

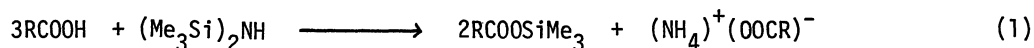
A FACILE SILYLATION OF CARBOXYLIC ACIDS WITH HEXAMETHYLDISILOXANE

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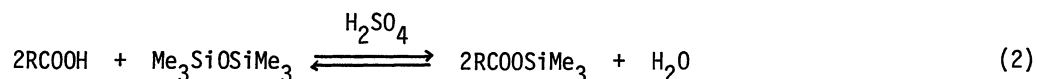
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It was found that, in the presence of a catalytic amount of sulfuric acid, hexamethyldisiloxane silylates carboxylic acids to give trimethylsilyl carboxylates in good yields.

The utility of the silylation of hydroxyl groups is well recognized.¹ Despite of the recent introduction of several useful reagents such as chlorosilanes,² hydrosilanes,³ silylamines,⁴ silylamides,⁵ silyl acetates,⁶ silyl trifluoromethanesulfonates,⁷ silyl acetals,⁸ allyl-silanes,⁹ and silyl perchlorates,¹⁰ there still exists a need for other silylating agents which are readily accessible and convenient enough to be handled. Recently, it has been reported that hexamethyldisiloxane can silylate alcohols with the aid of acids or bases.¹¹ Thus, Pinnick and coworkers have shown that, in the presence of a catalytic amount of pyridinium *p*-toluenesulfonate, the disiloxane reacts with aliphatic and aromatic alcohols to give trimethylsilyl ethers in good yields.^{11b} However, no example of the corresponding silylation of carboxylic acids has been reported yet. In connection with our ongoing synthetic work,¹² need for ready access to silyl carboxylates has forced us to explore the silylation of carboxylic acids of newer type. This is because the silylation of an acid with hexamethyldisilazane, a standard silylating agent, is often accompanied by the concurrent formation of a considerable amount of useless ammonium carboxylates (eqn. 1)^{4b} and the loss of an expensive carboxylic acid is of course undesirable.



We report herein our findings that, in the presence of a catalytic amount of sulfuric acid, hexamethyldisiloxane silylates effectively carboxylic acids (eqn. 2).



The silylation can be simply performed by refluxing a toluene solution of a binary mixture of

Table 1. Silylation of Carboxylic Acids with Hexamethyldisiloxane in the Presence of a Catalytic Amount of Sulfuric Acid^a

| Carboxylic acid | Time (h) | Product ^b | Yield,% ^c |
|---|----------|---|----------------------|
| CH ₃ (CH ₂) ₄ COOH | 72 | CH ₃ (CH ₂) ₄ COOSiMe ₃ | 71 (76) |
| CH ₂ =CH(CH ₂) ₈ COOH | 70 | CH ₂ =CH(CH ₂) ₈ COOSiMe ₃ | 67 (71) |
| CH ₂ ClCOOH | 32 | CH ₂ ClCOOSiMe ₃ | 64 (74) |
| CHCl ₂ COOH | 2 | CHCl ₂ COOSiMe ₃ | 74 (97) |
| CCl ₃ COOH | 1 | CCl ₃ COOSiMe ₃ | 93 (97) |
| CH ₃ CCl ₂ COOH | 4 | CH ₃ CCl ₂ COOSiMe ₃ | 78 (91) |
| cyclo-C ₆ H ₁₁ COOH | 90 | cyclo-C ₆ H ₁₁ COOSiMe ₃ | 70 (79) |
| C ₆ H ₅ COOH | 44 | C ₆ H ₅ COOSiMe ₃ | 73 |

^aConditions: [acid]/[siloxane]/[H₂SO₄] = 1:2:0.02-1:2:0.10; reflux in toluene.

^bIR and NMR spectra were in good agreement with the assigned structures.

^cIsolated yields (based on the carboxylic acid charged); in parentheses are given GLC yields.

a carboxylic acid and the disiloxane in the presence of a catalytic amount of sulfuric acid. The use of excess (approximately 2 equiv.) of the disiloxane and the continual removal of the resulting water from the reaction phase serves to shift the equilibrium far toward product side. The results are summarized in Table 1.

