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## Copper triflate [Cu(OTf)<sub>2</sub>] is an efficient and mild catalyst for the silylation of α-hydroxyphosphonates to α-trimethylsilyloxyphosphonates with HMDS at room temperature

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Abstract—A broad, adaptable, high yielding and convenient procedure for the fast conversion of various  $\alpha$ -hydroxyphosphonates to  $\alpha$ -trimethylsilyloxyphosphonates under mild conditions with HMDS in the presence of a catalytic amount of copper triflate is described. This procedure has also been applied successfully for the silylation of alcohols and phenols. © 2003 Elsevier Science Ltd. All rights reserved.

 $\alpha$ -Trimethylsilyloxyphosphonates are fascinating and versatile compounds in biology, industry and organic synthesis.<sup>1</sup> Having an  $\alpha$ -acidic hydrogen they can be deprotonated with bases such as lithium diisopropylamide.<sup>2</sup> This property and also easy cleavage of Si–O and C–P bonds in basic and acidic conditions, make  $\alpha$ -carbanionic  $\alpha$ -trimethylsilyloxyphosphonates efficient masked acyl anions.<sup>3</sup>

 $\alpha$ -Lithiated  $\alpha$ -trimethylsilyloxyphosphonates react with various acylating agents to produce the corresponding  $\alpha$ -acylated products, which can be converted to  $\alpha$ -hydroxy ketones after cleavage of the Si–O bond and elimination of dialkyl phosphate in alkaline media.<sup>2</sup> They react with various ketones to produce the corresponding  $\alpha$ -trimethylsilyloxyketones.<sup>4</sup> Carboxylic acids, unsymmetrical ketones and  $\beta$ , $\gamma$ -unsaturated ketones can be obtained by alkylation of  $\alpha$ -lithiated  $\alpha$ -trimethylsilyloxyphosphonates followed by cleavage of the Si–O bond and elimination of dialkyl phosphate in alkaline media.<sup>5</sup>

A review of the literature showed that the common methods for the synthesis of  $\alpha$ -trimethylsilyloxy phosphonates are definitely not easy ones. Harsh reaction conditions and long reaction times are required for the reaction of diethyl trimethylsilyloxyphosphite<sup>3,5</sup> or tri-

ethyl phosphite and trimethylsilyl chloride<sup>1b,c</sup> as the most common reagents for preparing  $\alpha$ -trimethylsilyloxyphosphonates from their corresponding aldehydes. The other method for the preparation of these compounds deals with the reaction of silyl phenyl ketones with trialkylphosphites at 80°C and over a long reaction time (12 h).<sup>6</sup> Trimethylsilyl chloride has been used to prepare diethyl  $\alpha$ -trimethylsilyloxybenzylphosphonate from the sodium salt of diethyl phosphite and benzaldehyde in a moderate yield (67%).<sup>5b</sup> A direct synthesis of  $\alpha$ -trimethylsilyloxyphosphonates from  $\alpha$ hydroxy phosphonates<sup>7</sup> was accomplished by using hexamethyldisilathiane at 50–70°C with 55–78% yields.<sup>8</sup>

Manipulation of the hydroxyl functional group of  $\alpha$ -hydroxyphosphonates without affecting Si–O and C–P bonds in these molecules is an important synthetic achievement. We have recently reported mild oxidation and silylation methods for this aim.<sup>9</sup> In our laboratories we have started an extensive study of new applications of triflates in organic synthesis. Now we report that copper triflate<sup>10</sup> [Cu(OTf)<sub>2</sub>] can be used as a mild



Scheme 1.

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**Table 1.** Silylation of diethyl  $\alpha$ -hydroxyphosphonates (1a– n) to diethyl  $\alpha$ -trimethylsilyloxyphosphonates (2a–n) with HMDS in the presence of Cu(OTf)<sub>2</sub> in CH<sub>3</sub>CN at room temperature

Product 2 <sup>Ref.</sup>	R-	Yield <sup>a</sup> (%)
<b>a</b> <sup>1a,c,5b,6</sup>	C <sub>6</sub> H <sub>5</sub> -	97 <sup>b</sup>
<b>b</b> <sup>11</sup>	$4-CH_3C_6H_4-$	90°
<b>c</b> <sup>12</sup>	$4-CH_3OC_6H_4-$	95
<b>d</b> <sup>9c</sup>	$2,4,6-(CH_3)_3C_6H_2-$	90
<b>e</b> <sup>12</sup>	$2-ClC_6H_4$ -	97
<b>f</b> <sup>12</sup>	$3-ClC_6H_4$ -	95
<b>g</b> <sup>12</sup>	$4-ClC_6H_4-$	98
h <sup>9c</sup>	2,6-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> -	96
<b>i</b> <sup>12</sup>	$2 - O_2 NC_6 H_4$ -	91
<b>j</b> <sup>12</sup>	$3-O_2NC_6H_4-$	90°
<b>k</b> <sup>12</sup>	$4-O_2NC_6H_4-$	92
1 <sup>9c</sup>	2-Naphthyl-	90
m <sup>9c</sup>	3-Pyridyl-	91
n <sup>3</sup>	PhCH=CH-	90

<sup>a</sup> Isolated yields, reaction time = 15 min. The amount of copper triflate and HMDS were 0.12 and 0.7 equiv., respectively.

