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Kinetic Study for Addition Rates of Phenylthio Radicals to *cis*- and *trans*-β-Methylstyrenes

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The rate constants for the addition reactions of the substituted phenylthio radicals with *cis*- and *trans*-β-methylstyrenes were estimated by a flash photolysis method. The rate constants for these internal olefins are smaller than those for α-methylstyrene by a factor of ca. 10–20 for each phenylthio radical; this is ascribed to the blocking effect of the methyl group attached to the β-position. The rates for the trans isomer are faster than the corresponding ones for the cis isomer by a factor of ca. 2–3. Since the polar effect is similar for both isomers, the higher reactivity of the trans isomer is ascribed to the greater resonance stabilization of the transition state, which increases with the overlap of the π-orbitals between the olefinic double bond and the phenyl ring at C_α. This is confirmed by the relative equilibrium constants estimated by the flash photolysis method. The reactivity of indene was also examined as a model of the planar cis conformation.

For the addition reactions of the free radicals to the cis and trans olefins, Lewis and Mayo first reported that the trans isomer is more reactive than the cis isomer.[1] Szwarc et al. found a similar tendency in the methyl radical affinity.[2,3] These steric effects have been verified by the measurements of the monomer reactivity ratios in the copolymerization reactions.[4,5] These results, however, are discussed on the basis of the measurements of the relative rate constants. The object of the present investigation is to estimate the difference in the absolute rate constants between cis and trans isomers.

To obtain some desired information, we investigate the addition reactions of the phenylthio radicals (PhS·) with *cis*- and *trans*-β-methylstyrenes and indene by means of the flash photolysis. The addition process of the phenylthio radical is reversible, and the rate constant can be estimated by the addition of a selective radical trap which is reactive only to the adduct carbon-centered radical; in this reaction system oxygen acts as a selective radical trap as shown in Scheme I.[6,7]

Scheme I

$$\mathrm{PhS\cdot} + \mathrm{(CH_3)CH{=}CHPh} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{PhSCH(CH_3)C\cdot HPh} \xrightarrow[k_2]{O_2} \text{peroxy radical}$$

The forward rate constants (k_1) are obtained as the absolute values and the backward rate constants (k_{-1}) and the equilibrium constants ($K = k_1/k_{-1}$) are estimated as relative values to the k_2 value. These data permit us to discuss the reactivities on the basis of the thermodynamic parameters. In order to investigate the polar nature of the reactions, the substituent effect of the phenylthio radicals is examined. Then, the difference in the resonance stabilization energy in the transition state among the isomers will be discussed.

Table I. Rate Constants (k_1) and the Equilibrium Constants (Kk_2) for the Addition Reactions of $p\text{-}XC_6H_4S\cdot$ toward *cis*-β-Methylstyrene in Cyclohexane at 23 °C[a]

X	k_1, $M^{-1}\ s^{-1}$	Kk_2, $M^{-2}\ s^{-1}$
Br	4.8×10^6	2.0×10^9
Cl	3.7×10^6	2.1×10^9
H	2.1×10^6	1.1×10^9
$t\text{-}C_4H_9$	8.8×10^5	4.2×10^8
CH_3	6.2×10^5	4.2×10^8
OCH_3	9.3×10^4	3.5×10^7
NH_2	9.1×10^3	4.8×10^6

[a] Estimation errors of ±10%.

Table II. Rate Constants (k_1) and the Equilibrium Constants (Kk_2) for the Addition Reactions of $p\text{-}XC_6H_4S\cdot$ toward *trans*-β-Methylstyrene in Cyclohexane at 23 °C[a]

X	k_1, $M^{-1}\ s^{-1}$	Kk_2, $M^{-2}\ s^{-1}$
Br	1.2×10^7	6.1×10^9
Cl	1.2×10^7	5.2×10^9
H	6.8×10^6	3.4×10^9
$t\text{-}C_4H_9$	2.2×10^6	8.4×10^8
CH_3	2.0×10^6	8.3×10^8
OCH_3	2.7×10^5	1.2×10^8
NH_2	3.7×10^4	1.1×10^7

[a] Estimation errors of ±10%.

