

Dealkylation of esters via treatment with *N*-(trimethylsilyl)diethylamine and methyl iodide

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Abstract

A method for the conversion of esters to carboxylic acids has been reported. Reaction of methyl *o*-methoxybenzoate with *N*-(trimethylsilyl)diethylamine and methyl iodide, followed by hydrolysis, afforded *o*-methoxybenzoic acid with a 94% yield based on 96% conversion. Methyl esters of not only aromatic acids but also aliphatic acids were converted to the corresponding acids with high yields. A combination of *N*-(trimethylsilyl)dimethylamine and methyl iodide was also effective to give *p*-methylbenzoic acid with a 85% yield based on 90% conversion from the corresponding methyl ester.

Keywords: Silicon; Ester dealkylation; Trimethylsilyl; *N*-(trimethylsilyl)diethylamine

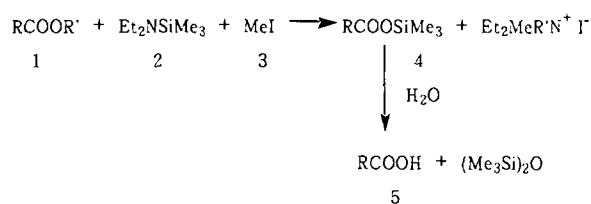
1. Introduction

The dealkylation of alkyl esters using trimethylsilyl iodide is well known [1]. Trimethylsilyl iodide, however, is very unstable and careful handling is required. Meanwhile, it is known that the basicity of amine is decreased by silylation [2]. However, we considered that the silylated derivatives of aliphatic amines still have sufficient basicity to interact with reactive organohalides, such as alkyl iodide, allyl bromide and benzyl bromide. In the preceding paper, we reported that the adducts formed from *N*-(trimethylsilyl)dialkylamines and alkyl iodides are quite efficient reagents to silylate the second hydrogen atom of primary amines [3]. During the course of investigation regarding the reactivity, we found that the above adducts are also effective for dealkylation of esters.

2. Results and discussion

A carboxylic ester (**1**) is mixed with *N*-(trimethylsilyl)diethylamine (**2**) and methyl iodide (**3**) in toluene

and the mixture is gradually heated to 90°C; continuous heating of the mixture at 100–15°C, followed by hydrolysis, gives the corresponding acid **5**:



The results for a series of esters are summarized in Table 1. Gas chromatographic conversions of benzoic esters to silyl esters were plotted vs. reaction time in Fig. 1.

From the results in Table 1 and Fig. 1, it is obvious that benzoic esters substituted with an electron-donating substituent such as methoxy group or methyl group are readily dealkylated in comparison with esters carrying an electron-withdrawing substituent such as a chlorine atom, and methyl esters are more reactive than ethyl esters. Under this reaction condition, a methoxy group directly bonded to aromatic ring is slightly influenced. Gas chromatography (GC) analysis showed that the

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decomposition of the anisyl moiety of methyl *p*-methoxybenzoate and methyl *o*-methoxybenzoate was less than 2%.

When carbon atoms adjacent to carboxyl groups in the case of aliphatic carboxylic acid esters were primary or secondary, the esters were comparatively readily demethylated, but an ester group adjacent to tertiary carbon was less reactive. Methyl 2,2-dimethylpropanoate was converted to trimethylsilyl 2,2-dimethylpropanoate with only 54% yield by heating at 100–110°C for 92 h.

A combination of **2** and allyl bromide is much less reactive in comparison with that of **2** and **3**. For example, the demethylation of methyl *p*-methoxybenzoate by **2** and allyl bromide at 100–110°C for 48 h proceeded only to give a 5% yield. Therefore the procedure using bromide is impractical for dealkylation of esters, being practically efficient to silylate the second hydrogen of primary amines [3].

As a process for this reaction, it may be suggested that the adduct **6** formed from **2** and **3**, for which spectral characteristics were discussed in the preceding paper [3], is a reactive species because **2** does not react alone with esters. The dealkylation proceeds via the silylation of the carbonyl oxygen atoms promoted by initial attack of iodide ion on carbonyl carbon or the silylation by direct attack of activated trimethylsilyl

