C–H/N–H Tautomerism of Tetrakis-(2-benzothiazolyl)ethane

J. Chem. Research (S),
1999, 410–411
J. Chem. Research (M),
1999, 1737–1749

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C–H and N–H tautomers of the title compound are obtained and their structural properties determined by ^{1}H and ^{13}C NMR spectroscopy and X-ray diffraction; solvent and base effects on the rate of the C–H to N–H transformation are investigated.

Usually, tautomeric processes are investigated by means of the spectroscopic properties of 'fixed parents'. This involves the assumption that the substitution of a hydrogen atom with an alkyl group does not affect the spectroscopic properties of the molecule.[1] This method overcomes the difficulty to obtain pure samples of the tautomeric forms, the separation of both tautomers being an uncommon event.

Herein, we report on the synthesis and isolation of both the N–H and C–H tautomers of tetrakis(2-benzothiazolyl)ethane **2** and on some kinetic data on the transformation of the C–H into the N–H tautomer.

The reaction of bis(2-benzothiazolyl)methane **1** with BuLi in the presence of $CBrCl_3$ affords tetrakis(2-benzothiazolyl)ethane **2**. Solutions of **2** are unstable spontaneously giving **3** (Scheme 3).

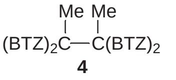
$$\underset{\mathbf{1}}{(BTZ)_2CH_2} \longrightarrow \underset{\mathbf{2}}{(BTZ)_2CH{-}CH(BTZ)_2} \longrightarrow \underset{\mathbf{3}}{(BTZ)_2C{=}C(BTZ)_2}$$

Scheme 3

As indicated in Scheme 4, **2** can exist in tautomeric (N–H and C–H) forms and the separation of the tautomers of tetrakis(2-benzothiazolyl)ethane (**2A** and **2B**) has been performed by flash chromatography on silica gel (eluent dichloromethane).

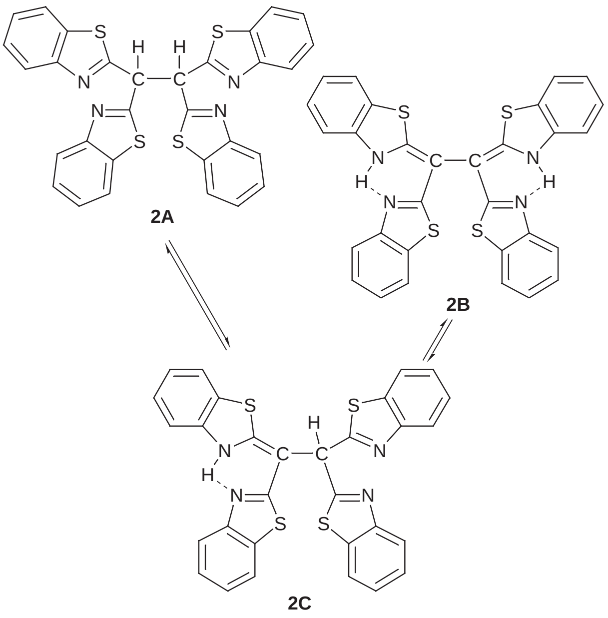
The oxidation **1** → **2** was performed also with Cr_2O_3 obtaining only **2A** in 10% yield.

The structure of the two tautomers **2A** and **2B** and of their oxidation product **3** was tentatively assigned by ^{1}H and ^{13}C NMR spectroscopy in $CDCl_3$ and in CH_2Cl_2. In $CDCl_3$, compound **2A** undergoes a very slow and incomplete conversion into the N–H tautomer **2B**. To confirm the structure of **2A** we synthesized 2,2,3,3-tetrakis-(2-benzothiazolyl)butane **4**, the spectroscopic properties of which are in accord with those of **2A**.



$$\underset{\mathbf{4}}{(BTZ)_2\overset{Me}{\overset{|}{C}}{-}\overset{Me}{\overset{|}{C}}(BTZ)_2}$$

