

A Novel Method for the Synthesis of Thiols from the Corresponding Olefins by Using Thiocarbonates and Ti(IV) Halides

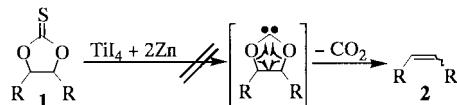
Teruaki Mukaiyama, Terunobu Saitoh, and Hideki Jona

Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162-8601

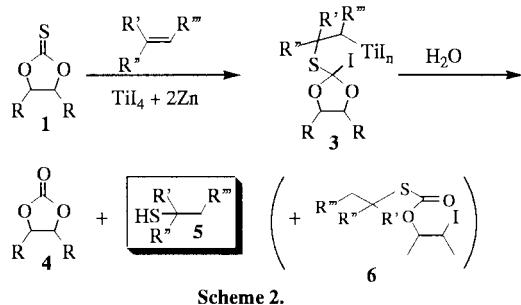
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A convenient method for the preparation of secondary or tertiary thiols from the corresponding olefins was established by using thiocarbonate, titanium(IV) chloride or fluoride and copper(II) oxide. Various thiols were obtained regioselectively in good to excellent yields according to the Markovnikov rule.

Recently, it was reported from our laboratory that diastereoselective pinacol coupling reaction of various aldehydes proceeded smoothly by using low valent titanium¹ halides such as chloride, bromide and iodide.² Then, it was thought that reductive deoxygenation of thiocarbonate **1**³ would be effected by the above low valent titanium species to afford the corresponding olefins **2** along with the loss of CO₂ via carbene intermediate formed by desulfurization. Contrary to expectation, the desired olefin **2** was not obtained at all when the reductive desulfurization of thiocarbonate was tried by using low valent titanium iodide formed in situ from titanium(IV) iodide and zinc powder (Scheme 1). Next, in order to scavenge iodine originated from titanium iodide, the same reaction was tried by adding of 2-methyl-2-butene. It was found that carbonate **4**, instead of the desired olefin **2**, was unexpectedly isolated together with adduct **6** (Scheme 2). The formation of **4** indicated the existence of intermediate **3** which in turn afforded thiol **5** on hydrolysis. This gave us an important hint that thiols would be prepared from the corresponding olefins. Actually, thiol **5** was isolated on careful treatment of the above reaction mixture with 1 M aqueous HCl. After screening the reaction conditions, it was found that the similar reaction proceeded smoothly by using just TiCl₄ without extra addition of such reducing agents as Zn powder. In this communication, we would like to report a convenient method for the preparation of secondary and tertiary thiols from the corresponding olefins by using thiocarbonate and titanium(IV) halide.



Scheme 1.



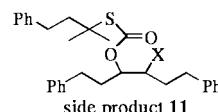
Scheme 2.

Various titanium(IV) halides were examined further in order to check their activities as Lewis acid under those reaction conditions as listed in Table 1. Then, TiCl₄ and TiF₄ proved to be more effective reagents compared with TiI₄ and TiBr₄ (Table 1, Entries 1–3, 6). In the latter cases, large amounts of side product **11** were formed. All these results indicated the reactions to be influenced by size, nucleophilicity, and electronegativity of the halogen atoms contained in the titanium salts.⁴ Next, various solvents and reaction temperatures were examined by using both TiCl₄ and TiF₄ (Table 1, Entries 3–5, 6–8). When TiCl₄ was used, the reaction proceeded smoothly at 0 °C in toluene to afford the desired thiol **9** in good yield (Table 1, Entry 5). Thiol **9** was also obtained in good yield when the reaction was carried out in CH₂Cl₂ at room temperature using TiF₄ (Table 1, Entry 6). In every case, the corresponding co-product of carbonate **10**, formed by oxygenation of thiocarbonate **8**, was obtained without an exception. Further, side product **11** was obtained in some cases, but it was not hydrolyzed during the above work up procedure.

Table 1. Synthesis of thiol **9** from the corresponding olefin **7** using thiocarbonate **8** and titanium(IV) halide

Entry	TiX ₄	Solvent	Temp.	9 /%	10 /%
				9 /%	10 /%
1	TiI ₄	CH ₂ Cl ₂	rt	19	25
2	TiBr ₄	CH ₂ Cl ₂	rt	10	18
3	TiCl ₄	CH ₂ Cl ₂	rt	43	41
4	TiCl ₄	CH ₂ Cl ₂	0 °C	57	52
5	TiCl ₄	Toluene	0 °C	81	81
6	TiF ₄	CH ₂ Cl ₂	rt	72	67
7	TiF ₄	CH ₂ Cl ₂	0 °C	66	62
8	TiF ₄	Toluene	0 °C	22	22

^aDetermined by GC analyses using an internal standard.



Next, various Lewis acids and additives were examined under the conditions as shown in Table 2. Concerning the effect of Lewis acids, TiCl₄ gave the best result. (Table 2, Entries 1–4). Further, several metal oxides⁵ were added to the above reaction mixture to improve the yield. Among the additives, copper(II) oxide was the most effective and thiol **9** was obtained in excellent yield. However the role of copper(II) oxide is not yet clear (Table 2, Entries 5–8).

