183. Isomerization of *N*-[α-(Alkylthio)alkyl]- and *N*-[α-(Arylthio)alkyl]benzotriazoles

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The thermal isomerizations of *N*-[α-(alkylthio)alkyl]- and *N*-[α-(arylthio)alkyl]benzotriazoles have been investigated under N_2 atmospheres *i*) in toluene, xylene, MeOH, or EtOH, in the presence of acid catalysts and *ii*) in the absence of solvent. The sulfide isomerization rates depend on the number of H-atoms carried by the C-atom attached to the N-atom of the benzotriazole: *tertiary* (no hydrogen) > *secondary* (1 hydrogen) > *primary* (2 hydrogens). The results support an isomerization mechanism involving a heterolytic N–C bond cleavage with formation of sulfonium/carbonium and benzotriazolate ions.

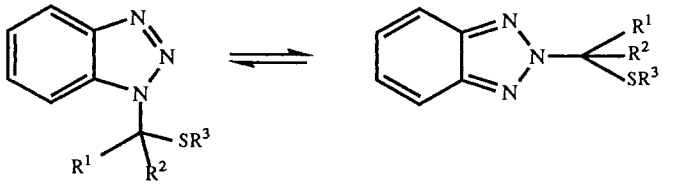
Introduction. – *N*-[α-(Dialkylamino)alkyl]benzotriazoles usually exist exclusively in the 1*H* form in the solid state, while in solution they exist as equilibrium mixtures of the 1*H* and 2*H* isomeric forms undergoing rapid interconversion [1–3]. Extensive investigations [2] [3] have revealed that these isomerizations proceed by intermolecular rearrangements involving an ionic dissociation-recombination mechanism. Recently, we reported similar results on the thermal isomerizations of *N*-(arylmethyl)benzotriazoles [4] in the absence of solvent. In both series the 1*H* isomer generally predominates over the 2*H* isomer, but the ratio diminishes with increasing steric bulk of the substituent group.

We have recently [5] prepared a number of *N*-[α-(alkylthio)alkyl]- and *N*-[α-(arylthio)alkyl]benzotriazoles, which on treatment with *Grignard* reagents, provide a convenient source for the preparation of *tert*-alkyl sulfides. We now report our results on the thermal isomerization of *N*-[α-(arylthio)alkyl]benzotriazoles. Our study, besides elucidating the mechanism of the isomerization process, provides information important to optimising the yields of synthetic transformations.

Results and Discussion. – The preparations of the compounds employed in this study are reported in [6]. We studied the potential isomerizations of *primary* (**1**), *secondary* (**2–4**), and *tertiary* (**5–9**) (1*H*-benzotriazol-1-yl)methanethiols by heating them either *i*) as neat, dry samples under N_2 (for compounds **1** and **2**) or *ii*) in solution in toluene, xylene, MeOH, or EtOH in the presence of an acid catalyst. The ^{1}H-NMR spectra were used to estimate the isomeric ratios.

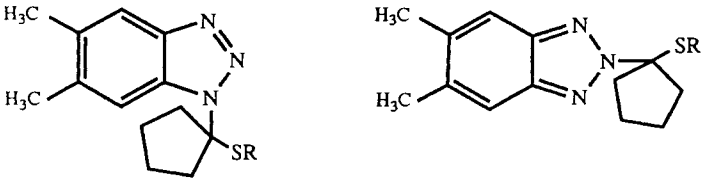
Isomerization in the Absence of Solvent. Compound **2** underwent isomerization together with some decomposition in the presence of a catalytic amount of anhydrous $ZnCl_2$. Sulfide **1** underwent only decomposition under these conditions.

Isomerization in Toluene or Xylene in the Presence of Acids. With a view to minimizing the formation of by-products, isomerizations of the sulfides were also carried out in toluene, xylene, MeOH, or EtOH in the presence of acid catalysts. The results are listed in



A B

Compound	1	2	3	4	5	6	7	8	9	10
R^1	H	i-Pr	Pr	Et	Me	$-(CH_2)_4-$	$-(CH_2)_5-$	$-(CH_2)_4-$	$-(CH_2)_4-$	$-(CH_2)_5-$
R^2	H	H	H	H	Me					
R^3	Ph	Ph	Ph	Ph	Ph	Ph	Ph	CH_2Ph	C_8H_{17}	CH_2Ph



A B

11 R = $PhCH_2$
12 R = C_8H_{17}

Table 1. Among the various catalysts employed, TsOH enhanced the isomerization the most effectively and allowed temperatures as low as 100° to be used in the cases of *N*-[α-(arylthio)alkyl]benzotriazoles **2**, **3**, **5**–**7**. *N*-[α-(Alkylthio)alkyl]benzotriazoles **9**, **10** isomerized in solution at room temperature even in the absence of catalyst. In all the cases (except compounds **5** and **10** in MeOH at room temperature), concomitant decomposition (7–15%) was observed due to the formation of vinyl sulfides by elimination of benzotriazole. Compound **7** underwent extensive decomposition, when H_2SO_4 was used as catalyst. The isomerization results summarized in *Table 1* indicate that the rate of isomerization is highest for the sulfides which possess a quaternary C-atom attached to the benzotriazole N-atom, especially when *N*-[α-(alkylthio)alkyl]benzotriazoles were isomerized.

