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Regioselective Alkylation of 1,3-Dioxolan-2-ylium Cation Derived from α,β-Unsaturated Aldehyde Ethylene Acetal with Lithium Organo Compounds

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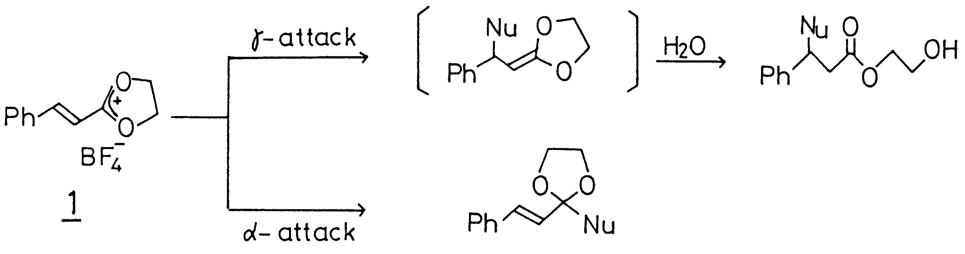
1,3-Dioxolan-2-ylium cations derived from α,β-unsaturated aldehyde ethylene acetals regioselectively react with lithium organocuprate and lithium organoaluminate to give the corresponding esters and ketals, respectively.

Recently it was shown from our laboratory that the trityl cation, a Lewis acid, effectively promotes various synthetic reactions.[1,2] For the exploitation of a new possibility of the trityl cation in organic synthesis, the generation of 1,3-dioxolan-2-ylium cations from α,β-unsaturated ethylene acetals by way of a hydride abstraction with the trityl cation, and the reactions of these stable cations with several nucleophiles were studied. It is well known that the trityl cation acts as an oxidant in certain cases,[1] for example, a 1,3-dioxolan-2-ylium cation[3] is formed from an ethylene acetal via hydride abstraction. However, there are few examples,[4] in which these kinds of carbocations, stabilized by two oxygen atoms, are employed as the active species in C-C bond-forming reactions. So we examined the reaction of 1,3-dioxolan-2-ylium cations with various carbon nucleophiles and now would like to report here the successful results.

First, 2-styryl-1,3-dioxolan-2-ylium tetrafluoroborate (1),[5] formed by the reaction of cinnamaldehyde ethylene acetal and trityl tetrafluoroborate (83% yields) according to the procedure of H. Meerwein,[6] was chosen as a model compound. There are two possible electrophilic centers in the 2-styryl cation 1 and, as shown in Scheme 1, ketals will be formed when the nucleophilic attack takes place at the α-position of 1, whereas saturated esters would be produced after hydrolysis of the ketene acetal initially formed by γ-attack of the nucleophiles on the cation. Therefore, it becomes important to control the regiochemistry of the above mentioned nucleophilic attack, as well as to find suitable carbon nucleophiles in the reaction with this isolatable carbocation.



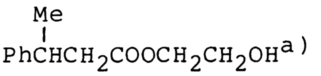
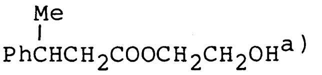
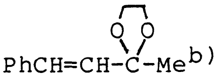
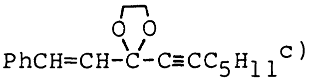
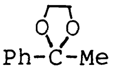
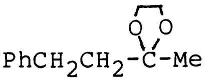
Nu=Nucleophile

Scheme 1.

After screening various nucleophiles (MeMgBr, Me_3Al, Et_2Zn, MeLi, Me_2CuLi, Me_4AlLi etc.), the following observations are noteworthy. 1) Organometallics exhibiting Lewis acidic characters, such as trimethylaluminium and diethylzinc, were not effective in this reaction. 2) Methyllithium gave the desired products in good yields, however, the regioselectivity was not so high (92%, α/γ = 72/28). 3) The ate complexes were effectively employed in this reaction and the desired products were isolated in good yields. It should be noted that, among these ate complexes, a lithium organocuprate gave only the saturated ester, while a lithium organoaluminate gave the ketal predominantly. The observed regioselectivity of alkylation may be explained as follows; the reaction using Me_2CuLi proceeds via electron transfer process, similar to that of the 1,4-addition of Me_2CuLi to α,β-unsaturated carbonyl compounds, to give the γ-adduct selectively. On the other hand, the reaction may proceed via ionic process in the case of Me_4AlLi; that is, exchange of the counter anion of the salt from BF_4^- to Me_4Al^- takes place first along with the formation of $LiBF_4$. Then, methyl group of Me_4Al^-, the counter anion, predominantly attacks the γ-carbon which may be more electron deficient compared with the α-carbon.

