BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 43 1234—1238 (1970)

The Reaction of Sulfenyl Chlorides with Thioethers. III. The Configuration and the Isomerization of *cis*- and *trans*-α-Methylthio-β-phenylthiostyrenes

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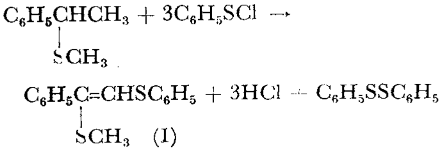
(Received November 17, 1969)

Various α-methylthio-β-arylthiostyrenes were prepared by the action of arenesulfenyl chloride on α-methylthiostyrene. The configuration of the stereoisomers of the styrene derivatives was determined by studying the nuclear Overhauser effect in the proton magnetic resonance. The relative stabilities of α-methylthio-β-phenylthiostyrene isomers were determined by equilibrating with the aid of hydrogen chloride at various temperatures.

It has been found that the treatment of methyl α-phenethyl sulfide with benzenesulfenyl chloride in carbon tetrachloride gives an isomeric mixture of *cis*- and *trans*-α-methylthio-β-phenylthiostyrenes in a 45% yield according to the following stoichiometry:



$$\underset{\displaystyle SCH_3}{C_6H_5CHCH_3} + 3C_6H_5SCl \rightarrow \underset{\displaystyle SCH_3}{C_6H_5C}{=}CHSC_6H_5 + 3HCl + C_6H_5SSC_6H_5$$

(I)

As has been shown in our previous papers,[1,2] one isomer which was predominant in the earlier stage of the reaction gradually decreased in quantity and another isomer became predominant in the later stage. That is, the formation of the olefins is kinetically-controlled, but these isomers are equilibrated even at room temperature under the present reaction conditions.

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[1] M. Ōki and K. Kobayashi, This Bulletin, **43**, 1223 (1970).

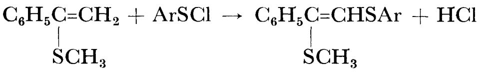
[2] M. Ōki and K. Kobayashi, *ibid.*, **43**, 1229 (1970).

Since this phenomenon seemed interesting from the standpoints of stereochemistry and the reaction mechanism, an extensive study was made of the stereochemistry of the olefins. The purpose of this paper is to report the assignment of the configuration and some pertinent data on the geometrical isomers of α-methylthio-β-phenylthiostyrene.

Results and Discussion

Separation of Isomers. The NMR spectrum of the isomeric mixture of α-methylthio-β-phenylthiostyrene shows two sharp singlets for CH_3S protons at τ 8.08 and 8.02 and two singlets for olefinic protons at τ 3.53 and 3.85. From the integration of the peaks, the signals at τ 8.08 and 3.53 are assigned to one isomer and those at τ 8.02 and 3.85 to another. Hereafter, the isomer which is obtained in a higher yield at the equilibrium will be called the isomer A, and the other, the isomer B, for the sake of simplicity in discussion. The ratio of the formation of IA and IB is calculated from the NMR integration to be approximately 3 : 1 under the present reaction conditions.

All attempts at separating isomer IA and IB ended in failure. Therefore, we aimed to separate the corresponding isomers with a substituent at the *p*-position of the phenylthio group, since it seemed that the introduction of a substituent might help the separation owing to the change in intermolecular forces. Thus, α-methylthiostyrene was treated with *p*-nitrobenzene-, *p*-bromobenzene-, *p*-chlorobenzene-, *p*-methylbenzene-, and *p*-methoxybenzene-sulfenyl chlorides; the corresponding α-methylthio-β-arylthiostyrenes (II—VI) were thus obtained:



$$\underset{\textstyle SCH_3}{C_6H_5C}{=}CH_2 + ArSCl \rightarrow \underset{\textstyle SCH_3}{C_6H_5C}{=}CHSAr + HCl$$

II: Ar=p-$NO_2C_6H_4$
III: Ar=p-BrC_6H_4
IV: Ar=p-ClC_6H_4
V: Ar=p-$CH_3C_6H_4$
VI: Ar=p-$CH_3OC_6H_4$

The *p*-nitrophenylthio derivatives (IIA and IIB) could be separated by fractional recrystallization from ethanol. The less soluble isomer was found from its NMR spectrum to be the isomer IIA; the isomer which was richer at the equilibrium was found to be less soluble. Therefore the more soluble isomer was IIB. The less soluble isomers of the *p*-bromo derivative (IIIA) and the *p*-chloro derivative (IVA) were also isolated by recrystallization.

