

Allylation of hydrates of aldehydes and activated aromatic aldehydes with allyltrimethylsilane in H₂O-CH₃CN catalyzed by Sc(OTf)₃[†]

Ming-Wen Wang, Yong-Jun Chen, Li Liu, Dong Wang* and Xiao-Ling Liu

Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China

Sc(OTf)₃-catalysed allylations of hydrates of α -keto aldehydes and glyoxylates and activated aromatic aldehydes with allyltrimethylsilane in H₂O-CH₃CN were examined. α -Keto and α -ester homoallylic alcohols **3a-d** and aromatic homoallylic alcohols **3e-f** were obtained in good to excellent yields, depending on the reaction temperature and the ratio of H₂O to CH₃CN in co-solvent.

Recently, aqueous organic reaction has received considerable attention in view of the synthetic efficiency and environmental friendliness.¹ Accordingly, the development of Lewis acid catalysed carbon-carbon bond forming reactions in aqueous media becomes one of the most challenging topics in organic synthesis. On the basis of Kobayashi's pioneering work,² lanthanide trifluoromethanesulfonates [lanthanide triflates, Ln(OTf)₃] have been used as effective water-tolerant Lewis acid catalysts for many carbon-carbon bond forming reactions in aqueous media, such as Diels-Alder reactions,³ Michael reactions,⁴ Mukaiyama aldol reactions,⁵ allylation with tetraallyltin⁶ and tetraallylgermane,⁷ and so on. As is well known, the allylation of carbonyl compounds with allylsilanes under Lewis acid conditions (Hosomi-Sakurai reaction⁸) is one of the most important carbon-carbon bond forming reactions. But it must be carried out under strict anhydrous condition due to the use of moisture-sensitive Lewis acids (such as TiCl₄, ZnCl₂, AlCl₃, etc.). So far, no paper on Hosomi-Sakurai reaction in aqueous media has been reported. Herein, we wish to report the allylation reaction of carbonyl compounds bearing active protons with allyltrimethylsilane in H₂O-CH₃CN, catalysed by scandium triflates, Sc(OTf)₃.

In our previous report,⁹ the allylation reactions of hydrates of α -keto aldehyde and glyoxylate with allyltrimethylsilane can be catalysed by Yb(OTf)₃ which proved to be tolerant to the substrates bearing active protons. Unfortunately, it was found that in the case of aqueous allylation reaction (CH₃CN:H₂O = 10:1) with allylsilane, Yb(OTf)₃ did not show an effective catalytic capability. Sc(OTf)₃ is also a water-tolerant Lewis acid^{2,10} and can be used as a catalyst for addition of allyltrimethylsilane to aldehydes in non-aqueous media.¹¹ Thus, the allylation reactions of hydrates of α -keto aldehyde (**1b-d**) and glyoxylate (**1e**), as well as aromatic aldehyde (**1f-g**) with allyltrimethylsilane (**2**) catalysed by Sc(OTf)₃ in water-acetonitrile were examined (Table 1). For comparison, the allylation reactions of **1a-g** in acetonitrile were also carried out. The catalytic capability of Sc(OTf)₃ appears not to be affected by hydroxyl group in the substrates **1b-e** and it superior to that of Yb(OTf)₃ for carrying out allylation with **2** in aqueous media (the yield of corresponding homoallylic alcohol is only 20%). Sc(OTf)₃ can efficiently activate carbonyl compounds in aqueous media (H₂O-CH₃CN). On the other hand, comparing with the reactivity of tetraallyltin⁶ in THF-H₂O (9:1) and tetraallylgermane⁷ in CH₃NO₂-H₂O (20:1), allyltrimethylsilane is less reactive in CH₃CN-H₂O (10:1). Furthermore, it was indicated¹² that allyltrimethylsilane is likely hydrolysed in aqueous media, especially in acidic media. The solution of Sc(OTf)₃ in H₂O-CH₃CN was found to be acidic (pH = 2 ~ 3). In fact, there is a competition between the

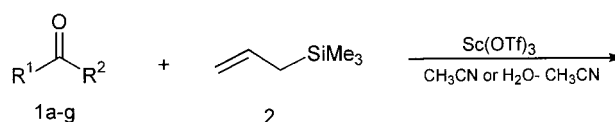
allylation of aldehydes with **2** and hydrolysis of **2** in the aqueous media. Therefore, activated aldehydes are desired to accelerate allylation reaction and prevail against the hydrolysis of **2**. For the activated aldehydes bearing α -carbonyl (**1a-d**), α -ester (**1e**), *p*-nitrophenyl (**1f**) and *p*-chlorophenyl (**1g**) groups, the allylations with **2** proceeded smoothly in acetonitrile at room temperature in the presence of 10 mmol % of Sc(OTf)₃. However, 20 mmol % of Sc(OTf)₃ and relatively higher reaction temperature (45–70 °C) must be employed in aqueous allylation reactions (co-solvent: 1:10 of H₂O-CH₃CN) to give the homoallylic alcohols (**3a-f**) in good to excellent yields (70–92%).

