A CONVENIENT METHOD FOR THE TEMPORARY PROTECTION OF CARBOXYLIC ACIDS USING TRIBUTYLTIN HYDRIDE OR TRIBUTYLTIN METHOXIDE: SCOPE AND LIMITATIONS

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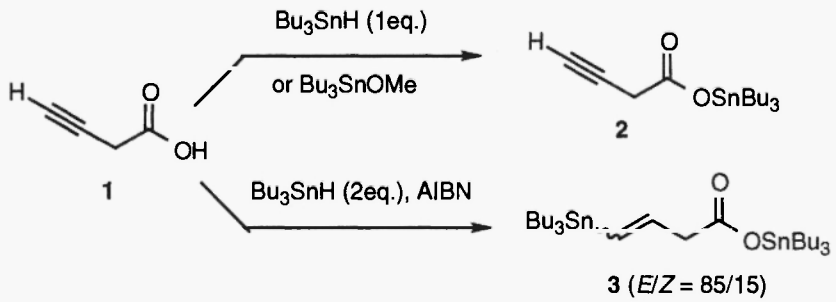
Abstract

Numerous acids have been protected as tributyltin esters using tributyltin hydride or tributyltin methoxide. Protection with tributyltin hydride was found limited when the use of tributyltin methoxide affords stannylesters in quantitative yield. Deprotection step proceeds in good yields using potassium fluoride followed by a slightly acidic solution. This protection have been successfully applied in Stille cross-coupling reactions between vinyltributyltins and vinyl iodide bearing a protected carboxylic function.

Introduction

In a polyfunctional substrate, a selective chemical reaction on one site needs in many cases the protection of the other reactive sites. For this purpose, many protective groups have been proposed in the past and this field remains under investigations.[1] For the protection of carboxylic acid function, different anhydrides,[2] amides[3] or esters,[4] particularly unsaturated esters,[5] have proven to be very efficient. In the last case, numerous deprotection procedures use specific reagents such as palladium[6] or rhodium[7] catalysts.

As part of an ongoing effort in the direct synthesis of acids,[8] we found that the radical hydrostannation of but-3-ynoic acid with tributyltin hydride does not lead to the corresponding vinyltin but yields quantitatively tributyltin carboxylate **2** (and H_2 gas evolution). The same reaction, in the presence of two equivalents of tributyltin hydride leads effectively to the corresponding protected vinyltin as depicted in scheme 1.[9]



scheme 1

Furthermore, we found that the palladium cross-coupling of vinyltin **3** with arylhalides occurs in high yield. Attempts using the acid free equivalent of **3** consistently failed.

Taking into account the judicious Kocienski's remarks about the required qualities of a protecting group[1] and the precedent observations, we have evaluated the possibilities to propose tributyltin as a temporary protective group of the acid function in certain reactions like Stille's cross-coupling. Moreover, as evoked in the past, the tributylstannylation of acid functions generally increase the solubility of the products, especially in the case of polyacid compounds.

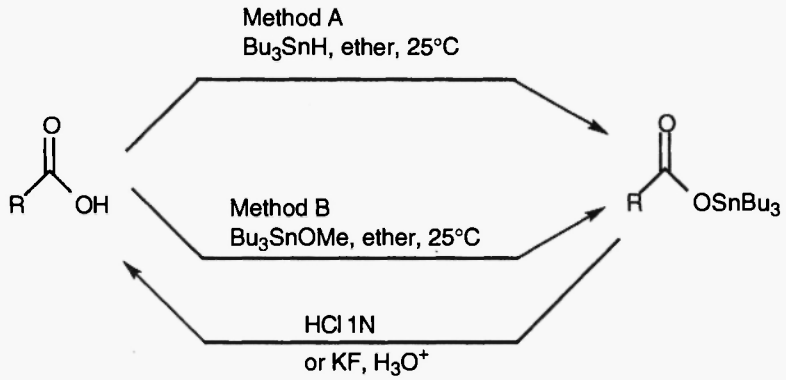
Tributyltin carboxylates have already been proposed as protective group in the total synthesis of penicillins and gibberelins.[10] The treatment with bistributyltin oxide of carboxylic acid function affords tributyltin carboxylates in good yields. However, the major drawback of this procedure is the generation of

water which must be removed by azeotropic distillation and, also, of numerous organotin by-products which impose a purification step.[11]

In this paper, we wish to report the easy formation of tributyltin carboxylates using tributyltin hydride or tributyltin methoxide and the application of this protection type in the Stille's cross-coupling reaction.

Results

Our results are summarised in the table 1. The synthesis of the stannylesters was realised using two methods. One involves the use of tributyltin hydride (A method) which gives stannylesters and H_2 gas evolution. A similar experiment conducted with one equivalent of tributyltin methoxide (B method) leads to the same carboxylate within a couple of minutes after removal of the methanol formed. The acid function is simply regenerated by treatment with an acidic solution or with a saturated potassium fluoride solution followed by a slightly acidic treatment (In this case, the saponification is quantitative giving acids in good yield).