Assignment of the Configuration. Since we will not attempt to assign all the configurations of the olefins, but to use analogy in making assignments, it will be necessary to establish the general tendency of the physical and/or chemical characteristics of the A or B series and to confirm that the analogy holds in this series. The relative stabilities have already been established from the equilibration, and it will be safe to say that the introduction of a substituent at the *p*-position of the phenylthio group will not affect the stability to such an extent that the relative stability will be reversed, since this is rather a minor change in the whole molecule.

The second criterion is the chemical shifts of the olefinic and methylthio protons of the series. As is shown in Fig. 1, the more stable isomers, the series A, always exhibit the methylthio signals at a higher field, and the olefinic proton signals, at a lower field, than the series B, except that the *p*-methoxy derivative (VI) happens to give signals of the methylthio protons of A and B at the same chemical shift. Here again, it may be assumed that the series A has the same configuration, since it is not usual to postulate that the introduction of a substituent may cause an abrupt anomaly in the chemical shifts of a series of compounds.

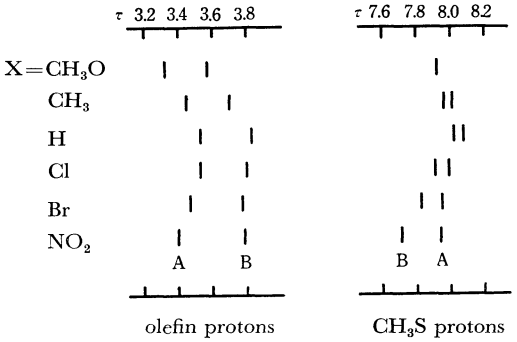


Fig. 1. Chemical shift data of the protons of α-methylthio-β-arylthiostyrenes in carbon tetrachloride solution (*ca.* 10%) except for the nitro derivative ($CDCl_3$).

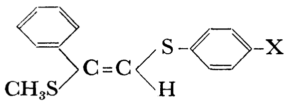
In spite of various attempts, we found it impossible to assign the configurations for the isolated isomers, IIA and IIB, on the basis of these chemical behavior: for example, attempted cyclization with ethylene iodide by heating ended only in the recovery of the starting material. The UV and the

TABLE 1. SPECTROSCOPIC DATA FOR THE GEOMETRICAL ISOMERS OF α-METHYLTHIO-β-*p*-NITROPHENYLTHIOSTYRENE (II)

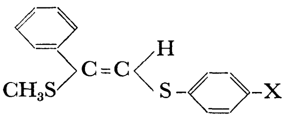
	A more stable	B less stable
mp (°C)	134—135	88—89
NMR (τ)	7.94 (3H, s)	7.71 (3H, s)
in $CDCl_3$	3.40 (1H, s)	3.79 (1H, s)
	aromatic protons	
	(5H, m: 4H, m)	(5H, s: 4H, m)
UV in C_2H_5OH	231 (14800)	223 (16800)
mμ (ε)	289 (9500)	280 (8600)
	367 (13900)	364 (12700)
IR (cm^{-1})	1337, 1095, 840	1339, 1095, 833
	761, 742, 700	761, 735, 700

IR spectra of these isomers, shown in Table 1, do not help much in assigning the stereochemistry. Although the former does show some difference in the absorption maxima, the coplanarity of the molecule can not be assumed because of the steric effect of the other groups; this assumption is, however, essential to establishing the configuration from the UV spectra.

However, the NMR spectral data in Table 1 do give some clue for elucidating the structure of the isomers. If it is assumed that the additivity rule of the chemical shifts in substituted ethylenes holds in these cases, as has been reported by Pascual and his co-workers,[3] the chemical shift of the olefinic protons in the *cis* isomer will be at a lower field than in the corresponding *trans* isomer, since it is expected that a proton *cis* to the phenyl ring and *trans* to the methylthio group will give a signal at a lower field than the counterpart, which is *trans* to the phenyl and *cis* to the methylthio group. Thus, from the additivity rule, the compounds of the series A should be assigned to the *cis* isomers:



trans



cis

It will not be safe, however, to rely too heavily on the additivity rule in the assignment, because the coplanarity of the molecule will not necessarily hold in these compounds. In order to confirm this tentative assignment, it will be necessary to use another technique in assigning the structure; the measurement of the intramolecular nuclear Overhauser effect (NOE) was chosen for this purpose.