A further confirmation of the structures of **2A** and **2B** is provided by the behaviour of their solutions in the presence of acids. By addition of an excess of methanesulfonic acid to CH_2Cl_2 solutions of **2A** and **2B** a rapid modification of the UV–VIS spectra is observed: both isomers giving the same spectrum ($\lambda_{max} = 420\,nm$, $\epsilon = 1.02 \times 10^5\,dm^3\,mol^{-1}\,cm^{-1}$), similar to that of **4** under the same experimental conditions ($\lambda_{max} = 435\,nm$, $\epsilon = 1.50 \times 10^5\,dm^3\,mol^{-1}\,cm^{-1}$).



Scheme 4

Complete structural definition of **2B** was obtained by X-ray diffraction of a single crystal. In order to distinguish between the N–H and the C–H isomer it is necessary to analyse the molecular geometry and in particular the bond distances in the penta-atomic rings. In fact at the resolution of the structure the hydrogen atoms could not be located. As found in other 2-benzothiazole systems,[8] each binuclear moiety is planar; the mutual orientation in the molecule is shown in Fig. 2.

Compound **2B** is a proton sponge-like molecule[10] and the hydrogen bond is resonance assisted[11] as depicted in Scheme 5.

The transformation **2A** → **2B** can be readily monitored by usual spectroscopic methods (colorless **2A** shows very different UV–VIS behaviour to the yellow **2B**): it is slow in apolar solvents such as dichloromethane or chloroform, but fast in polar solvents (dimethyl sulfoxide, dimethylformamide). Addition of dimethylformamide (DMF) to solutions of **2A** in CH_2Cl_2 enhances the rate of formation of **2B**.

Kinetic data concerning the conversion of **2A** into **2B** in CH_2Cl_2 in the presence of various additives such as dimethylformamide (DMF), tetrabutylammonium bromide

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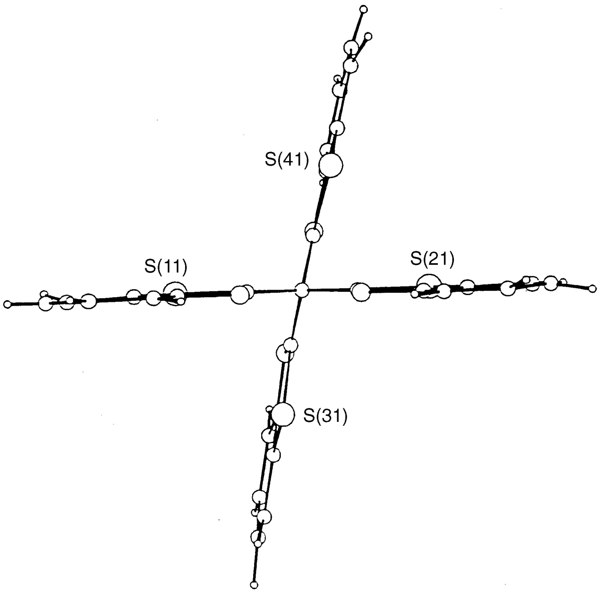


Fig. 2 Projection of tautomer **2B** along the C(1)–C(2) bond.

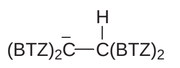
(TBAB), triethylamine (Et_3N) and piperidine (PIP) lead to the following conclusions: (i) the proton shift does not occur through an intermolecular mechanism involving two molecules of **2A**; (ii) the first addition of TBAB causes a significant increase of the reactivity, but a 'saturation' effect is rapidly observed; (iii) the variation of solvent composition by addition of DMF causes a large reactivity increase: a plot of k_{obs} *vs.* $[CH_2Cl_2]/[DMF]$ is linear with a zero intercept [$s = (3.02 \pm 0.06) \times 10^{-3}$, $i = -0.0007 \pm 0.0001$, $r = 0.9992$], thus confirming the very low reactivity in pure CH_2Cl_2; (iv) the activation parameters ($\Delta H\ddagger = 16.5\,kJ\,mol^{-1}$ and $\Delta S\ddagger = -237\,J\,K^{-1}\,mol^{-1}$) of this unimolecular reaction with a high value of the activation entropy indicate that transition-state formation involves a rather complex structural change or an (energetically) improbable structure involving solvent molecules.

