Tetrahedron Vol. 45, No. 4, pp. 1145 to 1154, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

[4+2] CYCLOADDITIONS OF ACETYLENIC ORGANOTINS : SYNTHETIC APPLICATIONS OF POLYFUNCTIONAL CYCLIC VINYLTINS

Bernard JOUSSEAUME * and Patrice VILLENEUVE

Laboratoire de Chimie Organique et Organométallique, UA 35, Université de Bordeaux I, 351, cours de la Libération, F-33405 - TALENCE CEDEX

(*Received in Japan* 19 *September* 1988)

ABSTRACT

A novel preparation of functional vinyltins is described. It involves the regiospecific [4+2] cycloaddition of functional alkynyltins with dienes such as 1,3-butadiene, 2,3-dimethyl-1,3-butadiene or 1-substituted 1,3-butadienes.

These cyclic vinyltins, bearing an ester, ketone, amide or nitrile group are converted into carbonylated, halogenated or sulfurized compounds. After reduction of the ester or ketone group, transmetallation leads to functional 1,4-cyclohexadienyllithiums which react easily with carbon dioxide, aldehydes or ketones to give substituted 1(3H)-4,7-dihydro-isobenzofuranones or 1,4-diols.

INTRODUCTION

Vinylic tin reagents are valuable intermediates in organic synthesis. One of the first examples, giving the most important and useful application, was the discovery by SEYFERTH of the transmetallation between vinyltins and lithium reagents allowing an easy preparation of vinylic lithium reagents (1). Since then, many other examples of synthetic utility have been found and applied to the synthesis of chemicals such as prostaglandins, antibiotics or vitamins (2). Vinyltins are obtained by many ways (3) but the most popular is the hydrostannation of acetylenic derivatives which is often very regio and stereoselective. Recently other routes have been developed involving the addition of tin-metal derivatives to acetylenic compounds (4) or the coupling of tin-metal reagents with heteroelement substituted vinylic derivatives (5). Only very few examples of cyclic vinyltins have been reported. They have been obtained either by the condensation of tributyltinlithium and a triflate (6) or by coupling a dilithium reagent derived from six-membered ring tosylhydrazone and tributyltin chloride (7). The first method has been applied to the synthesis of five, six or seven-membered ring bicyclic derivatives.

The Diels-Alder reaction provides powerful synthetic intermediates for constructing cyclic molecules. So far, only a limited number of studies have been made on the preparation of organotins in this way. The strong deactivating effect of the tin atom (8) explains why only few examples of these reactions are known. This unfavorable influence limited us to using hexachlorocyclopentadiene or coumarin as enophile with bis(trimethyltin)acetylene or phenyltrimethylstannylacetylene (9). Vinyltins have been shown to react with 2,3-dimethyl-1,3-butadiene or hexachlorocyclopentadiene under thermal or high pressure conditions : the use of high pressure prevents the isomerisation of the starting materials which occurs when the mixture is heated at the required temperature (10). We also reported the successful cycloaddition of p-

toluenesulfonyltrialkylstannylacetylene to various dienes. Unfortunately this reaction was not regiospecific with substituted dienes (11). We expected that Diels-Alder reactions with other alkynyltins could be achieved if a strongly activating group such as an ester, ketone, aldehyde, amide or nitrile was incorporated in the starting material.

In this paper, we describe a synthetic method for functional six-membered ring vinyltins and show that this reaction is regioselective with 1-alkyl-1,3-butadienes. Adducts can be reacted to give carbonylated, halogenated or sulfurized compounds. Their transmetallation and further reaction with carbonylated derivatives lead to 1(3H)-4,7-dihydroisobenzofuranones or 1,4-diols. All these compounds are shown to possess a 1,2,3-substituted-1-cyclohexene or 1,4-cyclohexadiene ring.

PREPARATION OF ALKYNYLTINS STARTING MATERIALS

Alkynyltins are usually prepared either by reaction of an acetylenic organometal or by condensation of a reactive organotin oxide, alkoxide or amine , with an alkyne (3). Among these methods, we prefered to use cheap bis(tributyltin)oxide (12) instead of an alkoxide or an amine for which an extra step is necessary. The reaction was conducted in warm cyclohexane with activated molecular sieves :

$$Bu_6Sn_2O + 2\ HC{\equiv}CR^1 \longrightarrow 2\ Bu_3SnC{\equiv}CR^1 + H_2O$$

R^1, yield (%) : COMe, 76*; COPh, 81*; $CONMe_2$, 96*; CN, 83.

