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A Convenient Synthesis of Thioacetates and Thiobenzoates Using Silica-Gel Supported Potassium Thioacetate

Tadashi Aoyama^a, Toshio Takido^a & Mitsuo Kodomari^b

^a Department of Materials and Applied Chemistry, College of Science and Technology, Nihon University, Kanda Surugadai, Chiyoda-ku, Tokyo, Japan

^b Department of Applied Chemistry, Shibaura Institute of Technology, Shibaura, Minato-ku, Tokyo, Japan

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A Convenient Synthesis of Thioacetates and Thiobenzoates Using Silica-Gel Supported Potassium Thioacetate

Tadashi Aoyama,^{1,*} Toshio Takido,¹ and Mitsuo Kodomari²

¹Department of Materials and Applied Chemistry, College of Science and Technology, Nihon University, Kanda Surugadai, Chiyoda-ku, Tokyo, Japan ²Department of Applied Chemistry, Shibaura Institute of Technology, Shibaura, Minato-ku, Tokyo, Japan

ABSTRACT

A simple and efficient procedure has been developed for the synthesis of thioesters by a reaction of alkyl halides with silica-gel supported potassium thioacetate or thiobenzoate under mild conditions.

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^{*}Correspondence: Tadashi Aoyama, Department of Materials and Applied Chemistry, College of Science and Technology, Nihon University, Kanda Surugadai, 1-8-14 Kanda Surugadai, Chiyoda-ku, Tokyo 101-8308, Japan; E-mail: aoyama@chem.cst.nihon-u.ac.jp.

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Key Words: Thioester; Potassium thioacetate; Thioacetates; Thiobenzoates; Silica-gel.

Thioesters are very important compounds in organic synthesis. For example, thioesters have been employed as mild acyl transfer reagents,^[1] building blocks of heterocyclic compounds,^[2] for aldol reactions^[3] and for the synthesis of ketones^[4] and amides,^[5] and precursors of thiols.^[6] Various synthetic procedures for synthesis of thiosters has been reported in the literature. Usually thioesters are prepared from the reaction of disulfides with carboxylic acid anhydrides,^[7] the reaction of carboxylic acids with thiols,^[8] thioacetic acids with alcohols,^[9] and organic halides with potassium thioacetate in polar solvents.^[10] These reactions are very efficient, but vigorous conditions, long reaction times and the use of environmentaly unfriendly reagents such as metal halides are often necessary to promote the reactions. The reaction of alkyl halides with potassium thioacetate in a nonpolar solvent did not proceed at all since the potassium thioacetate is insoluble in a nonpolar solvent. Therefore, the reaction of alkyl halides with potassium thioacetate should be carried out in a polar solvent such as ethanol or dimethyl formamide. Supported reagents are attractive in organic synthesis in view of their higher selectivity, milder reaction conditions, easier work-up, and environmentaly friendly reactions. Recently, many reactions using supported reagents have been reported. We have found that potassium thioacetate can be activated remarkably by supporting onto silica-gel, and silica-gel supported potassium thioacetate (AcSK/SiO₂) reacts with alkyl halides in nonpolar solvents such as benzene to give alkyl thioacetates in good yields. Herein we report a convenient procedure for the conversion of alkyl halides 1 into alkyl thioacetate 2 by using AcSK/SiO₂ (Sch. 1).

Benzyl bromide did not react with finely ground potassium thioacetate suspended in benzene at room temperature. In contrast, similar reaction with $AcSK/SiO_2$ proceeded easily under similar conditions to afford benzyl thioacetate in 83% yield after 1 h. As shown in Table 1, silica-gel was the most effective among the inorganic supports tested. Alumina was also effective but less than silica-gel. Molecular sieves 4A was much less effective. Celite and Montmorillonite K10 were ineffective for activating potassium thioacetate.



Scheme 1.

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Table 1. Comparative effectiveness of various supports for thioesterification of benzyl bromide using AcSK/support^a.

BrH ₂ C-	AcSK / Support Benzene	AcSH ₂ C
Support		Yield/(%)
None		no reaction
Montmorillonite K10		no reaction
Celite		no reaction
MS-4A		trace
Neutral-Al ₂ O ₃		53
Acidic-Al ₂ O ₃		48
Basic-Al ₂ O ₃		33
Silica-gel		83

^aA mixture of benzyl bromide (1 mmol) and AcSK/support (1 mmol, 1 g) in benzene (5 mL) was stirred at r.t. for 1 h. Yields were determined by GLC.

The reaction of a series of organic halides with $AcSK/SiO_2$ in benzene gave the corresponding thioacetates in high yields. The reaction of benzyl chloride with $AcSK/SiO_2$ required more strong conditions than that of benzyl bromide. Substituted benzyl halides were converted into the corresponding thioacetates in excellent yields at room temperature independent of the substituent (**2a–e**). For instance, 4-methyl and 4-nitrobenzyl bromide were converted into the corresponding thioacetates in 98 and 97% yields. Xylylene dibromides produced only disubstituted compound (**2f–h**). Mono substituted compound were not detected (Table 2).

