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Highly Chemoselective Allylation of Aldehydes in the Presence of Ketones

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Abstract: Highly chemoselective allylation of aldehydes in the presence of ketones has been achieved by preferential *in situ* conversion of aldehydes into 1-silyloxysulfonium salts and subsequent displacement with allyltributyltin.

The nucleophilic addition of allylmetal reagents to carbonyl compounds is very useful and fundamentally important organic reactions.¹ Reactive organometallic reagents such as allyllithium and allyl Grignard reagents often fail to react preferentially with aldehydes in the presence of ketones. Lewis acid promoted allylation of organic compounds does not normally exhibit high chemoselectivity.² Recently, highly chemoselective allylation of aldehydes in the presence of ketones was achieved with tetraallyltin in acidic aqueous media.^{2,3} We reported that selective dioxolanation of ketones in the presence of aldehydes could be achieved by preferential *in situ* conversion of aldehydes into 1-silyloxysulfonium salts, in which 1-silyloxysulfonium salts had been used as *in situ* protection of aldehydes.⁴ Furthermore, we also reported that 1-silyloxysulfonium salts were highly reactive species which underwent facile nucleophilic substitution reactions.⁵ In connection with our research interest in chemoselective reactions of carbonyl compounds, we wish to report a new chemoselective allylation of aldehydes in the presence of ketones.



Treatment of an equimolar mixture of nonylaldehyde and acetophenone with dimethyl sulfide (3.0 equiv) and trimethylsilyl triflate (TMSOTf) (1.0 equiv) in dichloromethane at -78°C for 5 min, followed by addition of allyltributyltin at -78°C, stirring at -40°C for 5 min, and subsequent addition of tetra-nbutylammonium fluoride afforded the homoallyl alcohol (A) with greater than 99% selectivity. When the same reaction was carried out in tetrahydrofuran, a same high aldehyde selectivity (99%) was obtained but the reaction was much slower, requiring 3 h at -40°C for completion of the reaction. As shown in Scheme 1, when the same reaction was performed without the addition of dimethyl sulfide, 1,3,5-trioxane derivative

Aldehyde	Ketone	Ratio(A:B)	Yield,% ^a	Aldehyde	Ketone	Ratio(A:B)	Yield,% ^a
PhCH ₂ CH ₂ CHO	PhCOCH ₃	> 99 : < 1	99	PhCH ₂ CH ₂ CHO	C∕=∘	> 99 : < 1	99
PhCHO	PhCOCH ₃	> 99 : < 1	99	🔶- сно	Î.	> 99 : < 1	98
С-сно	PhCOCH ₃	> 99 : < 1	95	PhCH ₂ CH ₂ CHO	Å.	> 99 : < 1	98
PhCH ₂ CH ₂ CHO) =0	> 99 : < 1	95	PhCH ₂ CH ₂ CHO) =0	93:7	93
С-сно	◯=∘	> 99 : < 1	98	🔶- сно	○ =0	92:8	91

Table 1. Selective Allylation of Aldehydes in the Presence of Ketones

^a The yield refers to GC yield of a homoallyl alcohol (A).

was isolated in 75% yield⁶ along with the homoallyl alcohol (21%) and acetophenone was recovered unchanged. Therefore, the initial conversion of an aldehyde into 1-silyloxysulfonium salt is essential for thesuccessful chemoselective allylation. Several experimental results of this chemoselective allylation of aldehydes are summarized in Table 1 and allylation of aldehydes in the presence of ketones has been consistently achieved in a highly selecitive manner with the exception of cyclohexanone. In the competition reaction of hydrocinnamaldehyde or cyclohexyl aldehyde and cyclohexanone, the aldehyde addition products were obtained with 93% and 92% selectivity due to a relatively high reactivity of cyclohexanone toward nucleophiles. The same high selectivity was also obtained with polycarbonyl compounds such as ketoaldehydes and the ketone addition product was not detected as shown below.



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