*estimated by ^1H NMR

Heating was stopped when the signal of the acetylenic hydrogen disappeared in the ^1H NMR spectrum of the mixture. This procedure was not suitable to prepare tributylstannylpropynal due to intensive polymerisation of propynal when it was mixed with an oxygenated triorganotin. This method gave methyl tributyltinpropiolate with a yield not exceeding 50% . It was prepared with a higher yield from methoxytributyltin (13). The stannylated alkynyl nitrile and ester were purified by distillation. The stannylated alkynyl ketones and amides were used without further purification because intensive polymerisation which occured during distillation lowered the yields.

REACTIONS WITH SYMMETRICAL DIENES

We used 1,3-butadiene, 2,3-dimethyl-1,3-butadiene, cyclopentadiene and 1,3-cyclohexadiene as enophiles. As expected the activating effect of the ketone, ester, amide or nitrile groups was strong enough to expand the scope of the [4+2] cycloaddition of alkynyltriorganotins (14).

The reaction occured smoothly at moderate temperature usually within 48 hours, without solvent, with a twofold excess of the diene. The products were purified either by distillation (for the esters) or by column chromatography on silica gel. Reaction conditions were not very different from those required for the cycloadditions of the corresponding esters or alkynyl

ketones and yields were similar (15). An intensive polymerisation of the diene was encountered with cyclopentadiene under our standard conditions : a lower temperature and a shorter reaction time had to be used to obtain a good yield. With 1,3-cyclohexadiene, the substituted benzene resulting from the loss of an ethylene molecule was isolated.

TABLE I : Cycloadditions with symmetrical dienes.

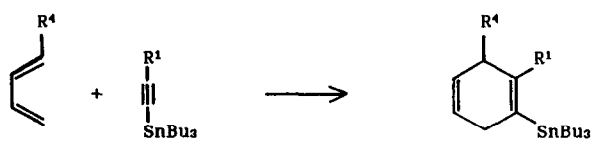
Diene			Experimental conditions		Yield* (%)
R^1	R^2	R^3			
COMe	H	H	110°C	48h	72
COMe	Me	Me	110°C	48h	54
COMe	cyclopentadiene		90°C	16h	60
CO_2Me	H	H	110°C	48h	71
CO_2Me	Me	Me	110°C	48h	56
CO_2Me	cyclopentadiene		90°C	16h	55
CN	H	H	110°C	48h	74
CN	Me	Me	110°C	48h	69
CN	cyclopentadiene		96°C	16h	34
$CONMe_2$	H	H	130°C	60h	36

*Isolated, pure products.

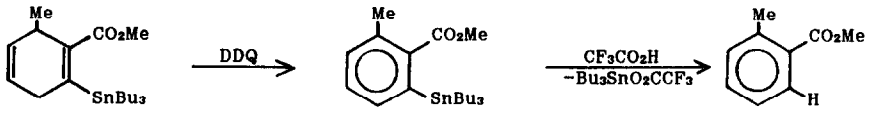
The stannylated dienes had to be kept at -20°C in the dark : after few weeks of storage at room temperature a small amount of aromatization could be detected by ^1H NMR.

REACTION WITH UNSYMMETRICAL DIENES

As it has been mentioned earlier, the [4+2] cycloaddition of isoprene with stannylated acetylenic compounds, like with many other derivatives (16), was not regiospecific. In our case, if the 1,3-butadiene unit was substituted at one end, the reaction gave only one regio-isomer. With methyl tributylstannylpropiolate and 1,3-pentadiene, we isolated, after the usual work-up, a compound of which ^{119}Sn NMR spectrum showed only one resonance at -56,7 ppm. As ^{119}Sn NMR shifts are extremely sensitive to their environment (17), that was a good indication of the selectivity of the reaction.



We elucidated the stereochemistry of the adduct by a chemical correlation. Methyl 2-tributylstannyl-6-methyl-1,4-cyclohexadiene-1-carboxylate was aromatized (vide infra) with DDQ (18) and the tin-ring bond of this new derivative cleaved by trifluoroacetic acid. The product was then compared with authentic samples of methyl 2- and 3-methylbenzoate and found to be identical to methyl 2-methylbenzoate. The regiospecificity of the [4+2] cycloaddition was then established.



