

벤질브로미드와 티오벤즈아미드의 반응에 있어서의  
 반응속도와 반응메카니즘

洪 淳 瑛 · 呂 壽 東\*

한양대학교 화학과

(1972. 5. 10 접수)

Kinetics and Mechanism of the Reaction of  
 Benzyl Bromide with Thiobenzamides

Soon-Yung Hong and Soo-Dong Yoh\*

Department of Chemistry, Hanyang University

(Received May 10, 1972)

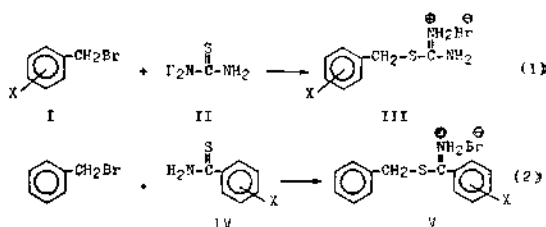
**요약** 벤질브로미드와 여러가지 *m*- 또는 *p*-핵치환 티오벤즈아미드류와의 반응속도를 전기전도도법으로 측정하였다. 이들 반응에서 전자흡인치환기는 반응속도를 촉진하였고 한편 전자공여치환기는 반응속도를 억제하였다. 이 사실에 부합하는 반응 메카니즘을 고찰하였다. 추가하여 이들 반응에 있어서의 활성화에너지와 활성화엔트로피를 산출하였다.

**Abstract** Rates of the reactions of *m*- and *p*-ring-substituted thiobenzamides with benzyl bromide in acetone have been determined by an electric conductivity method. The Hammett rule has been adopted for these reactions. It has been observed that an electron-attracting substituent accelerates the reaction while an electron-donating substituent retards the reaction, and a mechanism which accounts for the observed kinetics has been postulated. The activation energies and entropies of activation for these reactions have also been calculated.

Introduction

Previously we have studied the kinetics of the reactions of *m*- and *p*-substituted benzyl bromides with thiourea in ethanol<sup>1</sup>, and postulated that the C-Br bond cleavage in benzyl bromide is the rate-determining step in this S<sub>N</sub>2

reaction (Eq. 1). The present work has been undertaken to determine the quantitative effect of substituent on the nucleophilic sulfur atom



\* Department of Chemistry, Osaka University, Osaka, Japan

Table 1. Physical Properties of Thiobenzamides

Compounds	Melting Point (°C)		Appearance
	Observed	Literature	
Thiobenzamide	116	115-116	Colorless needles
<i>p</i> -Methylthiobenzamide	167	168	Colorless needles
<i>m</i> -Methylthiobenzamide	88-89	90-91	Colorless needles
<i>p</i> -Methoxythiobenzamide	149	149	Colorless needles
<i>p</i> -Chlorothiobenzamide	131	130	Colorless needles
<i>p</i> -Nitrothiobenzamide	159-160	158.5-159.5 <sup>a</sup>	Pale yellow needles

of thioamide, and to investigate a pertinent mechanism for the reaction of benzyl bromide with thioamide. To do so, *m*- and *p*-ring-substituted thiobenzamides were utilized as nucleophilic reagents as shown in Eq. 2.

### Experimental

**Preparation of thiobenzamides** Thiobenzamide and *m*- or *p*-substituted thiobenzamides were prepared from their corresponding benzonitriles (Reagent Grade, Aldrich Chemicals, U. S. A.). Hydrogen sulfide was bubbled through pyridine solution of benzonitriles using triethylamine as a catalyst.<sup>2</sup> The products as charac-

terized are shown in Table 1. Since the physical properties of the products are well coincided with those in the literature, a further analysis has not been attempted.

**Preparation of *s*-benzylisothiobenzamidinium bromide** This compound was prepared according to the procedure of *s*-benzylisothiobenzamidinium chloride synthesis.<sup>4</sup> A mixture of 0.1 mole of thiobenzamide and 0.1 mole of benzyl bromide (Aldrich Chemicals) dissolved in 200 ml of acetone was refluxed for 30 min. The product was collected by suction, and recrystallized twice from acetone. Colorless needles were obtained with mp 177-178°.

