

Notes

The Thiazolation Reaction of Substituted Phenacyl Arenesulfonates with Substituted Thiobenzamides. I.

Soo-Dong Yoh*, Jeong-Wan Seo, and Jong-Hwan Park

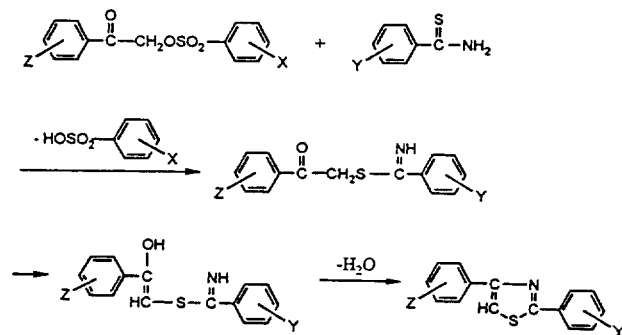
Department of Chemistry Education,
Kyungpook National University, Taegu 702-701

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We have previously studied the kinetics of the reactions of *m*- and *p*-substituted benzyl bromides with thiourea in ethanol, and postulated that the C-Br bond cleavage in benzyl bromide is the rate determining step in these reactions.¹ Additionally, the kinetic study for the reactions of benzyl bromide with substituted thiobenzamides have led to a conclusion that the rate determining step would be N-H bond cleavage rather than S-C bond formation between thiocarbonylic sulfur and benzylic carbon.² These results supported that the reaction would be so-called a "push-and-pull" model. Although the nucleophilic substitution reactions of α -halogenocarbonyl compounds, e.g. phenacyl halides, have attracted considerable attention over decades, many aspects of the reaction mechanism remain still unresolved.³ This is attributed to two available reaction sites in α -halogenocarbonyl compounds for a nucleophile to attack leading to different types of transition state structures.

In 1965 Okamiya studied the kinetics of the reactions of phenacyl bromides with substituted thiobenzamides in ethanol, and concluded that this reaction is a typical S_N2 reaction.⁴ In other words, the resonance of amino group increased the electron density of sulfur to be typical S_N2 attacking the carbon adjacent to bromine atom rather than carbonyl carbon. We also reported the substituents effects of substrate, nucleophile, and leaving group for the reactions of substituted phenacyl arenesulfonates with pyridine, respectively and proposed that the reaction proceeds by an S_N2 mechanism in which bond formation was relatively dominant due to the electronic interaction between nucleophile and the carbonyl group of the substrate.⁵

The kinetics of the nucleophilic substitution reactions of



Overall Reaction Scheme

Table 1. Second-Order Rate Constants ($10^3 k_2/l \cdot \text{mole}^{-1} \cdot \text{sec}^{-1}$) for the Reaction of Phenacyl Arenesulfonates with Substituted Thiobenzamides in Ethanol at 50°C

X\Y	<i>p</i> -OCH ₃	<i>m</i> -CH ₃	H	<i>p</i> -Cl	ρ_Y
<i>p</i> -OCH ₃	2.64	1.83	1.37	0.807	-1.05
<i>p</i> -OCH ₃	4.08	2.64	2.13	1.12	-1.13
H	6.52	4.30	3.05	1.58	-1.26
<i>p</i> -Br	15.5	8.76	6.29	3.35	-1.34
<i>m</i> -NO ₂	76.4	40.4	29.5	14.4	-1.46
ρ_X	1.48	1.36	1.33	1.27	

Table 2. Second-Order Rate Constants ($10^3 k_2/l \cdot \text{mole}^{-1} \cdot \text{sec}^{-1}$) for the Reaction of Substituted Phenacyl Arenesulfonates with *m*-methyl Thiobenzamides in Ethanol at 50°C

Z\X	<i>p</i> -OCH ₃	<i>p</i> -CH ₃	H	<i>p</i> -Br	<i>m</i> -NO ₂	ρ_X
H	1.83	2.64	4.30	8.76	40.4	1.36
<i>p</i> -CH ₃	1.70	2.59	3.94	8.61	38.8	1.37

substituted phenacyl arenesulfonates with substituted thiobenzamides in ethanol has been investigated in order to give more precise information on the reaction mechanism of phenacyl system with thiobenzamides.

The second-order rate constants for the reaction of substituted (*Z*) phenacyl arenesulfonates (*X*) with substituted (*Y*) thiobenzamides are summarized in Table 1. The rate constants for the reaction of phenacyl (*X*)-arenesulfonates with *m*-methylthiobenzamide were summarized in Table 2. The Hammett ρ_X value was obtained to be about 1.36.

As shown in Table 1, electron-donating substituents on thiobenzamides enhance the rate of substitution reactions of phenacyl arenesulfonates with thiobenzamides, while electron-withdrawing substituents reduce the rates. Opposite to the effects of substituents of nucleophile, electron-withdrawing substituents on the leaving group increase the rate of the reactions of phenacyl arenesulfonates with thiobenzamides, while electron-donating substituents decrease the rates. In general S_N2 reactions, larger electron density on nucleophile results in faster nucleophilic substitution reaction rate. The reaction rates of the phenacyl arenesulfonates with substituted thiobenzamides correlate well with regard to the σ constants to give a linear Hammett plot (Table 1). Our ρ_Y values (-1.0~ -1.5) are slightly larger than Okamiya's (-0.93). The $|\rho_Y|$ values are increased with electron-withdrawing substituents on the leaving group, while $|\rho_Y|$ ones are decreased with electron-withdrawing substituents on the nucleophile. These results indicate that these reactions proceed by an S_N2 mechanism in which bond formation and bond cleavage are all advanced. In order to figure out the detail reaction mechanism, the studies of the substituents effects of substrates and solvent effects will be needed in the future.