Results and Discussion

Transient absorption bands at 490–550 nm generated by the flash photodecomposition of diaryl disulfides were attributed to the corresponding substituted benzenethio radicals.[8] From second-order kinetics for the decay of PhS·, the concentration of PhS· produced by each flash exposure was estimated to be lower than ca. 10^{-6} M by assuming the diffusion-controlled recombination reaction.[9] The low reactivity of PhS· toward oxygen dissolved in solution was confirmed by the flash photolysis experiment.[6] The reversibility of the addition process of PhS· toward β-methylstyrenes was confirmed by the finding that the decay rate of PhS· was not accelerated by the addition of β-methylstyrene into the degassed solution. Oxygen acts as a selective radical trap to the adduct carbon-centered radical since the decay rate of PhS· increases when β-methylstyrene and oxygen coexist.[6] These findings are shown in Scheme I. The addition products for the reaction of PhS· with indene in the presence of oxygen were identified by Ford, Pitkethly and Young.[10]

When oxygen (10^{-4}–10^{-2} M) and olefins (10^{-3}–10^{-1} M) are in large excess compared with PhS· (ca. 10^{-6} M), decay kinetics of PhS· approaches first order. The pseudo-

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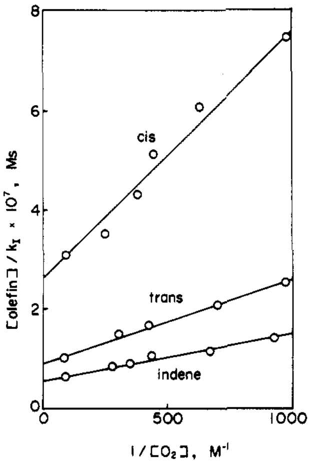

Figure 1. Plots of [olefin]/k_I vs. $1/[O_2]$ (eq 1) for the reaction systems of p-$ClC_6H_4S\cdot$ and olefins.

Table III. Rate Constants (k_1) and the Equilibrium Constants (Kk_2) for the Addition Reactions of p-$XC_6H_4S\cdot$ toward Indene in Cyclohexane at 23 °C[a]

X	k_1, M^{-1} s^{-1}	Kk_2, M^{-2} s^{-1}
Br	2.9×10^7	1.9×10^{10}
Cl	1.8×10^7	1.1×10^{10}
H	1.2×10^7	7.7×10^9
t-C_4H_9	4.2×10^6	2.2×10^9
CH_3	3.0×10^6	2.0×10^9
OCH_3	3.1×10^5	2.4×10^8
NH_2	4.7×10^4	7.2×10^7

[a] Estimation errors of ±10%.

first-order rate constant (k_I) can be represented by eq 1, since the concentration of the carbon-centered radical is approximated by the steady-state assumption (Scheme I).[6]

$$[(CH_3)CH{=}CHPh]/k_I = 1/k_1 + k_{-1}/k_1k_2[O_2] \quad (1)$$

Figure 1 shows the plots of eq 1 for the reaction systems of p-$ClC_6H_4S\cdot$ with *cis*- and *trans*-β-methylstyrenes and indene. Fairly good straight lines were obtained. The intercept and slope yield $1/k_1$ and k_{-1}/k_1k_2, respectively. From these values the k_1, k_{-1}/k_2, and Kk_2 values were calculated. The k_1 and Kk_2 values are summarized in Table I for the cis isomer, in Table II for the trans isomer, and in Table III for indene. The k_{-1}/k_2 values can be calculated by dividing k_1 by Kk_2. The above method was first found by us and recently confirmed by Kuntz et al.[11]