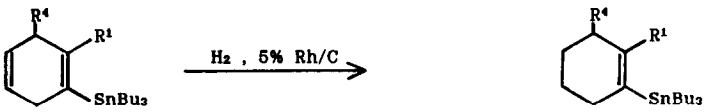
We also used successfully 1,3-decadiene and 5-ethyl-1,3-nonadiene. They required higher reaction temperature and gave slightly lower yields. 1-Phenyl-1,3-butadiene, 2,4-dimethyl-1,3-butadiene and 2,4-hexadiene were found to be unreactive with our dienophiles even at higher temperatures.

TABLE II : Cycloadditions with unsymmetrical dienes.

R^1	R^4	Experimental conditions		Yield (%)
COMe	Me	125°C	50	71
COMe	Et	125°C	48	72
COPh	Me	125°C	48	81
CO_2Me	Me	120°C	50	75
CO_2Me	CH(nBu)Et	150°C	24	40
CO_2Me	nHex	135°C	60	44
CN	Me	125°C	50	76

AROMATIZATION AND HYDROGENATION OF SUBSTITUTED-1,4-CYCLOHEXADIENES

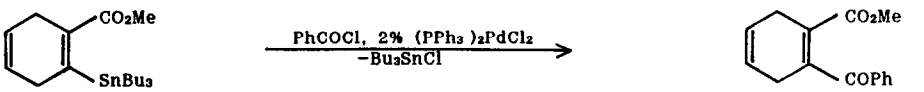
Adducts have been easily aromatized by treatment with DDQ (18). From this step substituted stannylated benzenes can be obtained in good yield. Adducts have been selectively hydrogenated to give functional stannylated cyclohexenes in the presence of 5% rhodium on carbon at atmospheric pressure. As it could be expected (19) the tetrasubstituted bond was unreactive and only the disubstituted bond was reduced.



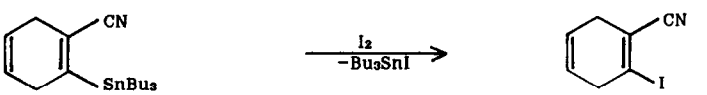
R^1, R^4, yield (%) : COMe, H, 94; COMe, Me, 92; CO_2Me, H, 90; CO_2Me, Me, 95.

PREPARATION OF FUNCTIONAL 1,4-CYCLOHEXADIENYL KETONES, HALIDES, SULFIDES AND SULFONES

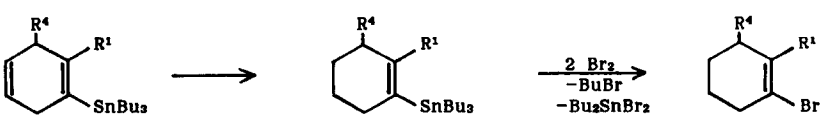
Cross-coupling of organotin reagents with a variety of organic electrophiles, catalyzed by palladium, provides a versatile and very usefull method for generating a carbon-carbon bond (20). We applied this novel method to the coupling of methyl 1-tributylstannyl-1,4-cyclohexadiene-1-carboxylate with acid chlorides. Indeed the reaction took place easily and allowed us to isolate the keto-ester in good yield. The cross coupling reaction with allyl bromides (21) was unsuccessful , giving a low yield of partially isomerized compound.



Halodemetallation of unsymetrical tetraorganotins has been developed because the very high selectivity of electrophilic demetallation provides useful synthetic applications for the preparation of organic halides (2). In our case, the preferential cleavage of the tin-vinyl bond might provide an easy route to halocyclohexadienes. These compounds could not be obtained by Diels-Alder reaction from halogenated alkynyl derivatives because of the very poor thermal stability of these derivatives (22). With 2-tributylstannyl-1,4-cyclohexadiene-1-carbonitrile the reaction with iodine gave the desired product.

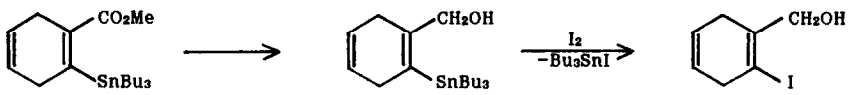


With our ketones and esters the carbonyl induced a reversal of selectivity by intramolecular nucleophilic assistance : a butyl bond was cleaved instead of a vinyl bond (23). This drawback could be overcome by the use of the hydrogenated substrates for which the reaction with a first equivalent of bromine was the cleavage of a butyl-tin bond and with a second equivalent resulted in the cleavage of the vinyl-tin bond.

