$Yb(OTf)_3$ catalysed allylation of the hydrates of α-keto aldehydes and glyoxylates with allylsilane

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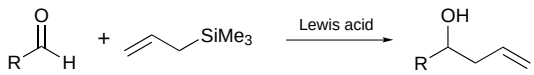
$Yb(OTf)_3$ catalysed allylation reactions of the hydrates of α-keto aldehydes and glyoxylates with allyltrimethylsilane at room temperature give α-keto and α-ester homoallylic alcohols in good yield.

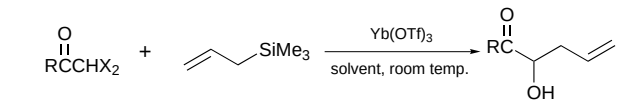
Recently, lanthanide trifluoromethanesulfonates [lanthanide triflates, $Ln(OTf)_3$] have attracted attention[1] because of their catalytic ability in various Lewis acid promoted carbon–carbon bond forming reactions, including Diels–Alder reactions,[2] Michael reactions[3] and allylation reactions of carbonyl compounds by allyl metals, for example allyltributylstannane and tetraallylgermane.[4] Kobayashi[5] also reported the $Ln(OTf)_3$ catalysed reaction of enol silyl ethers with carbonyl compounds (Mukaiyama aldol reaction) in aqueous media. Among the Lewis acid promoted C–C bond forming reactions, the allylation of carbonyl compounds with allylsilanes (Sakurai reaction,[6] Scheme 1) is one of the most important reactions in organic synthesis. However, stoichiometric amounts of Lewis acid must be employed due to the low nucleophilicity of allylsilane and the tight binding of the produced homoallylic alkoxide to the Lewis acid. The reaction can be performed using sub-stoichiometric amounts of silylating reagent [Me_3SiOTf, Me_3SiI and $Me_3SiB(OTf)_4$],[7] while the $Ln(OTf)_3$ catalysed Sakurai reaction was not realized until quite recently.[8] Compared with typical Lewis acids such as $TiCl_4$, $SnCl_4$, BF_3 and $AlCl_3$, $Ln(OTf)_3$ possesses stronger Lewis acidity, and is water soluble or water-tolerant, air-stable and easy to handle, not requiring anhydrous treatment. On the basis of the tolerance of $Ln(OTf)_3$ to active protons, we examined the ytterbium trifluoromethanesulfonate [$Yb(OTf)_3$] catalysed allylation of α-keto aldehydes hydrates **2**–**4** and glyoxylate hydrates **5** and **6** with allyltrimethylsilane **1**. We also explored the extent of asymmetric induction in the allylation reactions of chiral glyoxylate hydrate **6** in the presence of catalyst $Yb(OTf)_3$.



Scheme 1

Oxidation of the substituted acetophenones with selenium dioxide gave the corresponding hydrates **2**–**4**, while the (−)-menthyl glyoxylate monohydrate **6** was prepared according to Kornblum's method,[9] starting from (−)-menthol. The allylation reactions (Scheme 2) were carried out following a standard procedure. To a solution of the hydrate (0.25 mmol) and $Yb(OTf)_3$ (0.025 mmol) in 2 ml of CH_2Cl_2, allyltrimethylsilane (0.3 mmol) was added, followed by stirring for a given time (Table 1) at room temperature. The reaction mixture was worked up with brine and extracted with Et_2O. The crude product was purified by flash chromatography. The experimental results are listed in Table 1.

Compounds with α-keto and α-ester homoallylic alcohol moieties have been used as precursors for a number of biologically active natural products such as antibiotics.[10] Among the procedures currently available for the preparation of these compounds, allylation of α-keto aldehydes and glyoxylates using allyltrimethylsilane promoted by Lewis acids is a convenient method. However, the α-keto aldehyde and glyoxylates are often moisture sensitive and easily hydrated and polymerized. In practice, although the hydrates are more stable to air and moisutre, it is necessary to transform them to the corresponding α-keto aldehydes and glyoxylates before carrying out the Lewis acid promoted reaction, in order to avoid interaction between the Lewis acid and the hydroxy group. Under conventional Lewis acid conditions, hydroxy



2 R = Ph, X = OH
3 R = *p*-HOC_6H_4, X = OH
4 R = *p*-$MeOC_6H_4$, X = OH
5 R = BuO, X = OH
6 R = menthylO, X = OH
7 R = BuO, X_2 = O
8 R = Ph, X_2 = O

