

13. Work done by Prof. C. T. Ahn, Hankuk Univ. of Foreign Studies, Seoul, Korea.
14.  $^1\text{H NMR}(\text{CDCl}_3)$  1.04(t,  $J = 7.3$  Hz, 3H, H-1), 1.15(t,  $J = 7.3$  Hz, 3H, H-6), 2.24(q,  $J = 7.3$  Hz, 2H, H-5), 2.36(s, 3H, methyl), 2.89(q,  $J = 7.3$  Hz, 2H, H-2), 7.15(d,  $J = 7.8$  Hz, 2H), 7.26(d,  $J = 7.8$  Hz, 2H); IR 1501, 1313  $\text{cm}^{-1}$ ; MS,  $m/z$ (relative intensity), 251(84,  $\text{M}^+$ ), 221(80),

- 177(35), 163(100), 123(32), 119(43), 79(64).
15.  $^1\text{H NMR}(\text{CDCl}_3)$  for E-2-*p*-toluenethio-3-nitro-2-butene, 2.04(s, 3H, methyl) 2.30(s, 3H, methyl), 2.39(s, 3H, methyl), 7.20(d,  $J = 8$  Hz, 2H), 7.36(d,  $J = 8$  Hz, 2H); for Z-2-*p*-toluenethio-3-nitro-2-butene, 1.91(s, 3H, methyl), 2.32(s, 3H, methyl), 2.39(s, 3H, methyl), 7.18(d,  $J = 8$  Hz, 2H), 7.42(d,  $J = 8$  Hz, 2H).

## The Effect of Polarizability on Reactivity

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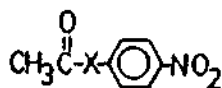
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As many as 17 factors have been suggested to be important in influencing nucleophilic reactivity,<sup>1</sup> and numerous relationships have been established to correlate nucleophilicity with one or more properties of the nucleophiles.<sup>2</sup> Polarizability has also been recognized as an important factors in determining nucleophilicity<sup>3</sup>. The best known description based on polarizability is Pearson's concept of hard and soft acids and bases, the so-called HSAB principle.<sup>4</sup>

The discovery that acylated coenzyme A, an intermediate in many biochemical reactions, is a thiol ester has accelerated the kinetic and spectroscopic investigations of thiol esters.<sup>5</sup> However, thionesters have not been studied intensively yet, largely due to their inaccessibility.<sup>6</sup> Recently the development of synthetic methods for the thiocarbonyl compounds has encouraged their systematic investigation.<sup>7</sup>

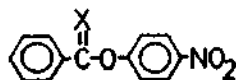
The replacement of oxygen atom by sulfur either in the carbonyl oxygen or in the ether-like oxygen in carboxylic esters has been reported to cause a significant increase in polarizability of the reaction center, and consequently to cause great differences in reactivity.<sup>8</sup> Although scattered information on the effect of polarizability on reactivity is available,<sup>9,10</sup> systematic studies have been lacking.

Thus we have prepared the following 4 esters (I, II, III, and IV) and performed kinetic studies of these esters with various nucleophiles of different nucleophilic atoms. Such a systematic change in the structure has been suggested to cause a significant difference in polarizability of the reaction center.<sup>8</sup> Thus any reactivity change upon the systematic structural change would be interpreted as an effect of polarizability on reactivity.



I: X = O, PNPA (*p*-nitrophenyl acetate)

II: X = S, PNTPA (*p*-nitrothiophenyl acetate)



III: X = O, PNPB (*p*-nitrophenyl benzoate)

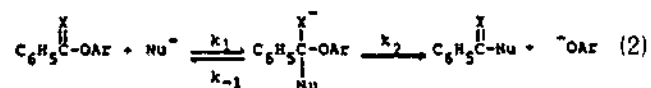
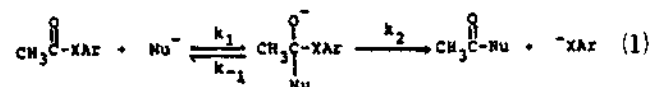
IV: X = S, PNPTB (*p*-nitrophenyl thionbenzoate)

**Table 1.** The second order rate constants ( $k$ ,  $\text{M}^{-1}\text{s}^{-1}$ ) for the reactions of the esters (I, II, III, and IV) with various types of nucleophiles at 25.0 °C

