Triphenylphosphine-Catalyzed Dehydrogenative Coupling Reaction of Carboxylic Acids with Silanes – A Convenient Method for the Preparation of Silyl Esters

Guo-Bin Liu,[a,*] Hong-Yun Zhao,[a] and Thies Thiemann[b]

[a] Department of Chemistry, Fudan University, 220 Handan Road, Shanghai 200433, People's Republic of China
Phone: (+86)-21-513-70613; fax: (+86)-21-513-201-101; e-mail: liuguobin@fudan.edu.cn
[b] Institute of Materials Chemistry and Engineering, Kyushu University, 6-1, Kasuga-koh-en, Kasuga, Fukuoka 816-8580, Japan

Abstract: Triphenylphosphine has been found to be an efficient catalyst for the dehydrosilylation of carboxylic acids with silanes. In the presence of 4 mol% of triphenylphosphine (PPh₃), dehydrosilylation reactions in DMF afforded the corresponding silyl esters at 120 °C in good yield.

Keywords: carboxylic acids; organocatalysts; phosphines; silanes; silylation

Silyl esters are very important intermediates for the preparation of functional polymeric substrates such as easily degradable poly(silyl ester)s, widely employed as recyclable materials, gene delivery carriers, matrices for drug delivery and biodegradable surgical devices.[1a–j] Simple, economical and practical procedures for the conversion of carboxylic acids into silyl esters, are not only needed in normal organic synthesis, but are also prerequisities for the accurate performance of gas-chromatographic analyses in organic and biological chemistry.[1k,l] From the viewpoint of synthetic chemistry, silylation of carboxylic acids is one of the most commonly used protocols for their protection because deprotection of silyl esters is easily realized under the mild reaction conditions.[2] Much attention has been devoted to the development of a simple, practical and atom-economical method for the preparation of stable and easily isolable silyl esters.

Usually, silyl esters are prepared by cross-coupling reactions of carboxylic acids and chlorosilanes.[3] Hydrogen chloride is unavoidably formed in these procedures, and a stoichiometric or even an excess amount of bases such as amines or ammonia is needed to consume the HCl gas formed thereby. Since chlorosilanes themselves are prepared by the chlorination of silanes, either with chlorine gas[1g] or with hydrochloric acid under Pd/C catalysis,[4] the synthesis of silyl esters from the corresponding silanes necessitates two reaction steps. Although some newer synthetic methods to silyl esters have been published and while a lot of literature concerns itself with the transition metal-catalyzed cross-coupling of OH-containing compounds such as water and alcohols with silanes,[5] there are still but few examples of the dehydrogenative coupling reaction of carboxylic acids with silanes. Silylating agents such as hexamethyldisilazane, N-trimethylsilylalkanamines, N-trimethylsilylacetamide, N-trimethylsilyl-2-oxazolidinone, aminosilanes, or trialkylsilyl methallylsulfinates have been extensively utilized for the the transformation of carboxylic acids into the desired silyl esters.[6a–f] However, some shortcomings have been noted in these reported methods. The silylations of carboxylic acids with hexamethyldisilazane usually require prolonged reaction times under heating and continuous removal of the ammonia or amine formed thereby and the silylating agents are generally expensive. A few examples have been disclosed for dehydrosilylation reactions catalyzed by metal salts such as zinc chloride or, more frequently, by transition metals and metal complexes such as [(Ph₃P)CuH], HPtCl₆, Rh, and Pd.[6g–n] Generally, catalysts such as transition metals are expensive. [(Ph₃P)CuH] requires a multiple-step synthetic approach and *in situ* generation protocols. Moreover, the transition metal-catalyzed dehydrocoupling of unsaturated carboxylic acids and silanes always results in the formation of by-products due to the known ability of Rh, Pd or Pd/C to act as hydrogenation catalysts in the reduction of carbon-carbon double bonds in the desired olefinic silyl esters, leading to a troublesome purification.

In this communication, we report that triphenylphosphine (Ph₃P) effectively catalyzes the dehydrogenative coupling of carboxylic acids with silanes, yielding the corresponding silyl esters selectively without formation of any reduced by-products in the case
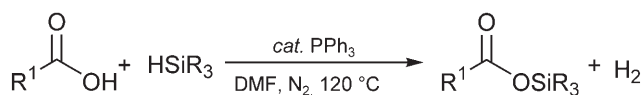
Scheme 1.

of unsaturated silyl esters. The results are summarized in Scheme 1 and Tables 1–4.