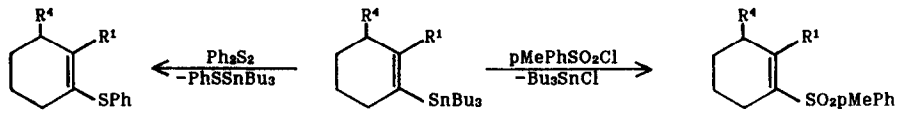


R^1, R^4, yield (%) : COMe, H, 70; COMe, Me, 69; CO_2Me, H, 83.

The reversal of selectivity also disappeared if the carbonyl was reduced by diisobutylaluminium hydride : assistance was too weak to change the normal course of the reaction. The 1-(2-iodo-1,4-cyclohexadienyl)methanol was then produced (yield : 78 %).



A radical substitution of the tributyltin group was successfully performed with diphenyldisulfide or p-toluenesulfonylchloride to get functional vinyl sulfide or sulfone (24). The addition-elimination reaction occured under UV irradiation in toluene as solvent.



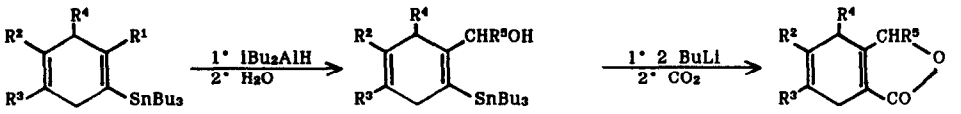
R^1, R^4, yield (%) : CO_2Me, H, 67; COMe, Me, 72; CO_2Me, H, 58;

PREPARATION OF SUBSTITUTED 1(3H)-4,7-DIHYDROISOBENZOFURANONES AND SUBSTITUTED 1,2-BIS(HYDROXYMETHYL)-1,4-CYCLOHEXADIENES

Transmetallation of vinylorganotins with lithium reagents is one of their most important applications in organic synthesis and is the only practical access to vinyllithiums. It had been shown that monotransmetallation of methyl 2,3-bis(trimethylstannyl)-2-butenoate was easy, leaving the carbonyl unchanged and involving only the tin nearest to the carbonyl (25), not the other one. We treated methyl 2-tributylstannyl-1,4-cyclohexadiene-1-carboxylate with butyllithium but at low temperatures no transmetallation occured. When the mixture was warmed, addition on the oxygenated function took place. Changes of solvent from THF to DME or HMPA did not improve the reaction selectivity. Steric effects are probably involved in this lack of selectivity : (E) vinyltins are always transmetallated more rapidly than (Z) ones (26) (27). Our attempts to protect the carbonyl by formation of 1,3-dioxolane or cyclic or not dithioacetals were unsuccessful: coordination of the tin by the carbonyl lowered its reactivity (28). Although WITTIG reaction on (E) and (Z)-3-trimethylstannyl-2-butenal (29) has been realized, we were unable to transform 1-acetyl-2-tributylstannyl-1,4-cyclohexadiene into the corresponding triene by the same reaction, which seemed to be inhibited.

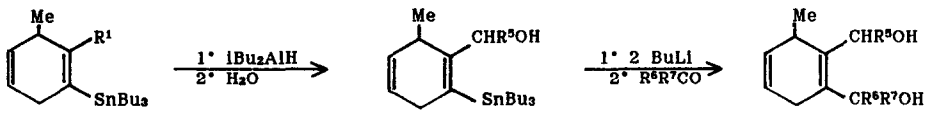
Transformation of the oxygenated function into alcohol allowed the wanted transmetallation. With lithium aluminium hydride variable amounts of demetallated cyclohexadienes were recovered. Diisobutylaluminium hydride at low temperature was of better use. Attempted distillation or column chromatography on silica gel or deactivated alumina led to decomposition products. Crude alcohols have then been used for the next step. They reacted smoothly at -50°C in THF with 2.2 equivalents of n-butyllithium to give a reddish solution of vinyllithium. Internal coordination by oxygen lowered the reactivity of these species. They did not couple at low temperature with reactive halides. When the temperature of the solution was raised to 20°C or when the reaction time was lengthed, partial decomposition occured. With carbonyls, normal addition took place. Reaction with carbon dioxide gave, after acidic hydrolysis, bicyclic lactones [1(3H)-4,7-dihydroisobenzofuranones] apparently unreported up to now. 1(3H)-5,6-dimethyl-4,7-dihydroisobenzofuranone was described but obtained as a mixture with 1(3H)-5,6-dimethyl-7,7a-

