

and thione esters show remarkable increases in reactivity toward sulfur centered nucleophile (*p*-ClPhS⁻), *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⁻ > PhO⁻ > CN⁻ > *p*-ClPhS⁻ > N₃⁻ for the oxygen esters (I & III), as expected from their pK_a values. However the nucleophilic reactivity order toward the thionester increases in order of CN⁻ < OH⁻ < *p*-ClPhO⁻ < PhO⁻ < N₃⁻ < *p*-ClPhS⁻, which is quite unexpected based on the Bronsted correlation. Although the basicity of *p*-ClPhS⁻ is over 8 pK_a unit lower than that of HO⁻, *p*-ClPhS⁻ is 45.6 folds more nucleophilic than HO⁻ toward the thionester.

Thus the present results seem to be consistent with the so-called HSAB principle, *i.e.* very polarizable *p*-ClPhS⁻ is highly reactive toward the polarizable substrate while relatively nonpolarizable HO⁻ shows an extremely low reactivity. The small reactivity change for N₃⁻ 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⁻ ion shows very little reactivity difference upon the structural change. Since CN⁻ has recently been suggested to be much softer than N₃⁻,¹¹ it would have been expected to be much more reactive than N₃⁻ 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⁻ is not so polarizable¹² as was originally suggested based on calculation.^{4,11}

The present result seems to be consistent with the argument that CN⁻ is not so polarizable from the view point of the HSAB principle. However, one can not exclude the possibility that CN⁻ 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,^{2b-c,9,10,14,15} 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,¹ diethyl carbonate,² and pentacarbonyl iron³ can af-

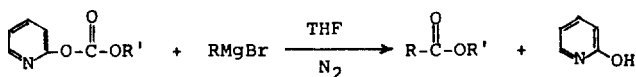
Table 1. Preparation of Carboxylic Esters from 2-Pyridyl Carbonates and Grignard Reagents
$$\text{R}'\text{O}-\text{COO}-2\text{-Py} + \text{RMgBr} \xrightarrow[\text{N}_2]{\text{THF}} \text{R}-\text{COO}-\text{R}'$$

RMgBr R	R'O-COO-Py R'	Reaction temp., °C	Isolated yield, % ^a
(CH ₂) ₅	C ₂ H ₅ ^b	0	81
<i>c</i> -C ₆ H ₁₁	C ₂ H ₅	0	91
2,4,6-(CH ₃) ₃ -C ₆ H ₂	C ₂ H ₅	0	94
<i>c</i> -C ₆ H ₁₁	(CH ₃) ₂ CH	0	89
C ₆ H ₅	(CH ₃) ₂ CH	0	92
CH ₃ (CH ₂) ₇	C ₆ H ₅ CH ₂	-78	88
C ₆ H ₅ CH ₂ ^f	C ₆ H ₅ CH ₂	-78	87
2,4,6-(CH ₃) ₃ -C ₆ H ₂	C ₆ H ₅ CH ₂	-78→0	88
CH ₃ (CH ₂) ₄	CCl ₃ CH ₂	0	75(8) ^d
		-78	85
C ₆ H ₅	C ₆ H ₅	-78	88
CH ₃ (CH ₂) ₇	<i>t</i> -C ₄ H ₉	0	95
<i>c</i> -C ₆ H ₁₁	<i>t</i> -C ₄ H ₉	0	80
C ₆ H ₅	<i>t</i> -C ₄ H ₉	0	93

^aYields represent purified products by distillation (Kugelrohr) and all products had identical spectral and physical properties with reported data. ^b2 equiv of ethyl 2-pyridyl carbonate was used. ^cGrignard reagent was prepared from benzyl chloride. ^dThe number indicates the isolated yield of di-2,2,2-trichloroethyl carbonate.

for the corresponding esters, their usefulness are limited due to competing side reactions, low yields, and scope. Carboxylic ester synthesis by treatment of alkyl chloroformates with organomagnesium reagents⁴ is useful, however its utility is confirmed to the preparation of unhindered esters. Thus, the success of carboxylic ester synthesis by carboxylation of organic halides depends largely on the nature of alkoxy-carbonyl derivatives and organometallic reagents employed.

As part of our study on the synthetic utility of active carbonates containing 2-pyridyl moiety we have reported that *t*-butyl 2-pyridyl carbonate⁵ and benzyl 2-pyridyl carbonate⁶ are very effective in the *t*-butoxycarbonylation and benzyloxycarbonylation of amines and amino acids. We now wish to report convenient method for the preparation of carboxylic esters by the reaction of Grignard reagents with 2-pyridyl carbonates.



In a typical experiment, 4 ml of 0.5 M solution of Grignard reagent in THF was added to the solution of 2 mmol of 2-pyridyl carbonate in 3 ml of THF at 0° or -78° under nitrogen atmosphere. Within 0.5 h the reaction was normally completed, quenched by 1 ml of saturated NH₄Cl, and the product was isolated in the usual manner.

As shown in Table 1, structurally different carboxylic esters can be synthesized without side products by this method. The reaction works well with both aliphatic and aromatic magnesium halides, including the hindered Grignard reagent such as 2,4,6-trimethylphenyl magnesium bromide. Significantly, the structure of alkyl group in the 2-pyridyl carbonate doesn't have influence on the synthesis of carboxylic esters under the present reaction conditions. Thus, even in case of the reaction of cyclohexylmagnesium bromide with *t*-butyl 2-pyridyl carbonate there was no side reaction such as elimination. Although the reaction of Grignard reagent with benzyl, 2,2,2-trichloroethyl, and phenyl 2-pyridyl carbonate at 0° gave a small amount of the side product such as corresponding dialkyl carbonate, which was decreased to trace at -78°C.

The preferential formation of carboxylic esters seems to result from the formation of six-membered chelate, stabilized by the coordination of the nitrogen atom and oxygen atom of carbonyl group to the magnesium atom, between 2-pyridyl carbonate and Grignard reagent. This can be partially confirmed by the following results. i) Ethyl benzoate was obtained in 98% yield by the reaction of ethyl 2-pyridyl carbonate with phenylmagnesium bromide in the presence of an equimolar amount of ethyl benzoate. ii) Ethyl benzoate was obtained in 92% yield by the reaction of ethyl 2-pyridyl carbonate with 2 equiv of phenylmagnesium bromide at 0° for 15 min without accompanying appreciable side products. However, employment of 3 equiv of phenylmagnesium bromide at 0° for 1.5 h produced ethyl benzoate, benzophenone, and triphenylmethanol in 70%, 4%, and 13% yield, respectively, indicating that six-membered chelate decomposes slowly with excess Grignard reagent.

In conclusion, the present method provides a useful alternative to other reported methods with respect to availability of 2-pyridyl carbonate, mild conditions, and high yields.

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