

KINETIC ISOTOPE EFFECT IN THE SULFONYLATION REACTION

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Electrophilic aromatic substitution is generally accepted as proceeding in two steps through a σ complex. Whether the second step involving the carbon-hydrogen bond rupture is rate determining may be deduced by examining the hydrogen kinetic isotope effect (1). Several examples of the kinetic isotope effect have been observed in the aromatic substitutions. Sulfonation reaction is the representative one, showing the primary isotope effect, $k_H/k_D = 1.4 - 2.1$ (2,3). Sulfonylation reaction has the common feature with sulfonation, being the reaction introducing the carbon-sulfur bonding to the aromatic ring. So far, the kinetic isotope effect in the sulfonylation has been mentioned only in two papers. Jensen and Brown (4) studied the kinetics of the aluminum chloride catalyzed sulfonylation with benzenesulfonyl chloride and reported the absence of the primary isotope effect, but the detail of the experiments has not been described. Diphenyl sulfone is formed as a by-product in the sulfonation of benzene with sulfur trioxide. Under these reaction conditions, the secondary kinetic isotope effect, $k_H/k_D = 0.86 - 0.96$ at 25.0°C , was observed for the sulfonylation (5). Both groups of the investigators concluded that the proton removing step from the σ complex is not the rate determining for the sulfonylation reaction, based on the absence of the primary kinetic isotope effect.

Recently Holt et al. discovered the high solubility of the aluminum chloride-sulfonyl chloride complex in methylene chloride and succeeded to sulfonate several aromatic compounds with this homogeneous reagent (6).

We have studied the kinetics of the sulfonylation under these reaction conditions and found the primary isotope effect as described below.

Reactions were followed to approximately 70% completion by determining the formed sulfone. Solutions of the mixture of the known amounts of p-toluene-sulfonyl chloride, benzene (or benzene-d₆) and aluminum chloride in methylene chloride were sealed in the ampoules and kept at given temperature for the appropriate reaction time. At suitable period, the ampoule was opened and the reaction was quenched with the mixture of ice chips and hydrochloric acid. Organic layer was separated, washed for few times with aqueous sodium carbonate, dried over magnesium sulfate, and the concentration of phenyl (or phenyl-d₅) p-tolyl sulfone in the solution was determined by infrared method. Incidentally, the competitive method between benzene and hexadeuteriobenzene was shown to be unsuccessful, due to the faster exchange of the ring hydrogen with the formed hydrogen chloride than the sulfonylation itself.

The rate followed cleanly the third order kinetic equation, first order in each of benzene, p-toluenesulfonyl chloride and aluminum chloride. Data for a typical kinetic run are shown in the Table 1.

TABLE 1

Typical Data for Sulfonylation of Benzene at 0.0°C.

Time, sec.	Phenyl p-Tolyl Sulfone (mole/l)	Rate Constant k_H (l ² mole ⁻² sec ⁻¹)
0.360 × 10 ⁴	0.0110	1.38 × 10 ⁻⁴
0.720	0.0181	1.12
1.080	0.0256	1.18
1.500	0.0336	1.04
1.800	0.0406	1.11
2.16	0.0466	1.16
9.360	0.1106	1.097
10.44	0.1226	1.253
17.64	0.1444	1.156
	mean	1.16

Initial concentrations; TsCl = 0.3003; C₆H₆ = 0.1905; AlCl₃ = 0.4332 mole/l.

Rate constants for benzene and for benzene-d₆ are given in the Table 2.

TABLE 2

Rate Constants for Sulfonation of Benzene and Benzene-d ₆		
Temperature	k _H (l ² mole ⁻² sec ⁻¹)	k _D (l ² mole ⁻² sec ⁻¹)
0.0°C	1.18 ± 0.10 × 10 ⁻⁴	0.48 ± 0.014 × 10 ⁻⁴
7.0	1.92 ± 0.16	1.01 ± 0.07
15.5	4.02 ± 0.26	1.93 ± 0.16

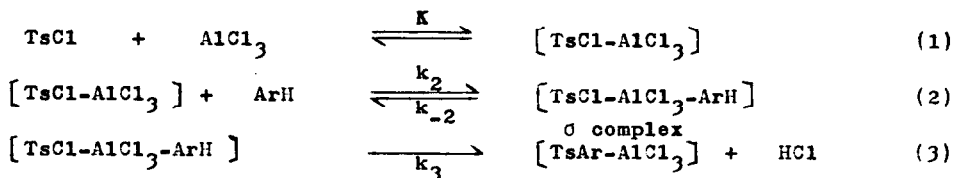
From these figures, the kinetic isotope effect can be calculated as below:

$$\begin{aligned}
 k_H / k_D &= 2.44 \pm 0.3 \quad (0.0^\circ\text{C}) \\
 &1.91 \pm 0.3 \quad (7.0^\circ\text{C}) \\
 &2.09 \pm 0.3 \quad (15.5^\circ\text{C})
 \end{aligned}$$

Activation parameters for these reactions are estimated as follows:

$$\begin{aligned}
 \text{Energy of activation; } E_H &= 11.9 \text{ Kcal/mole} \quad (\pm 1.0 \text{ Kcal/mole}) \\
 E_D &= 14.0 \quad (\pm 1.0) \\
 \text{Entropy of activation; } \Delta S_H^\ddagger &= -34.6 \text{ e.u. at } 0.0^\circ\text{C} \quad (\pm 3.6 \text{ e.u.}) \\
 \Delta S_D^\ddagger &= -28.9 \text{ e.u. at } 0.0^\circ\text{C} \quad (\pm 3.5 \text{ e.u.})
 \end{aligned}$$

Reaction mechanism of the sulfonation reaction with a sulfonyl chloride-aluminum chloride complex in methylene chloride described in this paper is considered as shown in the following scheme:



When the step 3 is the rate determining and steps 1 and 2 are reversible, the rate will be expressed by the following third order equation:

$$v = k [\text{TsCl}] [\text{AlCl}_3] [\text{ArH}]$$

where $k = k_2 k_3 K / (k_{-2} + k_3)$.

Since the primary kinetic isotope effect has been established in the present study, k_3 should be smaller than k_{-2} or at least comparable order of

magnitude with k_{-2} , and carbon-hydrogen bond may be stretched in a considerable degree in the transition state. Although the observed value of the kinetic isotope effect, $2.4 - 1.9$, is lower than the theoretical value, $6 - 7$, the extent of the rupture of the carbon-hydrogen bond in the transition state is not necessarily small, this aspect of the kinetic isotope effect being fully discussed by Westheimer (7) and Melander (1).

Preliminary studies on the sulfonylation of bromobenzene and bromobenzene- d_4 with *p*-toluenesulfonyl chloride-aluminum chloride complex in methylene chloride also showed the primary hydrogen kinetic isotope effect. Found value of k_H/k_D was 1.77 ± 0.2 at 0.0°C . The sole reaction product was 4-methyl-4'-bromodiphenyl sulfone. Detail of this kinetics will be reported later.

References

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