For various free radicals, the relative reactivities of *cis*- and *trans*-β-methylstyrenes, indene, and α-methylstyrene were measured by the conventional methods;[3,12] some of them are summarized in Table IV. A fairly good agreement among the reactivity ratios is found except for the reaction of $\cdot SCH_2COOCH_3$ with indene.[12] The k_1 value for the PhS·–α-methylstyrene reaction system is cited from our data previously estimated by the flash photolysis method.[13] The blocking effect of the methyl substituent at the β-position in the styrene moiety is apparent. The higher reactivity of the trans isomer than the cis isomer observed for the phenylthio radical is in good agreement with the methyl affinity;[3] the reactivity ratios are compatible with the relative rates of the acrylonitrile radical (trans/cis ratio of 2.8).[5] Indene is more reactive than *trans*-β-methylstyrene; the ratio is ca. 2 for the phenylthio radical.

Table IV. Relative Reactivities of α- and β-Methylstyrenes and Indene for Various Radicals

	relative reactivity[d]			
radical	α-MSt	*trans*- β-MSt	*cis*- β-MSt	indene
$\cdot SPh$	1.0[a]	0.10	0.03	0.17
$\cdot SCH_2COOCH_3$[b]	1.0	0.14		0.47
$\cdot CH_3$[b]	1.0	0.10	0.04	0.11

[a] Reference 13. [b] Reference 12. [c] Reference 3. [d] Abbreviations of olefins: α-MSt, α-methylstyrene; β-MSt, β-methylstyrene.

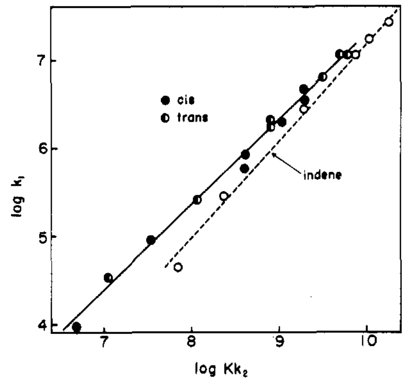

Figure 2. Plots of log k_1 vs. log Kk_2: ●, *cis*-β-methylstyrene; ◐, *trans*-β-methylstyrene; ○, indene. The slope for *cis*- and *trans*-β-methylstyrenes is 0.95 ± 0.02 and that for indene is 1.10 ± 0.04.

The K and k_{-1} values can be calculated from the values in Tables I–III by assuming an appropriate k_2 value; for example, by assuming $k_2 = 10^8$–10^9 M^{-1} s^{-1},[14-16] one can see that the K values are in the range of 10^{-2}–10^2 M^{-1} and that the k_{-1} values are 10^5–10^6 s^{-1}. Since the flash duration of the xenon lamp is ca. 10 μs, the equilibrium in Scheme I is established during the flash duration. From the K values, the reactions of the phenylthio radicals with the electron-withdrawing substituents are more exothermic than those for the electron-donating substituents for each olefin.[17]

Figure 2 shows the plots of log k_1 vs. log Kk_2; a fairly good linear free-energy relationship is found. Since the log K values for each olefin are a measure of the thermodynamic stabilities of the substituted phenylthio radicals, the substituent effect on the k_1 values is mainly determined by the stabilities of the phenylthio radicals at the reactants. The line for *trans*-β-methylstyrene overlaps with that for the cis isomer (slope = 0.95 ± 0.02). This suggests the same frequency factor of the Arrhenius equation for both isomers; i.e., the entropy of activation is quite similar for both isomers.[18,19] The slope for indene (1.10 ± 0.04) is slightly different; this may be caused by a different frequency factor and/or by some other factors such as the polar nature of the reactions and a release of the strain energy.

In order to investigate the polar nature of the reactions, we plotted the rate constants for the forward reaction and the equilibrium constants against the Hammett substitu-

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(16) The k_2 values for the resonance-stabilized radicals such as the benzyl-type radicals are ca. 10^2 lower than the diffusion-controlled limit.[15]

(17) Since negative entropy is expected for the addition reaction, the reaction may be quite exothermic even when $K \approx 1$.

