Tetrakis(trifluoromethanesulfonyl)propane: highly effective Brønsted acid catalyst for vinylogous Mukaiyama–Michael reaction of α,β-enones with silyloxyfurans†

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Received (in Cambridge, UK) 21st January 2008, Accepted 7th March 2008
First published as an Advance Article on the web 8th April 2008
DOI: 10.1039/b800815a

1,1,3,3-Tetrakis(trifluoromethanesulfonyl)propane was found as an excellent Brønsted acid catalyst for the Mukaiyama–Michael reaction of α,β-enones with 2-silyloxyfurans; using β,β-disubstituted enones as a Michael acceptor, an excellent yield construction of quaternary carbon centers could be achieved; in addition, very low catalyst loading of Brønsted acid was used in a range from 0.05 to 1.0 mol%.

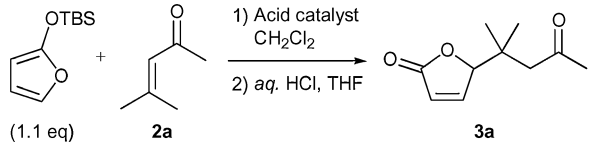
Organic Brønsted acids such as carboxylic acids, phosphonic acid and urea are useful and popular catalysts in modern organic synthesis.[1] These organic acids are essentially green due to avoiding the use of metal salts, although the catalyst loading of Brønsted acids is generally higher than those of transition metal catalysts or Lewis acids. In addition, the low catalyst activity of organic catalysts severely limits their application to synthetic reactions. For these reasons, the development of highly active Brønsted acid catalysts is an important task.

Recently, to realize low catalyst loading of Brønsted acid catalysts, Yamamoto and Boxer proposed the generation of silylated bis(triflyl)imide, which is known as a highly active silicon Lewis acid, featuring its 'self repairing' by *in situ* reaction of a catalytic amount of Tf_2NH (Tf = CF_3SO_2) and silyl enol ethers.[2] For instance, the Mukaiyama-aldol reaction of aldehydes with tris(trimethylsilyl)silyl (TTMS) enol ethers was nicely catalyzed by only 0.05 mol% of Tf_2NH. Efficient low catalyst loading was achieved only in the cases using bulky TTMS enol ethers as silylated nucleophiles, while the use of widely used *tert*-butyldimethylsilyl (TBS) enol ethers instead of TTMS enol ethers resulted in a significant decrease in the yield of aldol products. On the other hand, Jung and co-workers reported that the Mukaiyama–Michael reaction of cyclic enones with 2-TBSO-1,3-diene is catalyzed by Tf_2NH.[3,4] However, high catalyst loading, typically 1–5 mol%, remained a problem in this reaction.

As one of our ongoing researches on acid catalysis,[5,6] we reported the aluminium methide complex $Me_2AlCHTf_2$ prepared by the reaction of Me_3Al and bis(trifluoromethanesulfonyl)methane (Tf_2CH_2).[7] Since the Tf_2CH-structure acts as a good proton donor due to *gem*-disubstitution by two triflyl groups, highly acidic $Tf_2CHC_6F_5$ was reported as a 'super Brønsted acid' catalyst.[8] In addition, Yamamoto, Ishihara and co-workers reported a chiral organocatalyst equipped with a Tf_2CH-structure.[9] We have examined the catalyst activity of various carbon acids having a Tf_2CH-unit in the molecule. In this paper, we report on the vinylogous Mukaiyama–Michael reaction catalyzed by 1,1,3,3-tetrakis(trifluoromethanesulfonyl)propane **1** ($Tf_2CHCH_2CHTf_2$) having two acidic protons attached on the 1,3-carbons.[10,11] This is the first example of synthetic reactions catalyzed by carbon acid **1**.[12]

At first, to survey the activity of acid catalysts, the reaction of 4-methyl-3-penten-2-one **2a** with TBSO-furan (1.1 molar equivalent) as a model reaction was carried out (Table 1).[13] In the presence of 0.25 mol% of propane diacid **1**, the reaction for 2 h at −78 °C provided Michael adduct **3a** in 88% yield (entry 1). The catalyst loading of **1** could be reduced to 0.05 mol% without significant decrease in the product yield (entry 2). Interestingly, Tf_2CH_2 did not catalyze this reaction (entry 3), while a weak catalyst activity was observed by replacing a hydrogen of Tf_2CH_2 with a methyl or C_6F_5 group. That is, Tf_2CHMe (1.0 mol%) and $Tf_2CHC_6F_5$ (0.05 mol%) catalyzed the 1,4-addition reaction to give **3a** in 7% and 36% yield, respectively (entries 4, 5). Compared to the high catalyst