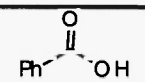
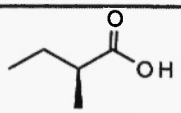
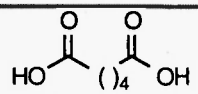
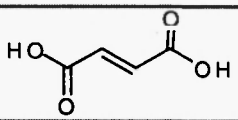
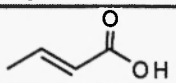
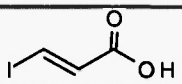
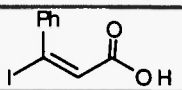
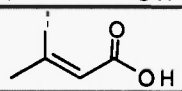
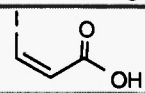
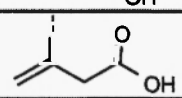
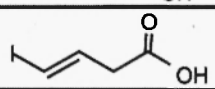
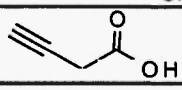
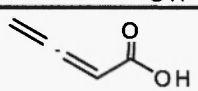
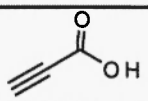
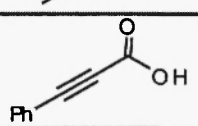
Scheme 2

Due to the simpleness of this methodology, we decided to verify the general character of this reaction to protect and deprotect numerous acids. The use of tributyltin hydride must be avoided with substrates bearing a triple bond or an halide group which are partially reduced. On the contrary the use of tributyltin methoxide affords good yields and seems to have a general character excepted for aminoacids. The deprotection step gives excellent yields under mild experimental conditions. No racemisation (entry 2), no isomerisation of double bond and no polymerisation of unsaturated systems occur during the protection or deprotection steps giving to this methodology a potential way of protection/deprotection system.

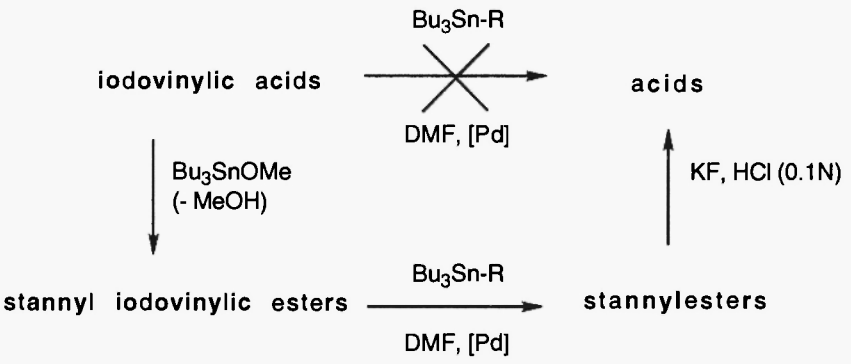
Applications

We have shown that, in some cases, functional groups can be introduced via organotin reagents in the presence of palladium complexes on iodovinylic acids without any protection of the carboxylic acid function.[8,12] Nevertheless, the use of vinyltin reagents bearing, in 2 position, an electron-donating group such as for example isobutenyltributyltin does not allow the transfer of a vinyl unit. A possible explanation for these observations is that the intermediate vinylpalladium, resulting from the oxidative addition onto the $C(sp^2)$-I bond, reacts with the free carboxylic acid giving a carboxylate palladium specie in which the electrophilic character of the palladium atom has significantly decreased. So, in the case of vinyltins (or tin acetylides) the transmetallation of the tin atom becomes inoperative, due to deactivated by an electrondonating-group in β position. And we decided to protect the iodovinylic acids with a tributylstannyl moiety and check the corresponding cross-coupling reaction under palladium catalysis.

Table 1 : Synthesis of tributyltinesters

Entry	acid	Method, conditions	N°	Yield of tributyltinesters	Yield of deprotected acid
1		A, 50°C, 1h, DMF	4	62	50
		B, 60°C, 1h, ether		98	72
2		A, 20°C, 1h	5	100	60#
3		A, 20°C, 2h	6	0	
		B, 20°C, 0.5h, (2 eq.)		100	76
4		B, 60°C, 3h, (2 eq.)	7	96	73
5		A, 20°C, 12h	8	98	80
6		B, 60°C, 0.5h	9	97	95
7		B, 20°C, 0.25h	10	98	93
8		A, 20°C, 1h	11	polymers	
		B, 20°C, 0.25h		95	90
9		B, 20°C, 0.25h	12	100	95
10		A, 0°C, 1h	13	reduction	
		B, 20°C, 0.25h		100	92
11		B, 20°C, 0.25h	14	100	94
12		A, 0°C, 1h	1	80*	
		B, 0°C, 1h		98	80
13		A, 20°C, 0.25h	15	reduction**	
		B, 20°C, 0.25h		97	88
14		A, 20°C, 3h	16	60***	
		B, 20°C, 0.25h		100	65
15		A, 20°C, 0.25h	17	50***	
		B, 20°C, 0.25h		98	73
16	L-Valine	A, 20°C, 2h		0	
		B, 20°C, 0.25h		-	-