The NOE has been increasingly used in assigning the stereochemistry of the organic compounds by identifying those protons which are in close proximity and which are coupled by dipole-dipole interaction. The transient method[4] was utilized for the NOE measurement with degassed solutions of IIA and IIB in deuteriochloroform. The magnetization of the methylthio protons was saturated by irradiating them at τ 7.94 for IIA and at τ 7.71 for IIB. After the irradiation, a transient recovery of the enhanced signal intensity of the olefinic proton to the thermal equilibrium was observed; IIB showed a definite enhancement in this process, while no change in signal intensity took place upon this treatment in IIA. From Fig. 2, it can be estimated that a 25% Overhauser enhancement is associated with IIB, whereas IIA does not show any intramolecular NOE.

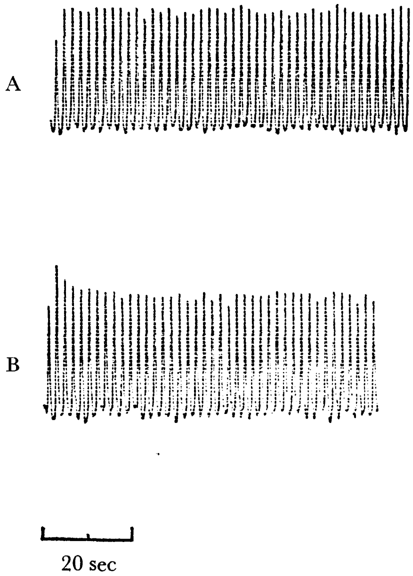


Fig. 2. Nuclear Overhauser enhancement and recovery to the thermal equilibrium of the olefinic proton.

The spin-lattice relaxation time (T_1) of the olefin proton was also measured. The estimation of T_1 is necessary because the following correlation[4,5] should be used in comparing the internuclear distance between two protons in a pair of configurational or conformational isomers:

$$d \propto \left[\frac{T_1}{\eta}\right]^{1/6}$$

where η is the nuclear Overhauser enhancement parameter; d is, in this case, the internuclear distance between the methylthio and the olefinic protons. Namely, if the T_1 of one proton is much larger than the other, it may affect the observed enhancement.

T_1 was found to be 4.7 sec for the olefinic proton of the isomer IIB, which showed a 25% enhancement of the signal intensity, whereas that for IIA was 5.8 sec. These results establish that the distance between two kinds of protons in IIB is shorter than that in IIA, since the T_1 for the olefinic proton of IIB is the smaller; if it were T_1 that was affecting the enhancement, IIA would show more enhancement than IIB.

The distance between the olefinic proton and a closest proton in the methylthio group in the *trans* isomer is estimated to be 1.5 Å from the Dreiding model, if the molecule assumes a conformation which possesses these protons at the

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[3] U. E. Matter, C. Pascual, E. Pretsch, A. Pross, W. Simon and S. Sternhell, *Tetrahedron*, **25**, 691 (1969).

[4] T. Fukumi, Y. Arata and S. Fujiwara, *J. Mol. Spectrosc.*, **27**, 443 (1968).

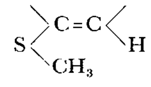
[5] F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, **87**, 5250 (1965).

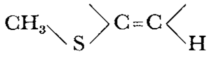
closest approach, whereas the protons in the *cis* isomer are far apart. Thus, IIA is assigned to the *cis* isomer, and IIB, to the *trans*, confirming the results obtained by the use of the additivity rule.

The NOE of the *p*-methoxyphenylthio derivative (VI) was also examined by the usual stationary state method. Although the isomers could not be separated, and although they happened to give methylthio signals at the same chemical shift, τ 7.92, the situation was rather auspicious for the NOE measurements: simple irradiation at τ 7.92 and observation of the intensities at the olefinic proton region sufficed in comparing the isomers. A degassed sample of VI, which contained *ca.* 2 : 1 isomers of A and B, was irradiated. The olefinic signal due to VIB showed 21% NOE, the amount of which was estimated from the relative change in the intensities of the two singlets at τ 3.57 (VIB) and τ 3.32 (VIA). Thus, VIB can be assigned to the *trans* isomer, and VIA, to the *cis*.

