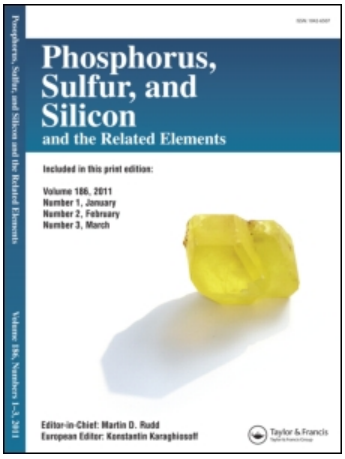

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Chalcogeno-Morita-Baylis-Hillman Reaction of Chalcogenide-Enones with Carbonyl Compounds

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The Chalcogeno-Morita-Baylis-Hillman reaction was achieved by the reactions of 2-(methylchalcogeno)phenyl vinyl ketones with carbonyl compounds or acetals in the presence of $BF_3{\cdot}Et_2O$. This reaction proceeds via the intramolecular Michael addition of the chalcogenide group to an enone moiety followed by the aldol reaction of the resulting chalcogenonio-enolate with an aldehyde. The reactions were worked up with triethylamine or saturated aqueous $NaHCO_3$ to give the α-methylene aldols (the Morita-Baylis-Hillman adducts).

Keywords Acetal; electron-deficient alkene; Morita-Baylis-Hillman reaction; selenide; sulfide; tandem Michael-aldol reaction

INTRODUCTION

We studied the chalcogenide-$TiCl_4$-mediated tandem Michael-aldol reaction of enones[1,2] or ynones[3] with aldehydes. This reaction proceeded quite rapidly and gave the methylene aldols (the Morita-Baylis-Hillman adducts) in good yields after purification of the raw products by preparative TLC on silica gel or after treatment of them with a base. Therefore, this reaction can be used instead of the Morita-Baylis-Hillman reaction. The reaction was extended to the reaction of chalcogenide-enones with aldehydes in the presence of a Lewis acid triggered by the intramolecular Michael addition of a chalcogenide followed by an aldol reaction and β-elimination.[4] This domino reaction can be called the chalcogeno Morita-Baylis-Hillman reaction. We herein describe the novel chalcogeno Morita-Baylis-Hillman reaction of chalcogenide-enones or -ynones with carbonyl compounds.

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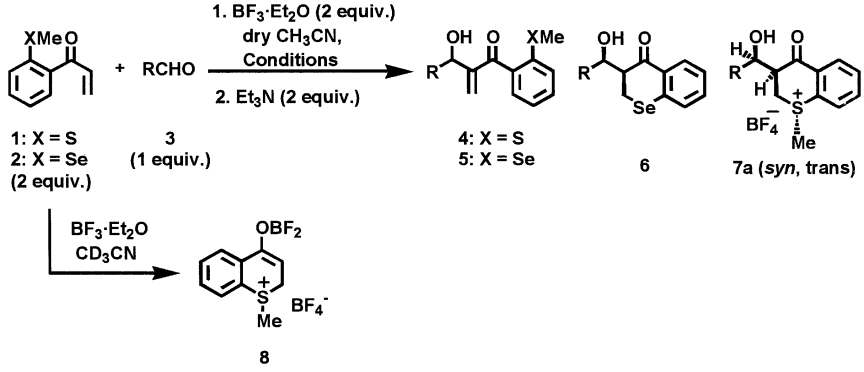
RESULTS AND DISCUSSION

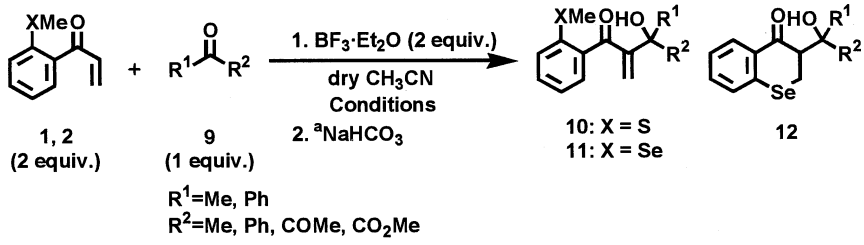
We first examined a Lewis acid whose conjugate base has low nucleophilicity to allow a chalcogenide to react with an enone and found that $BF_3{\cdot}Et_2O$ was the most effective Lewis acid. Reactions of enones **1** and **2** with aldehyde **3** were conducted using two equivilants of $BF_3{\cdot}Et_2O$ because one equivilants of $BF_3{\cdot}Et_2O$ is consumed for the formation of the alkoxyborane and the other becomes a counter anion (BF_4^-) of the onium salt after combination with the liberated fluoride.