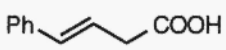
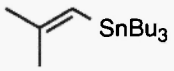
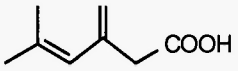
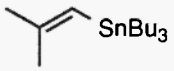
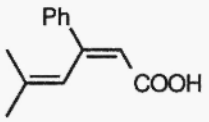
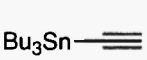
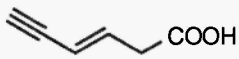
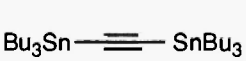
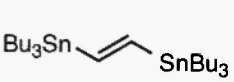
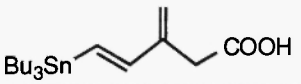
* 20% of vinyltin acid have been recovered.** Only but-3-enoic acid was detected at the end of the reaction ***obtained as a mixture with the hydrostannation products of the triple bond. #The regenerated (*S*)-2-methylbutenoic acid exhibits the same optical rotation than the starting material.



Scheme 3

The cross-coupling reactions affords dienes or enyne products in good yields (table 2). The same reaction has also been performed with vinyltin **3** and phenyl iodide under tetrakistriphenylphosphine palladium (0) catalysis. The mild experimental conditions of the Stille cross-coupling reactions leads to dienes free of polymerisation or isomerisation products.

Table 2 : Palladium catalysed cross-coupling reactions

Stannylester	A	Products	N°	yield
3	Ph-I		**18b**	65
10			**19b**	66
13			**20b**	68
14			**21b**	76
9*			**22b**	72
10			**23b**	77

* 2 equivalents of **9** have been used.

The synthetic potential of theses compounds have not been completely studied at the moment, however dienic compounds undergo Diels-Alder type reactions affording functionalised cycloadducts in good yields. Work is underway in our laboratory to delimit the synthetic application of this method.

In summary, we have demonstrated that numerous acids can be protected as tributyltin esters using tributyltin hydride or tributyltin methoxide. This protection have been successfully applied in Stille cross-coupling reactions between vinyltributyltins or tin acetylides and vinyl iodide bearing a tributyltin protected carboxylic function.

Experimental section

All reactions were carried out under inert atmosphere (N_2). Ether was dried and freshly distilled from sodium/benzophenone. DMF was dried by distillation over calcium hydride. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 (200MHz and 50MHz) nuclear magnetic resonance spectrometer using

$CDCl_3$ as solvent. Chemical shifts are given in ppm relative to Me_4Si. The mass spectra were obtained on a Hewlett Packard (engine 5989A) in direct introduction mode (70eV) . The isotopic patterns are given for ^{120}Sn (isotopic abundance 33%) in organotin fragments ; this means that the reported abundances (values in brackets) for organotin fragments are only roughly one third of the correct value taking account of the 10 isotopes of tin compared with those of organic fragment. IR spectra were recorded on a Nicolet 250FT-IR spectrophotometer. Raman spectra were recorded on a Brucker RFS 100, excitation with a laser Nd: YAG (1064nm, 130mW). Melting points are uncorrected. Tributyltin methoxide and tributyltin hydride are commercialy available (or prepared according to references 13 and 14). Acids 4-8 and 16-17 are also commercially available ; acids 1[15], 9-14[16] were preprared by previously reported procedures. Isobutenyltributyltin[17] is prepared from isobutenyl magnesium bromide and bistributyltin oxide. Tributyltinacetylide[18] is prepared from lithium acetylide, ethylenediamine complex and tributyltin chloride.

General procedure for the preparation of tributyltin carboxylates

5 mmol of acid are dissolved in 10 mL of diethylether and then 1.605 g (5 mmol) of tributyltin methoxide is added (syringe method). After further stirring at room temperature for 15 min, the methanol formed and the diethylether are removed under reduced pressure. The obtained tributyltin carboxylates are pure enough and can be used without purification.Tributylstannylbenzoate 4 and tributylstannyl-3-phenylpropionate **17** are commercially available.

Tributylstannylbut-3-ynoate 2

Mp = 73°C ; IR: 3313, 2129 (w), 1593-1572 ; RAMAN: 2127 (strong), 1155

^1H NMR δ (ppm): 0.88 (9H, t, $^3J_{2H}$ = 7.1Hz), 1.2-1.8 (18H, m), 2.17 (1H, t, $^4J_{2H}$ = 2.7Hz), 3.27 (2H, d, $^4J_{1H}$ = 2.7Hz)

^{13}C NMR δ (ppm): 13.5 (3C), 16.6 (3C, $^1J_{Sn-C}$ = 341-354Hz), 26.2, 26.9 (3C), 27.7 (3C), 70.9, 77.6 , 172.6

MS (70 eV) : m/z = 317 (20), 273 (25), 177 (46), 159 (24), 121 (31), 57 (21), 41 (100), 40 (11), 39 (66), 38 (11)

Tributylstannyl-4-tributylstannylbut-3-enoate 3

is prepared by hydrostannation of the but-3-ynoic acid under radicalar conditions (AIBN) with two equivalents of tributyltin hydride and uses as a thermodynamic mixture of **3** (*E/Z* = 85/15).