**Anal.** The elemental analysis was performed by the Galbraith Laboratories, Inc., Knoxville, Tenn., U. S. A. Calcd for C<sub>14</sub>H<sub>14</sub>NSBr: C, 54.55; H, 4.58; N, 4.54; S, 10.40; Br, 25.92. Found: C, 54.02; H, 4.58; N, 4.81; S, 10.07; Br, 27.51.

**IR Spectrum** Eliminated hydrogen bromide from this compound by aqueous ammonium hydroxide and obtained a product supposed to be *s*-benzylisothiobenzamide, C<sub>8</sub>H<sub>8</sub>CH<sub>2</sub>SC(=N)C<sub>6</sub>H<sub>5</sub>. An IR spectrum and mp (125°) of this amide were exactly the same as those of the amide obtained from the known compound, *s*-benzylisothiobenzamidinium chloride. Absorptions around 3400 cm<sup>-1</sup> and 1670 cm<sup>-1</sup> supposed

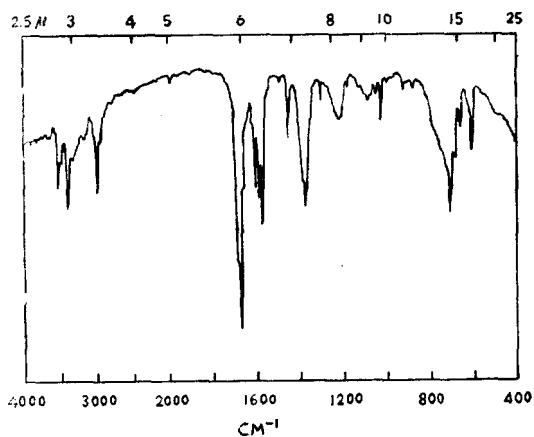


Fig. 1. IR Spectrum of *s*-benzylisothiobenzamide in chloroform.

to correspond with the N-H stretching vibration<sup>5</sup> of the imino group, =N-H, and the C=N stretching vibration<sup>6</sup> were observed respectively. The spectrum was obtained by the Hitachi Grating Infrared Spectrophotometer, Model EPI-G<sub>2</sub> with a KBr cell using CHCl<sub>3</sub> as a solvent.

**NMR Spectrum** The NMR spectrum was recorded on a Varian A-60(60 Mc) spectrometer using tetramethylsilane (TMS) as an internal standard. A solvent, CDCl<sub>3</sub> was employed. The NMR spectrum, together with the IR spectrum, provides an almost confirmative conclusion of the structure of this compound to be V in Eq. 2. Two protons at 5.1 ppm (singlet) corresponding to the methylene group substituted by a phenyl group and an isothiobenzamidinium group, ten phenylic protons at 7.5 ppm (multiplet), and two protons at 8.2 ppm (two doublet) supposed to be caused by the imidinium group were observed (Fig. 2).

**Kinetics** The kinetic apparatus and procedure to measure the rates of the reactions of benzyl bromide, with substituted thiobenzamides by an electric conductivity method, were exactly the same as those used previously.<sup>1</sup> The electric conductivity of 10 ml of 0.005 mole acetone solution of thiobenzamide ( $\kappa_a$ ) and that of 0.005 mole acetone solution of benzyl bromides ( $\kappa_b$ ) were measured respectively. Then the electric

conductivity of the mixture of the above two solutions ( $\kappa$ ) was measured at given times. Second-order rate constants of the reaction were derived from the following equations<sup>7</sup> (3) and (4).

$$kC_0t = \frac{\kappa_\infty - \kappa_t}{\kappa_\infty - \kappa} - 1 \quad (3)$$

$$\kappa = \frac{\kappa_a + \kappa_b}{2} \quad (4)$$

$C_0$ : Initial concentration of the mixture of the two acetone solutions of thiobenzamide and benzyl bromide

$\kappa_\infty$ : Electric conductivity at the terminal period

The electric conductivity,  $\kappa_\infty$ , is that measured after 4 days from the initiation of the reaction. This value was almost the same as that obtained from the solution of *s*-benzylisothiobenzamidinium bromide itself (10 ml of 0.0025 mole acetone solution). Two examples of the results are shown in Tables 2 and 3.

