Conrotatory Ring Opening of a Cyclobuteno-benzo[*b*]thiepine and Rearrangement of the Resulting *cis,trans*-Benzo[*b*]thionine

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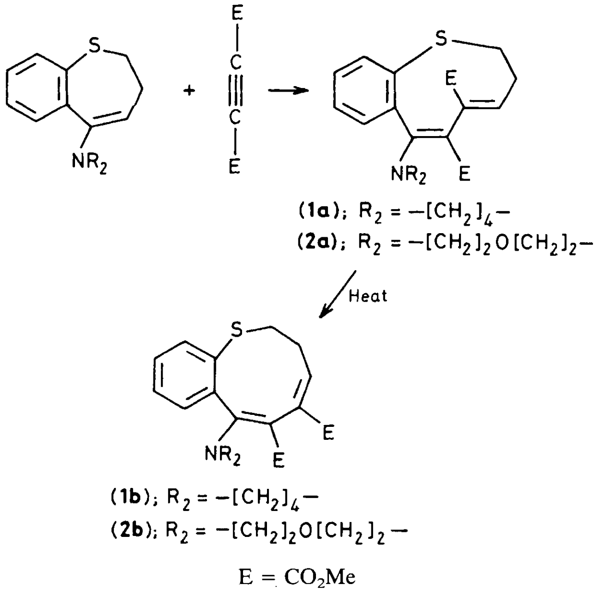
The opening of a bicyclic cyclobutene to a nine-membered ring with *cis,trans* configuration of the resulting butadiene, and the consecutive thermal transformation of this compound to the *cis,cis* isomer has been demonstrated by *X*-ray analysis; the kinetics of the *cis,trans* to *cis,cis* transformation have been studied, and both the *cis,trans* and the *cis,cis* compounds have been resolved into optical antipodes by chromatography on swollen, microcrystalline triacetylcellulose.

The recent communication by Reinhoudt *et al.*[1] on the conrotatory ring opening of *cis*-fused 3-aminocyclobutenes to *cis,trans*-cyclodienes, followed by thermal rearrangement to the *cis,cis* isomers, prompts us to publish our observation of the same reaction in a compound belonging to the benzo[*b*]-thionine system. Two of us have recently[2] described the synthesis of 2,3-dihydro-5,6-bismethoxycarbonyl-7-pyrrolidin-1-ylbenzo[*b*]thionine (**1**) *via* cycloaddition of dimethyl acetylenedicarboxylate (DMAD) to the pyrrolidine enamine of 5-oxo-2,3,4,5-tetrahydrobenzo[*b*]thiepine. In this publication the thionine was represented as the *cis,cis* isomer, in analogy with a similar eight-membered compound, for which this configuration has been found by *X*-ray crystallography.[3]



(**1a**); $R_2 = -[CH_2]_4-$
(**2a**); $R_2 = -[CH_2]_2O[CH_2]_2-$

(**1b**); $R_2 = -[CH_2]_4-$
(**2b**); $R_2 = -[CH_2]_2O[CH_2]_2-$

$E = CO_2Me$

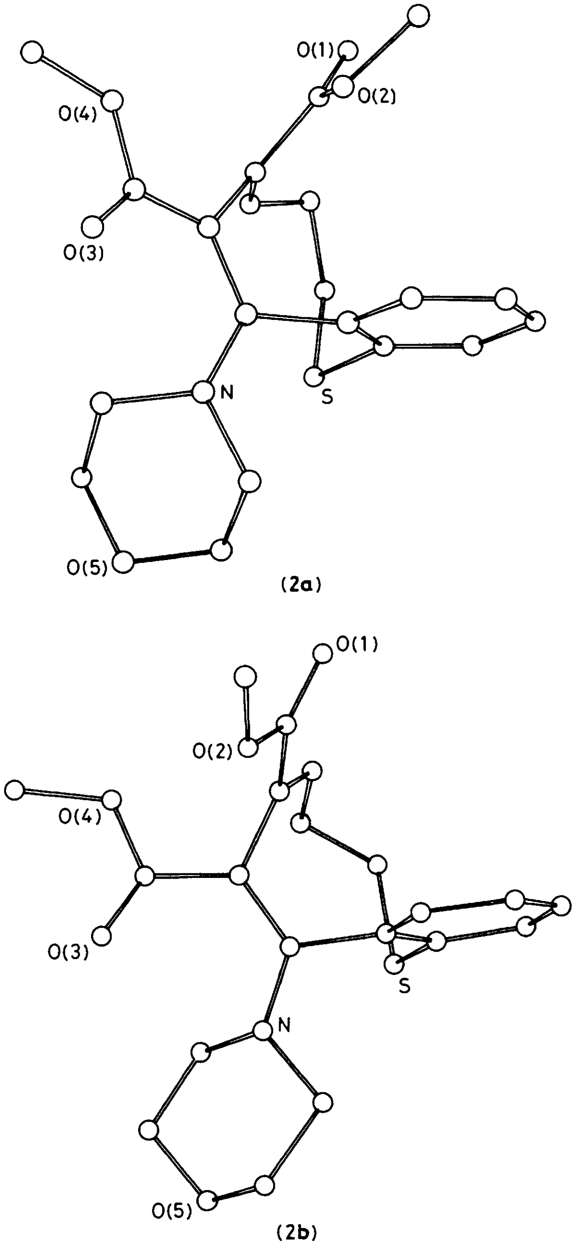


Figure 1. Computer generated pictures of the *cis,trans* (**2a**) and *cis,cis* (**2b**) forms.