IR: 1655, 1580-1550, 1074

^1H NMR δ (ppm): *E* Isomer: 0.8-1.65 (54H, m), 3.18 (2H, d, $^3J_{1H}$ = 5.0Hz), 6.0-6.2 (2H, m, ABX_2 system, Homo-Decoupling at 640Hz gives δ_{H3} = 6.00 and δ_{H4} = 6.08 and J_{AB} = 18.9Hz)

Z Isomer: 3.07 (2H, dd, $^3J_{1H}$ = 7.0Hz, $^4J_{1H}$ = 1.4Hz), 6.00 (1H, dt, $^3J_{1H}$ = 12.7Hz, $^4J_{2H}$ = 1.4Hz), 6.69 (1H, dt, $^3J_{1H}$ = 12.7Hz, $^3J_{2H}$ = 7Hz)

^{13}C NMR δ (ppm): -OSnBu_3: 13.5 (3C), 16.6 (3C, $^1J_{Sn-C}$ = 345-355Hz), 26.9 (3C, $^3J_{Sn-C}$ = 64Hz), 27.8 (3C, $^2J_{Sn-C}$ = 21Hz), -SnBu_3: 9.3 (3C, $^1J_{Sn-C}$ = 340-346Hz), 13.4 (3C), 27.1 (3C), 28.8 (3C, $^2J_{Sn-C}$ = 20Hz)

E Isomer: 44 (1C, $^3J_{Sn-C}$ = 65Hz), 130.7 (1C, $^1J_{Sn-C}$ = 369-386Hz), 141.7, 176.7

Z Isomer: 42.3, 130.9, 141.9, 176.6

MS (70 eV) : m/z = 611 (15), 609 (55), 507 (29), 319 (21), 291 (100), 271 (25), 267 (45), 235 (60), 213 (16), 179 (17), 84 (13), 57 (51), 49 (29), 41 (90)

Tributylstannyl-2-methylbutanoate 5

Mp = 73°C, $[\alpha]^{22;D}$ = 6.97 ° (c = 3.2, $CHCl_3$) ; IR: 1645, 1230, 1075

^1H NMR δ (ppm): 0.94 (9H, t, $^3J_{2H}$ = 7.1Hz), 1.13-1.80 (32H, m), 2.37 (1H, m)

^{13}C NMR δ (ppm): 11.7, 13.5 (3C), 16.2 (3C, $^1J_{Sn-C}$ = 342-360Hz), 17.2, 26.8 (3C, $^3J_{Sn-C}$ = 63Hz), 27.2, 27.7 (3C, $^2J_{Sn-C}$ = 21Hz), 41.5, 182

MS (70 eV) : m/z = 335 (100), 291 (17), 233 (16), 221 (28), 177 (24), 137 (18), 121 (13), 41 (11), 29 (13)

Bis(tributylstannyl)hexanedioate 6

Mp = 103°C ; IR: 1579-1556, 1151, 1080

^1H NMR δ (ppm): 0.92 (18H, t, $^3J_{2H}$ = 7.1Hz), 1.21-1.65 (40H, m), 2.33 (4H, t, $^3J_{2H}$ = 5.6Hz)

^{13}C NMR δ (ppm): 13.5 (6C), 16.2 (6C, $^1J_{Sn-C}$ = 346-362Hz), 25.4 (2C), 26.9 (6C, $^3J_{Sn-C}$ = 64.3Hz), 27.7 (6C, $^2J_{Sn-C}$ = 19.4Hz), 34.5 (2C), 179 (2C)

MS (70 eV) : m/z = 317 (100), 291 (22), 273 (38), 251 (15), 233 (10), 217 (20), 203 (29), 199 (19), 177 (99), 159 (45), 137 (38), 121 (34), 69 (13), 57 (23), 55 (10), 43 (14), 41 (32), 39 (10)

(*E*)-Bis(tributylstannyl)but-2-endioate 7

Mp = 134°C ; IR: 1572, 1081

^1H NMR δ (ppm): 0.92 (18H, t, $^3J_{2H}$ = 7Hz), 1.29-1.63 (36H, m), 6.79 (2H, s)

^{13}C NMR δ (ppm): 13.5 (6C), 16.4 (6C, $^1J_{Sn-C}$ = 340-356Hz), 26.8 (6C, $^3J_{Sn-C}$ = 64Hz), 27.6 (6C, $^2J_{Sn-C}$ = 19.6Hz), 134.5 (2C), 170.4 (2C)

MS (70 eV) : m/z = 636 (14), 323 (13), 291 (11), 233 (24), 177 (48), 137 (10), 121 (20), 57 (38), 41 (100).