The significant effect upon addition of DMF (without any detectable saturation effect) can be explained by the higher normalized donicity of DMF with respect to CH_2Cl_2 (DMF and CH_2Cl_2: DN^N 0.69 and 0.00, respectively)[12b] *i.e.* on their relative basicitiy (or nucleophilicity). Accordingly addition of triethylamine or piperidine causes a large enhancement of the reactivity. The dependence of the kinetic constant on the amine concentration is linear and can be expressed by eqns. (1) and (2) (errors are standard deviations).

$$k_{obs} = (-7 \pm 18) \times 10^{-5} + (5.77 \pm 0.02) \times 10^{-2}[Et_3N] \qquad (r = 0.997) \qquad (1)$$

$$k_{obs} = (6 \pm 3) \times 10^{-4} + (1.00 \pm 0.05)[PIP] \qquad (r = 0.992) \qquad (2)$$

Consequently, the transformation **2A** → **2B** is difficult to be termed a spontaneous 1,3-proton shift process, but probably involves a proton donor/acceptor interaction for the formation of anion **5** and its resonance structures.



$$(BTZ)_2\overset{-}{C}\text{—}\overset{H}{\overset{|}{C}}(BTZ)_2$$

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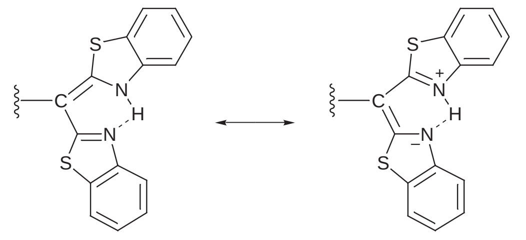
We were able to observe the transformation **2A** → **2B** but not the reverse reaction. While deprotonation of ammonium ions[13] is a very fast process, deprotonation of proton sponges usually shows a very low rate[14] of proton transfer to other bases (such as hydroxide ion in water) in agreement with the present findings.



Scheme 5

Experimental

Crystal Data for **2B**.—$C_{30}H_{18}N_4S_4 \cdot CH_2Cl_2$, $M = 647.6$, monoclinic, space group $P2_1/C$, $a = 20.069(3)$, $b = 13.375(2)$, $c = 21.650(3)$ Å, $\beta = 95.4(1)$, $V = 5785.6(18)$ Å^3, $Z = 8$, $F(000) = 2656$, linear absorption coefficient, $\mu = 49.6\,cm^{-1}$, unique total data = 11781, unique observed data = 3647, $R = 0.056$, $R_w = 0.059$.

We thank the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST, Roma), the Consiglio Nazionale delle Ricerche (CNR, Roma) and the University of Bologna (Progetto d'Ateneo: Biomodulatori organici: sintesi, proprietà ed applicazioni).

Techniques used: NMR (^1H, ^{13}C, DEPT, COSY, HETCOR), UV–VIS, crystallography

Schemes: 5

Figure 1: Numbering scheme of tetrakis(2-benzothiazolyl)ethane **2B**

Table 1: ^1H and ^{13}C NMR data of **2A**, **2B**, **3** and **4**

Table 2: Selected bond lengths and angles for **2B**

Table 3: Rates of conversion of **2A** in to **2B**

Table 4: Experimental data for the X-ray diffraction studies on **2B**

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Received, 21st January 1999; Accepted, 16th February 1999
Paper E/9/00579J

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