As a preliminary to a study of the ring inversion of benzo[*b*]-thiocines and -thionines, the ^{1}H n.m.r. spectra of (**1**) were recorded at elevated temperatures. In the range 120—130 °C a fast, irreversible change was observed, indicating the formation of an isomeric compound. A similar behaviour was observed with the morpholine enamine adduct (**2**), and we decided to study the rearrangement in detail with this compound.

Reflux of (**2a**) in toluene for 4 h brought about complete isomerization, as shown by h.p.l.c. analysis. Both starting material and product have been studied by single crystal *X*-ray diffraction.† The initially formed adduct (**2a**) was found to have the *cis,trans,* and the rearranged product (**2b**) the *cis,cis* configuration (Figure 1). The most notable change in the ^{1}H n.m.r. spectrum is shown by the vinylic proton resonance, which is shifted from δ 6.51 to δ 6.25. It appears in both forms as a doublet of doublets, with *J* 10.6 and 3.8 Hz in (**2a**) and 9.7 and 6.1 Hz in (**2b**). Since the corresponding dihedral angles in the crystal are 160° and 79° in (**2a**), and 48° and 157° in (**2b**), assumption of a Karplus type relation[4] indicates similar conformations in solution and in the crystal.

The doublet of doublets is observed without band broadening even at +170 °C, indicating no rapid inversion of the thionine ring (on the n.m.r. time scale) even at this temperature. We have been able to resolve both (**2a**) and (**2b**) into enantiomeric pairs by liquid chromatography on swollen, microcrystalline triacetylcellulose,[5,6] and a study of the barriers to ring inversion by polarimetry is under way.

The rate of isomerization (**2a**) → (**2b**) has been determined by h.p.l.c. analysis of samples from a 1,1,2,2-tetrachloroethane solution at +90.7 °C in the presence of dry sodium carbonate to give $\Delta G^{\ddagger} = 125.0\,\text{kJ mol}^{-1}$. No product except (**2b**) is observed. The isomerization involves rotation about a double bond in an acrylic ester moiety. Free energy barriers to *cis* → *trans* isomerization in similar systems, *e.g.* methyl crotonate[7] and crotononitrile[8] (241 and 244 kJ mol^{-1} at 450 °C, respectively) are typically about twice as high as the one measured for the (**2a**) → (**2b**) isomerization, and the difference must to a large extent be ascribed to strain in the *cis,trans* thionine ring. This is corroborated by the *X*-ray structure of (**2a**), for which a dihedral angle of 145.4° is found for the *trans* C–C=C–C bonds. The reaction is strongly

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† *Crystal data:* $C_{20}H_{23}NO_5S$, $M_r = 389.5$. *cis,trans* (**2a**): monoclinic, space group $P2_1/c$, $a = 9.375(3)$, $b = 11.791(3)$, $c = 17.875(6)$ Å, $\beta = 104.37(3)°$, $U = 1914(1)$ Å^3, $F(000) = 824$, $Z = 4$, $D_c = 1.35\,\text{Mg m}^{-3}$, $\mu(\text{Mo-}K_\alpha) = 2.03\,\text{cm}^{-1}$, 2077 reflections with $I > 3\sigma(I)$. *cis,cis* (**2b**): monoclinic, spacegroup $C2/c$, $a = 17.499(3)$, $b = 16.815(6)$, $c = 13.244(6)$ Å, $\beta = 91.55(3)°$, $U = 3895(2)$ Å^3, $F(000) = 1648$, $Z = 8$, $D_c = 1.33\,\text{Mg m}^{-3}$, $\mu(\text{Mo-}K_\alpha) = 1.99\,\text{cm}^{-1}$, 2011 reflections with $I > 3\ \sigma(I)$. The two structures were solved with MULTAN 80 which revealed the positions of all non-hydrogen atoms. The atomic positions of 21 hydrogen atoms were found after least-squares refinement and difference Fourier analysis. The final refinement cycle included anisotropic temperature factors for the non-hydrogen atoms and fixed isotropic factors for the hydrogen atoms. The final *R* values were 0.060 ($R_w = 0.068$) and 0.060 ($R_w = 0.061$) for (**2a**) and (**2b**), respectively. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemistry Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

accelerated by acidic impurities, which indicates a polar mechanism for the C=C bond rotation.[9]

As was pointed out in reference 1, the orbital symmetry rules[10] predict conrotatory opening of a cyclobutene ring. As a consequence, a cyclobutene, which is *cis*-annelated to another ring, must yield a *cis,trans* or a *trans,cis* diene configuration in the expanded ring. It is worth noting that in (**2b**) (Figure 1) as well as in the *cis,cis* thiocine studied in reference 1, the tertiary amine group and the adjacent methoxycarbonyl group are *cis* related. A study of models indicates that ring opening in the opposite rotation sense would be subject to severe steric hindrance.

In our previous work[2] it was found that the six-membered thiochromanone enamine yields a cyclobutene adduct, which undergoes ring opening only at elevated temperatures, whereas the homologous seven-membered adducts open to the nine-membered ring compound so rapidly at room temperature that only the latter is observed. Reinhoudt *et al.*[1] found that the reaction between DMAD and *N*-cyclohexenylpyrrolidine yields an equilibrium mixture of the cyclobutene and its *cis,trans* cyclo-octadiene valence isomer, which is irreversibly transformed into the *cis,cis* isomer with a measurable rate at room temperature.

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