(18) Hammett, L. P. "Physical Organic Chemistry"; McGraw-Hill: London, 1970; p 107.

(19) The frequency factor and activation energy are related to $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$, respectively.[18]

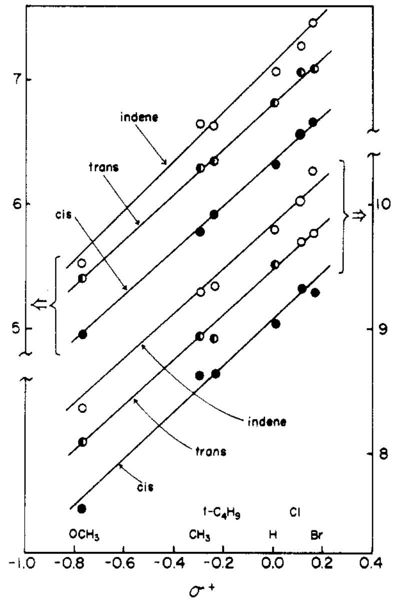


Figure 3. Hammett plots of log k_1 or log Kk_2 vs. σ^+:$\rho^+(k_1) = 1.76 \pm 0.04$ for *cis-* and *trans-β*-methylstyrene, $\rho^+(k_1) = 2.04 \pm 0.02$ for indene, and $\rho^+(Kk_2) = 1.85 \pm 0.02$ for these olefins. The values for *p*-$NH_2C_6H_4S\cdot$ are fitted to the lines at $\sigma^+ = 1.40$.

ent constants (σ^+) in Figure 3. Fairly good linear lines are obtained with the plots vs. σ^+, while the plots vs. σ show curves with downward curvatures. The linear correlation of log Kk_2 with σ^+ indicates that the stabilities of the phenylthio radicals are affected by the resonance effect in addition to the inductive effect. The positive slopes in the plots for the log Kk_2 values ($\rho^+ = 1.85 \pm 0.02$) show that the phenylthio radicals are stabilized by the electron-donating substituents.[20] In general, the substituent effect on the reactivities for each olefin is controlled both by the thermodynamic stabilities of the phenylthio radicals as the linear free energy relationship in Figure 2 suggests and by the polar nature of the transition state.[21] The ρ^+ values for the reactivities ($\rho^+(k_1)$) can be represented as eq 2.[21] Here α and γ denote the proportionality constant

$$\rho^+(k_1)/\rho^+(Kk_2) = \alpha + \gamma \qquad (2)$$

for the linear free energy relationship and the contribution of the polar resonance structures to the transition state, respectively. When there is the contribution of [PhS^-,-olefin$^+\cdot$], γ refers to a positive value; such a contribution may change linearly with the σ^+ constants. The slopes in Figure 2 are equal to $\rho^+(k_1)/\rho^+(Kk_2)$. The α value for *cis-* and *trans-β*-methylstyrenes is the same since the α value is not variable for the same type reactions with similar rates;[22] therefore, the similar $\rho^+(k_1)$ value observed in Figure 3 for both isomers (1.75 ± 0.04) suggests that the contribution of the polar transition state to the reactivities (γ) is also same. Thus, the difference in the reactivities between the cis and trans isomers can be attributed to the difference in the exothermicity of the reactions.

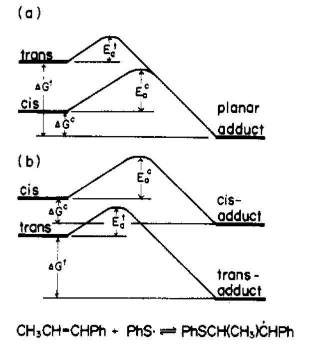
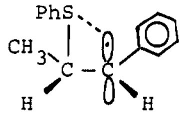
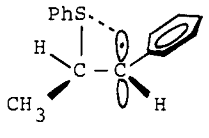


Figure 4. Energy diagrams for the addition reactions of the phenylthio radicals ($PhS\cdot$) with *cis-* and *trans-β*-methylstyrenes: (a) both adducts produced from cis and trans olefins are assumed to be the same structure, and (b) the planar trans adduct is more stable than the angular cis adduct. The activation energy for the trans isomer (E_{at}) is smaller than that for the cis isomer (E_a^c). The free-energy change for the trans isomer (ΔG^t) is greater than that for the cis isomer (ΔG^c) as the log Kk_2 values suggest. The slopes of the potential curves and the polar nature of the transition state are same for both isomers.