## Results and Discussion

Rates of reactions of benzyl bromide with several substituted thiobenzamides at three temperatures in acetone are given in Table 4. The reactions of benzyl bromide with thiobenzamides, which produce *s*-benzylisothiobenzamidinium bromides, are first-order in benzyl bromide and first-order in thiobenzamides, since the time-dependent rate constants ( $k'$ s), derived from equation (3) which is based on the second-order kinetics, showed good consistency (Tables 2 and 3). The Hammett plots based on these data are shown in Figure 3; the  $\sigma$  constants employed were taken from the tabulation of Hammett.<sup>8</sup> The plots show good linearity with slope of approximately +0.4 while a non-linear behavior was observed in the reaction of benzyl

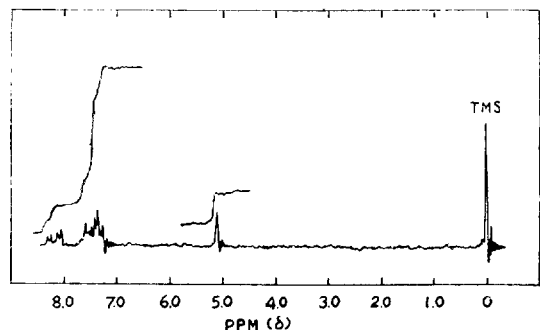


Fig. 2. NMR Spectrum (60 Mcps) of *s*-benzylisothiobenzamidinium bromide in CDCl<sub>3</sub> with TMS as internal standard.

Table 2. Rates of Reactions of Benzyl Bromide with *p*-Methoxythiobenzamide in Acetone at 25.0°  
( $C_0=0.0025$  mole/l,  $\kappa_0=4.17 \times 10^{-6}$ )

$t$ (min.)	$\kappa(10^{-6}U)$	$kC_0t$	$k$ (l/mole · min.)
10	4.31	0.0045	0.18
20	4.47	0.0090	0.18
40	4.76	0.0178	0.18
60	5.11	0.0320	0.21
80	5.32	0.0393	0.19
100	5.58	0.0488	0.19
140	6.00	0.0643	0.18
180	6.49	0.0829	0.18
220	6.95	0.1010	0.18
260	7.47	0.1222	0.18
300	7.90	0.1403	0.18
340	8.33	0.1591	0.18
380	8.61	0.1716	0.18
4 Days	34.48		Mean: 0.18

Table 3. Rates of Reactions of Benzyl Bromide with *p*-Nitrothiobenzamide in Acetone at 35.0°  
( $C_0=0.0025$  mole/l,  $\kappa_0=1.85 \times 10^{-6}$ )

$t$ (min.)	$\kappa(10^{-6}U)$	$kC_0t$	$k$ (l/mole · min.)
10	3.49	0.0255	1.02
20	5.06	0.0511	1.01
40	7.96	0.1020	1.02
60	10.69	0.1543	1.02
80	12.20	0.1855	0.92
100	14.49	0.2363	0.94
140	17.79	0.3176	0.90
180	21.07	0.4095	0.91
220	23.58	0.4895	0.90
260	26.16	0.5850	0.90
300	28.70	0.6825	0.91
340	30.67	0.7726	0.90
380	33.33	0.9087	0.95
4 Days	67.97		Mean: 0.95

bromide with thiourea.<sup>1</sup> A relatively small value indicates that the reaction is not so sensitive to substituent effects. The Arrhenius act-

ivation energies and entropies of activation derived from the data in Table 4 are shown in Table 5.

Table 4. Kinetic Data for the Reactions of Benzyl Bromide with Thiobenzamides in Acetone at 25°, 35°, and 45°

Thiobenzamides	Substituents	Second-order Rate Constant <sup>a</sup> , $k(l/mole \cdot min.)$		
		25.5°	35.0°	45.0°
<i>p</i> -Methoxythiobenzamide	<i>p</i> -CH <sub>3</sub> O	0.18	0.36	0.68
<i>p</i> -Methylthiobenzamide	<i>p</i> -CH <sub>3</sub>	0.19	0.38	0.70
<i>m</i> -Methylthiobenzamide	<i>m</i> -CH <sub>3</sub>	0.22	0.40	0.81
Thiobenzamide	H	0.23	0.42	0.91
<i>p</i> -Chlorothiobenzamide	<i>p</i> -Cl	0.25	0.46	0.99
<i>p</i> -Nitrothiobenzamide	<i>p</i> -NO <sub>2</sub>	0.43	0.95	1.86

a: Duplicate runs were made in each reaction studied.