<sup>b</sup> The amount of copper triflate was 0.11 equiv.

<sup>c</sup> The amount of HMDS was 1 equiv.

catalyst for the activation of HMDS to affect efficient silylation of various types of diethyl  $\alpha$ -hydroxyphosphonates (1a–n). The reactions proceeded smoothly and effortlessly in a few minutes in CH<sub>3</sub>CN at room temperature (Scheme 1, Table 1).

In all these reactions cleavage of C–P and Si–O bonds was not observed and only diethyl  $\alpha$ -trimethylsilyloxy

phosphonates as the sole products of the reactions were isolated in excellent yields (90-98%).<sup>13</sup>

In order to show the unique catalytic behavior of  $Cu(OTf)_2$  in these reactions, we have performed silylation of **1a** with HMDS in the presence of catalytic amounts of LiOTf,<sup>14</sup> Ce(OTf)<sub>4</sub><sup>15</sup> as other metal triflates and CuCl<sub>2</sub>. Production of benzaldehyde in 30–45% yields was observed which indicates a large amount of C–P bond cleavage in the presence of these catalysts.

Easy work-up, along with the high yields of the products and also the mildness of the catalyst and the reaction conditions encouraged us to apply this method for the protection of hydroxy functional groups in ordinary alcohols and phenols. Most of the reactions proceeded smoothly and cleanly in excellent yields in appropriate reaction times (Table 2).<sup>16</sup>

As shown in Table 2, treatment of a variety of ordinary alcohols with HMDS in acetonitrile at room temperature in the presence of catalytic amounts of  $Cu(OTf)_2$ gives the corresponding trimethylsilyl ethers in excellent yields. *p*-Substituted benzylic alcohols containing electron-donating and electron-withdrawing groups, primary and secondary aliphatic alcohols were protected efficiently in short reaction times (entries 1–12). Longer reaction times are required for complete conversion of allylic and tertiary aliphatic alcohols to the corresponding silylated products (entries 13–18). *p*-Cresol was silylated faster with higher yield than phenol (entries 19, 20). While even after 24 h stirring, conversion of

**Table 2.** Silylation of alcohols and phenols to trimethyl silyl ethers with HMDS in the presence of  $Cu(OTf)_2$  in  $CH_3CN$  at room temperature

Entry	Substrate	Time (min)	Yields <sup>a</sup> (%)
1	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	5	95 <sup>b</sup>
2	4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	5	90 <sup>b</sup>
3	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	15	95 <sup>b</sup>
4	4-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> OH	35	90 <sup>b</sup>
5	Anthracene-9-methanol	57	95°
6	Ph(CH <sub>2</sub> ) <sub>2</sub> CH <sub>2</sub> OH	25	98°
7	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>6</sub> CH <sub>2</sub> OH	30	91°
8	PhCH <sub>2</sub> CH <sub>2</sub> OH	5	95°
9	PhCH(C <sub>2</sub> H <sub>5</sub> )OH	40	95 <sup>b</sup>
10	(Ph) <sub>2</sub> CHOH	35	98 <sup>b</sup>
11	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CH(CH <sub>3</sub> )OH	40	98°
12	2-(6,6-Dimethylbicyclo[3.1.1]hept-2-ene-2-yl)ethanol	75	99 <sup>b</sup>
13	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>5</sub> CH(CH=CH <sub>2</sub> )OH	65	90 <sup>b</sup>
14	(CH <sub>3</sub> ) <sub>2</sub> C=CHCH <sub>2</sub> OH	80	85 <sup>b</sup>
15	α-Terpineol	24 h	93°
16	5-CH <sub>3</sub> -5-decanol	19 h	90°
17	1-Adamantanol	120	91°
18	CH <sub>3</sub> CH <sub>2</sub> C(CH <sub>3</sub> ) <sub>2</sub> OH	150	93°
19	C <sub>6</sub> H <sub>5</sub> OH	120	70°
20	$4-CH_3C_6H_4OH$	5	85°
21	$4-O_2NC_6H_4OH$	24 h	_d
22	4-AcetylC <sub>6</sub> H <sub>4</sub> OH	24 h	_d

<sup>a</sup> Isolated yields.

<sup>b</sup> The equivalent ratio of substrate/HMDS/Cu(OTf)<sub>2</sub> is 1/0.5/0.01.

<sup>c</sup> The equivalent ratio of substrate/HMDS/Cu(OTf)<sub>2</sub> is 1/0.7/0.01.

<sup>d</sup> No reaction.

phenols with electron-withdrawing groups to the corresponding trimethylsilyl ethers was not observed under similar reaction conditions (entries 21 and 22).

