_2H); 2.34 (3H,s, CH_3Ts); 2.02 (3H,s, R') ;1.46(3H,s,CH_3).^{13}C nmr δ ppm : 144.1 (s,C(9)); 133(s,C(8));67.0 (d,^{1}J=152,5 Hz, C(2));22.5 (qxq, ^{1}J=126.5 Hz ,CH_3); 21.6 (qxt, ^{1}J=127.3 Hz,CH_3Ts); 19.7(qxq,^{1}J=126.3 Hz, CH_3). ir ν, cm^{-1}1638 (C=C), 1358 , 1166 (SO_2), 812(1-4 disubstitution phenyl), 760,664 (mono and 1-2 disubstitution phenyl).

4b($R=C_6H_5, R'=H$) : **2-(1-phenyl--1propene)-3-tosylamino -2,3-dihydrobenzo thiazole.**

^1H nmr δ ppm:6.90-7.67(13H,m,phenyl);6.68 (1H,s,C(2)H); 6.00 (1H, q,J=6.91 Hz C(2')H)); 2.34(3H, s,CH_3Ts);1.49 (3H, dxd,J=6.91Hz;CH_3-C(2')). ir ν, cm^{-1} 1646 (C=C) , 1356,1168 (SO_2),812 (1-4 disubstitution phenyl),748,702(1-2 and monosubstitution phenyl).

4c($R=R'=CH_3$):**[(1,2-dimethyl)-1-propene]-3-tosylamino-2,3-dihydrobenzo thiazole.**

M.p.:94°C.^1H nmr δ ppm:6.49-7.64(8H,m,phenyl);6.70 (1H,s,C(2)H); 2.35(3H, s, CH_3Ts); 1.91 (3H,d,J= 1,2Hz,CH_3);1.51,1.69 (2s,3H,R,R').ir ν, cm^{-1}:1654 (C=C), 1354 -1170(SO_2), 814(1-4 disubstitution phenyl),748(1-2 disubstitution phenyl).

4d($R=CH_3$, R'=H) : **2-[(1-methyl)-1-propene]-3-tosylamino -2,3-dihydrobenzo thiazole.**

M.p.:111°C.^1H nmr δ ppm 6.97-7.68(8H,m,phenyl); 6.00(1H,s,C(2)H); 5.72(1H, q,J:6.62 Hz, C(2')H); 2.33(3H,s, CH_3Ts); 1.60 (3H,s,CH_3-C(1')) ;1.58(3H,d,J=6.94 Hz, CH_3-C(2')) .^{13}C nmr δ ppm: 144.8(s, C(9)); 133.0(s,C(8)); 73.4(d,^1J=153.6 Hz C(2));21.5(qxt,^1J=127.1 Hz,CH_3Ts); 13.2(q,1=126.2 Hz , CH_3- C(2')), 11.7(dxd, ^1J=127.0 Hz,CH_3-C(1')).ir ν, cm^{-1}:1644(C=C),1358 -1166(SO_2), 846(=CH) .

5c ($R=R'=CH_3$) **: (1-propenyl-3-methyl)-4-tosylamino-2H- 3,4-dihydro- 1,4 - benzothiazine**

^1H nmr δ ppm:7.00-7.52(8H,m,phenyl); 4.70-5.05 (2H, m,=CH_2); 3.12-3.19 (2H, AB, J=12.4Hz, S-CH_2); 2.41(3H,s,CH_3Ts); 1.77 (3H,s,CH_3-C(3)); 1.67(3H,s,

CH_3-C(1')). ^{13}C nmr δ ppm: 111.3CH(t,=CH_2); 62.9 (s, C(3));34.7(t,^1J=140.0 Hz,C(2)H $_2$);27.6(q,^1J=129.9Hz,CH_3-C(3)), 21.6 (qxt,^1J=127.2Hz,CH_3Ts); 18.3 (qx m,^1J=125.8Hz,CH_3-C(1')). ir ν,cm^{-1}:1644 (C=C), 1348-1166 (SO_2), 812(1-4 disubstitution phenyl),756(1-2 disubstitution phenyl) .

5d(R=CH_3,R'=H) : (3-vinyl)-3-methyl-4-tosylamino-2H-3,4- dihydro-1,4 - benzothiazine.