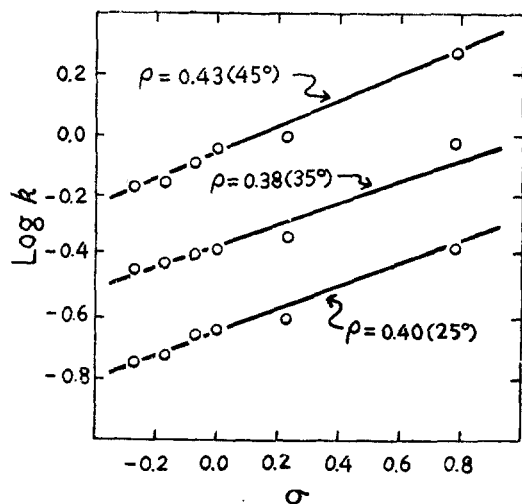
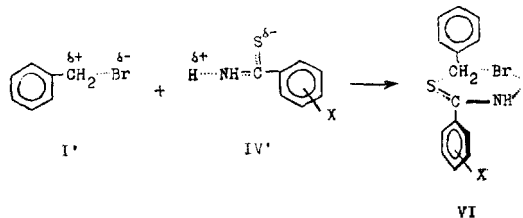


Fig. 3. Hammett plots for the rates of reactions of benzyl bromide with thiobenzamides in acetone at 25°, 35°, and 45°.

Table 5. Activation Parameters in the Reactions of Benzyl Bromide with Thiobenzamides in Acetone

Thiobenzamides	Activation Energy, $E_a$ (kcal)	Entropy of Activation, $\Delta S_{\ddagger}^{\ddagger}$ (e. u.)
<i>p</i> -Methoxythiobenzamide	10.16	-29.54
<i>p</i> -Methylthiobenzamide	9.75	-28.88
<i>m</i> -Methylthiobenzamide	10.17	-29.24
Thiobenzamide	9.32	-31.71
<i>p</i> -Chlorothiobenzamide	10.17	-27.36
<i>p</i> -Nitrothiobenzamide	6.80	-39.12

In the  $S_N2$  process of these reactions (Eq. 2), the benzylic carbon of benzyl bromide (I) is attacked by the nucleophile (IV) to form C-S bond, and it is assumed that an electron-donating substituent on the benzene ring of thiobenzamide accelerates the reaction, while an electron-attracting substituent retards the reaction. On the contrary, however, it was observed that the reaction is accelerated by an electron-attracting substituent, and is retarded by an electron-donating substituent (Table 4). This is rather surprising because the rate of reaction is increasing as the electron density of thiocarbonyl sulfur is decreasing, and this suggests that C-S bond formation is not a rate-determining step. This behavior would be most easily rationalized in terms of an activated complex such as structure VI. According to structure VI, it seems plausible that an electron-attracting group laying on the benzene ring of thiobenzamide makes amino hydrogen atom easy to



leave and to pull bromine atom from the benzylic carbon atom. And in this structure, N-H bond cleavage, rather than S-C bond formation between thiocarbonylic sulfur and benzylic carbon, would be the rate-determining step in the light of the positive  $\rho$  value. Then the electronic nature of a substituent of thiobenzamide will effects quantitatively the C-Br cleavage of benzyl bromide through amino hydrogen of thiobenzamide. However, it should be noted that transmission of an electronic nature of the substituent to the reaction center is insensitive due to the small value of  $\rho$ . A relatively large decrease of the entropy of activation (Table 5), as compared with that obtained from the reaction of benzyl bromide with thiourea ( $-18$  e. u.)<sup>1</sup> will also support the formation of the rigid and so-called "push-and-pull" model, as an activated complex structure (IV).

#### Acknowledgement

This work was partly supported by a grant provided by Hanyang Research Institute of

Industrial Sciences, Hanyang University.

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