dihydroisobenzofuranone (30). Yields involve three steps : reduction, transmetallation and addition to carbon dioxide.



R^2, R^3, R^4, R^5, yield (%) : Me, Me, H, Me, 41; H, H, Me, Me, 38; H, H, Me, Ph, 37; H, H, Me, H, 39

Aldehydes and ketones reacted with our vinylic lithium reagents giving diols, useful for furan (31) or furanones (32) synthesis, with a 1,2,3-substituted-1,4-cyclohexadiene backbone. Yields involve three steps : reduction, transmetallation and addition to the carbonylated compounds. These diols cannot be obtained by a [4+2] cycloaddition of acetylenic diols which are too unreactive. Furthermore a lack of selectivity would be expected for products of this disymetry (33).



One of the advantages of this method of diol synthesis is the possibility of producing regioisomers by a convenient choice of starting materials as it can be seen below.

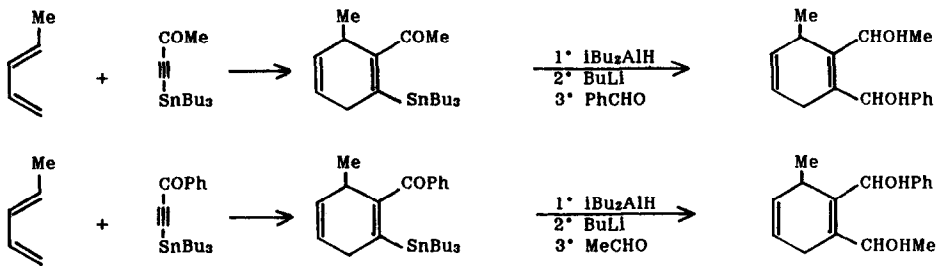


TABLE III : Preparation of diols.

R^5	R^6	R^7	yield (%)	R^5	R^6	R^7	yield (%)
Me	Me	Me	31	Me	Me	Ph	19
Me	H	nPr	26	Me	H	Ph	40
Ph	Me	Me	26	Ph	Ph	Me	17
Ph	H	nPr	24	Ph	H	Ph	41
H	Me	Me	34	H	Me	Ph	23
H	H	nPr	39	H	H	Ph	45

EXPERIMENTAL

Infrared spectra were recorded on a Perkin Elmer 683 spectrophotometer. Nuclear magnetic resonance spectra were obtained on either a Perkin-Elmer R 12 (^{1}H, 60 MHz) or a AC 200 spectrometer (^{1}H, 200 MHz ; ^{119}Sn, 93.98 MHz). Solutions in carbon tetrachloride with tetramethylsilane as internal standard were used for ^{1}H NMR unless otherwise stated. Solutions in benzene-d_6 with tetramethylstannane as internal standard were used for ^{119}Sn NMR unless otherwise stated. Chemical shifts are quoted in ppm downfield from TMS. Mass spectra were recorded on a VG Micromass 16 F apparatus. Column chromatography was performed on Merck silica gel or deactivated (6% H_2O) neutral alumina. Mass spectra and microanalysis data were consistent with the proposed structures. Dienes were prepared by the method of YAMAMOTO (34).

Alkynyltins. Methyl tributylstannylpropiolate. A solution of methylpropiolate (Aldrich) (4.2g, 50 mmol) and methoxytributyltin (15g, 50 mmol) in dry cyclohexane (150 ml) was heated for 15h at 50°C. After evaporation of the solvent and distillation, pure methyl tributylstannylpropiolate was obtained (12.4g, 70%). 1-tributylstannyl-1-butyne-3-one , 1-tributylstannyl-1-phenyl-1-propyne-3 one, 1-tributylstannyl-N,N-dimethylpropiolamide and 1-tributylstannylpropiolonitrile. A solution of acetylenic compound (50 mmol) and bis(tributyltin)oxide (23 mmol) in dry cyclohexane (100 ml) was heated at 50°C for 2h in the presence of activated molecular sieves (3 Å). After filtration and evaporation of the solvent the stannylated derivatives were used without further purification.