On the basis of the assumption that the adduct carbon-centered radicals generated from the cis and trans isomers have the same structure, i.e., the phenyl ring at the α-position is coplanar with the olefinic plane, the larger Kk_2 value of the trans isomer compared with that of the cis isomer for each phenylthio radical indicates that *trans-β*-methylstyrene in the reactant stage is less stable than the cis isomer (Figure 4a). The heats of hydrogenation, however, predict that the trans isomer is more stable than the cis isomer.[1,2] Therefore, we must consider other models for the adduct radicals; i.e., oxygen traps the adduct radicals having structures similar to those of the transition states which maintain conformations similar to those of the corresponding olefins in the reactants. This is reasonable if the adduct radicals react rapidly with oxygen before the relaxation to the stable planar benzyl-type radicals. This model suggests that the rotation of the C_α–C_β bond in the adduct is interfered with for some reason; i.e., there is the interaction between the sulfur atom and the radical center as was proposed from the analysis of the stereospecific product[23] and from the ESR measurements.[24] The following adduct radicals may be formed from *cis-* and *trans-β*-methylstyrenes.[23,24]



cis adduct



trans adduct

In the trans adduct the resonance stabilization of the unpaired electron on the radical center is greater than that of the cis adduct since the p orbital at C_α is coplanar with those of the phenyl ring. Thus, the trans adduct in the product and the trans olefin in the reactant are more stable than the corresponding ones for the cis isomer. Therefore, the low activation energy of the trans isomer can be expected when there exists a large free energy gap between the radical adducts than between the starting olefins, which is deduced from the observation that the K value for trans isomer is larger than that for the cis isomer (Figure 4b).[25]

Indene is more reactive than *trans-β*-methylstyrene. The slope of the linear free energy relationship (Figure 2)

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[20] The $\rho^+(Kk_2)$ values estimated in this study are slightly greater than those for vinyl monomers estimated by the same method (Ito, O.; Matsuda, M. *J. Am. Chem. Soc.* **1981**, *103*, 5871). Such a difference can be caused when the k_2 values are variable with the substituents of the phenylthio moiety in the adduct radical.

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[25] The entropy change between the reactant and product may be similar for both isomers since the radical adducts maintain the similar conformations to the corresponding olefins. It is also expected that the k_2 value for the cis adduct is greater than that for the trans adduct; thus, the difference in the K values between both isomer increases.

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indicates the difference in the frequency factor of the Arrhenius equation. The greater polar nature is deduced from the greater $\rho^+(k_1)$ value. The greater Kk_2 value for each phenylthio radical suggests that the reaction of indene is highly exothermic, owing to the release of the strain energy of the five-membered ring, or that the adduct radical of indene having cis planar conformation is more stable than that for the slightly angular trans adduct (dihedral angle of *trans*-β-methylstyrene is 12°).[26] Some of above factors cooperate in order to control the reactivity of indene.

Experimental Section

Indene and *cis*- and *trans*-β-methylstyrenes (Aldrich Chemical Co.) were distilled under reduced pressure before use. Disulfides were purified by recrystallization from ethanol. Cyclohexane used as a solvent was of spectrophotometric grade.