Dehydrogenative coupling reactions were carried out by heating a mixture of carboxylic acid, silane and a catalytic amount of phosphine in solvents under a nitrogen atmosphere for several hours (Scheme 1, Tables 1–3, the dehydrocoupling reaction was monitored by GC). The transformation of propionic acid with triethylsilane was used as a model to optimize the reaction conditions.

The dehydrogenative coupling was found to be finished after 15 h at 120°C, in the presence of 4 mol% PPh₃, affording the corresponding triethylsilyl propionate in 87% yield (Table 1, run 3). When the amount of catalyst was increased to 8, 16, or even 32%, the product yields were 85–88% (Table 1, runs 4–6). The reaction proceeded more slowly, however, when the amount of PPh₃ was decreased (to 1 or 2 mol%), when 48% and 30% of triethylsilane remained unreacted (GC ratio), even after 48 h at 120°C (Table 1, runs 1 and 2). The reaction progressed more slowly when carried out at 50, 80 or 100°C. Thus, a significant amount of Et₃SiH was found to be unreacted (88% at 50°C, 72% at 80°C and 51% at 100°C) after being heated for 48 h (Table 1, runs 8–10). No silyl

Table 1. Ph₃P-catalyzed dehydrocoupling of propionic acid with triethylsilane in DMF.[a]

Run	Ph₃P [mol%]	Temperature [°C]	Time [h]	HSiEt₃	CH₃CH₂CO₂SiEt₃
1	1	120	48	48	52
2	2	120	48	30	70
3	4	120	15	0	100 (87[6])
4	8	120	15	0	100 (88[6])
5	16	120	15	0	100 (85[6])
6	32	120	15	0	100 (87[6])
7	4	30	48	100	0
8	4	50	48	88	12
9	4	80	48	72	28
10	4	100	48	51	49

[a] Propionic acid (20 mmol), triethylsilane (20 mmol).
[b] GC ratio.
[c] Isolated yield in parenthesis.

Table 2. Ph₃P-catalyzed dehydrocoupling of propionic acid with triethylsilane in different solvents.[a]

Run	Solvent	Time [h]	HSiEt₃	CH₃CH₂CO₂SiEt₃
1	DMF	15	0	100 (87[6])
2	DMAc	15	8	92
3	NMP	15	9	94
4	DMI	15	12	94
5	HMPA	15	10	91
6	n-Octane	72	90	10
7	Xylene	72	62	38
8	t-Butylbenzene	72	81	19
9	Mesitylene	72	84	16
10	Chlorobenzene	72	89	11
11	1,2-Dichlorobenzene	72	91	9
12	Anisole	72	86	14
13	Di(ethylene glycol) diethyl ether	72	81	19
14	Benzonitrile	72	83	17

[a] Propionic acid (20 mmol), triethylsilane (20 mmol).
[b] GC ratio.
[c] Isolated yield in parenthesis.

Table 3. Catalyst-screening for the dehydrocoupling of propionic acid with triethylsilane in DMF at 120°C.[a]
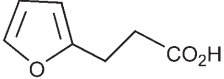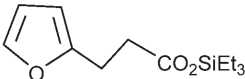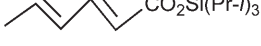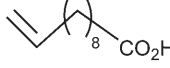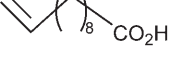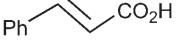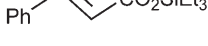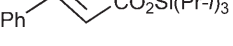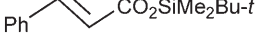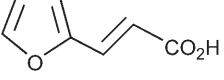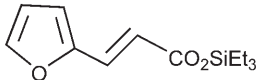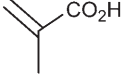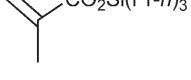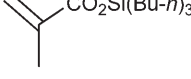
Run	Catalyst	Time [h]	HSiEt₃	CH₃CH₂CO₂SiEt₃
1	Ph₃P	15	0	100 (87[6])
2	Ph₃PO	24	98	2
3	(n-Bu)₃P	24	14	86
4	(t-Bu)₃P	24	16	84
5	Tricyclohexylphosphine	24	60	40
6	Tris(2-methylphenyl)-phosphine	24	70	30
7	1,2-Bis(diphenylphosphino)-ethane	24	65	35
8	1,3-Bis(diphenylphosphino)-propane	24	66	34
9	1,4-Bis(diphenylphosphino)-butane	24	69	31
10	rac-BINAP	48	78	22

[a] Propionic acid (20 mmol), triethylsilane (20 mmol).
[b] GC ratio.
[c] Isolated yield in parenthesis.