Table 1 Survey of effective acid catalysts for the reaction of **2a** with TBSO-furane



Entry	Acid catalyst (mol%)	*T*/°C	*t*/h	Yield[a] (%)
1	$Tf_2CHCH_2CHTf_2$ **1** (0.25)	−78	2	88
2	$Tf_2CHCH_2CHTf_2$ **1** (0.05)	−78 to −24	3	87
3	Tf_2CH_2 (1.0)	−78	3	0
4	Tf_2CHMe (1.0)	−78	3	7
5	$Tf_2CHC_6F_5$ (0.05)	−78 to rt	5	36
6	TfOH (0.25)	−78	6	7
7	Tf_2NH (0.25)	−78	6	7
8	Me_3Al (40)	−78	3	64
9	None	rt	5	NR[b]

[a] Isolated yield. [b] No reaction.

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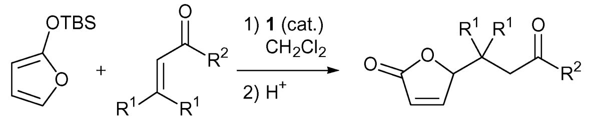
† Electronic supplementary information (ESI) available: Details of experiments, NMR data of **1** and all new compounds, and crystal structure of **1**. CCDC 674990. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b800815a

Table 2 Vinylogous Mukaiyama–Michael reaction of α,β-enones **2**[a]



(1.1 eq) **2** **3**

Entry	**2**	R[1]	R[2]	**1** (mol%)	**3**	Yield[b] (%)
1[c]	**2b**	$-(CH_2)_5-$	Me	0.25	**3b**	90
2[c]	**2c**	H	Me	0.05	**3c**	82
3[d]	**2d**	H	Ph	0.10	**3d**	89
4[d]	**2e**	H	4-BrC_6H_4	0.10	**3e**	88

[a] Reaction temperature, −78 to −24 °C; reaction time, 1–3 h. [b] Isolated yield. [c] Acidic workup by aq. HCl in THF. [d] Acidic workup by CF_3SO_3H in CH_2Cl_2.

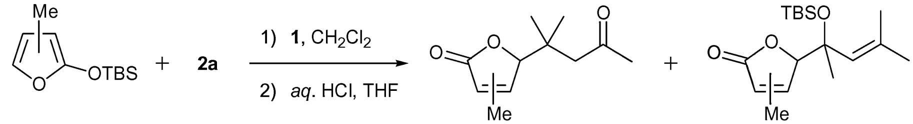
activity of **1**, the efficiency of other Brønsted acids such as TfOH and Tf_2NH was remarkably lower. For instance, in the presence of 0.25 mol% of TfOH, Michael adduct **3a** was obtained in only 7% yield (entry 6). The use of Tf_2NH also gave essentially the same result as the case of TfOH (entry 7). Additionally, the use of Me_3Al instead of Brønsted acid catalyst **1** required a notable increase in catalyst loading, but resulted in a low yield of **3a** (40 mol%, 64% yield) (entry 8).[13] The reaction in the absence of acid catalysts at room temperature also resulted in no change of **2a** and silyloxyfuran (entry 9).

Despite a number of reports demonstrating that Lewis acids can promote 1,4-addition of silicon enolate to sterically crowded β,β-disubstituted enones *via* a single-electron transfer mechanism,[14] the construction of a quaternary carbon through Brønsted acid-catalyzed Michael type addition to β,β-disubstituted enones has been limited.[3,15]