SCHEME 1

Methylene aldols **4** and **5** were obtained in good yields.[4,5] Selenochromanone derivative **6** was obtained from seleno derivative **2**. Sulfonium salt **7a** (26%) was isolated from the reaction of **1** with *p*-nitrobenzaldehyde **3a** when the reaction was worked up with a saturated aqueous $NaHCO_3$ solution.

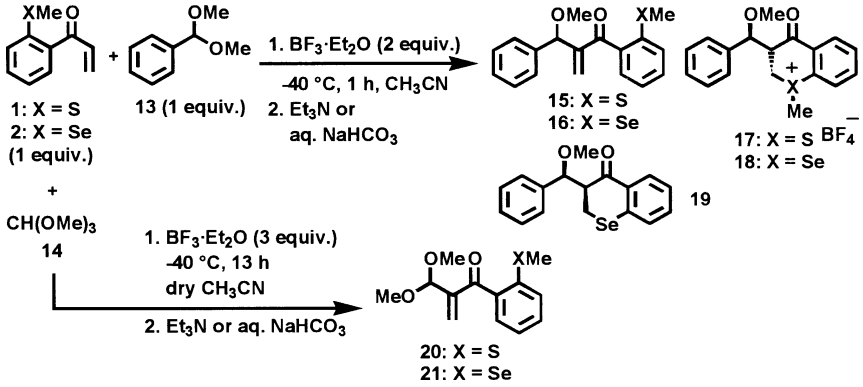
The sulfonio-enolate intermediate **8** was detected by ^{1}H-NMR spectroscopic analysis of the reaction of **1** and $BF_3{\cdot}Et_2O$ in CD_3CN (Scheme 1). This finding that the intermediate was a boron enolate encouraged us to conduct the reactions of **1** or **2** with ketones (Scheme 2),



SCHEME 2

α-diketones, and α-ketoesters, which do not react with enones under Morita-Baylis-Hillman reaction conditions. Reactions of these carbonyl compounds proceeded, but yields were low to moderate except for methyl pyruvate.[4,6]

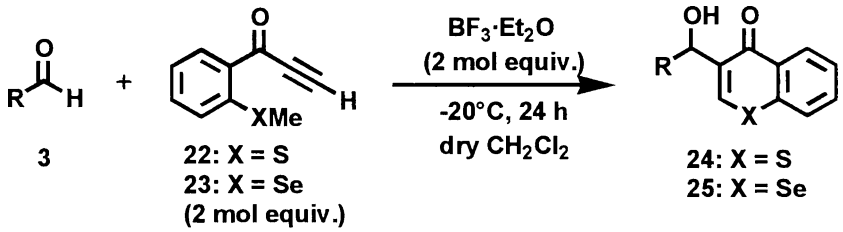
If acetals are used instead of aldehydes for our reaction, $BF_3{\cdot}Et_2O$ works for the formation of both sulfonio-enolate **8** and α-alkoxy carbocations. The alkoxy carbocations react with **8**, and α-alkoxyalkylation of enones can be achived. We carried out the reactions of **1** or **2** with benzaldehyde dimethyl acetal **13** in the presence of $BF_3{\cdot}Et_2O$. When the reaction was quenched with a saturated aqueous $NaHCO_3$ solution, chalcogenonium salt **17** or **18** was isolated together with **15** or **16**, respectively. The stereostructure of **18** was determined by X-ray analysis to be the anti-configuration between the methoxy group and the CH_2S moiety and the trans-configuration between the α-methoxybenzyl side chain and the *Se*-methyl group. Reaction of **1** or **2** with triethyl orthoformate **14** gave dimethoxy derivative **20** or **21** (Scheme 3), respectively, in good yield.



SCHEME 3

Reaction of ynone **22** or **23** with $BF_3{\cdot}Et_2O$ formed the boron allenolate as an intermediate, and it reacted with aldehydes to give 3-(hydroxyalkyl)chalcogeno-chromen-4-ones **24** or **25**, respectively, in moderate yields via 6-*endo-dig* cyclization and the aldol reaction (Scheme 4).[7]

Demethylation of the onium salts initially produced easily occurred because the carbonyl group is activated by the coordination of $BF_3{\cdot}Et_2O$ and the selenopyranone ring is more positively charged. This method is useful for the synthesis of 2-unsubstituted 3-(hydroxyalkyl)chalcogenochromen-4-ones.



SCHEME 4

In conclusion, we developed the tandem Michael-aldol reaction of chalcogenide-enones and carbonyl compounds using $BF_3{\cdot}Et_2O$ (the chalcogeno-Morita-Baylis-Hillman reaction) and demonstrated that this reaction can be used for reactions with not only aldehydes but also ketones, α-diketones, α-ketoesters, and acetals which cannot be applied to the Morita-Baylis-Hillman reaction.

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