Table 4. Ph_3P-catalyzed dehydrocoupling of carboxylic acids with silanes.[a]

Run	Acid	Silane	Time [h]	Product	Yield [%][b]
1	CH_3CO_2H	$(n\text{-}Pr)_3SiH$	12	$CH_3CO_2Si(Pr\text{-}n)_3$	88[7]
2	CH_3CO_2H	$(n\text{-}Bu)_3SiH$	14	$CH_3CO_2Si(Bu\text{-}n)_3$	86[7]
3	$CH_3CH_2CO_2H$	Et_3SiH	15	$CH_3CH_2CO_2SiEt_3$	84[6f]
4	$CH_3CH_2CO_2H$	$(n\text{-}Bu)_3SiH$	14	$CH_3CH_2CO_2Si(Pr\text{-}i)_3$	76[8]
5	$CH_3(CH_2)_8CO_2H$	$(i\text{-}Pr)_3SiH$	15	$CH_3CH_2CO_2Si(Pr\text{-}i)_3$	79[2]
6	$C_6H_5CO_2H$	$(i\text{-}Pr)_3SiH$	14	$C_6H_5CO_2Si(Pr\text{-}i)_3$	83[2]
7	$C_6H_5CO_2H$	$t\text{-}BuMe_2SiH$	16	$C_6H_5CO_2SiMe_2Bu\text{-}t$	77[2]
8	$3\text{-}BrC_6H_4CO_2H$	$(i\text{-}Pr)_3SiH$	15	$3\text{-}BrC_6H_4CO_2Si(Pr\text{-}i)_3$	80[9]
9	$3\text{-}BrC_6H_4CO_2H$	$t\text{-}BuMe_2SiH$	17	$3\text{-}BrC_6H_4CO_2SiMe_2Bu\text{-}t$	78[9]
10	$3\text{-}ClC_6H_4CO_2H$	$(i\text{-}Pr)_3SiH$	14	$3\text{-}ClC_6H_4CO_2Si(Pr\text{-}i)_3$	81[9]
11	$3\text{-}ClC_6H_4CO_2H$	$t\text{-}BuMe_2SiH$	18	$3\text{-}ClC_6H_4CO_2SiMe_2Bu\text{-}t$	77[9]
12	$4\text{-}ClC_6H_4CO_2H$	Et_3SiH	13	$4\text{-}ClC_6H_4CO_2SiEt_3$	85[10]
13	$4\text{-}O_2NC_6H_4CO_2H$	$t\text{-}BuMe_2SiH$	18	$4\text{-}O_2NC_6H_4CO_2SiMe_2Bu\text{-}t$	75[11]
14	$C_6H_5CH_2CO_2H$	Et_3SiH	14	$C_6H_5CO_2SiEt_3$	80[6]
15		Et_3SiH	12		79[13]
16		$(i\text{-}Pr)_3SiH$	14		78[2]
17		$(i\text{-}Pr)_3SiH$	14		74[9]
18		Et_3SiH	13		82[12]
19		$(i\text{-}Pr)_3SiH$	15		75[12]
20		$t\text{-}BuMe_2SiH$	18		72[12]
21		Et_3SiH	13		80[6k]
22		$(n\text{-}Pr)_3SiH$	14		86[13]
23		$(n\text{-}Bu)_3SiH$	15		78[5i]

[a] Propionic acid (20 mmol), triethylsilane (20 mmol).
[b] GC ratio.
[c] Isolated yield in parenthesis.

ester was formed at 30 °C even for 48 h and triethylsilane was recovered quantatively (Table 1, run 7).

The dehydrocoupling in different solvents was investigated (Table 2). In aprotic dipolar solvents such as *N,N*-dimethylacetamide (DMAc), 1,3-dimethyl-2-imidazolidinone (DMI), *N*-methylpyrrolidinone (NMP), and hexamethylphosphoramide (HMPA), the dehydrogenative coupling is slightly slower compared with that in DMF and small amounts of Et₃SiH were detected (8–12 %) (Table 2, runs 2–5). In xylene, *tert*-butylbenzene, mesitylene, chlorobenzene, 1,2-dichlorobenzene, *n*-octane, anisole, di(ethylene glycol) dimethyl ether, and benzonitrile, the dehydrocoupling could not be finished and even when heated at 120 °C for 72 h significant amounts of Et₃SiH were detected (62–90 %) (Table 2, runs 6–11).

