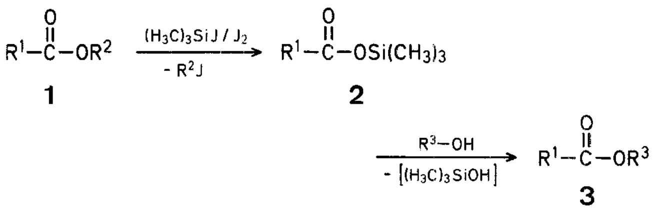
Synthetic Methods and Reactions; 90[1]. Iodotrimethylsilane-Mediated Mild and Neutral Transesterification of Esters

George A. Olah*, Subhash C. Narang, George F. Salem, B. G. Balaram Gupta

Hydrocarbon Research Institute, Department of Chemistry, University of Southern California, Los Angeles, California 90007, U.S.A.

Iodotrimethylsilane and its equivalents have been used by us[2-8] and others[9-15] in a wide variety of reactions in organic synthesis. These reactions include the cleavage of esters, lactones, carbamates, sulfoxides, ethers, acetals, epoxides etc. Iodotrimethylsilane is finding increasing utility as a reagent in the synthesis of novel and complex organic molecules[16,17,18]. In our continuing interest in silicon-based reagents, we report now that esters undergo iodotrimethylsilane-mediated transesterification.

When esters **1** are treated with iodotrimethylsilane and a catalytic amount of iodine, followed by the desired alcohol, the corresponding transesterified esters **3** are obtained in good to excellent yield (Table).



$$R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^2 \xrightarrow[-\,R^2J]{(H_3C)_3SiJ\,/\,J_2} R^1{-}\overset{O}{\overset{\|}{C}}{-}OSi(CH_3)_3 \xrightarrow[-\,[(H_3C)_3SiOH]]{R^3{-}OH} R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^3$$

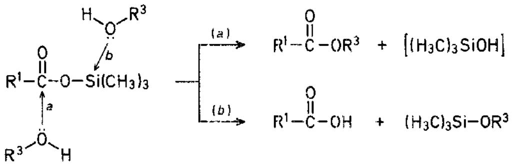
1 **2** **3**

The transesterification procedure is general for aryl, alkyl, and α,β-unsaturated carboxylic acid esters. Even hindered esters such as methyl pivalate underwent transesterification in good yield.

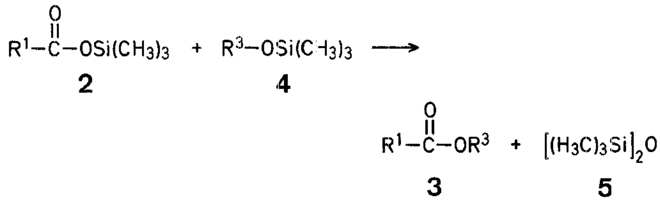
Transesterification of esters is generally carried out by heating them under reflux with a large excess of the alcohol in the presence of an acid catalyst (such as sulfuric acid[19]). In contrast, the iodotrimethylsilane-mediated transesterification occurs under strictly neutral conditions. Furthermore, diethyl diethylmalonate was transformed to dimethyl diethylmalonate in 44% yield using the present procedure. However, the scope of the reaction is limited to primary and secondary aliphatic alcohols.

The overall reaction is considered to be a composite of two successive transesterifications. In the first step, iodotrimethylsilane reacts with the starting alkyl ester **1** to form the corresponding trimethylsilyl ester **2**, which in turn reacts with the added alcohol to form the desired new ester and trimethylsilanol. Upon addition of the alcohol to the intermediate silyl ester, there are two possible alternative pathways:

- *(a)* the alcohol adds to the carbonyl carbon and subsequent loss of trimethylsilanol yields the desired ester;
- *(b)* the alcohol attacks the silicon, thus giving the alkyl trimethylsilyl ether and carboxylic acid as the products.



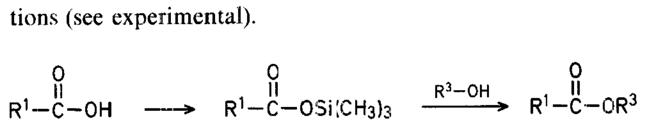
The latter pathway *(b)* seems to be the predominant one, when the intermediate trimethylsilyl ester is quenched with a large excess of alcohol. In this case, most of the product obtained is the carboxylic acid, instead of the desired ester. This is reflected in the reaction of phenol with trimethylsilyl benzoate which is obtained by the cleavage reaction of methyl benzoate with iodotrimethylsilane. Similar observations are also made in the reaction of benzyl alcohol with trimethylsilyl cinnamate (see experimental). In order to eliminate the possible formation of silyl ethers, the alcohols can be replaced by the corresponding trimethylsilyl ethers **4** to obtain high yields of the carboxylic acid esters **3** (see Table).