In conclusion, in this study we have found that  $Cu(OTf)_2$  is a mild and suitable catalyst for the activation of HMDS to silylate hydroxy functional groups of structurally different  $\alpha$ -hydroxyphosphonates under mild reaction conditions with excellent yields and without cleavage of C–P bonds. We have also applied this protocol for the efficient silylation of ordinary alcohols and phenols.

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## References

- (a) Kabachnik, M. M.; Synatkova, E. V.; Novikova, Z. S.; Abramova, G. L.; Rozhkova, N. G.; Andreeva, E. I. Vesthn. Mosk. Univ., Ser. 2: Khim. 1990, 31, 384–389; (b) Birum, G. H.; Richardson, G. A. US Patent 3, 113, 139 (to Monsanto Chem. Co), December, 3, 1963; Chem. Abstr. 1964, 60, 5551d; (c) Olah, G. A.; Wu, A. J. Org. Chem. 1991, 56, 902–904.
- Sekine, M.; Nakajima, M.; Hata, T. Bull. Chem. Soc. Jpn. 1982, 54, 218–223.
- 3. Hata, T.; Hashizume, A.; Nakajima, M.; Sekine, M. *Tetrahedron Lett.* **1978**, *19*, 363–366.
- Koenigkramer, R. E.; Zimmer, H. Tetrahedron Lett. 1980, 21, 1017–1020.
- (a) Evans, D. A.; Hurst, K. M.; Truesdale, L. K.; Takacs, J. M. *Tetrahedron Lett.* **1977**, *18*, 2495–2498; (b) Sekine, M.; Nakajima, M.; Kume, A.; Hashizume, A. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 224–238.
- Sekiguchi, A.; Ikeno, M.; Ando, W. Bull. Chem. Soc. Jpn. 1978, 51, 337–338.

- (a) Baraldi, P. G.; Guarneri, M.; Moroder, F.; Polloni, G. P.; Simoni, D. *Synthesis* **1982**, 653–655; (b) Sardarian, A. R.; Kaboudin, B. *Synth. Commun.* **1997**, *27*, 543–551; (c) Texier-Boullet, F.; Foucaud, A. *Synthesis* **1982**, 916.
- Lebedev, E. P.; Mizhiritskii, M. D.; Baburina, V. A.; Mironov, V. F.; Ofitserov, E. N. *Zh. Obshch. Khim.* 1979, 49, 1731–1737.
- (a) Firouzabadi, H.; Iranpoor, N.; Sobhani, S.; Sardarian, A. R. *Tetrahedron Lett.* 2001, 42, 4369–4371; (b) Firouzabadi, H.; Iranpoor, N.; Sobhani, S. *Tetrahedron Lett.* 2002, 43, 477–480; (c) Firouzabadi, H.; Iranpoor, N.; Sobhani, S. *Tetrahedron Lett.* 2002, 43, 3653–3655.
- Jenkins, C. L.; Kochi, J. K. J. Am. Chem. Soc. 1972, 94, 843–855.
- 11. Ernst, A.; Karola, H.; Hermann, M. Synthesis 1990, 323–326.
- 12. Yongzhen, Z.; Zhonghua, L. *Yingyong Huaxue* **1991**, *8*, 33–37.
- 13. Typical procedure for the preparation of diethyl  $\alpha$ -trimethylsilyloxyphosphonates from diethyl  $\alpha$ -hydroxyphosphonates catalyzed by copper triflate [Cu(OTf)<sub>2</sub>]: A solution of **1a** (1 mmol, 0.244 g) and HMDS (0.7 mmol) was prepared in CH<sub>3</sub>CN (5 mL). Cu(OTf)<sub>2</sub> (0.11 mmol) was added to the mixture at room temperature. After 15 min dichloromethane (10 mL) was added to the reaction mixture and it was washed with H<sub>2</sub>O (3×10 mL). The organic layer was separated and dried over anhydrous sodium sulfate. After evaporation of the solvent, the highly pure product **2a** was obtained in 97% yield.
- Firouzabadi, H.; Iranpoor, N.; Eslami, Sh. Tetrahedron Lett. 1999, 40, 4055–4058.
- 15. Iranpoor, N.; Shekarriz, M. Bull. Chem. Soc. Jpn. 1999, 72, 455–458.
- 16. Typical procedure for trimethylsilylation of alcohols with HMDS using copper triflate  $[Cu(OTf)_2]$  as catalyst: Cu(OTf)<sub>2</sub> (0.01 mmol) was added to a solution of benzyl alcohol (1 mmol) and HMDS (0.5 mmol) in acetonitrile (5 mL) at rt. The reaction progress was monitored by TLC. After completion of the reaction, dichloromethane (10 mL) was added to the reaction mixture and the solution washed with H<sub>2</sub>O (3×10 mL). The organic layer was separated and dried over anhydrous sodium sulfate. After evaporation of the solvent, the highly pure benzyl trimethylsilyl ether was obtained in 95% yield.