1

9 R = Ph
10 R = *p*-HOC_6H_4
11 R = *p*-$MeOC_6H_4$
12 R = BuO
13 R = menthylO

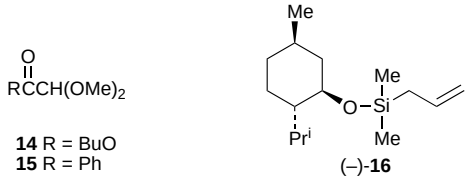
Scheme 2

Table 1 $Yb(OTf)_3$ catalysed allylation of hydrates **2**–**6** and glyoxylates **7** and **8** at room temperature

Entry	Substrate	Catalyst mol%	Solvent	*t*/h	Product	Yield[a] (%)	De (%) (Config.)
1	**2**	10	CH_2Cl_2	2	**9**	71	
2	**3**	10	MeCN	20	**10**	74	
3	**4**	10	MeCN	20	**11**	65	
4	**5**	10	CH_2Cl_2	1.5	**12**	76	
5	**6**	10	CH_2Cl_2	2	**13**	69	5 (*S*)
6[b]	**6**	10	CH_2Cl_2	24	**13**	49	8 (*S*)
7	**6**	10	MeCN	4	**13**	80	10 (*S*)
8	**6**	10	dioxane	20	**13**	76	30 (*S*)
9[c]	**6**	10	CH_2Cl_2	2	**13**	71	21 (*S*)
10[c]	**6**	10	dioxane	10	**13**	76	10 (*R*)
11	**7**	5	MeCN	0.5	**12**	75	
12	**8**	5	MeCN	0.5	**9**	83	

[a] Isolated yield. [b] Performed at 0 °C. [c] Using (−)-**16** instead of **1**.

groups in the substrates need to be protected. In contrast, the results (entries 1–5) obtained here show that the catalytic capability of $Yb(OTf)_3$ appears not to be affected by hydroxy groups on the substrate, including the phenoxy group in **3**. The reactions proceeded smoothly with a catalytic amount of $Yb(OTf)_3$ (10 mol%), giving α-keto homoallylic alcohols **9**–**11** and α-ester homoallylic alcohols **12** and **13** in good yields (65–83%). The various substrates exhibited different reactivity, the glyoxylate hydrates **5** and **6** being more reactive than the α-keto aldehyde hydrates **2**–**4** (*cf.* entry 7 *vs.* entries 2 and 3). The solvents used strongly influenced the reaction rate, which is fast in CH_2Cl_2 but slow in 1,4-dioxane. For the hydrates **3** and **4**, MeCN is the solvent of choice becasue of the low solubility of the hydrates in CH_2Cl_2 and 1,4-dioxane. On reducing the reaction temperature to 0 °C, the reaction slowed down noticeably (*cf.* entry 5 *vs.* entry 6). While the aldehyde hydrates can be considered as equivalent to an aldehyde carbonyl function in these catalytic allylation reactions, the aldehyde carbonyl groups themselves are more reactive (entries 11 and 12 *vs.* entries 4 and 1). On the other hand, if the corresponding acetals **14** and **15** were used, $Yb(OTf)_3$ catalysed allylation with



1 did not proceed at all, even in the presence of 20 mol% of catalyst.

When chiral glyoxylate hydrate **6** was employed, catalytic diastereoselective allylation occurred. The diastereoselectivity (de) of the reactions was low to moderate (5–30%), determined by the ratio of absorptions of diastereomeric protons in the ^1H NMR spectrum of the product **13**. The absolute configuration of the newly formed stereogenic centre was deduced through comparison with an authentic compound.[11] The de of the product strongly depended on the solvents used, with moderate de (30%) obtained in 1,4-dioxane, and rather poor de in CH_2Cl_2 and MeCN. Reducing the reaction temperature to 0 °C did not improve the de (entry 6). It is interesting to note that if (−)-allyldimethyl[(1*R*,2*S*,3*R*)-menthoxy]silane **16** was used, the de (*cf.* entry 5 *vs.* entry 9) increased noticeably (from 5 to 20%), but with 1,4-dioxane as the reaction solvent the absolute configuration of the new stereogenic centre was reversed. All these results indicated that the chiral group on the silicon participated in the stereocontrol of the allylation reaction. This is different from the conventional Lewis acid ($TiCl_4$, $AlCl_3$ and BF_3) promoted allylation of **6** with **16**, where the chiral group on the silicon did not affect the de of the product **13** to any significant extent.[11]

To our knowledge, these results are the first example of $Ln(OTf)_3$ catalysed allylation of aldehydes bearing unprotected hydroxy groups with allylsilane. $Ln(OTf)_3$ is therefore a novel mild catalyst for allylation with allylsilanes which is tolerant to substrates with active protons. It is expected that this $Ln(OTf)_3$ catalysed allylation reaction should also be effective in aqueous media.

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Footnote and References

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