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Silica Sulfuric Acid-promoted Deacylation of α-Bromo-β-diketones

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Novel deacylation of α-bromo-β-diketones using silica sulfuric acid (SSA) has been developed. Deacylation of 3-bromopentane-2,4-diones and 2-bromobutane-1,3-diones were carried out in the presence of SSA in dichloroethane under mild conditions to obtain the corresponding α-bromo ketones in good to excellent yields. SSA also promoted the Friedel–Crafts type alkylation of benzene with 3-(*sec*-alkyl)-2,4-pentanediones to give the corresponding triarylmethanes in high yields in benzene.

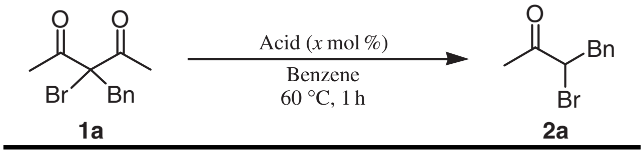
Deacylation is one of the most important transformations in organic synthesis because it has been widely used for the synthesis of natural products, biological active compounds, etc. Many methods for deacylation have been developed. The reactions are usually catalyzed by acids and bases. Base catalysts have been employed to catalyze deacylation of β-dicarbonyl compounds.[1–5] In contrast, acid catalysts are scarcely used for deacylations of β-dicarbonyl compounds. Adkins and co-workers[6] first reported acid-catalyzed deacylation using hydrogen chloride and alcohol, and Zinnes's group[7] reported deacylation of 3-acyl-2*H*-1,2-benzothiazin-4(3*H*)-one 1,1-dioxide using PTS and ethylene glycol in benzene.

In the course of our study of synthetic reactions using inorganic solid-supported reagents, we found out that silica sulfuric acid (SSA)[8] promotes deacylation of α-halo-β-dicarbonyl compounds to afford α-bromo ketones. To the best of our knowledge there are no reports of deacylation of α-halo-β-dicarbonyl compounds using an acid.

Deacylation of α-halo-β-dicarbonyl compounds is usually catalyzed by bases.[9–11] This transformation has been used in the synthesis of pharmaceuticals such as triamcinolone[12] and juvenile hormone.[13] α-Halo ketones are important compounds in organic synthesis, which are useful in the synthesis of a variety of heterocycles such as thiazoles,[14] imidazoles,[15] and pyran-2,5-diones,[16] as well as in other synthetic applications. In this paper we describe deacylation of α-halo-β-dicarbonyl compounds using SSA.

First, conversion of 3-benzyl-3-bromopentane-2,4-dione (**1a**) into 3-bromo-4-phenylbutane-2-one (**2a**) was carried out in the presence of various acids (Table 1). Among the acids tested, SSA showed the highest activity. The other acids without sulfuric acid were inactive. $NaHSO_4/SiO_2$ and Amberlyst-15® had slight effects for the reaction of **1a** into **2a**, but the yield was very low at 17% and 2% respectively. The activity of H_2SO_4 was the same as SSA, but the yield of **2a** was lower than that using SSA because some undesirable side reactions occurred. When HCl and *p*-toluenesulfonic acid (PTS) were used as an acid, **1a** was recovered quantitatively. Lewis acid, $ZnCl_2/SiO_2$, did not work for this reaction.

Table 1. Deacetylation of **1a** using various acids[a]



Entry	Acid	x/mol %	Yield/%	
			1a	**2a**
1	SSA	185	0	100
2	$NaHSO_4/SiO_2$	210	83	17
3	Amberlyst-15®	480	98	2
4	$HClO_4/SiO_2$	10	100	0
5	PPA/SiO_2	—	100	0
6	H_2SO_4	900	0	85
7	HCl	600	100	0
8	PTS	100	100	0
9	$ZnCl_2/SiO_2$	150	100	0

[a] Recovery and yield were determined by GLC area ratio.

Table 2. Deacetylation of **1a** in various solvents

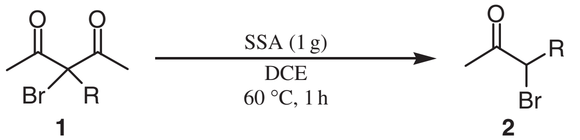
$$\mathbf{1a} \xrightarrow[\text{Solvent, 60 °C, 1 h}]{\text{SSA}} \mathbf{2a}$$

Entry	Solvent	Conversion (Isolated yield)/%
1	Benzene	100 (79)
2	Toluene	4 (—)
3	Chlorobenzene	100 (85)
4	1,2-Dichloroethane	100 (92)
5	Hexane	100 (69)

Various solvents can be used for this reaction except for toluene. 1,2-Dichloroethane was the most suitable solvent, whereas using toluene as a solvent, the conversion was only 4% and large amount of unchanged **1a** was observed in the reaction mixture (Table 2). In order to make clear this reaction profile, a suspension of SSA in toluene was stirred at 80 °C for 5 h. PTS was formed in good yield. Thus, in the reaction of **1a** with SSA in toluene, PTS did not work as an acid catalyst for deacylation. Hajipour and co-workers[17] have reported that active aromatics are sulfonated by SSA.

