percentage of additives will reduce the stability. Some compromise has been made in formation of both stable and tight bilayer membrane. To explain the optimum ratio (DLL/DPPC/DMPC=2/1/1), more thorough model study remains to be established. Presently we are undergoing projects of controlling permeability of bilayer for large molecules and "smart liposomes" capable of seeking the target site.

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TBSOTf Promoted Conjugate Addition of Enamines, Pyrrole, and Indole to α,β-Enones

Sunggak Kim,* Gyu-Jong Jeon, Deog-il Kim, Joo Hyun Park, and Joo Moon Lee

Department of Chemistry, Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea
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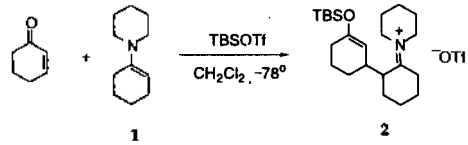
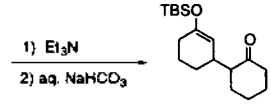
In connection with our research program toward functionalization of α,β-enones via conjugate addition approach,[1-3] we have studied the possibility of TBS triflate promoted conjugated addition of enamines and their related derivatives to α,β-enones. Enamines are normally considered as enol or enolate equivalents and they are often sufficiently reactive to add to conjugate acceptors when heated in solution.[4] If enamines would undergo the conjugate addition reaction to α,β-enones, it is expected that the resulting enolates might be trapped with TMSCl to afford synthetically very useful silyl enol ethers for further α-functionalizations.[5]



1 2

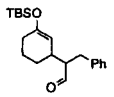
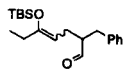
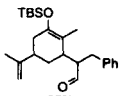
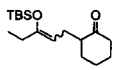
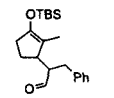
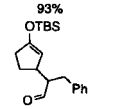
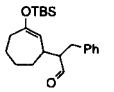
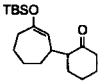
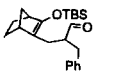
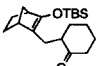
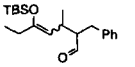
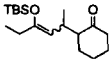


3 (84%) (1)

In order to assess that possibility, we began our studies by mixing 2-cyclohexen-1-one with piperidine enamine of cyclohexanone (**1**) in dichloromethane at room temperature for 24 h. Although the reaction proceeded to some extent, the conjugate addition product **3** was obtained in less than 20% yield. When the same reaction was carried out in toluene at 80 °C for 24 h, only a trace amount of the conjugate addition product was observed. Addition of TMSCl to the reaction mixtuire did not significantly speed up the reaction, indicating that TMSCl was not strong enough to activate the carbonyl group. Therefore, we turned our attention to much stronger reagent TBSOTf as a promoter.[6] When the same reaction was carried out in the presence of TBSOTf in dichloromethane, the reaction proceeded smoothly and was complete almost instantly at − 78 °C, yielding the 1,4-addition product **3** bearing a silyl enol ether group in 84% yield after aqueous workup (eq 1). Evidently, the reaction should proceed via intermediate **2**. The silyl enol ether group can be further utilized for the α-functionalization of α,β-enones.

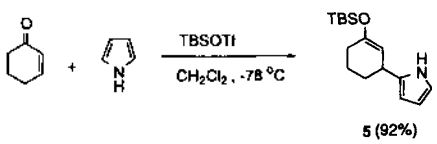
To determine the scope and limitations of the present method, the reactions were carried out with several structurally different α,β-enones using **1** and piperidine enamine of hydrocinnamaldehyde (**4**) in the presence of TBSOTf in dichloromethane at − 78 °C and experimental results are shown in Table 1. When 2-cyclohexen-1-one was treated with **4** under the similar conditions, 1,4-addition product was isolated in 93% yield. However, when the same reaction was carried out with 2-cyclopenten-1-one, a 69 : 13 mixture of 1, 4- and 1,2-addition product was obtained, whereas 2-methyl-2-cyclopenten-1-one was exclusively converted into 1,4-addition proudct under the similar conditions. Furthermore, 1,4-addition products were obtained exclusively with carvone and 3-methylene-2-norbornanone. However, with acyclic enones as Michael acceptors, a mixture of 1,2- and 1,4-addition products was obtained roughly in an equal ratio. Somewhat higher ratio of 1,4- and 1,2-addition products were obtained with **1**. Thus, 2-cyclopenten-1-one and 2-cyclohexen-1-one gave only 1,4-addtion products in high yield, although 2-cyclohepten-1-one gave a 74 : 7 mixture of 1,4- and 1,2-addition product. With acyclic enones, the ratio