(*E*)-Tributylstannylbut-2-enoate 8

Mp = 92°C ; IR: 3040, 1658, 1560-1535

^1H NMR δ (ppm): 0.93 (9H, t, $^3J_{2H}$ = 7.10Hz), 1.20-1.80 (18H, m), 1.87 (3H, d, $^3J_{1H}$ = 6.8Hz), 5.89 (1H, d, $^3J_{1H}$ = 15.4Hz), 6.89 (1H, m)

^{13}C NMR δ (ppm): 13.5 (3C), 16.3 (3C, $^{1}J_{Sn-C}$ = 344-360Hz), 17.6, 26.9 (3C, $^{3}J_{Sn-C}$ = 66.2Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 20Hz), 124, 143, 172
MS (70 eV) : m/z = 319 (100), 233 (12), 205 (39), 177 (17), 161 (14), 137 (17), 121 (13), 69 (12), 57 (11), 41 (37),
39 (12)

(*E*)-Tributylstannyl-3-iodoprop-2-enoate 9

Mp = 90°C ; IR: 1607, 1547
^{1}H NMR δ (ppm): 0.94 (9H, t, $^{3}J_{2H}$ = 7Hz), 1.27-1.65 (18H, m), 6.92 (1H, d, $^{3}J_{1H}$ = 14.7Hz), 7.73 (1H, d, $^{3}J_{1H}$ = 14.7Hz)
^{13}C NMR δ (ppm): 13. 5 (3C), 16.5 (3C, $^{1}J_{Sn-C}$ = 340-353Hz), 26.9 (3C, $^{3}J_{Sn-C}$ = 60Hz), 27.6 (3C, $^{2}J_{Sn-C}$ = 20Hz), 97.8, 138.3, 169
MS (70 eV) : m/z = 431 (47), 429 (35), 361 (20), 317 (18), 305 (17), 247 (25), 177 (26), 121 (28), 57 (45), 55 (14),
53 (12), 45 (11), 41 (100), 39 (27)

(*Z*)-Tributylstannyl-3-iodo-3-phenylprop-2-enoate 10

Mp = 66°C ; IR: 1606, 1543
^{1}H NMR δ (ppm): 0.96 (9H, t, $^{3}J_{2H}$ = 7.1Hz), 1.31-1.67 (18H, m), 6.7 (1H, s), 7.35-7.4 (3H, m), 7.55-7.57 (2H, m)
^{13}C NMR δ (ppm): 13.6 (3C), 16.7 (3C, $^{1}J_{Sn-C}$ = 334-349Hz), 26.8 (3C, $^{3}J_{Sn-C}$ = 58Hz), 28.3 (3C, $^{2}J_{Sn-C}$ = 20Hz), 127.9, 128 (2C), 128.5 (2C), 129.3, 131, 143.2, 170
MS (70 eV) : m/z = 507 (13), 361 (52), 305 (26), 247 (29), 177 (22), 147 (15), 121 (24), 103 (10), 102 (23), 77 (14), 76 (13), 69 (16), 57 (43), 51 (12), 50 (11), 41 (100), 39 (29).

(*Z*)-Tributylstannyl-3-iodobut-2-enoate 11

Mp = 71°C ; IR: 1623, 1561-1544, 1267
^{1}H NMR δ (ppm): 0.92 (9H, t, $^{3}J_{2H}$ = 7.1Hz), 1.26-1.72 (18H, m), 2.68 (3H, d, $^{4}J_{1H}$ = 1.1Hz), 6.31 (1H, bs)
^{13}C NMR δ (ppm): 13.5 (3C), 16.5 (3C, $^{1}J_{Sn-C}$ = 337-355Hz), 26.9 (3C, $^{3}J_{Sn-C}$ = 64Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 20Hz), 35.8, 109, 128.6, 168
MS (70 eV) : m/z = 445 (46), 361 (15), 331 (11), 305 (12), 247 (22), 177 (24), 121 (26), 85 (24), 69 (15), 67 (19),
57 (33), 43 (14), 41 (100), 40 (16), 39 (81), 38 (13)

(*Z*)-Tributylstannyl-3-iodoprop-2-enoate 12

Mp = 86°C ; IR: 1611, 1544, 1285
^{1}H NMR δ (ppm): 0.95 (9H, t, $^{3}J_{2H}$ = 7Hz), 1.29 1.73 (18H, m), 6.94 (1H, d, $^{3}J_{1H}$ = 8.7Hz), 7.22 (1H, d, $^{3}J_{1H}$ = 8.7Hz)
^{13}C NMR δ (ppm): 13.5 (3C), 16.5 (3C, $^{1}J_{Sn-C}$ = 337-353Hz), 26.9 (3C, $^{3}J_{Sn-C}$ = 50Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 20Hz), 90.8, 132.7, 169
MS (70 eV) : m/z = 431 (58), 361 (22), 317 (12), 305 (21), 247 (38), 233 (14), 177 (27), 121 (31), 57 (42), 55 (15), 41 (100), 39 (27).