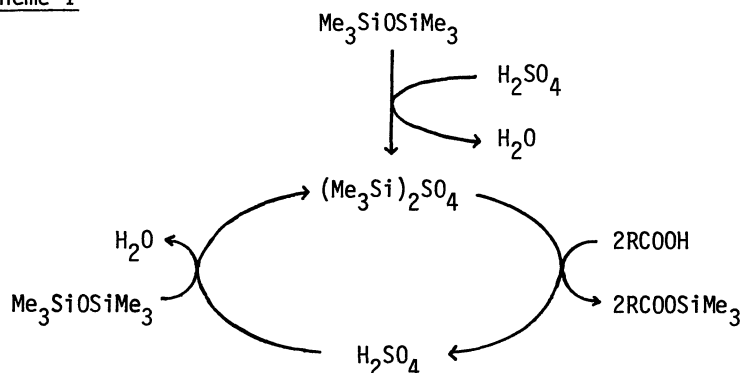
A typical procedure is as follows: In a 100 ml flask equipped with a Dean-Stark trap were placed hexanoic acid (17.5 g, 151 mmol), hexamethyldisiloxane (48.7 g, 301 mmol), sulfuric acid (1.5 g, 15 mmol), and toluene (40 ml). The flask was then heated to gentle reflux, and the course of the reaction was monitored by GLC. After 72 h, the reaction mixture was distilled under reduced pressure to give trimethylsilyl hexanoate (20.2 g, 71% yield based on the carboxylic acid charged) as a colorless liquid, bp 75-76°C/15 mmHg (lit.⁹ bp 79-81°C/19 mmHg); IR (neat) 1720 (s, C=O), 1254 (s, SiMe), 1185 (s, Si-O-C); NMR (CCl₄) δ 0.25 (s, 9H, SiMe), 0.90 (t, 3H, CH₃-), 1.07-1.74 (m, 6H, -(CH₂)₃-), 2.22 (t, 2H, -CH₂CO-); Mass (70 eV) m/e 173 (M⁺-Me).

Inspection of the Table reveals that the present silylation works well for various carboxylic acids such as alkanolic, alkenolic, and aromatic acids. The present system has the following distinct advantages: (i) Hexamethyldisiloxane is as inexpensive as trimethylchlorosilane, (ii) whereas the silylation with chlorosilanes has the disadvantages of producing amine hydrochlorides which are difficult to separate from the desired product, the present reaction is not

hampered by such problems; and (iii) the catalyst used here is also very inexpensive.

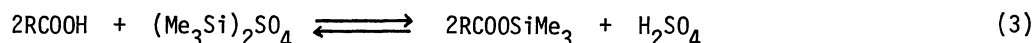
It has been reported by Calas and coworkers that hexamethyldisiloxane reacts with sulfuric acid to give bis(trimethylsilyl)sulfate in excellent yield.¹³ This silyl ester is then conceived to be an actual catalyst in the present silylation (Scheme I). This is supported by the fact

Scheme I



that, when a toluene solution of hexanoic acid and hexamethyldisiloxane (molar ratio 1:2) was refluxed for 70 h in the presence of 10 mol% of the bis(silyl)sulfate, trimethylsilyl hexanoate was obtained in 86% yield.

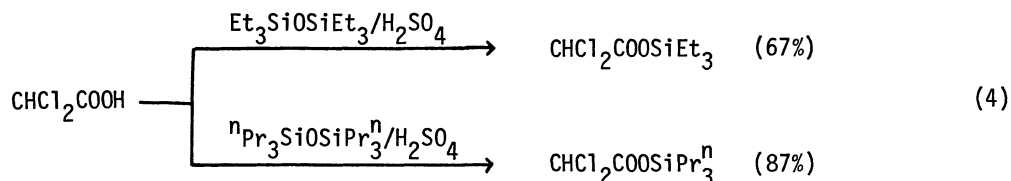
Table 1 also indicates that the present silylation can successfully be extended to α -chloro-carboxylic acids. A comparison of the reaction conditions for the silylation finds the reactivity order of the α -chloroacetic acids to be $\text{CCl}_3\text{COOH} > \text{CHCl}_2\text{COOH} > \text{CH}_2\text{ClCOOH}$. This order was further confirmed by the competitive silylation of pairs of the two of the three carboxylic acids with hexamethyldisiloxane in the presence of sulfuric acid which gave the relative rates, $\text{CCl}_3\text{COOH} : \text{CHCl}_2\text{COOH} : \text{CH}_2\text{ClCOOH} = 12:3:1$. It is thus meant that the silyl-proton exchange reaction between the carboxylic acid and bis(trimethylsilyl)sulfate (eqn. 3) proceeds more smoothly with increasing acidity of the carboxylic acids.



Catalyst efficiency was tested briefly for other acids or their silyl esters using the reaction of hexamethyldisiloxane with hexanoic acid as standard. Among them, pyridinium *p*-toluenesulfonate was found to catalyze the silylation. For example, the reaction in the presence of 10 mol% of this particular catalyst gave trimethylsilyl hexanoate in 54% yield after refluxing for 70 h. However, the reaction was accompanied by the concurrent formation of a considerable amount of tars. Trifluoromethanesulfonic acid, trimethylsilyl trifluoromethanesulfonate, and

p-toluenesulfonic acid also effect the silylation, but their catalytic ability was somewhat lower compared to sulfonic acid.

Finally, an attempt was made to silylate carboxylic acids with other hexaorganodisiloxanes in the presence of sulfuric acid and the results are quite satisfactory as is shown below.



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