[4+2] cycloaddition of alkynyltributyltins. The stannylated dienophile (10g) and the wanted diene (100% excess) were mixed in a glass ampoule (wall thickness 2 mm), frozen at -180°C. The ampoule was then sealed (external neck diameter 6 mm) under vacuum and placed in an autoclave, together with 100 ml of pentane. Once closed it was placed into an oven at the desired temperature. After complexion of the reaction, the cooled autoclave was cautionously opened, the ampoule frozen in liquid nitrogen and then its neck was brocken. In the case of butadiene, this enophile was condensed in the frozen ampoule. Methyl 2-tributylstannyl-1,4 cyclohexadienylcarboxylate was distilled under vacuum : $Eb_{0.03}$=135-40°C. Other cyclohexadienes were purified by column chromatography on silica gel (eluent pentane/Et_2O : 90/10). Mass spectra of these stannylated cyclohexadienes are characterized by a strong base peak at M-C_4H_9. 1-acetyl-2-tributylstannyl-1,4-cyclohexadiene. ^{1}H NMR δ : 0.7-1.9 (m,27H), 2.20 (s,3H), 2.9-3.3 (m, 4H), 5.5-5.8 (m,2H). ^{119}Sn NMR δ : -57.7. 1-acetyl-2-tributylstannyl-4,5-dimethyl-1,4-cyclohexadiene. ^{1}H NMR δ : 0.7-1.9 (m,33H), 2.21 (s,3H), 2.9-3.3 (m,4H). ^{119}Sn NMR δ : -59.8. 1-acetyl-2-tributylstannyl-1,4-norbornadiene. ^{1}H NMR δ : 0.7-1.9 (m,27H), 2.05 (m,2H), 2.20 (s,3H), 3.9-4.1 (m,2H), 6.5-6.9 (m,2H). RMN ^{119}Sn δ : -61.5. 1-acetyl-2-tributylstannyl-6-methyl-1,4-cyclohexadiene. ^{1}H NMR δ : 0.7-1.9 (m, 30H), 2.21 (s,3H), 2.8-3.5 (m,3H), 5.80 (m,2H). ^{119}Sn NMR δ : -56.7. 1-acetyl-2-tributylstannyl-6-ethyl-1,4-cyclohexadiene. ^{1}H NMR δ : 0.7-1.9 (m,32H), 2.34 (s,3H), 2.8-3.5 (m,3H), 5.82 (m,2H). ^{119}Sn NMR δ : -56.1. 1-benzoyl-2-tributylstannyl-6-methyl-1,4-cyclohexadiene. ^{1}H NMR δ : 0.7-1.9 (m,30H), 2.7-3.4 (m,3H), 5.81 (m,2H), 7.2-7.6 (m,5H), ^{119}Sn NMR δ : -46.9. Methyl 2-tributylstannyl-1,4-cyclohexadiene-1-carboxylate : ^{1}H NMR δ : 0.7-1.9 (m,27H), 2.97 (m,4H), 3.82 (s,3H), 5.5-5.8 (m,2H). ^{119}Sn NMR δ : -55.6. Methyl 2-tributylstannyl-4,5-dimethyl-1,4-cyclohexadiene-1-carboxylate. ^{1}H NMR δ : 0.7-1.90 (m,33H), 3.0 (m,4H), 3.82 (s,3H), ^{119}Sn NMR δ : -57.3. Methyl 2-tributylstannyl-1,4-norbornadiene-1-carboxylate. ^{1}H NMR : δ : 0.7-1.9 (m,27H), 2-2.1 (m,2H), 3.83 (s,3H), 3.97 (m,2H), 6.5-7.0 (m,2H). ^{119}Sn NMR δ : -50.7. Methyl 2-tributylstannyl-6-methyl-1,4-cyclohexadiene-1-carboxylate. ^{1}H NMR δ : 0.7-1.9 (m,30H), 2.7-3.4 (m,3H), 5.80 (m,2H), 7.2-7.6 (m,5H). ^{119}Sn NMR : -54.8. Methyl-2-tributylstannyl-6-(1-ethylpentyl)-1,4-cyclohexadiene-1-carboxylate. ^{1}H NMR δ : 0.7-1.9 (m,40H), 2.7-3.4 (m,3H), 3.81 (s,3H), 5.71 (m,2H). Methyl 2-tributylstannyl-6-hexyl-1,4-cyclohexadiene-1-carboxylate. ^{1}H NMR δ : 0.7-2 (m,40H), 2.8-3 (m,2H), 3.31 (m,1H), 3.83 (s,3H), 5.72 (m,2H). 2-tributylstannyl-1,4-cyclohexadiene-1-carbonitrile. ^{1}H NMR δ : 0.7-1.9 (m,27H), 3.05 (m,4H), 5.67 (m,2H). ^{119}Sn NMR δ : -42.6. 2-tributylstannyl-4,5-dimethyl-1,4-cyclohexadiene-1-carbonitrile. ^{1}H NMR δ : 0.7-1.9 (m,3H), 2.6-3.2 (m,4H), 5.66 (m,2H). ^{119}Sn NMR δ : -56.3. 2-tributylstannyl-1,4-norbornadiene-1-carbonitrile. ^{1}H NMR : δ : 0.7-1.9 (m,27H), 2-2.1 (m,2H), 3.7-4.1 (m,2H), 6.5-7 (m,2H), ^{119}Sn NMR δ : -38.1. 2-tributylstannyl-6-methyl-1,4-cyclohexadiene-1-carbonitrile. ^{1}H NMR δ : 0.7-1.9 (m,30H), 2.7-3.4 (m,3H), 5.67 (m,2H). ^{119}Sn NMR δ : -41.2. N,N-dimethyl-2-tributylstannyl-1,4-cyclohexadiene-1-carboxamide. ^{1}H NMR δ : 0.7-1.9 (m,27H), 2.1-3.1 (m,10H), 5.86 (m,2H).