Table 1. Conjugate Addition of Enamines to α,β-Enones

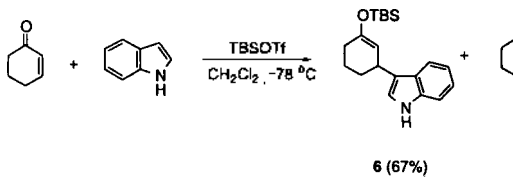
Enone	Products[a]	enone	Products
	 93%		 44% (36%)
	 95%		 58% (28%)
	 93%		 93%
	 69% (13%)		 92%
	 49% (37%)		 74% (7%)
	 65%		 70%
	 55% (44%)		 72% (17%)

[a] The numbers in parenthesis indicate the yield of the 1,2-addition product

of 1,4- and 1,2-addition products were increased to some extent, as compared with **4**, indicating that the ratio of 1,4- and 1,2-addition products depend very much on the nature of α,β-enones and enamines. Furthermore, we were unable to prepare enamines of acetaldehyde due to their tendency of polymerizations. It is also noteworthy that β-substituted α,β-enones did not undergo the conjugate addition reaction



5 (92%) (2)

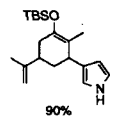
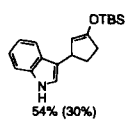
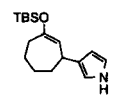
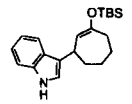
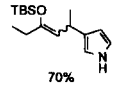


6 (67%) 7 (18%) (3)

under the present condtions.

We next studied the possibility of a conjugate addition of indole and pyrrole to α,β-enones since they were structurally and electronically related to enamines. When pyrrole was treated with 2-cyclohexen-1-one and TBSOTf in dichloromethane at − 78 °C, the conjugate addition reaction occurred cleanly, yielding **5** in 92% yield (eq 2). Similar results were obtained with 2-cyclohepten-1-one and 4-hexen-3-one. Furthermore, the reaction of indole with 2-cyclohexen-1-one in the presence of TBSOTf under the similar conditions also gave 1,4-addition products **6** and **7** (eq 3), in which the silyl enol ether group was partially hydrolyzed.[7] It is noteworthy that imidazole and *N*-methylimidazole did not undergo conjugate additions to 2-cyclohexen-1-one. Experimental results are summarized in Table 2.

Table 2. Conjugate Addition of Pyrrole and Indole to α,β-Enones

Enone	Product[a]	Enone	Product[a]
	 90%		 54% (30%)
	 88%		 64% (20%)
	 70%		45% (44%)
	73%		77%

[a] The numbers in parenthesis indicate the yield of the desilylated product

8 (82%) (4)

We also examined the conjugate addition reactions of aniline derivatives to α,β-enones. When the reaction was carried out with *N,N*-dimethylaniline under the similar conditions, the conjugate addition reaction did not occur. However, the reaction worked well with more electron-rich 3-methoxy-*N,N*-dimethylaniline, yielding the 1,4-addition proudct **8** in 82% yield under the similar conditions (eq 4). Similarly, 3-methoxy-*N,N*-dimethylaniline underwent clean conjugate addition reactions with 2-cyclopenten-1-one and 4-hexen-3-one. Furthermore, we also tested the possibility of conjugate addition of thiophene, furan, 2-dihydropyran, and benzofuran to 2-cyclohexene-1-one. When the reactions were carried out under the similar conditions using TBSOTf as a promoter, polymerized products were obtained with thiophene, furan, and 2-dihydrofuran, whereas the reaction did not occur with benzofuran under the same conditions.