M.p.:115°C.^1H nmr δ ppm: 7.04-7.52(8H,m,phenyl);4.98-6.08 (3H,m,CH=CH2); 2.96- 3.04 (2H, AB, J=12.2Hz, S-CH_2);2.41(3H,s, CH_3Ts); 1.52(3H,s,CH_3-C(3)). ^{13}C nmr δ ppm: 112.7 (t,^1J=155.0 Hz,=CH_2); 60.2(s,C(3)); 34.4 (t,^1J=142.2 Hz, C(2)); 28.4 (q, ^1J=129.6Hz, CH_3-C(3)) ; 21.5(qxt,^1J=127.2 Hz,CH_3Ts).ir ν, cm^{-1} 164 0 (C=C), 1348,1166 (SO_2), 812(1-4 disubstitution phenyl),754(1-2 disubstitu tion phenyl). ms (m/z):$C_{18}H_{19}O_2S_2N$ calculated mass:345.0857, found:345,0851.

6c(R'=CH_3):2-methane-(2-aminophenylthio)-3-methyl-butadiene.

^1H nmr δ ppm : 6.96-7.82(8H,m,phenyl);4.55, 5.00, 5.14, 5.15(4H,4sC =CH2); 3.36(2H, s, S-CH_2); 2.34(3H,s,CH_3Ts); 1.91(3H,s, CH_3-C(3)).^{13}C nmr δ ppm: 114.3(txq, ^1J=155.3Hz ,C(4)H_2);116.4 (txt, ^1J=157.8 Hz CH_2=C(2)); 40.1(txdxd, ^1J= 141.6 Hz, C(1)); 21.1(qxt,^1J=127.3, CH_3Ts); 20.9 (qxdxd,^1J= 127.0 Hz CH_3 -C(3)) .ir ν,cm^{-1}: 3254(NH), 1134 ,1160 (SO_2), 900(C=CH), 812 (1-4 disubstitu-tion phenyl), 754 (1-2disubstitution phenyl).ms (m/z): $C_{19}H_{21}O_2S_2N$, calculated : 359.013, found:359.1007.

6d(R'=H):2-methane-(2-aminophenylthio)-butadiene.

M.p.:113°C.^1H nmr δ ppm:6.97-7.82(8H,m,phenyl); 5.22-6.32 (3H, m,CH=CH_2);

4.53-4.89 (2H,m, C(2)=CH_2); 3.28(2H,s,S-CH_2); 2.35 (3H,s, CH_3Ts). ^{13}C nmr δ ppm: 115.3 (t,^{1}J=154.8Hz ,C(4)); 119.4(txm, ^{1}J=158. 1Hz,CH_2=C(2)); 38.1 (txm, ^{1}J=141.6Hz, S-CH_2); 21.4 (qxt,^{1}J=127.2 Hz, CH_3Ts).ir νcm^{-1} 3262 (NH),1634 (C=C), 1336, 1166(SO2), 906 (C=CH2), 814(1-4 disubstitution phenyl),756 (1-2 disubstitution phenyl). ms(m/z): $C_{18}H_{19}S_2O_2N$: calculated:345.0857 , found : 345.0853.

X-ray cristallography of 4d and 5d.[12,13,14]

for **4d** :C18H19O2NS2/Mr=345.49,orthorhombic, Pna21, a=13,454(1), b= 13.848 (4),c =9.473(2)A,V=1764,9(6)A^{-3},Z=4,D_x=1.300 Mg.m^{-3},λ(MoKα) = 0.70926 A μ=2.96cm^{-1}, F(000)=728,T=293K, final R=0.027 for 1448 observations.The sample (0.45*0.50*0.55mm) is studied on an automatic diffractometer CAD4 - ENRAF NONUS with graphite monochromatized MoKα radiation. The cell parameters are obtained by fitting a set of 25 high-tetha reflections. The data collection ($2\theta_{max}$= 50°, scan ω/2θ=1, t max=60s, range HKL : H 0,15 K 0,16 L 0,11 , intensity controls without appreciable decay (0,4%) gives 3208 reflections from which 1448 with I >3σ (I). After Lorenz and polarisation corrections the structure was solved with Direct Method which reveals all the non-hydrogene atom of the structure. After isotropic (R=0.095), then anisotropic refinement (R=0.051), all the hydrogene atoms are found with a Fourier Difference between 0.69 and 0.26 e.A^{-3}. The whole structure was refined by the full-matrix least-square techniques (use of F magnitude ; x,y,z, βij for S,N,O,and C, atoms and x,y,z for H atoms; 265 variables and 1448 observations ; w= $1/\sigma(Fo)^2 = [\ \sigma^2(I)+(0.04Fo^2)^2]^{-1/2}$) with the resulting R= 0.028, R_w=0.037 and S w=0.796 (residual $\Delta\rho \leq 12$ e A^{-3}).