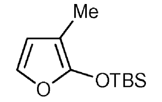
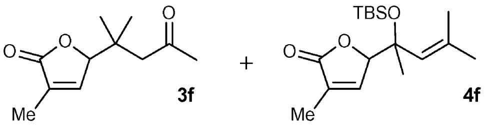
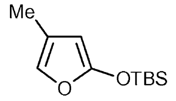
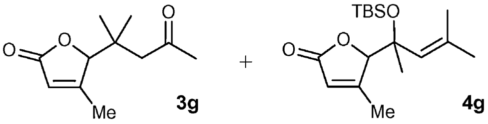
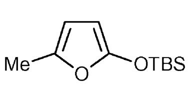
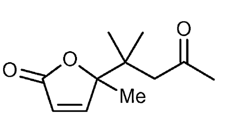
Next, in the presence of catalytic amount of propane diacid **1**, the vinylogous Mukaiyama–Michael reaction of various α,β-enones was conducted. The results are shown in Table 2. The reaction of cyclohexylideneacetone **2b** with silyloxyfuran was nicely catalyzed by 0.25 mol% of **1** to give 1,4-adduct **3b** in 90% yield (entry 1). Methyl vinyl ketone **2c** and aryl vinyl ketone derivatives **2d**, **2e** were also found as good substrates for the present reaction (**3c** 82% yield, **3d** 89% yield and **3e** 88% yield). Since effective catalyst loading was varied in a range from 0.05 to 0.25 mol% in these cases, excellent catalyst activity of propane diacid **1** was clearly demonstrated.

To reveal the substituent effect on the furan ring, we examined the reaction of **2a** with various methylated

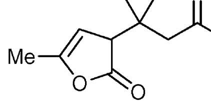
Table 3 Vinylogous Mukaiyama–Michael reaction of **2a** with methylated 2-silyloxyfurans



(1.1 eq) **3** (1,4-adduct) **4** (1,2-adduct)

Entry	2-Silyloxyfuran	**1** (mol%)	*T*/°C	*t*/h	Products	Yield[a] (%)	Ratio[b] (1,4 : 1,2)
1		0.25	−78	2	 **3f** + **4f**	86	42 : 1
2[c]		0.25	−78	4	 **3g** + **4g**	86	10 : 1
3[c]		1.00	−78	2	 **3h**	72[d]	1,4-only
4[c]		0.25	−24	2		55[e]	1,4-only

[a] Isolated yield. [b] Based on isolated yield. [c] 1.5 molar equivalent of 2-silyloxyfuran was used. [d] 25% of **5** was obtained. [e] 29% of **5** was obtained.



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silyloxyfuran derivatives (Table 3). In the presence of 0.25 mol% of **1**, the reaction of **2a** with 3-methyl-2-*tert*-butyldimethylsilyloxyfuran smoothly proceeded at −78 °C to give 1,4-adduct **3f** in 84% yield along with a small amount of 1,2-adduct **4f** (2% yield) after acidic work-up (entry 1). As shown in entry 2, in the case of 4-methyl-2-silyloxyfuran, the 1,4- : 1,2-selectivity was decreased to 10 : 1, although an excellent combined yield of **3g** and **4g** was observed (86% yield). Surprisingly, in the presence of 1 mol% of **1**, the reaction with 5-methyl-2-silyloxyfuran gave 1,4-adduct **3h**, which has consecutive quaternary carbons, in 72% yield without the formation of any 1,2-adducts. In this reaction, isomer **5** was also formed as a major byproduct (~25% yield) (entry 3). Since, as shown in entry 4, lower catalyst loading of **1** (0.25 mol%) resulted in a significant decrease of the reaction rate and poor yield of **3h**, >1 mol% of **1** was necessary to obtain a smooth reaction.

Regarding the reaction mechanism of the present reaction, we believe that Brønsted acid **1** initially reacts with silyloxyfurans to give a silane methide intermediate.[16] Since the silylation activity of this silane methide would be expected to be high due to I-strain between the silyl group and sterically bulky methide part,[17] the observed efficient activation of α,β-enones as a Michael accepter would involve a simultaneous coordination of this silane methide to the carbonyl oxygen and the following facile *O*-silylation of the enone carbonyl during the C–C bond formation (Michael addition step).

In conclusion, we found that tetrakis(trifluoromethanesulfonyl)propane **1** operates as an excellent catalyst for the vinylogous Mukaiyama–Michael reaction of α,β-enones with silyloxyfurans. Under the present catalyst conditions, an efficient construction of the quaternary carbons could be achieved in the reaction of β,β-disubstituted enones. A 1,4-adduct having consecutive quaternary carbons was also obtained in good yield by this Brønsted acid-catalyzed reaction of β,β-disubstituted enones with 5-methyl-2-silyloxyfuran. In addition, very low catalyst loading was realized in a range from 0.05 to 1.0 mol%. Further study on the synthetic application of **1** and the mechanistic insight are under progress in our laboratory.

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