At this stage, it has been established that the isomers of the A series, which are the more stable, have the *cis* configuration, while those of the series B have the *trans* configuration.

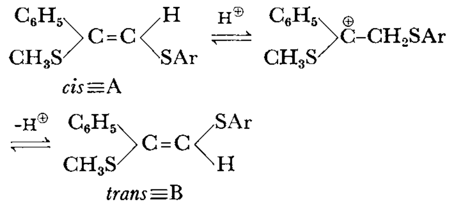
The observation of NOE enhancement for IIB and VIB indicates that the olefinic and methylthio protons are in close proximity, which would require that the carbon-sulfur bond in the methylthio group eclipse the carbon-carbon double bond (VII). If it were taking the S-*trans* conformation (VIII), the enhancement would be expected to be very small, since the distance between the two kinds of protons is estimated to be more than 4.6 Å from the Dreiding model, in contrast to 1.5 Å in the S-*cis* conformation.


(VII)


(VIII)

This conformation is supported by the analogy of the situation in methyl vinyl ether, which has been shown by microwave spectroscopy to possess the S-*cis* conformation.[6] There is also an example of NOE measurement with methyl vinyl ether derivatives in which NOE is observed between the *O*-methyl protons and the vinyl proton *cis* to each other.[7]

Relative Stabilities of the *cis-trans* Isomers. The *cis-trans* isomerization of the olefiins can be effected by the action of hydrogen chloride in carbon tetrachloride. The mechanism of the isomerization is assumed to proceed *via* a carbonium ion intermediate which is formed by addition of a proton and which forms olefins by the elimination of the proton. Incidentally, the intermediate is the same as that assumed in the addition of sulfenyl chloride to α-methylthiostyrene.



To estimate the thermodynamic parameters for the pair of *cis* and *trans* isomers, II was equilibrated with hydrogen chloride in carbon tetrachloride at four temperatures. The isomer distribution was calculated from the integration of the signal areas of the NMR spectra. The Arrhenius plot is shown in Fig. 3, while the parameters obtained therefrom are summarized in Table 2.

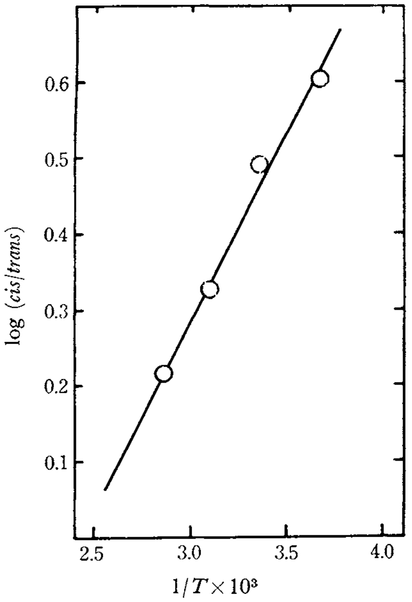


Fig. 3. Arrhenius plot for the *cis-trans* equilibration of α-methylthio-β-phenylthiostyrene.

TABLE 2. THE THERMODYNAMIC PARAMETERS FOR THE *cis-trans* EQUILIBRATION OF α-METHYLTHIO-β-PHENYLTHIOSTYRENE

ΔH	-2.2 ± 0.7 kcal/mol
ΔS	-5 ± 2 e.u.

Although the reasons for the stability of the *cis* isomer relative to the *trans* are not completely understood at the present time, two factors may be considered. The first factor may be of the steric origin. If it is assumed (and it is common to assume) that the steric effect in the olefinic compound is determined by the first atom which directly

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[6] P. Cahill, L. P. Gold and N. L. Owen, *J. Chem. Phys.*, **48**, 1620 (1968).

[7] M. C. Woods, I. Miura, A. Ogiso, M. Kurabayashi and H. Mishima, *Tetrahedron Lett.*, **1968**, 2009.