for **5d:** C18H19O2NS2/Mr=345.49,orthorhombic,Pna21, a=7.691(3), b= 12.049 (9),c =18.770(9)A,V=1739(6)A^{-3}, Z=4,D_x=1.300 $Mg.m^{-3}$,λ(MoKα) = 0.70926, A μ=3.08cm^{-1},F(000)=728,T=294K, final R=0.073 for 1148 observations.The sample (0.45*0.45*0.50 mm) is studied on an automatic diffractometer CAD4-ENRAF NONUS with graphite monochromatized MoKα radiation. The cell parameters are obtained by fitting a set of 25 high-tetha reflections. The data collection ($2\theta_{max}$= 50°, scan ω/2θ=1, t max=60s, range HKL : H 0,9 K 0,14 L 0,22 , intensity controls without appreciable decay (0,6%) gives 1785 reflections from which 1148 with I >3σ (I). After Lorenz and polarisation corrections the structure was solved with Direct Method which reveals all the non-hydrogene atom of the structure. . The whole structure was refined by the full-matrix least-square techniques (use of F magnitude ; x,y,z, βij for S,N,O,and C, atoms and x,y,z for H atoms; 209 variables and 1148 observations ; $w= 1/\sigma(Fo)^2 = [\ \sigma^2(I)+(0.04Fo^2)^2]^{-1/2}$) with the resulting R= 0.073, R_w=0.073 and S w=1.52 (residual $\Delta\rho \leq 12$ e A^{-3}).Atomic scattering factors from International Tables for X-ray Crystallography (1974). All the calculations were performed on a Digital Micro VAX 3100 computer with the MOLEN package (FAIR, 1990).

Acknowledgments to Mrs M. LE ROCH and Mr J.F. CUPIF for technical assistance.

Acknowledgments to Mr G.BOUER for the translation.

REFERENCES

1a. YAMAMOTO K.Y. , FUJITA M., TABASCHI K., KAWASCHIM Y.,

KATO A.E.,OYA M.,ISO T. and IWAO J.I., *J.Med.Chem.*, 1988, *31* ,919 and ref. cited.

1b. MORI M., KATAOKA T., SHIMURZU H., IMAI Y. and FUJIMURA H. , *Yakugaku Zasshi*,1978, *98*, 1019.

2. KALGUTKAR A.S. and MASHRAOUI S. H., *J.Chem.Research*,1991,*96*.

3 BABUDRI F. ,SAVERIO F. and INGUSCIO G., *Synthesis*,1985, *5*, 522.

4. MARTIN G., SAULEAU J. and SAULEAU A., *Sulfur Letters*,1993, *16*,195, and ref. 8 noted.

5. KERWIN J. F., McCARTY J. E. and VANDERWERF C.A., *J.Org. Chem.* , 1959,*24*,1719.

6. INOUE H., KONDA M., HASHIYAMA T. , OTSUKA H., TAKA- HASHI K., GAINO M., DATE T., AOE K.,TAKEDA M., MURATA S. , NARITA H., and NAGAO T. , *J.Med.Chem*, 1991, *34*,675 .

7. SCHWARTZ A. , MADAN P.B,MOHACSI E., O'BRIEN J.P., TODARO L.J. and COFFEN D.L., J.Org. *Chem*, 1992, *57*,851.

8.ROBILLARD B., HUGHES L, SLABY M., LINDSAY D.A and INGOLD K. U., *J.Org.Chem*, 1986, *51* , 1700.

9a. VOGELI U. and VON.PHILIPSON W.,*Org.Magn.Reson.*, 1975, 617.

9b. STOTHERS J.B. ,Carbon 13 in NMR Spectroscopy, Academic Press, New-York,1972, p.69.

10. SAWHNEY S.N. and BOYKIN D.W., *J.Org.Chem*, 1979, *44*,11.

11. SMIT W.A., ZEFIRON N.S., BODRIKOV I.V. and KRIMER M.Z, *Accounts of Chemical Research*, 1979, *12*, 282.

12. FAIR,C.K.(1990).MolEN."An Interactive Intelligent System for Crystal Structure Analysis".Enraf-Nonius, Delft, The Netherlands.

13. International Tables for X-ray Crystallography Birmingham : Kynoch Press 1974,4.

14. JOHNSON,C.K., Report ORNL-3794.Oak Ridge National Laboratory Tennessee, USA. 1965.

(Received in the UK 03 April 1995)