To find the best conditions to avoid elimination, the influences of solvent and catalyst concentration on compound **9** were studied (*Table 2*). The results show that less elimination occurred in toluene than in EtOH. When the concentration of catalyst was increased, more elimination was observed. The best results were obtained when 10 mol-% of catalyst was used; with more than 50% of catalyst other by-products were also formed.

Equilibrium Position. Data listed in *Table 1* reveal that *tert*-alkyl sulfides **5**–**10** have high or major contributions from the 2*H* isomers at equilibrium. As expected, increased bulk in the *N*-substituent increases the proportion of the 2*H* isomer at equilibrium. Easy

Table 1. *Results on the Isomerization of* N-*[α-(Alkylthio)alkyl]- and* N-*[α-(Arylthio)alkyl]benzotriazoles*

Compound	Isomer	Solvent	Catalyst	Temp. [°C]	Time [h]	1*H*/2*H*
1	1*H*	–	–	250	7.0	100:0[a])
	1*H*	Xylene	TsOH	135	4.5	100:0[a])
2	1*H*	–	–	200	0.12	100:0[a])
	1*H*	–	$ZnCl_2$	250	0.5	90:10[b])
	1*H*	Toluene	–	100	12.0	100:0[a])
	1*H*	Toluene	$ZnBr_2$	100	20.0	93:7
	1*H*	Toluene	TsOH	100	0.5	93:7
3	1*H*	Xylene	TsOH	135	4.5	73:27[b])
	1*H*	Toluene	TsOH	100	0.5	95:5[b])
4	1*H*	Toluene	TsOH	100	0.5	100:0[a])
	1*H*	Xylene	TsOH	135	4.5	75:25[b])
5	2*H*	Toluene	TsOH	50	0.5	5:95
	2*H*	Toluene	TsOH	80	0.5	50:50
	1*H*	Toluene	TsOH	100	0.5	50:50
6	1*H*	Toluene	TsOH	100	0.5	40:60[b])
	1*H*	Toluene	TsOH	100	0.5	40:60[b])
7	1*H*	Toluene	–	100	12.0	100:0[a])
	1*H*	Toluene	H_2SO_4	100	5.0	[c])
	1*H*	Toluene	$ZnBr_2$	100	0.5	100:0[a])
	1*H*	Toluene	$ZnBr_2$	100	20.0	80:20[b])
	1*H*	Toluene	$PhCH_2Br$	100	0.5	78:22[b])
	1*H*	Toluene	$PhCH_2Br$	100	5.0	50:50[b])
	1*H*	Toluene	TsOH	100	0.5	40:60[b])
	1*H*	Toluene	TsOH	100	5.0	40:60[b])
	2*H*	Toluene	TsOH	100	0.5	40:60[b])
8	1*H*	Toluene	TsOH	80	0.5	62:38[b])
	2*H*	Toluene	TsOH	80	0.5	62:38[b])
9	1*H*	Toluene	TsOH	100	0.12	42:58[b])
	1*H*	Toluene	TsOH	100	0.5	42:58[b])
10	1*H*	Toluene	TsOH	100	0.12	35:65[b])
	1*H*	Toluene	TsOH	100	0.5	35:65[b])
	2*H*	Toluene	TsOH	100	0.12	35:65[b])
	2*H*	Toluene	TsOH	50	0.25	18:82[b])
	1*H*	MeOH	–	20	0.5	85:15
	1*H*	MeOH	–	50	0.5	85:15
	1*H*	MeOH	TsOH	20	0.5	80:20[b])
	1*H*	MeOH	TsOH	50	0.5	53:47[b])
	2*H*	MeOH	TsOH	50	0.5	53:47[b])

[a]) 2*H* Isomer not detected in NMR. [b]) Some decomposition took place. [c]) Extensive decomposition observed.

isomerization in the case of *N*-[(alkylthio)alkyl]benzotriazoles is due to the lower stability of the carbocation which is formed during isomerization.

Crossover Experiment. An isomerization reaction carried out on a mixture of **9A** and **11A** in the presence of a catalytic amount (10 mol-%) of TsOH in (D_8)toluene (80°, 0.5 h) afforded a mixture of products. ^{1}H- and ^{13}C-NMR Spectra revealed the formation of the crossover products **8A** and **12A**. A study of the ^{1}H-NMR spectrum for the benzyl CH_2 *singlets* showed that the mixture of products included **11A** (19.4%), **11B** (12.7%), **8A** (16%), and **8B** (4.1%), and also (from the vinyl proton signals) products (7.6%) of elimination of benzotriazole. The rest of the ^{1}H spectrum consisted of overlapping

Table 2. *Influence of Concentration of TsOH on the Isomerization of 2*H *Isomer of* **9** *at 50° for 0.5 h*