Table 3. α-Methylthio-β-arylthiostyrenes ($C_6H_5C(SCH_3):CHSC_6H_4X$-*p*)

X	NMR (τ)		Molecular formula	Analyses			
				calcd		found	
	SCH_3	=CH		C	H	C	H
OCH_3	A 7.92 B 7.92	3.32 3.57	$C_{16}H_{16}OS_2$	66.63	5.59	66.86	5.48
CH_3	A 8.01 B 7.96	3.45 3.70	$C_{16}H_{16}S_2$	70.54	5.92	70.34	6.18
Cl	A 7.99 B 7.91	3.53 3.80	$C_{15}H_{13}ClS_2$	61.51	4.47	61.42	4.21
Br	A 7.95 B 7.91	3.53 3.80	$C_{15}H_{13}BrS_2$	53.41	3.88	53.63	3.94
NO_2	A 7.94 B 7.71	3.40 3.79	$C_{15}H_{13}NO_2S_2$	59.38	4.32	59.18 59.45	4.52 4.21

attaches to the double bond, when there is freedom of rotation for the other part, sulfur must play the main role in determining the steric effect in the methylthio and arylthio groups; by appropriate rotation, methyl and aryl groups can take conformations in which these groups have little steric effect. Therefore, it is the van der Waals radius of the sulfur atom that should be taken into account; it is usually taken as 1.85 Å. The half-thickness of the benzene ring is also estimated to be 1.85 Å. Therefore, if the benzene ring is perpendicular with respect to the olefinic bond, the steric effect on the conformational energy will be almost the same in both isomers. However, due to the delocalization energy to be gained at the coplanar conformation, the benzene ring will come as close by as possible to the planar conformation. This, of course, increases the apparent van der Waals radius of the benzene ring; the steric interaction between the phenyl and the arylthio groups is then larger than that between the methylthio ant the arylthio groups. The steric factor, therefore, may favor the *cis* configuration.

There is another factor to be considered; it may be called the electrostatic interaction. It has been well known that the *cis* isomer is more stable than the *trans* in 1,2-dihaloethylenes,[8-10] although halogens are much larger than hydrogen. The cause for this phenomenon may be the dispersion force, and the same effect may be operating in the series of compounds discussed in this paper.

The separation of these factors is not at all possible at the present time and awaits further studies.

Experimental

The General Method for the Preparation of α-Methylthio-β-arylthiostyrenes. To a solution of 6 g (0.04 mol) of α-methylthiostyrene[2] in 50 m*l* of dry carbon tetrachloride, equimolar arenesulfenyl chloride in 25 m*l* of carbon tetrachloride was slowly added at 0°C; hydrogen chloride was then evolved. The solution was allowed to stand for another hour after the color of the sulfenyl chloride had essentially faded, and then poured into 100 m*l* of aqueous sodium carbonate. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was chromatographed on alumina to give 75—95% yields of α-methylthio-β-arylthiostyrene.

Isolation of Isomers. In the case of α-methylthio-β-*p*-nitrophenylthiostyrene, the remaining yellow solid was fractionally recrystallized from ethanol to give the *cis* isomer, mp 134—135°C, as a less soluble part and the *trans*, mp 88—89°C, as a more soluble part.

In the cases of α-methylthio-β-*p*-chlorophenylthiostyrene and α-methylthio-β-*p*-bromophenylthiostyrene, on long standing they gave crystals which were then separated from the oil and recrystallized from petroleum ether to give the *cis* isomers. The mp's of the chloro and bromo derivatives were 91°C and 92—93°C respectively.

Equilibration of *cis*- and *trans*-α-Methylthio-β-phenylthiostyrenes. The title isomers were equilibrated by maintaining a carbon tetrachloride solution, into which hydrogen chloride was introduced, at the specific temperature for 30 min. The temperatures at which the equilibration was carried out were 0, 25, 50, and 77°C. The products were analyzed by means of the NMR spectra of the reaction mixture after washing the solution with aqueous alkali and then drying it.

NOE Measurements. The NOE measurements were carried out with a Japan Electron Optics 4H-100 spectrometer operating at 100 MHz. The transient NOE was observed in the "HR mode," employing the usual double-resonance technique. In measuring the spin-lattice relaxation time, the magnetization of the olefin proton was inverted adiabatically and the recovery of the magnetization was observed by scanning through the resonance with a weak rf field.

The samples were dissolved in deuteriochloroform (in the case of II) or in carbon tetrachloride (in the case cf VI) to make a *ca.* 15% solution, which was then degassed and sealed.

The authors are indebted to Mr. T. Fukumi for the NOE measurements.

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[8] H. Steinmetz and R. M. Noyes, *J. Amer. Chem. Soc.*, **74**, 4141 (1952).

[9] K. S. Pitzer and J. L. Hollenberg, *ibid.*, **76**, 1493 (1954).

[10] H. G. Viehe, *Chem. Ber.*, **93**, 1697 (1960).