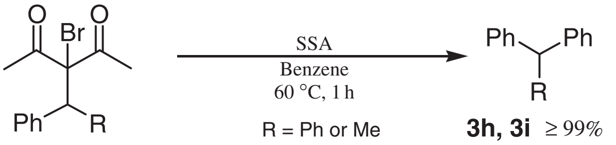
We tried to synthesize various α-bromo ketones **2** from 3-bromo-3-substituted pentane-2,4-diones **1** using SSA (Table 3). A mixture of **1a** (1 mmol) and SSA (1 g) in 1,2-dichloroethane

Table 3. Deacylation of **1** using SSA[a]



Entry	–R		Yield[b]/%
1	$–CH_2Ph$	**2a**	92
2	$–(CH_2)_2Ph$	**2b**	77
3	$–(CH_2)_7CH_3$	**2c**	>99
4	$–(CH_2)_{17}CH_3$	**2d**	>99
5	$–(CH_2)_5Br$	**2e**	94
6	$–(CH_2)_3COOEt$	**2f**	N.D.
7	–Ph	**2g**	>99
8	$–CH(CH_3)Ph$	**2h**	11[c]
9	$–CHPh_2$	**2i**	49

[a] In all reactions were carried out using **1** (1 mmol), 1,2-dichloroethane (10 mL), and SSA (1 g). [b] Isolated yield. [c] Yield was determined by GLC internal standard method.

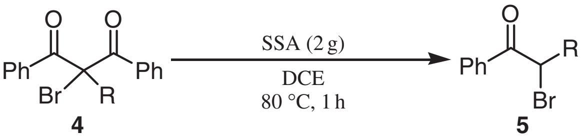


Scheme 1.

(DCE, 10 mL) was stirred at 60 °C for 1 h, and then SSA was removed by filtration and the filtrate was evaporated under reduced pressure to give the product **2a** in 92% yield.[18] Deacylation of the other α-bromo-β-diketones **1** was also promoted by SSA, and the corresponding **2** was obtained in good yield. The length of the alkyl group at the 3-position in **1** did not affect the yields of the product **2** (Entries 1–4). Compound **1e** which contained bromine at the ω-position gave **2e** in 94% yield, whereas in the reaction of **1f** having ester group **2f** was not observed (Entries 5 and 6). In the reactions of 2,4-pentanediones with a *sec*-alkyl group at the 3-position, **1h** and **1i**, **1h** did not give **2h** in good yield, whereas **1i** gave **2i** in moderate yield (Entries 8 and 9). When these reactions were carried out in benzene, unexpected products, 1,1-diphenylethane (**3h**) and triphenylmethane (**3i**), were obtained (Scheme 1). We are very interested in these results. To the best our knowledge, these Friedel–Crafts type alkylations have not been reported. Now these reactions are under investigation in detail.

SSA promoted not only deacetylation but also debenzoylation reactions. Results are summarized in Table 4. Reactions were carried out in the presene of SSA (2 g) at 80 °C for 1 h. All 2-bromo-1,3-diphenylpropane-1,3-diones **4** employed were debenzoylated to give the corresponding debenzoylated analogs **5** along with a small amount of benzoic acid. Benzoic acid was removed by adding Na_2CO_3/SiO_2 into the reaction mixture or extracting with concd $NaHCO_3$ (aq.) after the reaction. This transformation did not proceed effectively under basic conditions. For instance reaction of 2-benzyl-2-bromo-1,3-diphenylpropane-1,3-dione **4b** (1 mmol) in the presence of Na_2CO_3/SiO_2 (6 mmol) gave **5b** in 12% yield after 5 h at 80 °C.

Table 4. Deacylation of **4** using SSA[a]



Entry	–R		Yield[b]/%
1	$–CH_3$	**5a**	79
2	$–CH_2Ph$	**5b**	>99
3	$–CH_2C_6H_4\text{-}4\text{-}CH_3$	**5c**	44
4	$–CH_2C_6H_4\text{-}4\text{-}Cl$	**5d**	92
5	$–(CH_2)_7CH_3$	**5e**	>99

[a] In all reactions were carried out using **4** (1 mmol), 1,2-dichloroethane (10 mL), and SSA (2 g). [b] Isolated yield.

In conclusion, we developed a novel method for deacylation of α-halo-β-dicarbonyl compounds using SSA. SSA promoted not only deacetylation of 3-bromo-3-substituted pentane-2,4-dione but also debenzoylation of 2-bromo-2-substituted 1,3-diphenylpropane-1,3-diones in excellent yield. Deacetylation of α-halo-β-dicarbonyl compounds has been used in the total synthesis of natural products and hormones. We believe this procedure has a beneficial effect on a deacylation of α-halo-β-dicarbonyl compounds having functional groups which are sensitive to base. Notably, we found a novel Friedel–Crafts type alkylation using α-alkyl-β-dicarbonyl compound as an alkylating agent. These results in detail will be reported in a subsequent paper.

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18 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.