Although the reaction with *n*-alkyl halides did not proceed at room temperature, when the reaction temperature was increased to 80° C the reactions occurred to give the corresponding thioacetates. The reactivity of *n*-alkyl halides decreased as follow; I > Br > Cl (See Table 3). Octyl thioacetate was obtained quantitatively from octyl iodide after 3 h, whereas, octyl chloride gave only 32% yield of octyl thioacetate after 24 h. Secondary alkyl halides were less reactive than primary alkyl halides. 2-Bromooctane was converted to corresponding thioacetate at 80° C, but the yield was only 26% after 24 h. In the case of 1,4-dibromopentane, 4-Bromopentyl thioacetate was formed along with a small amount of disubstituted compound, but 4-bromo-1-methylbutyl thioacetate was not detected. The other bromides such as allylic bromides and α -bromoketones were also converted into the corresponding

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Table 2. Synthesis of thioesters from substituted benzyl halides and $AcSK/SiO_2$.^a

R-X	Products		Temp./ (°C)	Time/ (h)	Yield ^b / (%)
CIH ₂ C	AcSH ₂ C	2a	50	3	90
BrH ₂ C	AcSH ₂ C	2a	r.t.	1	91
BrH ₂ C	AcSH ₂ C	2b	r.t.	1	98
BrH ₂ C	AcSH ₂ C-V-NO ₂	2c	r.t.	1	97
BrH ₂ C-CN	AcSH ₂ C-CN	2d	r.t.	1	97
BrH ₂ CI	AcSH ₂ C	2e	r.t.	1	99
BrH ₂ C-CH ₂ Br	AcSH ₂ C-CH ₂ SAc	2f	r.t.	1	91 ^c
CH ₂ Br	CH ₂ SAc	2g	r.t.	1	96 ^c
BrH ₂ C	AcSH ₂ C				
BrH ₂ C	AcSH ₂ C	2h	r.t.	1	94 ^c
BrH ₂ C	AcSH ₂ C				

^aA mixture of substituted benzyl halide (5 mmol) and AcSK/SiO₂ (7.5 mmol, 7.5 g) in benzene (20 mL) was stirred and then filtered to remove the used supported reagents. The filtrate was evaporated to afford the product.

^bYield of isolated and purified (>98%) product.

 $^{c}AcSK/SiO_{2}\ (15\,mmol,\ 15\,g)$ and benzene (40 mL) were used.

thioacetates at room temperature. Ethyl 2-bromopropionate required 3 h to complete the reaction, and afford the corresponding thioacetate in 84% yield. In contrast, α -bromobenzyl phenyl ketone produced 2-oxo-1, 2-diphenylethyl thioacetate in 72% yield in 1 h, and small amount of unexpected product, benzyl phenyl ketone, was formed along with the thioacetate. Using silica-gel supported potassium thiobenzoate

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R-X	Products		Temp./ (°C)	Time/ (h)	Yield ^b / (%)
ci~~~5~	AcS ()5	2i	80	24	32 ^{c,d}
Br ()5	Acs ()5	2i	80	8	89 ^{c,d}
1~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Acs (1)5	2i	80	3	100 ^d
Br (1)4	Acs ()4	2j	80	24	26 ^{c,d}
Br	AcS	2k	60	7	75 ^e (11) ^f
Br	AcS-	21	r.t.	5	85°
Br — Ph	Ph AcS	2m	r.t.	1	76
Ph Br——Ph Ph	AcS Ph Ph Ph	2n	r.t.	1	82
Br	Acs	20	r.t.	1	96
Br	Acs	2p	r.t.	1	92
Br	Acs	2q	r.t.	3	84
Br	Acs	2r	r.t.	1	91
Br	AcS Ph	2s	r.t.	1	72 ^c (19) ^g
Ph	Ph				

Table 3. Synthesis of thioesters from alkyl halides and AcSK/SiO₂.^a

^aA mixture of alkyl halide (5 mmol) and AcSK/SiO₂ (7.5 mmol, 7.5 g) in benzene (20 mL) was stirred and then filtered to remove the used supported reagents. The filtrate was evaporated to afford the product.

^bYield of isolated and purified (>98%) product.

^cThe product was isolated with column chromatography.

 $^{d}AcSK/SiO_{2}$ (10 mmol, 10 g) and benzene (25 mL) were used.

eAcSK/SiO₂ (15 mmol, 15 g) and benzene (40 mL) were used.

^fYield of disubstituted compound.

^gYield of benzyl phenyl ketone.