The reactivity of the hydrates of α -keto aldehydes **1b** is similar to that of the corresponding aldehydes **1a** in the same conditions. However, when the acetal (**4**) of α -keto aldehyde **1a** was used, the Sc(OTf)₃-catalysed allylation with **2** did not proceed at all in either CH₃CN or H₂O-CH₃CN (entry 8). The formation of **1a** in the course of the Sc(OTf)₃-catalysed reactions of **1b** with **2** in H₂O-CH₃CN was observed. It is suggested that there would be an equilibrium between **1a** and **1b** in Sc(OTf)₃-H₂O-CH₃CN mixture, and the formed **1a** be activated by Sc(OTf)₃ to react with **2**, driving the equilibrium to the side of the aldehyde **1a**.

The yields of the products **3a-f** strongly depend on the amount of water in the co-solvent system. The yields decrease with the increase of the ratio of water to acetonitrile. If the ratio was more than 1:5 of H₂O:CH₃CN, the allylation reaction did not work. Excessive water in the co-solvent would dismiss the catalytic activity of Sc(OTf)₃.

It is noted that higher reaction temperature (45–70 °C) is necessary for Sc(OTf)₃-catalysed aqueous allylation with **2**. For the aqueous reaction of **1f**, only a trace of the produce **3e** was detected at ambient reaction temperature, but 44% yield was obtained in the reaction at 45 °C. With increasing the reaction temperature to 70 °C, the yield of **3e** increased up to 92% markedly (entry 6). In the case of **1g**, the yield of **3f** increased from 10% at reaction temperature 45 °C up to 68% at 70 °C. It is clear that higher reaction temperature is favourable to the aqueous allylation, but not to the hydrolysis of **2**, even in acidic Sc(OTf)₃-H₂O-CH₃CN system.

The crotylations of **1b** with crotyltrimethylsilane (*Z*)- and (*E*)-**5** catalysed by Sc(OTf)₃ were carried out to give the mixtures of the homoallylic alcohols *syn*-**6** and *anti*-**6** (Scheme 2). The yields of the products in CH₃CN (80–82%) are relatively higher than that in H₂O-CH₃CN (60–65%).



Scheme 1

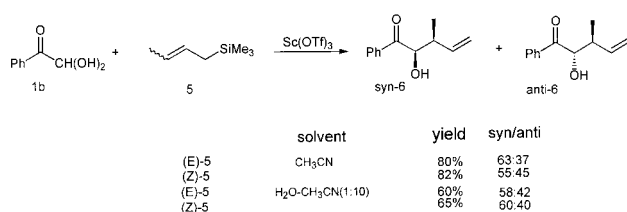
* To receive any correspondence.

[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 1 Sc(OTf)₃-catalysed allylation reactions of carbonyl compounds

Entry	R ¹	Substrate	R ²	Product	R ³	Catalyst (mmol%)	Solvent ^a	Temp (°C)	Time (1h)	Yield (%)
1	1a	Ph	CHO	3a	PhCO	10	A	20	12	75
						20	C	45	20	71
2	1b	Ph	CH(OH) ₂	3a	PhCO	10	A	20	15	78
						20	C	45	20	76
						10	C	45	20	30
						20	B	45	20	trace
3	1c	<i>p</i> -MeOC ₆ H ₄	CH(OH) ₂	3b	<i>p</i> -MeOC ₆ H ₄ CO	10	A	20	15	79
						20	C	45	20	79
4	1d	<i>p</i> -HOC ₆ H ₄	CH(OH) ₂	3c	<i>p</i> -HOC ₆ H ₄ CO	10	A	20	15	81
						20	C	45	20	83
5	1e	BuO	CH(OH) ₂	3d	BuOCO	10	A	20	6	65
						20	C	45	30	70
6	1f	<i>p</i> -NO ₂ C ₆ H ₄	H	3e	<i>p</i> -NO ₂ C ₆ H ₄	10	A	20	10	91
						20	C	45	10	44
						20	C	70	10	92
						20	C	45	10	10
7	1g	<i>p</i> -ClC ₆ H ₄	H	3f	<i>p</i> -ClC ₆ H ₄	10	A	20	10	88
						20	C	45	10	10
						20	C	70	10	68
						20	C	45	20	— ^c
8	4	Ph	CH(OEt) ₂	—	—	10	A	20	20	— ^c
						20	C	45	20	— ^c

^aA: CH₃CN; B: H₂O:CH₃CN (V/V) = 1:5; C: H₂O:CH₃CN (V/V) = 1:10; ^bisolated yield; ^cstarting materials were recovered.



