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Oxidative Carbon-Carbon Bond Forming Reaction via a 1,3-Dioxolan-2-ylium Cation

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1,3-Dioxolan-2-ylium cations, derived from aldehyde ethylene acetals and trityl cation, react with ketene silyl acetals and enamines to give the corresponding β-keto esters and 1,3-diketones, respectively.

Carbocationic species are some of the most important reactive intermediates in organic synthesis, especially in carbon-carbon bond forming reactions. Most of these cationic species are generated in situ by the use of appropriate reagents such as Lewis acids, enabling further reactions with various nucleophiles. However, few examples are known concerning the reaction of isolated carbocations with nucleophiles.

Among several methods for the generation of isolable carbocations, hydride-abstraction with trityl cation$^{1)}$ is unique, because net oxidation of the substrate can be achieved. Thus it is expected that generation of a cation by hydride-abstraction, followed by treatment with a carbon nucleophile should afford a novel oxidative carbon-carbon bond formation.

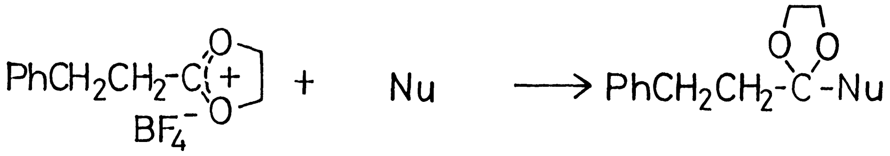
In this context, we have already reported that the 1,3-dioxolan-2-ylium cation,$^{2)}$ derived from ethylene acetal and trityl cation, reacts with lithium organo compounds to give esters or ketals in good yields.$^{3)}$ In the present communication, we would like to report the preparation of β-keto esters and 1,3-diketones by the reactions of the 1,3-dioxolan-2-ylium cations with several carbon nucleophiles such as ketene silyl acetals and enamines.

1,3-Dithiolan-2-ylium cation$^{4)}$ and 1,3-dithian-2-ylium cation,$^{5)}$ isolable carbocations, are known to react with silyl nucleophiles. However, there has been only one report$^{6)}$ about this type of reaction between 1,3-dioxolan-2-ylium cation with silyl nucleophiles, and this cation has been seldom used for carbon-carbon bond forming reactions. This is probably because 1,3-dioxolan-2-ylium cation seems unstable and difficult to handle compared with the cations stabilized by two sulfur atoms. It has already been reported$^{2)}$ that 1,3-dioxolan-2-ylium cation is also an isolatable, stable cation, and synthesized easily by the hydride abstraction with trityl cation.

When these cations are treated with silyl nucleophiles, such as silyl enol ethers or ketene silyl acetals, the formation of selectively monoprotected 1,3-diketones or of β-keto esters is expected, the former result being generally difficult to achieve according to the usual synthetic procedures.

Moreover, an ethylene ketal, the protecting group in the present reaction, is easily deprotected by acid hydrolysis. Based on these considerations of synthetic advantage, we started to examine the synthesis of β-keto esters and 1,3-diketones using 1,3-dioxolan-2-ylium cations.

2-Phenethyl-1,3-dioxolan-2-ylium tetrafluoroborate (1), formed by the reaction of 3-phenylpropanal ethylene acetal and trityl tetrafluoroborate according to the procedure of H. Meerwein,$^{7)}$ was chosen as a model compound, and in the first place various silyl nucleophiles were screened with the expectation of carrying out the reaction under non-basic conditions.