Solvent	TsOH [mol-%]	1*H*/2*H*	Decomposition [%]
Toluene	0	10:90	4
Toluene	10	18:82	7
Toluene	25	20:80	14
Toluene	50	22:78	25
Toluene	100	34:66	52
Toluene	200	64:36	95
EtOH	0	10:90	8
EtOH	10	15:85	25
EtOH	25	22:78	60
EtOH	50	50:50	80
EtOH	100	60:40	90
EtOH	200	60:40	95

aliphatic and aromatic *multiplets*, so it was not possible to determine the concentrations of **9A/B** and **12A/B**. In the ^{13}C-NMR spectrum, 8 signals could be clearly seen for the quaternary C-atoms between 77.8 and 85.1 ppm. The ratio of the weakest to the strongest was *ca.* 1:3. Thus, the mixture **9A/11A** gave the four possible 1*H*-benzotriazol-1-yl isomers along with the four possible 2*H*-benzotriazol-2-yl isomers, all in significant amounts.

Conclusion. – These results indicate that isomerization proceeds *via* an intermolecular rearrangement by N–C(SR) bond cleavage and support the previously published mechanism [4].

Experimental Part

General. The ^{1}H-NMR spectra were taken in $CDCl_3$ and $C_6D_5CD_3$ at 300 MHz on a *VXR-300* (FT mode) spectrometer with TMS as internal reference. The ^{13}C-NMR spectra at 75 MHz were obtained on the same instrument with internal lock. *N*-[α-(Arylthio)alkyl]benzotriazoles **1**–**7** and *N*-[α-(alkylthio)alkyl]benzotriazoles **9**, **10** were prepared according to the procedure in [6].

Preparation of Substituted N-*[1-(Alkylthio)cyclopentyl]benzotriazoles* **8**, **11**, *and* **12**. A mixture of 1*H*-benzotriazole or 5,6-dimethyl-1*H*-benzotriazole (0.05 mol), a thiol (0.05 mol), and cyclopentanone (0.05 mol) was refluxed in toluene (100 ml) in the presence of TsOH (0.2 g) under a *Dean-Stark* head for 24 h. The product was poured into NaOH soln. (200 ml, 5%) and stirred for 10 min. Et_2O (150 ml) was added to the mixture and the org. layer separated, washed with H_2O, dried ($MgSO_4$), and the solvent removed. The 1*H* and 2*H* isomers were separated by flash chromatography (*Table 3*). Typical ^{1}H-NMR: for **8A** ($CDCl_3$): 1.81 (*m*, 2 H); 1.99 (*m*, 2 H); 2.55 (*m*, 2 H); 2.92 (*m*, 2 H); 3.35 (*s*, 2 H); 6.91 (*m*, 2 H); 7.04 (*m*, 3 H); 7.35 (*m*, 1 H); 7.43 (*m*, 1 H); 7.88 (*d*, 1 H); 8.01 (*d*, 1 H). ^{13}C-NMR ($CDCl_3$): 23.2; 34.6; 39.3; 77.6; 113.0; 119.8; 123.8; 126.5; 126.7; 128.1; 128.4; 131.6; 136.6; 147.0. ^{1}H-NMR: for **8B** ($CDCl_3$): 1.74 (*m*, 2 H); 1.95 (*m*, 2 H); 2.52 (*m*, 2 H); 3,12 (*m*, 2 H); 3.73 (*s*, 2 H); 7.11 (*m*, 5 H); 7.37 (*m*, 2 H); 7.87 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 23.3; 35.2; 39.7; 82.3; 118.2; 126.3; 126.8; 128.1; 128.7; 136.8; 144.0.

Table 3. *Preparation of Substituted* N-*[1-(Alkylthio)cyclopentyl]benzotriazoles*

	8A	**8B**	**11A**	**11B**	**12A**	**12B**
Yield [%]	50	25	33	22	50	25
M.p. [°C] [a])	79–81	66–68	68–70	98–100	oil	oil

[a]) All compounds gave satisfactory elemental analyses.

Isomerization Procedure. Isomerizations were carried out under N_2 with pure dry 1*H* or 2*H* isomers. The samples **1** to **10** (60–100 mg) were dissolved in the appropriate solvents with 10 mol-% of the appropriate catalyst and heated at the temp. and for the times shown in *Table 1*. H_2O was added to the mixture, and it was extracted with Et_2O (3 × 2 ml). The combined org. layers were dried ($MgSO_4$), and the solvent was evaporated at r.t. under reduced pressure. The residue was dissolved in a deuterated solvent and the spectrum recorded. Samples **1** and **2** were also heated without solvent and, after reaction, were cooled rapidly, dissolved in $CDCl_3$ and the spectra recorded.

Crossover Experiment. A mixture of pure compounds **9A** and **11A** (0.1 g of each), and TsOH (0.01 g) was dissolved in deuterated toluene (2 ml) and kept at 80° for 0.5 h in an NMR tube and the spectra recorded.

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