

References

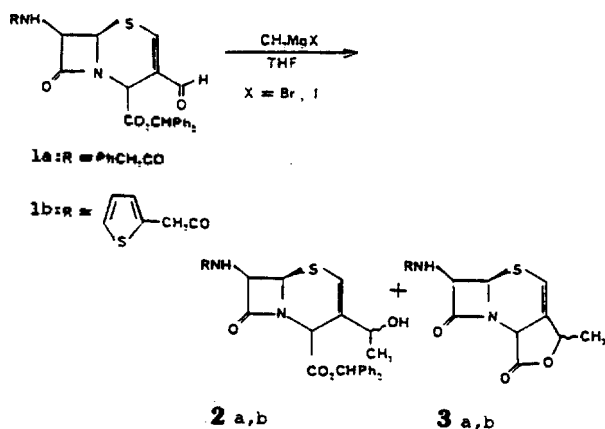
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- Zinc was less effective than magnesium. The reaction of 2-pyridyl isobutyrate with ethyl 2-bromoisobutyrate proceeded slowly and required 7 h for completion of the reaction. Furthermore, the reaction of 2-pyridyl benzoate with ethyl 2-bromoisobutyrate afforded the product in only 10% yield for 6 h with recovery of 2-pyridyl benzoate in 86% yield.

Remarkable Effects of Lithium Salt in Grignard Reaction

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During our ongoing efforts to develop new antibiotics, we discovered remarkable effects of lithium salt in Grignard reaction. We needed compound **2a** as a key intermediate for new compounds which had broad spectrum antibacterial activities. Preparation of the compound **2b** from corresponding aldehyde **1b** was documented in the literature¹. However, when we tried this transformation of **1a**, we isolated less than 30% of a mixture of diastereoisomeric carbinols **2a** with 50% of lactone **3a** and 10% of recovered starting material **1a** under the optimized condition (e.g. 5 equivalents of Grignard reagent $-\text{CH}_3\text{MgBr}$ or CH_3MgI at -78°C).²



It was believed that an alkoxide which was generated *in situ* by addition of Grignard reagent to aldehyde at C-3 attacked ester at C-4 to form lactone **3a**. In order to obtain considerable amount of key intermediate-compound **2a**, we were looking for a condition to suppress lactone formation and facilitate the addition to completion.

Trimethylsilyl chloride was known to activate carbonyl groups for various nucleophilic attack. Recently, it was elegantly employed to promote 1,4-addition of cuprate by different researchers.³ It was also known that it did not react with cuprate^{3a} at -78°C . We expected that it might trap the

resulting alkoxide from Grignard reaction and also facilitate the addition by activation of carbonyl group. We tried the reaction with 2 equivalents of trimethylsilyl chloride and 7 equivalents of Grignard reagent at -78°C . Under this condition, we isolated 40% of desired carbinols **2a** and 50% of lactone **3a**. We could not detect any starting material **1a**. It showed that trimethylsilyl chloride promoted addition but failed to trap the alkoxide to prevent lactone formation. We changed ratios of reagents but obtained similar results. From these results, we turned our attention to more effective reagents. Lithium salts were widely used for stereoselective aldol condensations⁴ and regioselective enolate formations.⁵ They were also used to control E and Z geometry in Wittig reaction.⁶ Lithium cation was known to tightly coordinate with oxygen atom. When we tried reaction with 7 equivalents of anhydrous lithium chloride and 7 equivalents of Grignard reagent, we obtained remarkable result. There was no starting material remaining. We isolated 80% of desired carbinols **2a** and less than 5% of lactone **3a**. We increased the amount of lithium chloride but obtained almost the same result.

It was believed that lithium cation was very effectively coordinated to oxygen atom at carbonyl group to prevent lactone formation and also to facilitate the addition to completions. From these results, we expected that methyllithium might give similar results. However, when we tried reaction with methyllithium. We observed that methyllithium attacked both aldehyde and ester function to give no desired carbinols. We are presently looking for possible extension of the reaction.