Tributylstannyl-3-iodobut-3-enoate 13

Mp = 81°C ; IR: 1624, 1597-1572
^{1}H NMR δ (ppm): 0.94 (9H, t, $^{3}J_{2H}$ = 7.1Hz), 1.18-1.70 (27H, m), 3.57 (2H, s), 5.87 (1H, s), 6.18 (1H, s)
^{13}C NMR δ (ppm): 13.5 (3C), 16.5 (3C, $^{1}J_{Sn-C}$ = 317-346Hz), 26.9 (3C, $^{3}J_{Sn-C}$ = 64Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 20Hz), 51.4, 100.6, 129, 174
MS (70 eV) : m/z = 445 (13), 361 (31), 313 (14), 305 (18), 247 (22), 177 (24), 121 (26), 57 (47), 41 (100), 40 (20), 39 (71), 38 (11)

(*E*)-Tributylstannyl-4-iodobut-3-enoate 14

Mp = 70°C ; IR: 3028, 1583, 1216, 1151
^{1}H NMR δ (ppm): 0.94 (9H, t, $^{3}J_{2H}$ = 7.2Hz), 1.16-1.7 (18H, m), 3.08 (2H, d, $^{3}J_{1H}$ = 7.3Hz), 6.18 (1H, d, $^{3}J_{1H}$ = 14.5Hz), 6.69 (1H, dt, $^{3}J_{1H}$ = 14.5Hz, $^{3}J_{2H}$ = 7.3Hz)
^{13}C NMR δ (ppm): 13.5 (3C), 16.4 (3C, $^{1}J_{Sn-C}$ = 339-359Hz), 26.9 (3C, $^{3}J_{Sn-C}$ = 66.7Hz), 27.6 (3C, $^{2}J_{Sn-C}$ = 20.5Hz), 41.4, 77.2, 139.4, 172.6
MS (70 eV) : m/z = 445 (30), 361 (15), 305 (14), 291 (15), 247 (32), 177 (28), 121 (26), 97 (18), 85 (15), 57 (33), 55 (93), 41 (100), 40 (16), 39 (69)

Tributylstannylbuta-2,3-dienoate 15

Mp = 97°C ; IR: 3065, 1969, 1942, 1574-1550, 1282, 1076
^{1}H NMR δ (ppm): 0,94 (9H, t, $^{3}J_{2H}$ = 7.2Hz), 1.20-1.80 (18H, m), 5.16 (2H, d, $^{4}J_{1H}$ = 6.5Hz), 5.69 (1H, t, $^{4}J_{2H}$ = 6.5Hz)
^{13}C NMR δ (ppm): 13.4 (3C), 16.3 (3C, $^{1}J_{Sn-C}$ = 359-343Hz), 26.8 (3C, $^{3}J_{Sn-C}$ = 64.3Hz), 27.6 (3C, $^{2}J_{Sn-C}$ = 19.4Hz), 77.9, 88.9, 170.5, 215.4
MS (70 eV) : m/z = 317 (27), 177 (37), 159 (16), 121 (27), 57 (25), 41 (100), 39 (58)

Tributylstannylpropiolate 16

Mp = 62°C ; IR: 3300, 2110, 1580-1560
^{1}H NMR δ (ppm): 0.92 (9H, t, $^{3}J_{2H}$ = 7Hz), 1.21-1.80 (18H, m), 2.78 (1H, s)

^{13}C NMR δ (ppm): 13.4 (3C), 16.9 (3C, $^{1}J_{Sn-C}$ = 340-356Hz), 26.8 (3C, $^{3}J_{Sn-C}$ = 68Hz), 27.5 (3C, $^{2}J_{Sn-C}$ = 21Hz), 71.9, 76.6, 157
MS (70 eV) : m/z = 359 (M^{+}, 1), 303 (100), 293 (26), 259 (35), 203 (42), 189 (16), 177 (28), 145 (31), 137 (10), 121 (21), 57 (10), 41 (28)

General procedure for the deprotection of tributyltin carboxylates
5 mmol of tributyltin carboxylate are dissolved in 10 mL of diethylether and then 20 mL of an aqueous solution of 1M hydrochloric acid are added dropwise. After stirring for 15 min, the aqueous phase is extracted with ether (3x20 mL); then the organic layers are treated with 1M NaOH and the obtained aqueous phase is acidified with
1M HCl, extracted with diethylether (3x20 mL) and after usual workup the crude acid is recovered by cristallisation from petroleum ether/Et_2O (95/5) or purified by column chromatography on silica gel (petroleum ether / diethylether: 95/5). For deprotection using potassium fluoride see experimental procedure (*vide infra*).

Applications
Procedure for the preparation of dienoic acids
To a DMF solution (15 mL) of 4.14g (12 mmol) of isobutenyltributyltin, 10 mmol of **13** (or 10) diluted into 5 mL of DMF is added dropwise. At the end of the addition, 129 mg (0.5 mmol) of dichlorobis(acetonitrile)-palladium(II) is added. The mixture is stirred for 3h at 25°C. In the case of **3**, the reaction is run with chloroform as the solvant and with tetrakistriphenylphosphine palladium (O) as catalyst.

a) Isolation of the tincarboxylates **18a, 19a and 20a:**
The solution is hydrolysed with 25 mL of a 1M solution of potassium fluoride and 25 mL of acetone to precipitated the formed tributyltin iodide. After strongly stirring for 2h, the reaction mixture was filtered, washed with NH_4Cl solution (2x15 mL) and extracted with diethylether (3x30 mL) After usual treatments, the crude tincarboxylates **18a, 19a and 20a** are purified by cristallisation (petroleum ether/diethylether) (90/10). The corresponding acids **18b, 19b and 20b** are obtained by treatment of the tin carboxylates with a saturated solution of potassium fluoride and then are acidified with 0.1M HCl solution and extracted with diethylether (3x30 mL). After usual treatments, the crude acids were purified by cristallisation (petroleum ether/diethylether: 95/5).