$$R^1{-}\overset{O}{\overset{\|}{C}}{-}OSi(CH_3)_3 + R^3{-}OSi(CH_3)_3 \longrightarrow R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^3 + [(H_3C)_3Si]_2O$$

2 **4** **3** **5**

In addition, the trimethylsilyl esters **2** are indeed involved as reactive intermediates in these transesterification processes as is shown by treating preformed trimethylsilyl ester **2** with alcohols to obtain the corresponding alkyl esters **3** under similar conditions (see experimental).



$$R^1{-}\overset{O}{\overset{\|}{C}}{-}OH \longrightarrow R^1{-}\overset{O}{\overset{\|}{C}}{-}OSi(CH_3)_3 \xrightarrow{R^3{-}OH} R^1{-}\overset{O}{\overset{\|}{C}}{-}OR^3$$

2 **3**

Transesterification of Methyl Benzoate to Ethyl Benzoate; Typical Procedure:

A solution of methyl benzoate (**1**; $R^1=C_6H_5$, $R^2=CH_3$; 1.4 g, 10 mmol), iodotrimethylsilane (2.0 g, 10 mmol) and iodine (0.25 g, 1 mmol) in chloroform (20 ml) is heated under reflux for 3 h under nitrogen. The mixture is allowed to cool to ambient temperature and stirred with a drop of mercury till the color of iodine disappears. A solution of ethanol (1.15 g, 25 mmol) in chloroform (2 ml) is then added and the mixture is again heated under reflux overnight. The mixture is then allowed to cool to room temperature, quenched with 5% aqueous sodium hydrogen carbon-

0039-7881/81/0232-0142 $ 03.00

Table. Transesterification of Esters **1** to Esters **3** using 1. Iodotrimethylsilane/Iodine, 2. Alcohol R^3-OH

Ester **1**		Reaction Conditions for **1**→**2**	R^3 in Alcohol and Ester **3**	Yield [%][a] of **3**	m.p. [°C] or b.p. [°C]/torr of **3**	
R^1	R^2				Observed	Reported
C_6H_5	CH_3	60 °C/3 h	C_2H_5	98	68–70°/1.9	87°/10[20]
C_6H_5	CH_3	60 °C/3 h	i-C_3H_7	72	74–77°/3	218°/760[20]
C_6H_5	C_2H_5	25 °C/8 h	CH_3	98	52–53°/1.6	198–199°/760[20]
t-C_4H_9	t-C_4H_9	80 °C/3 h	CH_3	50	98–101°/760	101°/760[20]
t-C_4H_9	CH_3	80 °C/6 h	C_2H_5	96	117–118°/760	118–118.2°/760[20]
t-C_4H_9	CH_3	80 °C/6 h	i-C_3H_7	71	128°/760	121.3 ± 0.2°/670[21]
$C_6H_5-CH=CH-$	CH_3	25 °C/6 h	C_2H_5	98	108–109°/1.8	271°/760[20]
$C_6H_5-CH=CH-$	CH_3	25 °C/6 h	i-C_3H_7	70	106–107°/1.7	153–155°/20[20]
C_6H_5	CH_3	60 °C/3 h	$C_6H_5CH_2$[b]	85	105–108°/0.05	170–171°/11[20]
C_6H_5	CH_3	60 °C/3 h	C_6H_5[b]	40	67.4°	71°[20]

[a] Yield of isolated product. The product purity (≥95%) was determined by G.L.C. analysis using a Varian 3700 gas chromatograph, equipped with a 150 ft × 0.01 in glass capillary column packed with OV 101 at 120 °C using helium (40 psi) as a carrier gas.

[b] The corresponding silylethers were used.

ate solution (50 ml) and extracted with ether (2 × 50 ml). The ether extract is washed with water and dried with anhydrous sodium sulfate. Evaporation of the solvent and distillation of the residue gives ethyl benzoate (**3**; $R^1 = C_6H_5$, $R^3 = C_2H_5$); yield: 1.47 g (98%); b.p. 68–70 °C/1.9 torr (Lit.[20], b.p. 87 °C/10 torr).

Other transesterifications were carried out similarly. Product esters **3** were purified by distillation or recrystallization. The obtained esters were characterized by T.L.C. (silica gel, benzene), I.R., U.V., and ^{1}H-N.M.R. spectroscopy.