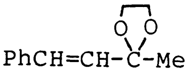
The reactions of the ate complexes or alkyllithiums with various 2-substituted 1,3-dioxolan-2-ylium cations were carried out, and results are summarized in Table 1. As shown in entries 7 and 8, 2-phenyl or 2-phenethyl-1,3-dioxolan-2-ylium cation gave a ketal by employing an alkyllithium as a carbon nucleophile.

Table 1. The reaction of 2-substituted 1,3-dioxolan-2-ylium tetrafluoroborate with carbon nucleophiles

Entry	2-Substituent	Nucleophile	Yield/%	Product
1	$\mathrm{PhCH{=}CH{-}}$	$\mathrm{Me_2CuLi}$	92	 $\mathrm{Ph\overset{Me}{C}HCH_2COOCH_2CH_2OH}^{a)}$
2	$\mathrm{PhCH{=}CH{-}}$	$\mathrm{Ph_2CuLi}$	79	$\mathrm{Ph_2CHCH_2COOCH_2CH_2OH}^{a)}$
3	$\mathrm{CH_3CH{=}CH{-}}^{5,7)}$	$\mathrm{Me_2CuLi}$	64	$\mathrm{Me_2CHCH_2COOCH_2CH_2OH}^{a)}$
4	$\mathrm{CH_3CH{=}CH{-}}$	$\mathrm{Ph_2CuLi}$	79	 $\mathrm{Ph\overset{Me}{C}HCH_2COOCH_2CH_2OH}^{a)}$
5	$\mathrm{PhCH{=}CH{-}}$	$\mathrm{Me_4AlLi}$	80	 $\mathrm{PhCH{=}CH{-}\overset{O\;\;O}{C}{-}Me}^{b)}$
6	$\mathrm{PhCH{=}CH{-}}$	$\mathrm{LiAlMe_3(C{\equiv}CC_5H_{11})}$	63	 $\mathrm{PhCH{=}CH{-}\overset{O\;\;O}{C}{-}C{\equiv}CC_5H_{11}}^{c)}$
7	$\mathrm{Ph{-}}^{8)}$	MeLi	81	 $\mathrm{Ph{-}\overset{O\;\;O}{C}{-}Me}$
8	$\mathrm{PhCH_2CH_2{-}}^{8)}$	MeLi	71	 $\mathrm{PhCH_2CH_2{-}\overset{O\;\;O}{C}{-}Me}$

a) α-Adduct is not detected.

b) Yield of γ-adduct is 8%.

c)  $\mathrm{PhCH{=}CH{-}\overset{O\;\;O}{C}{-}Me}$ is obtained in 20% yield.

Typical procedure of entry 1 is as follows: To an ethereal suspension (1.5 ml) of 2-styryl-1,3-dioxolan-2-ylium tetrafluoroborate (0.37 mmol) was added lithium dimethylcuprate (I) in ether (0.55 mmol) at -78 °C. The reaction mixture was stirred at that temperature for 1 hour and then at 0 °C for 6 hours. The reaction was worked up by adding aqueous sodium hydrogencarbonate and the mixture was filtered through a celite pad and organic materials were extracted with ether.

After the organic layer was dried and evaporated, the residue was purified by thin layer chromatography to give 2-hydroxyethyl 2-phenylpropanoate (0.34 mmol, 92% yield).

Thus, it is noted that the present reaction affords a very useful method for the oxidative carbon-carbon chain extention of aldehyde ethylene acetals to ketals by a one pot procedure. Especially, in the cases of the cations from α,β-unsaturated aldehyde ethylene acetals, both possible regioisomeric products, ketals or esters, can be respectively prepared by simply changing the center metal of the ate complexes used.

References

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2) T. Mukaiyama, H. Nagaoka, M. Ohshima, and M. Murakami, Chem. Lett., 1986, 1009; T. Mukaiyama, M. Tamura, and S. Kobayashi, ibid., 1986, 1017.
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4) A. Pelter and M. E. Colclough, Tetrahedron Lett., 27, 1935 (1986); K. Dimroth, P. Heinrich, and K. Schromm, Angew. Chem., 77, 863 (1965).
5) H. Hart and D. A. Tomalia, Tetrahedron Lett., 1966, 3383.
6) H. Meerwein, V. Hederich, H. Morschel, and K. Wunderlich, Justus Liebigs Ann. Chem., 635, 1 (1960).
7) This compound is synthesized according to the procedure of D. J. Raber. D. J. Raber and W. C. Guida, Synthesis, 1974, 808.
8) This compound is synthesized according to the procedure of H. Meerwein.(6)

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