References and Notes

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- All yields refer to isolated products and all new compounds gave satisfactory spectral data.
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Salt Effects in Electron-Transfer Induced Photooxygenation of 1,1-Diphenyl-2-Vinylcyclopropane; in the Presence of LiClO_4 , NaClO_4 , and $(n\text{-Bu})_4\text{NClO}_4$

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The influence of alkali cation on the photoreaction of organic compounds has been the subject of extensive investigation in recent years.¹ The effect of alkali cations on the photoreduction of carbonyl compound has been recently examined by picosecond transient laser spectroscopy and the interactions between the solvent and the salts have been probed by Raman spectroscopy.² These interactions between the molecules of solvent and the cations constitute the driving force for the formation of the solvent separated ion pairs. The main factors affecting the interactions between the solvent and the cations at any temperature and pressure are the ionic size, charge, and the solvent size, viscosity, and dielectric constant.³

In an attempt to elucidate the role of cation-solvent interactions in the exchange mechanism, we now report the salt effect on a novel photooxygenation of 1,1-diphenyl-2-vinylcyclopropane (VCP-DPh, **1**) cosensitized by 9,10-dicyanoanthracene (DCA) and biphenyl (BP).⁴ Photooxygenation of **1** (10^{-4}M) DCA (10^{-4}M) and BP (10^{-2}M) in the presence of LiClO_4 , NaClO_4 and $(n\text{-Bu})_4\text{NClO}_4$ in dry acetonitrile solution was carried out. The solution was irradiated at 10°C under oxygen with a 450-W medium-pressure mercury arc lamp through a CuSO_4 -filter solution. The reaction was monitored by HPLC.

In a given temperature, pressure, solvent, and ionic charge of salt cation, each salt of different cation influences the VCP-DPh photooxygenation quantum yield differently. The quantum yield of VCP-DPh photooxygenation increased in the order of $\text{LiClO}_4 < \text{NaClO}_4 < (n\text{-Bu})_4\text{NClO}_4$, as shown in Figure 1.

For alkaline salts, this observation may be explained as the following. A small ion, like Li^+ , binds with acetonitrile more strongly than larger ions, like Na^+ ,^{5,6} suggesting that the effective ionic radius of solvated Li^+ could be larger than that of Na^+ because the smaller ions carry the thicker solvent sphere. Consequently, an increase in the size of Stoke's radius results in the lower mobility of alkali cations and causes the quantum yield to increase less effectively.^{7,8}

In addition, the strong solvent-cation interaction formed by the smaller alkali cations such as Li^+ relative to Na^+ and the polar solvent such as acetonitrile results in an increase in the thermodynamic barrier for exchange process. For ion-pair exchange between salt and radical ions to occur, these ion-dipolar forces must be overcome. Thus, a high barrier as-

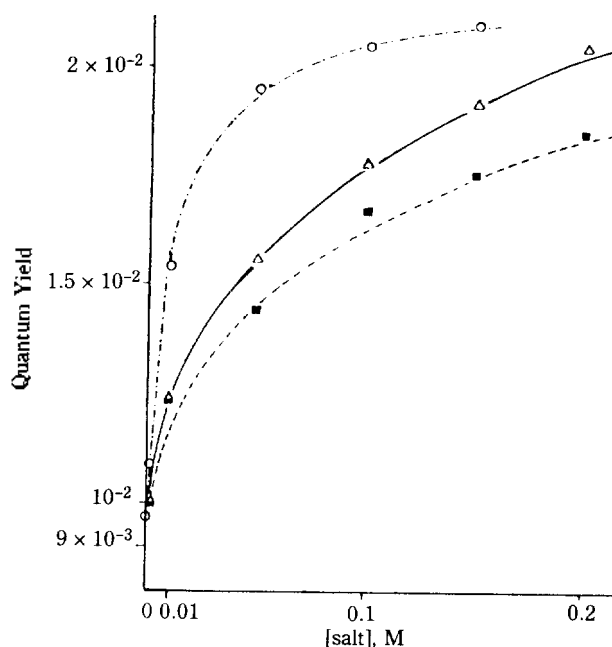
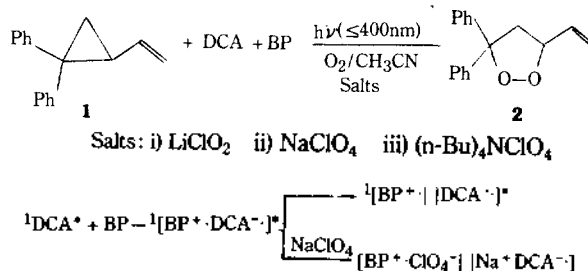


Figure 1. Salt effect on the Photooxygenation of 10^{-2}M VCP-DPh, 10^{-4}M DCA, and 10^{-2}M BP; LiClO_4 (■), NaClO_4 (△), and $(n\text{-Bu})_4\text{NClO}_4$ (○).



Scheme 1

sociated with the desolvation of alkali metal cation causes the formation of solvent separated ion pairs to decrease. The difference in overall rates of ion-pair exchange reaction for NaClO_4 and LiClO_4 was demonstrated by the Raman analysis of acetonitrile-salt solutions in recent years.² The larger alkali cation in acetonitrile increases the formation of solvent