Phosphines other than Ph₃P were also tested as catalysts for the dehydrogenative coupling and the results are summarized in Table 3 (all at 4 mol %, DMF, 120 °C). Only a trace amount of silyl ester was formed when triphenylphosphine oxide (Ph₃PO) was used as a catalyst (Table 3, run 2). In the case of using tri-*n*-butylphosphine and tri-*tert*-butylphosphine as catalysts, 14 % and 16 % of Et₃SiH were still detected even being heated for 24 h at 120 °C (Table 3, runs 3 and 4). Under the catalysis of 1,2-bis(diphenylphosphino)ethane, 1,3-bis(diphenylphosphino)propane, 1,4-bis(diphenylphosphino)butane, tricyclohexylphosphine, tris(2-methylphenyl)phosphine, and *rac*-2,2′-bis(diphenylphosphino)-1,1′-naphthyl (*rac*-BINAP), the dehydrocoupling was sluggish (Table 3, runs 5–10) and some amounts of Et₃SiH were detected even after being heated for 24 h or 48 h at 120 °C.

A number of carboxylic acids were reacted with triethylsilane, tri-*n*-propylsilane [(*n*-Pr)₃SiH], tri-*n*-butylsilane [(*n*-Bu)₃SiH] or *tert*-butyldimethylsilyl (*t*-BuMe₂SiH) and all afforded the corresponding silyl esters in good yields (all with 4 mol % PPh₃, DMF, 120 °C) (Table 4). In the case of the reaction of bromo- and chlorobenzoic acids, the desired silyl esters were obtained in 77–85 % yield, free of dehalogenated by-products (Table 4, runs 8–12). Also, the dehydrocoupling of 4-nitrobenzoic acid with *tert*-butyldimethylsilane afforded the corresponding silyl ester in good yield without any over-reduced by-product (Table 4, run 13). In the case of 2-phenylacetic acid and 3-furylpropionic acid, the corresponding silyl esters were obtained in good yields (Table 4, runs 14 and 15). Under similar reaction conditions, the desired unsaturated silyl esters were produced by dehydrogenative coupling reaction of silanes with unsaturated acids such as cinnamic acid, furylacrylic acid, 1,3-hexadienoic acid, and methacrylic acid. No formation of over-reduced by-products was observed (Table 4, runs 16–23).

In conclusion, we have demonstrated that PPh₃ is an efficient catalyst for the dehydrogenative coupling of carboxylic acids with silanes. The dehydrogenative coupling reactions proceed efficiently to give the corresponding silyl esters in good yields. No over-reduced silyl esters are formed in the case of coupling unsaturated carboxylic acids, bromo-, chloro- or nitrobenzoic acids, and unsaturated acids with silanes. We believe that the PPh₃-catalyzed dehydrogenative coupling reaction of carboxylic acids with silanes provides another important protocol for a one-step, metal-free, highly selective, atom-economical and efficient synthetic method. Also, the PPh₃-catalyzed dehydrocoupling reaction of carboxylic acids with silanes offers a useful method for protecting carboxylic acid because the silyl ester is easily hydrolyzed to give the corresponding carboxylic acid. Further work on the dehydrosilylation of carboxylic acids and silanes is currently in progress in our laboratory and the results will be published in due course.

Experimental Section

Typical Procedure

To a mixture of propionic acid (40 mmol, 2.96 g), and triethylsilane (40 mmol, 4.64 g) in DMF (20 mL) was added triphenylphosphine (1.6 mmol, 0.42 g, 0.04 equivs.) at room temperature under a nitrogen atmosphere. The reaction mixture was stirred at 120 °C for 15 h (monitored by GC). The desired triethylsilyl propionate was obtained as a colourless oil (yield: 87 %) after distillation under reduced pressure (run 3).

Triethylsilyl propionate:[6f] IR (neat): $\nu = 684$, 740, 824, 998, 1062, 1241, 1410, 1464, 1714, 2870, 2954 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): $\delta = 0.72$ (6 H, q, ³*J* = 7.8 Hz), 0.95 (9 H, t, ³*J* = 7.8 Hz), 1.14 (3 H, t, ³*J* = 7.6 Hz), 2.36 (2 H, q, ³*J* = 7.6 Hz); ¹³C NMR (100 MHz, CDCl₃): $\delta = 4.42$, 6.46, 9.34, 28.46, 175.20.

All of the silyl esters are known compounds and were compared with authentic samples [prepared by cross-coupling of carboxylic acids and chlorosilanes in the presence of a base such as triethylamine or imidazole (*tert*-butylsilyl esters) in dichloromethane] and were identified on the basis of their IR, ¹H NMR, ¹³C NMR and GC-mass spectral data.

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