Table 2. Effect of metal chlorides and additives

Entry	MX	Additive (0.25 equiv)	Yield /% ^a	Reaction scheme	
				1.2 equiv)	12
1	TiCl ₄	—	87		
2	SnCl ₄	—	62		
3	AlCl ₃	—	complex mixture		
4	ZrCl ₄	—	N.R.		
5	TiCl ₄	ZnO	89		
6	TiCl ₄	MgO	90		
7	TiCl ₄	CuO	98		
8	TiCl ₄	CuO ^b	quant.		

^aDetermined by GC analyses using an internal standard.^bCuO (0.5 equiv) was used.**Table 3.** Syntheses of thiols from various olefins

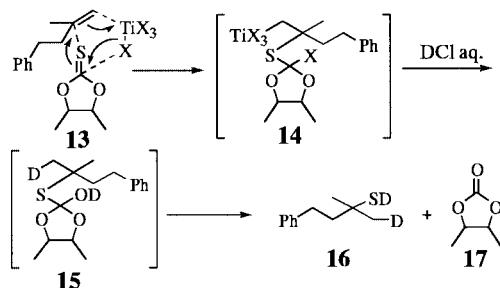
Entry	Olefin	Thiol	Conditions ^a	Yield /% ^b	Reaction scheme	
					TiX ₄ (3.0 equiv), CuO (0.5 equiv)	(1.2 equiv)
1	Ph-CH=CH ₂	Ph-CH ₂ CH ₂ SH	A	99		12
2	Ph-CH=CH ₂	Ph-CH ₂ CH ₂ CH ₂ SH	A	76		
3	Ph-CH=CH ₂	Ph-CH ₂ CH ₂ CH ₂ CH ₂ SH	A	quant.		
4	Ph-C ₆ H ₄ =CH ₂	Ph-C ₆ H ₄ CH ₂ SH	A	88 ^{c,d}		
5	CH ₂ =CH-CH ₂	(CH ₂ -CH ₂) ₂ S	B	66 ^c		
6	CH ₂ =CH-CH ₂	CH ₂ -CH ₂ CH ₂ SH	A	6		
7	CH ₂ =CH-CH ₂	CH ₂ -CH ₂ CH ₂ CH ₂ SH	C	62		
8	CH ₂ =CH-CH ₂	CH ₂ -CH ₂ CH ₂ CH ₂ CH ₂ SH	A	6		
9	CH ₂ =CH-CH ₂	CH ₂ -CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ SH	C	58		
10	Ph-CH=CH ₂	Ph-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ SH	A	26		
11	Ph-CH=CH ₂	Ph-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ SH	C	67		

^aReaction conditions: A TiCl₄, Toluene, 0 °C, 1 h. B i) TiCl₄, Toluene, 0 °C, 1 h, ii) HCl aq. iii) I₂. C TiF₄, CH₂Cl₂, rt, 12 h. ^bDetermined by GC analyses using an internal standard. ^cIsolated yield. ^dDiastereomeric ratio = ca. 2:1 by ¹H NMR and the relative stereochemistries have not been clear.

In order to extend the scope of the present thiol forming reaction, various olefins were treated under the reaction conditions shown in Table 3. Tertiary thiols were obtained in good to excellent yields when geminal di-, tri-, or tetra-substituted olefins were used (Table 3, Entries 1–5). In the cases of using vicinal di- or mono-substituted olefins, on the other hand, secondary thiols were obtained in good yields only when TiF₄ was used (Entries 6–11). Furthermore, it should be noted here that

all thiols were obtained in perfectly regioselective manner according to Markovnikov rule (Entries 1–4, 10, 11).

Finally, the mechanism of the present reaction using olefin, thiocarbonate, and titanium(IV) halide was investigated by quenching the reaction mixture with D₂O–DCl, and deuterated thiol **16** and carbonate **17** were formed as shown in Scheme 3. The result was thus explained by considering the initial formation of the key intermediate **14** by way of TiX₄-induced cyclic six-membered transition state **13**. The formed **14** was in turn hydrolyzed on treatment with DCl–D₂O to afford the deuterated thiol **16** and carbonate **17**.

**Scheme 3.**

Thus, a novel method for direct synthesis of thiols from the corresponding olefins by using of TiCl₄ or TiF₄ in the coexistence of copper(II) oxide was established. Since there are only a few reports on direct synthesis of thiols⁶ especially on that of the hindered ones,⁷ this method provides a useful tool in the field of organic synthesis.

The typical experimental procedure is as follows: to a stirred suspension of CuO (8.0 mg, 0.1 mmol), **7** (28.9 mg, 0.2 mmol) and **12** (32.4 mg, 0.24 mmol) in toluene (3.0 mL) was added TiCl₄ (0.066 mL, 0.6 mmol) at 0 °C. After the reaction mixture was stirred for 1 h at 0 °C, it was quenched by addition of 1 M HCl aq. The mixture was stirred vigorously and aqueous layer was extracted with CH₂Cl₂. The combined organic layer was washed with H₂O and brine. The yield was determined by GC analysis using an internal standard.

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