Xenon flash photolysis apparatus was of standard design;[27] the flash duration and energy of the xenon lamps (Xenon Corp., N-851C) were ca. 10 μs and 130 J, respectively. Flash photolysis of the disulfides was performed in a 10-cm cylindrical cell with light of wavelength longer than 350 nm, which does not excite the olefins. Kinetic observations were made with a continuously monitored light source and photomultiplier detection. The oxygen concentration in cyclohexane was calculated from Henry's law using the partial oxygen pressure.[28]

Registry No. *p*-$BrC_6H_4S\cdot$, 31053-90-4; *p*-$ClC_6H_4S\cdot$, 31053-91-5; $C_6H_5S\cdot$, 4985-62-0; *p*-*t*-$C_4H_9C_6H_4S\cdot$, 81372-23-8; *p*-$CH_3C_6H_4S\cdot$, 31053-92-6; *p*-$CH_3OC_6H_4S\cdot$, 31053-93-7; *p*-$NH_2C_6H_4S\cdot$, 31053-95-9; *cis*-β-methylstyrene, 766-90-5; *trans*-β-methylestyrene, 873-66-5; indene, 95-13-6.

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Stereoelectronic Effects in Tertiary Amine Nitrosation: Nitrosative Cleavage vs. Aryl Ring Nitration

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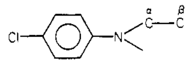
The nitrosation (acetic acid) of *N*-(4-chlorophenyl)pyrrolidine gives at least 30% *N*-(4-chloro-2-nitrophenyl)pyrrolidine while the corresponding aryldibenzylamine gives no nitration and only nitrosative dealkylation at nitrogen. This difference in reaction site has been probed with *N*-(4-chlorophenyl)diethylamine. This substance undergoes competitive ring nitration to *N*-(4-chloro-2-nitrophenyl)diethylamine (50%) and nitrosative dealkylation to (4-chlorophenyl)ethylnitrosamine (50%). The former compound nitrosates further to give (4-chloro-2-nitrophenyl)ethylnitrosamine. This substance denitrosates to give the corresponding secondary amine. The reactivity differences result from stereoelectronic factors controlling the amine nitrogen unshared pair delocalization into the aryl ring. This interpretation is supported by ^{13}C NMR data and mechanistic arguments.

As the awareness that certain environmental chemicals cause cancer has grown, so has the realization that prevention or, at least, reduction of the disease prevelance can be attained through a knowledge of the chemistry of carcinogen production and transformation. Tobacco products and smoke, for example, are known to contain variable trace quantities of nitrosamines,[1] substances that are recognized as potent animal carcinogens.[2] In a fundamental study of nitrosation of nicotine in aqueous acid, Hecht and co-workers[3] found a number of unusual trace nitrosamine products to be formed from the pyrrolidine ring in addition to those major ones, which were produced in accord with expectations from previous studies of tertiary amine nitrosation.[4] With the exception of Hecht's work, there has been no published thorough investigation of heterocyclic tertiary amine nitrosation despite the ubiquity of such compounds in the environment.

To initiate our study of heterocyclic tertiary amine nitrosation we began by investigating the reaction of *N*-(4-chlorophenyl)pyrrolidine (1) with nitrous acid at 80–90 °C. While this reaction gives a complex array of products, the characterization and chemistry of which will be the subject of a forthcoming publication from our laboratory, we found a major product to be *N*-(4-chloro-2-nitrophenyl)pyrrolidine (2). Aryl ring nitration accompanying tertiary amine nitrosation certainly has precedent and is not new.[4,5] In this case, however, it was unexpected because *N*-(4-chlorophenyl)dibenzylamine (3) apparently gave only nitrosative debenzylation and no aryl ring nitration.[4]

Table I. ^{13}C NMR Chemical Shifts for Amines (ppm)



compd[a]	1	2	3	4	α	β
1	147.0	112.9	129.0	120.7	48.1	25.9
4	147.0	113.3	129.3	120.6	45.0	12.6
3	148.4	114.2	129.0	122.1	55.0	

[a] Ph C_1–C_4: 138.8, 129.0, 127.0, 127.3

In this paper we present the results of our investigation into this apparent discrepancy. We have reinvestigated the nitrosation of 3 and found the initial report to be

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