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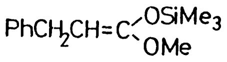
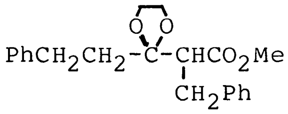
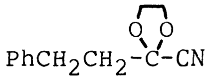
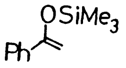
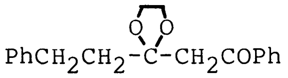
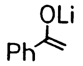
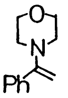
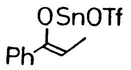
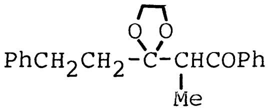
Nu = Nucleophile

Table 1. Reaction of 1 with carbon nucleophiles

Nucleophile	Product	Yield/%
		80
$Me_3SiCH_2CH=CH_2$	————	0
Me_3SiCN		42
		43
 a)	"	61
	"	75
 b)		47

a) Lithium enolate is prepared by the procedure of H. O. House.$^{8)}$

b) Stannous enolate is prepared by the procedure of T. Mukaiyama.$^{9)}$

Silyl enol ethers, which gave good results in the cases of the reactions with 1,3-dithiolan-2-ylium cation$^{4)}$ and 1,3-dithian-2-ylium cation,$^{5)}$ did not afford the desired products in good yields. This result indicates that 1,3-dioxolan-2-

ylium cation is not as electrophilic as those cations stabilized by two sulfur atoms. So we tried to find a more reactive nucleophile, and ketene silyl acetals proved to react smoothly with the cation to give the corresponding β-keto esters in good yields.

Next, we tested other "ketone enolate equivalents" in order to prepare 1,3-diketone derivatives. As shown in Table 1, a good result is achieved when an enamine is used as the nucleophile. This is because the reaction is carried out under almost neutral conditions suppressing the side reactions such as an acetal opening and also because the enamine has a stronger nucleophilicity toward the positive center of the carbocation.

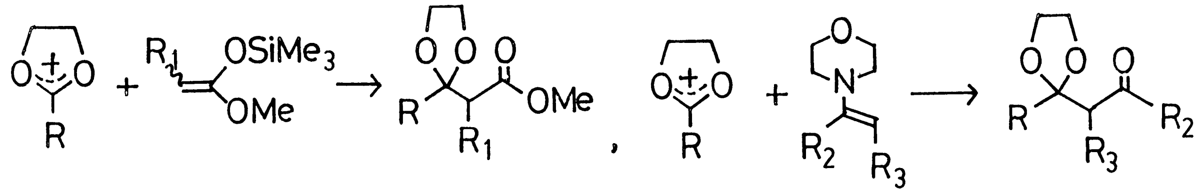
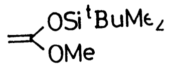
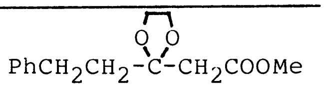
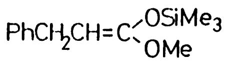
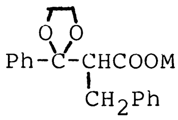
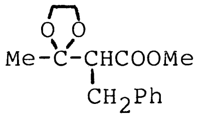
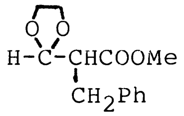
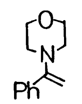
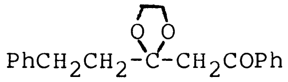
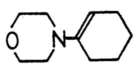
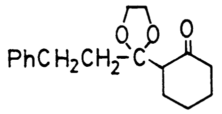
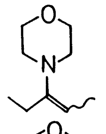
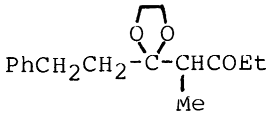
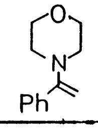
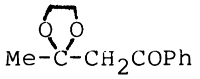


Table 2. Reaction of 2-substituted 1,3-dioxolan-2-ylium cation with ketene silyl acetal and enamine