Nu <sup>-</sup>	pKa (NuH) <sup>a</sup>	k, M <sup>-1</sup> s <sup>-1</sup>			
		I	II	III <sup>d</sup>	IV <sup>d</sup>
N <sub>3</sub> <sup>-</sup>	4.0	0.0342	0.853	0.00288	10.1
CN <sup>-</sup>	9.3	0.164	0.174	0.0698	0.0852
<i>p</i> -ClPhO <sup>-</sup>	9.38	0.683 <sup>b</sup>	3.27 <sup>b</sup>	0.144	2.20
PhO <sup>-</sup>	9.95	0.967 <sup>b</sup>	3.77 <sup>b</sup>	0.303	2.30
OH <sup>-</sup>	15.7	12.0	6.01	6.3	0.71
				1.45 <sup>c</sup>	0.172 <sup>c</sup>
<i>p</i> -ClPhS <sup>-</sup>	7.50	0.143	42.7	0.02-0.03 <sup>e</sup>	342
PhS <sup>-</sup>	7.80	0.36 <sup>b</sup>	36 <sup>b</sup>		

<sup>a</sup>reference 13. <sup>b</sup>reference 9. <sup>c</sup>reference 10(a). <sup>d</sup>The reactions for III and IV were performed in 10 mole % DMSO-H<sub>2</sub>O mixture due to a solubility problem. <sup>e</sup>A large error might be expected due to a long reaction time which caused the oxidation of thiophenoxide to disulfide.

In Table 1 is presented a summary of the second-order rate constants for the nucleophilic substitution reactions, as shown in the following equation 1 and 2. The reaction mechanism of the present system has generally been suggested as a two-step reaction, *i.e.* the formation of a tetrahedral intermediate followed by the breakdown of it.<sup>2b-c,9,10</sup>



It is clearly demonstrated in Table 1 that the effect of polarizability on the substrate reactivity is strongly dependent on the polarizability of nucleophiles. The reactivity of the sulfur containing substrates toward HO<sup>-</sup> ion is decreased by two to ten folds when the substrate changes from I to II and from III to IV, respectively. On the contrary, the thiol

and thione esters show remarkable increases in reactivity toward sulfur centered nucleophile (*p*-ClPhS<sup>-</sup>), *i.e.* 300 to about 17,000 folds rate enhancements compared to the corresponding oxygen esters.

It is also interesting to note that the nucleophilicity decreases in the order of HO<sup>-</sup> > PhO<sup>-</sup> > CN<sup>-</sup> > *p*-ClPhS<sup>-</sup> > N<sub>3</sub><sup>-</sup> for the oxygen esters (I & III), as expected from their pKa values. However the nucleophilic reactivity order toward the thionester increases in order of CN<sup>-</sup> < OH<sup>-</sup> < *p*-ClPhO<sup>-</sup> < PhO<sup>-</sup> < N<sub>3</sub><sup>-</sup> < *p*-ClPhS<sup>-</sup>, which is quite unexpected based on the Bronsted correlation. Although the basicity of *p*-ClPhS<sup>-</sup> is over 8 pKa unit lower than that of HO<sup>-</sup>, *p*-ClPhS<sup>-</sup> is 45.6 folds more nucleophilic than HO<sup>-</sup> toward the thionester.

Thus the present results seem to be consistent with the so-called HSAB principle, *i.e.* very polarizable *p*-ClPhS<sup>-</sup> is highly reactive toward the polarizable substrate while relatively nonpolarizable HO<sup>-</sup> shows an extremely low reactivity. The small reactivity change for N<sub>3</sub><sup>-</sup> and aryloxy ions upon the substrate change is well understandable if one admits that their polarizability is not so great as that of the sulfur centered nucleophile.

Interestingly CN<sup>-</sup> ion shows very little reactivity difference upon the structural change. Since CN<sup>-</sup> has recently been suggested to be much softer than N<sub>3</sub><sup>-</sup>,<sup>11</sup> it would have been expected to be much more reactive than N<sub>3</sub><sup>-</sup> toward the sulfur containing substrates on the basis of the HSAB principle. However experimental studies based on the data from free energy of transfer and solvent effect on rate have revealed that CN<sup>-</sup> is not so polarizable<sup>12</sup> as was originally suggested based on calculation.<sup>4,11</sup>

The present result seems to be consistent with the argument that CN<sup>-</sup> is not so polarizable from the view point of the HSAB principle. However, one can not exclude the possibility that CN<sup>-</sup> has showed an exceptional result in the present study. Also any changes in the rate limiting step, which have recently been a subject of controversy,<sup>2b-c,9,10,14,15</sup> could be responsible for the present result. A more quantitative and mechanistic study is under way for a complete interpretation of the present work.

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## Convenient Synthesis of Carboxylic Esters Using 2-Pyridyl Carbonates

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Carboxylic esters are usually prepared by the reaction of carboxylic acids or their derivatives with alcohols. However, only a few methods have been reported on the derivation of

carboxylic esters from carboxylation of organic halides. Although reaction of Grignard reagents with methyl chloroformate,<sup>1</sup> diethyl carbonate,<sup>2</sup> and pentacarbonyl iron<sup>3</sup> can af-