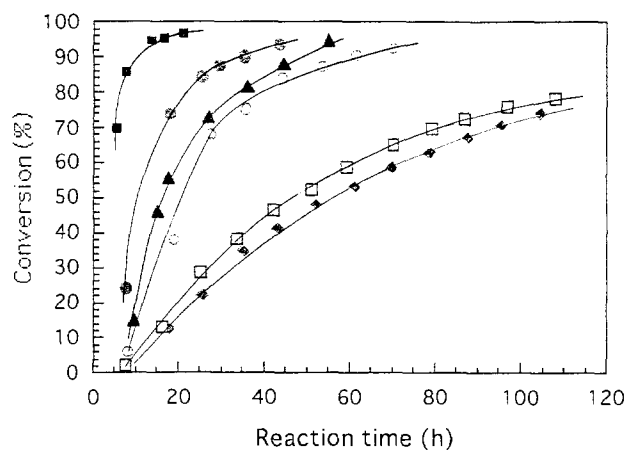
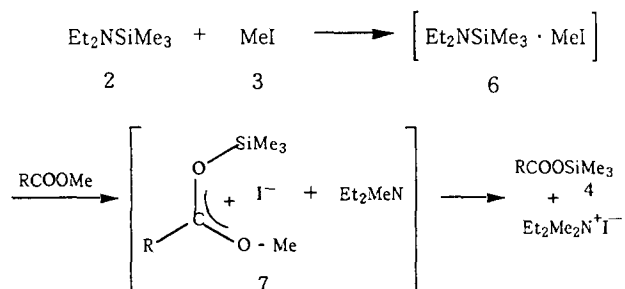


Fig. 1. Plot of conversion of alkyl benzoate to trimethylsilyl benzoate vs. time: ○, methyl benzoate; ■, methyl *o*-methoxybenzoate; ●, methyl *p*-methoxybenzoate; ▲, methyl *p*-methylbenzoate; ◆, methyl *p*-chlorobenzoate; □, ethyl *p*-methylbenzoate. The conversions were evaluated from GC peak areas using toluene as an internal standard.

group of adduct **6** on carbonyl oxygen, followed by formation of a silyl ester iodide salt **7**, as suggested by Jung and Lyster [1a]:



From the fact that iodide is more reactive than bromide, it is considered that the halide ion plays an important part for the silylation.

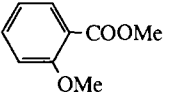
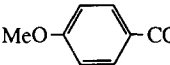
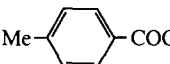
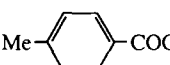
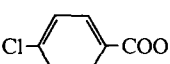
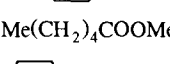
Although additional experiments are necessary to discuss the reaction mechanism in detail, we may conclude that the reagent given by the combination of *N*-(trimethylsilyl)diethylamine and methyl iodide has a reactivity similar to that of trimethylsilyl iodide in regard to the dealkylation of esters.

3. Experimental section

3.1. General remarks

Commercially available toluene, esters and methyl iodide were used without purification. *N*-(Trimethylsilyl)diethylamine and *N*-(trimethylsilyl)dimethylamine were prepared by the reaction of diethylamine and dimethylamine with trimethylsilyl chloride respectively.

Table 1
The dealkylation of esters by Et₂NSiMe₃ and MeI

RCOOR'	Temperature (°)	Time (h)	Conversion (%)	Yield ^b (%)
	90–100	19	96	94
	100–115	40	94	92
	90–115	53	95	86
	100–115	100	79	93
	100–115	100	75	83
Me(CH ₂) ₄ COOMe	90–115	42	94	76
	95–115	75	92	81
Me ₃ CCOOMe	100–110	92	54	68
MeOOC(CH ₂) ₈ COOMe	100–110	60	95	68

^a Conversions were estimated from GC peak areas of starting materials and products.

^b The yields are given as yields of isolated acids, calculated on the bases of conversion, after aqueous work-up.

The authentic trimethylsilyl esters of acids were prepared from the corresponding acids with hexamethyldisilazane [4].

IR spectra were recorded on a JASCO IR-810 spectrometer. GC–mass spectroscopy was measured with a Hewlett–Packard 5970 mass-selective detector with a Hewlett–Packard 5890 gas chromatograph. The dealkylated esters were verified as acids by hydrolysis, followed by comparison of IR spectra with those reported in the literature [5]. The trimethylsilyl esters of acids contained in the reaction mixtures were verified by comparison of retention times of GC peaks and mass spectra with those of authentic samples.

3.2. General procedures for dealkylation of esters: reaction of methyl benzoate with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a 200 ml flask with a condenser, a thermometer and a stirrer was placed a mixture of 13.6 g (0.1 mol) of methyl benzoate, 17.4 g (0.12 mol) of *N*-(trimethylsilyl)diethylamine, 18.5 g (0.13 mol) of methyl iodide and 50 ml of toluene, and the temperature of the mixture was raised gradually with stirring to 90°C over 4 h. Stirring was continued at 100–110°C for 58 h until the GC showed that 93% conversion of the methyl ester to the trimethylsilyl ester was performed. After removal of the precipitated ammonium salt by filtration, the reaction mixture was treated with 30 ml of water for 30 min and alkalified with a 10% aqueous solution of NaOH to dissolve the acid into the water. After separation of the toluene-soluble materials, the water layer was acidified with 10% hydrochloric acid. The precipitated acid was filtered and dried in vacuo to give 9.5 g (84% yield based on conversion) of benzoic acid.