Entry	R	Nucleophile	Yield/%	Product
1	$PhCH_2CH_2$-a)		80	 $\mathrm{PhCH_2CH_2\text{-}\overset{O\ O}{C}\text{-}CH_2COOMe}$
2	Ph-a)	 $\mathrm{PhCH_2CH{=}C\!\begin{smallmatrix}OSiMe_3\\ OMe\end{smallmatrix}}$	80	 $\mathrm{Ph\text{-}\overset{O\ O}{C}\text{-}\underset{CH_2Ph}{CH}COOMe}$
3	Me-a)	"	66	 $\mathrm{Me\text{-}\overset{O\ O}{C}\text{-}\underset{CH_2Ph}{CH}COOMe}$
4	H-a)	"	71	 $\mathrm{H\text{-}\overset{O\ O}{C}\text{-}\underset{CH_2Ph}{CH}COOMe}$
5	$PhCH_2CH_2$-b)		75	 $\mathrm{PhCH_2CH_2\text{-}\overset{O\ O}{C}\text{-}CH_2COPh}$
6	"		70	
7	"		73	 $\mathrm{PhCH_2CH_2\text{-}\overset{O\ O}{C}\text{-}\underset{Me}{CH}COEt}$
8	Me-b)		62	 $\mathrm{Me\text{-}\overset{O\ O}{C}\text{-}CH_2COPh}$

a) Reaction conditions are in the text.

b) Molar ratio, 1,3-dioxolan-2-ylium cation : enamine = 1 : 1.5, CH_2Cl_2, 0 °C, 30 min.

After screening the reaction conditions (solvent, temperature, time), the reactions of ketene silyl acetals or enamines with various 2-substituted-1,3-dioxolan-2-ylium cations were tried and these results are summarized in Table 2.

Typical procedure of entry 1 of Table 2 is as follows: To a dichloromethane suspension (5 ml) of 2-phenethyl-1,3-dioxolan-2-ylium tetrafluoroborate (0.39 mmol) was added the ketene silyl acetal of methyl acetate (0.55 mmol) in dichloromethane (1 ml) at -45 °C. After the reaction mixture was stirred at this temperature for 2.5 hours, the reaction was worked up by adding aqueous sodium hydrogencarbonate and the organic materials were extracted with dichloromethane. After the organic layer was dried and evaporated, the residue was purified by thin layer chromatography to give methyl 3,3-ethylenedioxy-5-phenylpentanoate (80%).

This reaction has the following unique characteristics that should be pointed out. Firstly, according to the present procedure, one of the carbonyl functions of the product is selectively protected as an ethylene ketal, which is a synthetically useful protecting group as mentioned previously. Secondly, the reaction with enamine is driven by the successive production of increasingly stable cations. That is, initially, the trityl cation, stabilized by three phenyl groups, is converted into 1,3-dioxolan-2-ylium cation, stabilized by two oxygen atoms. This cation in turn produces an immonium ion stabilized by the nitrogen atom along with the formation of a new carbon-carbon bond.

References

1) M. E. Yung, J. Org. Chem., 41, 1479 (1976); M. E. Yung and Y. -G. Pan, ibid., 42, 3961 (1977); H. J. Dauben, Jr.,F. A. Gadecki, K. M. Harmon, and D. L. Pearson, J. Am. Chem. Soc., 79, 4557 (1957).

2) C. V. Pittman, Jr., S. P. Mcmanus, and J. W. Larsen, Chem. Rev., 72, 357 (1972).

3) T. Mukaiyama, Y. Hayashi, and Y. Hashimoto, Chem, Lett., 1986, 1627.

4) Y. Hashimoto and T. Mukaiyama, Chem. Lett., 1986, 755, 1623.

5) E. J. Corey and S. W. Walinsky, J. Am. Chem. Soc., 94, 8932 (1972); I. Paterson and L. G. Price, Tetrahedron Lett., 22, 2829, 2833 (1981); C. Westerlund, ibid., 23, 4835 (1982).

6) Y. S. Yokoyama, T. Inoue, and I. Kuwajima, Bull. Chem. Soc. Jpn., 57, 553 (1984).

7) H. Meerwein, V. Hederich, H. Morschel, and K. Wunderlich, Justus Liebigs Ann. Chem., 635, 1 (1960).

8) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, J. Org. Chem., 34, 2324(1969).

9) T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, Tetrahedron, 40, 1381 (1984).

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