Experimental

Materials and Instruments

Ethanol was purified by distillation after refluxing with sodium metal and ethylphthalate for 2 hours. Conductance measurement were carried out with BARNSTED Model PM-70 CB conductivity bridge.

Preparation of Reagents. Substituted Thiobenzamides were prepared from their corresponding benzonitrile.^{4,8} Hydrogensulfide was bubbled through pyridine solution of benzonitriles using triethylamine as a catalyst. Substituted Phenacyl Arenesulfonates were synthesized as following.^{5b} A solution of 0.055 mole of silver arenesulfonate in 500 ml of dry acetonitrile was placed in a dry three necked flask fitted with mechanical stirrer, reflux condenser, and thermometer. Substituted phenacyl bromide (0.05 mole) was introduced and then the solution was heated in a water bath at 50°C for fifteen hours. After filtering silver bromide precipitated and evaporating the solution, white crystals were obtained and recrystallized from benzene-isopropyl alcohol. Thiazoles were prepared as following.⁴ A mixture of 0.02 mole thiobenzamide and 0.02 mole substituted phenacyl arenesulfonate dissolved in 50 ml of ethanol was refluxed for hours. After evaporating the solution and adding ammonia water, white or yellow crystals were obtained and then recrystallized from ethanol.

Kinetic Measurements. The kinetic apparatus and procedure to measure the rates of the reactions of substituted phenacyl arenesulfonates with substituted thiobenzamides by an electric conductivity method were the same as those used previous study. Reactions were generally run to about 3 to 4 half-lives of substrate. Pseudo first-order rate constants were determined by the Guggenheim method with substituted thiobenzamides in large excess, and second-order rate constants were obtained by dividing the observed first-order rate constants by nucleophile concentration.

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A Synthesis of 4-Phenyl-2-phenylsulfonyl-3-vinylcyclopentanone via Palladium-Catalyzed 1,3-Oxygen-to-Carbon Alkyl Shift

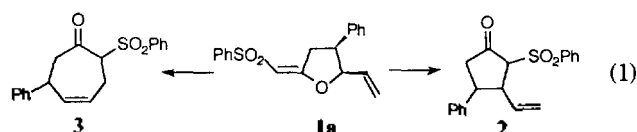
Phil Ho Lee^{a*}, Jong Soon Kim^a, and B. M. Trost^{b*}

^aDepartment of Chemistry, Kangwon National University, Chuncheon 200-701

^bDepartment of Chemistry, Stanford University, Stanford, CA 94305, U.S.A.

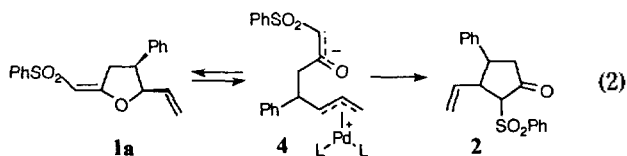
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The discovery of natural products that contain five-membered rings has led to increasing investigation of cyclopentanone syntheses.¹ In this respect, a number of synthetic methods were developed over the past years and used to synthesize natural products.² In connection with our recent research for Pd-chemistry, we have had an occasion to study the isomerization of **1a** to **2** and it has been found that palladium-catalyzed 1,3-oxygen-to-carbon alkyl shift occurred cleanly to provide cyclopentanone (Eq. 1).³



The fact that an allyl vinyl ether such as **1a** is converted to a cyclopentanone by a Pd(0) catalyst contrasts to the normal chemical reactivity of such compounds which isomerize to cycloheptanones under thermal conditions.⁴ In order to find optimum conditions, a variety of Pd(0) catalysts and solvents were tested and these results are shown in Table 1. The use of refluxing 1,4-dioxane under the influence of a Pd₂dba₃CHCl₃/dppp catalyst gave cyclopentanone in 51% yield, although many reaction conditions produced only unknowns whose structures may be related to coupling compounds of **1a** and **2** due to two carbonyl peaks (1750 and 1725 cm⁻¹) and many vinyl protons. Thus, cyclopentanone formation proved sensitive to the reaction conditions. Solvent and concentration played a dominant role.

The mechanism of this 1,3-shift can be thought to involve an oxidative addition of palladium(0) catalyst to the allyl ether as in Eq. 2 to form a zwitterion **4**. This intermediate collapses by C-alkylation to form the observed product. The regiochemistry of the collapse is quite interesting in that a five-membered ring product is observed. This reaction illustrates an ability of a transition metal to change the normal rules of reactivity of an organic system.



The experimental procedure for cyclopentanone formation is as follows. To a solution of Pd₂dba₃CHCl₃ (4.1 mg, 4 × 10⁻³ mmol) and 1,3-bis(diphenylphosphino)propane (8.3 mg, 0.02 mmol) in 2 ml of 1,4-dioxane was added **1a** (52.2 mg, 0.08