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Table 4. Synthesis of thiobenzoate from alkyl bromides and PhCOSK/SiO2.^a

	R-Br PhCOSK / SiO ₂	 Ph 	COS-R		
	1	3a-f			
R-Br	Products		Temp./ (°C)	Time/ (h)	Yield ^b / (%)
	PhCOS	3a	80	24	52 ^c
Br (1)5	PhCOS	3a	80	4	94 ^c
BrH ₂ C	PhCOSH ₂ C	3b	r.t.	1	99
BrH ₂ C	PhCOSH ₂ C-CH ₂ SCOPh	3c	r.t.	1	100 ^d
Br	PhCOS	3d	r.t.	1	100
Br	PhCOS	3e	r.t.	1	98
Br	PhCOS	3f	r.t.	1	98

^aA mixture of alkyl bromide (5 mmol) and PhCOSK/SiO₂ (7.5 mmol, 7.5 g) in benzene (20 mL) was stirred and then filtered to remove the uesd supported reagents. The filtrate was evaporated to afford the product.

^bYield of isolated and purified (>98%) product.

^cPhCOSK/SiO₂ (10 mmol, 10 g) and benzene (25 mL) were used.

^dPhCOSK/SiO₂ (15 mmol, 15 g) and benzene (40 mL) were used.

(PhCOSK/SiO₂), the reaction rapidly occurred at room temperature to give the corresponding thiobenzoates in high yields (See Table 4). The reactivity of PhCOSK/SiO₂ was higher than AcSK/SiO₂. Octyl bromide reacted with AcSK/SiO₂ to afford the octyl thioacetate in 89% yield at 80°C after 8 h, whereas, the reaction with PhCOSK/SiO₂ gave octyl thiobenzoate (3a) in 94% yield after 4 h. Moreover, octyl chloride gave **3a** in 52% yield after 24 h.

In conclusion, the present procedure using silica-gel supported potassium thioacetate and thiobenzoate allows for an efficient transformation of organic halides into thioesters. The notable advantages of this procedure are: operational simplicity, good yield, and mild reaction conditions. Moreover, the products are easily isolated by filtering the

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used supported reagent and removing the solvent under vacuum, and are generally spectroscopically pure.

EXPERIMENTAL

Preparation of supported reagent $AcSK/SiO_2$: Silica-gel supported potassium thioacetate was prepared as follows. Silica-gel (Wakogel C-200(Wako pure chemical ind. Ltd.), 8.86g) was added to a solution of potassium thioacetate (10 mmol, 1.14g) in methanol, and the mixture was stirred at room temperature for 0.5h. The methanol was removed by rotary evaporator under reduced pressure, and the resulting reagent was dried in vacuo (10 mmHg) at room temperature for 1 h.

In a typical procedure, a mixture of benzyl bromide (5 mmol) and AcSK/SiO₂ (7.5 mmol, 7.5 g) was stirred in benzene at room temperature for 1 h, and then filtered to remove the uesd supported reagents. The filtrate was evaporated to afford the product, benzyl thioacetate, in 91% yield, and the purity was >99%.

2b. liquid; IR(neat): 1691 cm⁻¹. ¹H NMR(CDCl₃) δ 2.31 (3H, s), 2.33 (3H, s), 4.08 (2H, s), 7.10 (2H, d, J=8Hz), 7.17 (2H, d, J=8Hz). MS(EI). m/z = 180(M⁺).

2d. M.p. 53–54°C. IR(KBr): 2233, 1685 cm⁻¹. ¹H NMR(CDCl₃) δ 2.37 (3H, s), 4.13 (2H, s), 7.41 (2H, d, J = 8Hz). 7.59 (2H, d, J = 8Hz). MS(EI) $m/z = 191(M^+)$.

2r. M.p. 43–44°C. IR(KBr): 1695, 1684 cm⁻¹. ¹H NMR(CDCl₃) δ 2.41 (3H, s), 4.41 (2H, s), 7.48 (2H, t, J=8Hz), 7.60 (1H, d, J=8Hz), 7.99 (2H, d, J=8Hz). MS(EI) m/z = 194(M⁺).

3c. M.p. 52–53°C. IR(KBr): 1662 cm⁻¹. ¹H NMR(CDCl₃) δ 4.30 (4H, s), 7.27 (3H, m), 7.38 (1H, s), 7.43 (4H, t, J=8Hz), 7.56 (2H, d, J=8Hz), 7.96 (4H, d, J=8Hz). MS(EI) m/z=378(M⁺).

3f. M.p. 84–85°C (Lit.^[11] 79–80°C). IR(KBr): 1697, 1657 cm⁻¹. ¹H NMR(CDCl₃) δ 4.59 (2H, s), 7.46 (2H, t, J=8Hz), 7.50 (2H, t, J=8Hz), 7.59 (1H, t, J=8Hz), 7.61 (1H, t, J=8Hz), 8.00 (2H, d, J=8Hz), 8.07 (2H, d, J=8Hz). MS(EI) m/z=256(M⁺).

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