Similarly, methyl *o*-methoxybenzoate, methyl *p*-methoxybenzoate, methyl *p*-methylbenzoate, ethyl *p*-methylbenzoate and methyl *p*-chlorobenzoate were dealkylated as given in Table 1.

3.3. Reaction of methyl *p*-methylbenzoate with *N*-(trimethylsilyl)dimethylamine and methyl iodide

In a 200 ml flask with a condenser, a thermometer and a stirrer was placed a mixture of 15.0 g (0.1 mol) of methyl *p*-methylbenzoate, 17.6 g (0.15 mol) of *N*-(trimethylsilyl)dimethylamine, 24.1 g (0.17 mol) of methyl iodide and 100 ml of toluene, and the temperature of the mixture was raised gradually with stirring to 90°C over 1.5 h. Stirring was continued at 100–110°C for 79 h until the GC showed that 90% conversion of methyl ester to trimethylsilyl ester was performed. Similar work-up of the reaction mixture gave 10.4 g (85% yield based on conversion) of *p*-methylbenzoic acid.

3.4. Reaction of methyl hexanoate with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a 200 ml flask with a condenser, a thermometer and a stirrer was placed a mixture of 19.5 g (0.15 mol) of methyl hexanoate, 26.1 g (0.18 mol) of *N*-(trimethylsilyl)diethylamine, 28.4 g (0.20 mol) of methyl iodide and 100 ml of toluene, and the temperature of the mixture was raised gradually with stirring to 90°C over 3.5 h. Stirring was continued at 90–115°C for 42 h until GC showed that 94% conversion of methyl ester to trimethylsilyl ester was performed. After removing the precipitated ammonium salt by filtration, the reaction mixture was treated with 45 ml of water for 30 min and alkalified with a 10% aqueous solution of NaOH to dissolve the acid into the water. After the separation of toluene-soluble materials, the water layer was acidified with 10% hydrochloric acid and the separated acid was extracted with ether. The ether layer was washed with a saturated aqueous solution of Na₂SO₄ three times and dried over Na₂SO₄. Distillation under reduced pressure gave 12.3 g (75% yield based on conversion) of hexanoic acid (boiling point (b.p.), 76–77°C (4 Torr)).

Similarly, methyl cyclohexanecarboxylate was demethylated as given in Table 1.

3.5. Reaction of methyl 2,2-dimethylpropanoate with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a 300 ml flask with a condenser, a thermometer and a stirrer was placed a mixture of 23.2 g (0.20 mol) of methyl 2,2-dimethylpropanoate, 34.8 g (0.24 mol) of *N*-(trimethylsilyl)diethylamine, 37.0 g (0.26 mol) of methyl iodide and 100 ml of toluene. The temperature of the mixture was raised gradually with stirring to 100°C over 4.5 h and stirring was continued at 100–110°C for 92 h. The conversion of methyl ester to trimethylsilyl ester, evaluated from GC peak areas, was 54%. After removal of the precipitated ammonium salt by filtration, the reaction mixture was treated with 30 ml of water for 1 h and alkalified with a 10% aqueous solution of KOH to dissolve the acid into the water. After the separation of toluene-soluble materials, the water layer was evaporated to dryness under reduced pressure. The sodium salt obtained was acidified with 20% hydrochloric acid and the separated acid was extracted with ether. The ether layer was washed with a saturated aqueous solution of Na₂SO₄ twice and dried over Na₂SO₄. Distillation under reduced pressure gave 7.5 g (68% yield based on conversion) of 2,2-dimethylpropanoic acid (b.p., 68–70°C (14 Torr)).

3.6. Reaction of dimethyl decanedioate with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a 200 ml flask with a condenser, a thermometer and a stirrer was placed a mixture of 23.0 g (0.10 mol)

of dimethyl decanedioate, 43.5 g (0.30 mol) of *N*-(trimethylsilyl)diethylamine, 42.6 g (0.30 mol) of methyl iodide and 60 ml of toluene. The temperature of the mixture was raised gradually with stirring to 110°C over 3 h and the stirring was continued for 60 h at 100–110°C. The GC analysis showed that the peak of dimethyl ester had disappeared completely and the relative ratio of bis(trimethylsilyl) ester and partially demethylated ester MeOOC(CH₂)₈COOSiMe₃ contained in the reaction mixture was 95 : 5.

After removal of the precipitated ammonium salt by filtration, the reaction mixture was treated with 60 ml of water for 10 min and alkalified with a 10% aqueous solution of NaOH to dissolve the acid into the water. After separation of the toluene-soluble materials, the water layer was acidified with 10% hydrochloric acid. The precipitated acid was filtered, dried in vacuo and recrystallized from hot water to give 13.0 g (68% yield based on conversion) of decanedioic acid.

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