b) Direct obtention of the acids **18b, 21b, 22b and 23b**
The solution is hydrolysed with 25 mL of a saturated solution of potassium fluoride and 25 mL of acetone. After strongly stirring for 2h, the reaction mixture was filtered and washed with water, the aqueous layer is acidified with 1M HCl solution, extracted with diethylether (3x30 mL) and washed with a saturated NH_4Cl solution. After usual treatments, the crude acids are purified by cristallisation (petroleum ether/diethylether: 95/5). (*E*)-4-Phenylbut-3-enoic acid **18b** is commercially available.

(*E*)-Tributylstannyl-4-phenylbut-3-enoate 18a
IR: 3065, 3026, 1651, 1587-1568, 1155, 1076, 964
^{1}H NMR δ (ppm) : 0.94 (9H, t, $^{3}J_{2H}$ = 7Hz), 1.27-1.65 (18H, m), 3.28 (2H, d, $^{3}J_{1H}$ = 5.9Hz), 6.39 (1H, dt, $^{3}J_{1H}$ = 16Hz, $^{3}J_{2H}$ = 5.9Hz), 6.51 (1H, d, $^{3}J_{1H}$ = 16Hz), 7.24-7.43 (5H, m)
^{13}C NMR δ (ppm): 13.5 (3C), 16.4 (3C, $^{1}J_{Sn-C}$ = 357-341Hz), 26.9 (3C, $^{3}J_{Sn-C}$ = 64.5Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 18.8Hz), 39, 123.8, 126.1 (2C), 127, 128.3 (2C), 132, 137.2, 176.8
MS (70 eV): m/z = 395 (13), 235 (16), 177 (20), 121 (13), 57 (34), 55 (11), 43 (31), 42 (11), 41 (100), 39 (42)

Tributylstannyl-5-methyl-3-methylenehex-4-enoate 19a
IR: 3089, 1653, 1630, 1590, 1218
^{1}H NMR δ (ppm): 0.89 (9H, t, $^{3}J_{2H}$ = 7.2Hz), 1.20-1.67 (18H, m), 1.76 (3H, s), 1.78 (3H, s), 3.07 (2H, s), 4.90 (1H, s), 5.08 (1H, s), 5.66 (1H, s)
^{13}C NMR δ (ppm): 13.4 (3C), 16.2 (3C, $^{1}J_{Sn-C}$ = 362-346Hz), 19.3, 26.4, 26.9 (3C, $^{3}J_{Sn-C}$ = 34-32Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 20Hz), 43.8, 115.7, 125.2 , 135.1, 140.1, 176.7
MS (70 eV) : m/z = 373 (12), 329 (28), 217 (16), 177 (28), 135 (14), 121 (22), 57 (30), 55 (14), 53 (10), 41 (100),
39 (26)

5-Methyl-3-methylenehex-4-enoic acid 19b
IR: 3090, 2972, 2924, 2721, 2681, 1711, 1655, 1631, 1450, 1300, 1219, 1188
^{1}H NMR δ (ppm): 1.82 (6H, s), 3.16 (2H, s), 5.03 (1H, s), 5.18 (1H, s), 5.67 (1H, s), 11.20 (1H, bs)
^{13}C NMR δ (ppm): 19.4, 26.5, 42.8, 117.1, 124.3, 136.5, 138.1, 178.2
MS (70 eV) : m/z = 140 (M^{+}, 40), 125 (100), 97 (11), 95 (22), 83 (10), 81 (17), 80 (12), 79 (67), 77 (20), 72 (10), 67 (26), 55 (22), 53 (20), 51 (10), 45 (10), 41 (39), 39 (32), 27 (19)

(*E*)-Tributylstannyl-5-methyl-3-phenylhexa-2,4-dienoate 20a
only the *E* isomer of 1 is reactive under our experimental conditions
IR: 3063, 3028, 1630, 1602, 1580-1560, 1148
^{1}H NMR δ (ppm): 0.94 (9H, t, $^{3}J_{2H}$ = 7Hz), 1.27-1.65 (18H, m), 1.37 (3H, d, $^{4}J_{1H}$ = 1.4Hz), 1.36 (3H, d, $^{4}J_{1H}$ = 1Hz), 6.08 (1H, d, $^{4}J_{1H}$ = 1.4Hz), 6.66 (1H, m), 7.3-7.45 (5H, m)
^{13}C NMR δ (ppm): 13.4 (3C), 16.9 (3C, $^{1}J_{Sn-C}$ = 334-349Hz), 26.8 (3C, $^{3}J_{Sn-C}$ = 55Hz), 27.7 (3C, $^{2}J_{Sn-C}$ = 22Hz), 119, 123, 127.5 (2C), 128.2 (2C), 128.5, 140, 141.7, 155, 172