Trimethylsilyloxybenzene from Trimethylsilyl Benzoate and Phenol:
Trimethylsilyl benzoate (**2**; $R^1 = C_6H_5$) is prepared according to the procedure described above. To this solution of **2** (10 mmol) is added a solution of phenol (2.82 g, 30 mmol) in chloroform (5 ml) and the mixture is again heated under reflux overnight. The mixture is then cooled and worked up in the usual manner to give trimethylsilyloxybenzene (1.4 g) which is slightly contaminated with phenyl benzoate (90% pure as determined by G.L.C.). The sodium hydrogen carbonate extract contains pure benzoic acid; yield: 1.1 g; m.p. 122 °C (Lit.[20], m.p. 122.4 °C).

Ethyl Benzoate from Trimethylsilyl Benzoate:
Trimethylsilyl benzoate (**2**; $R^1 = C_6H_5$) is prepared separately by the procedure of Morita et al.[22]. A solution of trimethylsilyl benzoate (**2**; 1.94 g, 10 mmol) and ethanol (1.15 g, 25 mmol) in chloroform (15 ml) is then heated under reflux overnight. Cooling of the reaction mixture and usual work up affords ethyl benzoate (**3**; $R^1 = C_6H_5$, $R^3 = C_2H_5$); yield: 1.41 g (94%); b.p. 68–70 °C/1.9 torr (Lit.[20] b.p., 87 °C/10 torr).

Support of our work by the National Science Foundation and the National Institutes of Health is gratefully acknowledged.

Received: July 7, 1980
(Revised form: September 15, 1980)

---

[1] For part 89, see G. A. Olah, M. Arvanaghi, Y. D. Vankar, G. K. S. Prakash, *Synthesis* **1980**, 662.

[2] T. L. Ho, G. A. Olah, *Angew. Chem.* **88**, 847 (1976); *Angew. Chem. Int. Ed. Engl.* **15**, 774 (1976).

[3] T. L. Ho, G. A. Olah, *Synthesis* **1977**, 417.

[4] T. L. Ho, G. A. Olah, *Proc. Natl. Acad. Sci. U.S.A.* **75**, 4 (1978).

[5] G. A. Olah, B. G. B. Gupta, S. C. Narang, *Synthesis* **1977**, 583.

[6] G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra, *Synthesis* **1979**, 61.

[7] G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra, *J. Org. Chem.* **44**, 1247 (1979).

[8] G. A. Olah, S. C. Narang, B. G. B. Gupta, R. Malhotra, *Angew. Chem.* **91**, 848 (1979); *Angew. Chem. Int. Ed. Engl.* **18**, 612 (1979).

[9] M. E. Jung, M. A. Lyster, *J. Am. Chem. Soc.* **99**, 968 (1977).

[10] R. A. Benkeser, E. C. Mozdzen, C. L. Muth, *J. Org. Chem.* **44**, 2185 (1979).

[11] H. R. Kricheldorf, *Angew. Chem.* **91**, 749 (1979); *Angew. Chem. Int. Ed. Engl.* **18**, 689 (1979).

[12] M. E. Jung, M. A. Lyster, *J. Chem. Soc. Chem. Commun.* **1978**, 315.

[13] M. E. Jung, M. A. Lyster, *J. Org. Chem.* **42**, 3761 (1977).

[14] M. E. Jung, W. A. Andrus, P. L. Ornstein, *Tetrahedron Lett.* **1977**, 4175.

[15] J. N. Denis, R. Magnane, M. van Eenoo, A. Krief, *Nouv. J. Chim.* **3**, 705 (1979).
For a recent review see: W. C. Groutas, D. Felker, *Synthesis* **1980**, 861.

[16] K. C. Nicolaou, W. E. Barnette, R. L. Magolda, *J. Am. Chem. Soc.* **100**, 2567 (1978).

[17] J. D. Bryant, G. E. Keyser, J. R. Barrio, *J. Org. Chem.* **44**, 3733 (1979).

[18] R. B. Silverman, R. E. Radak, N. P. Hacker, *J. Org. Chem.* **44**, 4970 (1979).

[19] C. E. Rehberg, *Org. Synth. Coll. Vol.* III, 146 (1955).

[20] *Handbook of Tables for Organic Compound Identification*, 3rd Ed., Chemical Rubber Company, Cleveland, Ohio, 1978.

[21] B. S. Lennon, V. R. Stimson, *Aust. J. Chem.* **21**, 1659 (1968).

[22] T. Morita, Y. Okamoto, H. Sakurai, *Tetrahedron Lett.* **21**, 835 (1980).