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Tellurium Dioxide-Catalyzed Chlorination of Alcohols with Chlorotrimethylsilane

Dong Soo Ha* and Guen Seok Chai

Department of Chemistry, Sunchon National University, Sunchon 540-742, Korea
Received June 15, 1997

Recently, Palomo and Aizpurua[1] reported that chromic anhydride easily react with chlorotrimethylsilane in methylene chloride forming a dark red chromium oxidizing agent. This neutral reagent was proved to be efficient for the oxidation of secondary alcohols to ketones, thiols to disulfides, and oximes to the corresponding carbonyl compounds.[1] A simple insertion of chromic anhydride into silicon-chlorine bond of chlorotrimethylsilane would produce trimethylsilylchlorochromate which Palomo *et al.* proposed as an active oxidant.[1] In the study on the insertion reaction of inorganic compounds to reactive silicon-halogen bond, we reported some valuable reactions for the oxidation of toluenes,[2] alcohols[3] and olefins[4] and chlorinations of alcohols.[5]

Halosilanes were known to be useful for halogenation of alcohols. Silicon tetrachloride can convert reactive alcohols to the corresponding chlorides at high temperature.[6,7] Reactive iodotrimethylsilane also converts primary alcohols to alkyl iodides under mild conditions.[8] Bromotrimethylsilane requires a higher temperature to react with primary alcohols to produce alkyl bromides.[9] Use of chlorotrimethylsilane generally fails to produce alkyl chlorides. There are a few reports on the use of chlorotrimethylsilane for the preparation of alkyl chlorides.[10] Potassium carbonate[11] and bismuth (III) chloride[12] were known to activate the chlorinating power of chlorotrimethylsilane, but the former is appeared to be limited to some reactive allylic alcohols.[11] Dimethylsulfoxide catalyzed chlorotrimethylsilane was known to convert primary and tertiary alcohols to the corresponding chlorides.[13] Selenium dioxide was known to react with chlorotrimethylsilane to produce insertion products.[14] A trimethylsilylchloroselenite was displaced rapidly by a chloride, forming selenium(IV) oxodichloride. The selenium(IV) oxodichloride generated *in situ* from the reaction of selenium dioxide and chlorotrimethylsilane is known to convert various alcohols into corresponding chlorides.[14]

Taking into account the structural similarity of tellurium (IV) oxodichloride to those chlorinating agents such as thionyl chloride and selenium(IV) oxodichloride, we expected that tellurium(IV) oxodichloride can be developed as a new chlorinating agent for many organic functional groups. Indeed, when benzyl alcohol was treated with 2 equivalents of chlorotrimethylsilane and one equivalent of tellurium dioxide, the reaction was complete within an hour at room temperature (Equation 1).[15] The conversion was almost quantitative without any side products in the reaction mixtures.

$$ArCH_2OH + TMSCl \xrightarrow[CH_2Cl_2]{TeO_2} ArCH_2Cl \qquad (1)$$

A number of examples of the chlorination are summarized in Table 1. For most alcohols, the yields were almost quantitative. The conversion can be easily achieved in the chlorinated solvents such as methylene chloride or carbon tetrachloride of an alcohol and chlorotrimethylsilane containing tellurium dioxide. Most of primary alcohols as well as benzylic alcohols were chlorinated efficiently without any skeletal rearrangement and competing side reactions such as elimination. Cyclic alcohols and other secondary alcohols were also easily converted into the corresponding alkyl chlorides without rearrangement of carbon skeleton. Conversion of tertiary alcohols into corresponding chlorides were appeared to have some problems due to competing elimination. Allylic alcohol such as *trans*-cinnamyl alcohol also produced allylic chloride at room temperature without any side reactions.

This reaction was found during the course of our study of the functional group transformations using inorganic oxides/organosilanes.[2-5] Tellurium dioxide first reacts with chlorotrimethylsilane to form trimethylsiloxytellurium(IV) oxochloride which rapidly decomposes into tellurium(IV) oxodichloride (Equation 2). The unstable tellurium(IV) oxodichloride reacts with another molecule of chlorotrimethylsilane to form tellurium tetrachloride eventually (Equation 3).