MS (70 eV) : m/z = 435 (12), 361 (52), 305 (17), 247 (25), 177 (24), 121 (27), 77 (32), 57 (43), 55 (13), 51 (11), 41 (100), 39 (24)

(*E*)-5-Methyl-3-Phenylhexa-2,4-dienoic acid 20b

IR: 3445, 2957, 2920, 2852, 1681, 1638, 1589, 1284, 1215

^{1}H NMR δ (ppm): 1.37 (3H, d, $^4J_{1H}$ = 1Hz), 1.98 (3H, d, $^4J_{1H}$ = 1.4Hz), 6.05 (1H, d, $^4J_{1H}$ = 1.2Hz), 6.7 (1H, m), 7.4-7.46 (5H, m), 11.5 (1H, bs)

^{13}C NMR δ (ppm): 20.8, 26.7, 116.1, 122.7, 127.7 (2C), 128.4 (2C), 129, 141.2, 142.9, 154.2, 168.7

MS (70 eV): m/z = 203 (M+1, 5), 202 (M^+, 26), 188 (12), 187 (100), 169 (12), 157 (20), 156 (41), 155 (16), 143 (24), 142 (34), 141 (75), 129 (28), 128 (44), 127 (14), 115 (50), 102 (14), 91 (30), 89 (10), 85 (11), 78 (15), 77 (36), 76 (11), 65 (16), 63 (25), 57 (19), 55 (20), 53 (22), 52 (19), 51 (59), 50 (31), 45 (55), 43 (78), 42 (11), 41 (47), 40 (13), 39 (98), 38 (12)

(*E*)-Hex-5-yn-3-enoic acid 21b

IR: 3303, 3043, 2673, 2106, 1712, 1649, 1419, 1293, 1229, 1073, 1020

^{1}H NMR δ (ppm): 2.93 (1H, s), 3.24 (2H, d, $^3J_{1H}$ = 7Hz), 5.64 (1H, d, $^3J_{1H}$ = 16Hz), 6.32 (1H, dt, $^3J_{1H}$ = 16Hz, $^3J_{2H}$ = 7Hz), 11.36 (1H, bs)

^{13}C NMR δ (ppm): 37.6, 77.7, 81.1, 112.9, 136, 177

MS (70 eV): m/z = 110 ($M^{\cdot+}$, 34), 71 (100), 68 (30), 66 (24), 65 (59), 63 (19), 62 (11), 60 (11), 57 (11), 45 (22), 44 (10),
43 (81), 42 (51), 41 (43), 40 (37), 39 (100), 38 (19), 37 (10)

(2*E*, 4*E*)-Oct-4-yn-2,6-diendioic acid 22b

IR (KBr): 3075, 2821, 2520, 2341, 2191 (w), 1683, 1622, 1301, 1274, 1211

RAMAN: 3039 (w), 2192 (strong), 1610

^{1}H NMR δ (ppm) (acetone d^6): 6.40 (1H, d, $^3J_{1H}$ = 15Hz), 6.95 (1H, dd, $^3J_{1H}$ = 15Hz, $^5J_{1H}$ = 2.2Hz), 10.05 (1H, bs)

^{13}C NMR δ (ppm) (acetone d^6): 74 (2C), 123.4 (2C), 132.4 (2C), 166 (2C)

MS (70 eV) : m/z = 166 ($M^{\cdot+}$, 40), 121 (52), 120 (87), 103 (15), 93 (10), 92 (25), 84 (13), 82 (28),76 (14), 75 (43),
74 (56), 73 (16), 72 (13), 71 (54), 69 (16), 67 (13), 66 (21), 65 (67), 64 (29), 63 (20), 62 (10), 60 (11), 55 (27), 54 (17), 53 (20), 51 (60), 50 (73), 45 (49), 44 (21), 43 (35), 42 (61),41 (42), 40 (14), 39 (100), 38 (40), 37 (21)

(4*E*)-5-Tributylstannyl-3-methylenepent-4-enoic acid 23b

IR: 3095, 2973, 2922, 2682, 1713, 1640, 1628, 1180

^{1}H NMR δ (ppm): 0.96 (9H, t, $^3J_{2H}$ = 7Hz), 1.25-1.65 (18H, m), 3.28 (2H, bs), 6.27 (1H, d, $^3J_{1H}$ = 19.4Hz), 6.63 (1H, d, $^3J_{1H}$ = 19Hz, $^1J_{Sn\text{-}C}$ = 68Hz)

^{13}C NMR δ (ppm): 9.4 (3C, $^1J_{Sn\text{-}C}$ = 328-343Hz), 13.5 (3C), 27.1 (3C, $^3J_{Sn\text{-}C}$ = 50Hz), 29 (3C, $^2J_{Sn\text{-}C}$ = 20Hz), 38.2, 117.6, 129.2 (1C, $^1J_{Sn\text{-}C}$ = 360-377Hz), 141.8, 147, 176.7

MS (70 eV) : m/z = 345 (87), 301 (86), 300 (26), 291 (74), 269 (100), 253 (32), 235 (58), 213 (23), 177 (72), 57 (51), 42 (16), 41 (40)

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