Scheme 2

Both (Z)- and (E)-**5** gave moderate *syn*-selectivity, *syn:anti* = 55:45–63:37, where the ratios of *syn*- to *anti*-isomer were deduced by ¹H NMR of the product mixture in terms of the peaks of double bond [$\delta_{\text{CH}} = 5.96$ (*syn*) and 5.51 ppm (*anti*) and methyl group [$\delta_{\text{CH}} = 0.77$ (*syn*) and 1.21 ppm (*anti*)]. However, the presence of water has no impact on the diastereoselectivity of the crotylation reactions.

The products, α -keto and α -ester homoallylic alcohols **3a–e**, are useful precursors for a number of biologically active natural products.¹³ Among the procedures for the preparation of these compounds, the allylation of α -keto aldehydes and glyoxylates with **2** catalysed by Lewis acid is a conventional method. However, the α -keto aldehydes and glyoxylates are often moisture sensitive and easily hydrated and polymerized. In practice, although the hydrates are more stable to air and moisture, it is necessary to transform hydrates into corresponding α -keto aldehyde or glyoxylate before carrying out Lewis acid-catalysed reactions.¹⁴ Meanwhile, under conventional Lewis acid conditions, hydroxyl group in the substrates must be protected. The allylation of the hydrate of α -keto aldehyde and glyoxylate with **2** in CH₃CN and H₂O – CH₃CN catalysed by Sc(OTf)₃ provides a convenient approach to the α -keto and α -ester homoallylic alcohols. The investigation for expanding the generality of the aqueous allylation reaction with allylsilane is in process.

Experimental

General procedure: To a solution of hydrate of α -keto aldehyde (0.5 mmol) and Sc(OTf)₃ (0.1 mmol) in 2 ml of co-solvent (H₂O/CH₃CN = 1:10 v/v), allyltrimethylsilane (1 mmol) was added. The mixture was stirred for given reaction time at given temperature. The reaction mixture was quenched by brine and extracted with ether. Organic layer was dried over MgSO₄. The crude product was purified by flash chromatography on silica gel to give corresponding homoallylic alcohol **3a**¹⁵, **3e–f**¹⁶ and **3b–d**.

3b⁹ colourless oil, $V_{\text{max}}/\text{cm}^{-1}$ (film) 3470, 2940, 1670, 1570, 1260, 965, δ_{H} 2.33–2.38 (1H, m), 2.63–2.65 (1H, m), 3.90 (3H, s), 5.00–5.12 (2H, m), 5.72–5.85 (1H, m), 6.98 (1H, d, $J = 9$ Hz), 7.91 (2H, d, $J = 9$ Hz). m/z 206 (M^+ , 2.5), 135 (100).

3c⁹ colourless oil, $V_{\text{max}}/\text{cm}^{-1}$ (film) 3430, 2950, 1660, 1510, 1280, 1070, 960, δ_{H} 2.29–2.42 (1H, m), 4.99–5.16 (2H, m), 5.74–5.82 (1H, m), 6.50 (1H, s), 6.92 (2H, d, $J = 9.0$ Hz), 7.88 (2H, d, $J = 9.0$ Hz).

3d, colourless oil (Found: C, 62.65; H, 9.27. C₉H₁₆O₃ requires C, 62.76; H, 9.35%). $V_{\text{max}}/\text{cm}^{-1}$ (film) 3480, 3070, 1760, 1635, 1460, 910 δ_{H} (CDCl₃) 0.87 (3H, t, $J = 7.3$ Hz, CH₃), 1.20–1.50 (2H, m, CH₂), 1.55–1.70 (2H, m, CH₂), 2.18 (1H, s, OH) 2.35–2.80 (2H, m, CH₂), 4.12 (2H 2 x t, $J = 6.6$ Hz, OCH₂), 4.19 (1, dd, $J = 4.8$, 6.4 Hz, CH), 5.05–5.22 (2H, m, =CH₂), 5.7–5.9 (1H, m, =CH). δ_{C} 13.57, 19.01, 30.57, 38.69, 65.52, 69.92, 118.58, 132.48, 174.48.

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