Catalytic hydrogenation. A flask containing a mixture of organotin diene (20 mmol) , 5% rhodium on carbon (0.3g) , 75ml of methanol and 25ml of ether was degazed, filled with hydrogen at atmospheric pressure and vigorously stirred. After 6h the mixture was filtered and the solvents evaporated. The product was chromatographied on a short column of silica gel with a mixture of pentane and diethylether (90/10). 1-acetyl-2-tributylstannyl-1-cyclohexene. ^{1}H NMR δ : 0.7-1.9 (m,31H), 2.23 (s,3H), 2.3-2.6(m,4H). 1-acetyl-2-tributylstannyl-6-methyl-1-cyclohexene. ^{1}H NMR δ : 0.7-1.9 (m,34H), 2.25 (s,3H), 2.35-2.7 (m,3H). Methyl 2-tributylstannyl-1-cyclohexene-1-carbonylate. ^{1}H NMR δ : 0.7-1.9 (m,31H), 2.3-2.6 (m,4H), 3.77 (m,3H), ^{119}Sn NMR δ : -58.3. Methyl 2-tributylstannyl-6-methyl-1-cyclohexene-1-carboxylate. ^{1}H NMR δ : 0.7-1.8 (m,34H), 2.3-2.7 (m,3H), 3.75 (m,3H).

Preparation of 2-iodo-1,4-cyclohexadiene-1-carbonitrile. To a solution of 2-tributylstannyl-1,4-cyclohexadiene-1-carbonitrile (3g, 8 mmol) were added crystals of iodine until persistance of a pink coloration. The solution was washed with a solution of sodium thiosulfate

until discoloration, dried on magnesium sulfate and evaporated. The residu was chromatographied on silica gel with a mixture of pentane and ether (80/20) as eluent. Yield : 1.61g, 70%.

Preparation of 1-(2-iodo-1,4-cyclohexadienyl)methanol. To a solution of stannylated ester (3g, 7 mmol) in diethylether (50 ml) at -50°C was added a solution (10 ml) of diisobutylaluminium (1.0 M, 10 mmol) in hexanes. Temperature was raisen to -20°C, the mixture hydrolyzed with a saturated solution of ammonium chloride, dried with magnesium sulfate, and the solvents evaporated. The crude alcohol was then diluted in CCl_4 (20 ml) and iodine slowly added until persistance of a pink coloration. The solution was washed with a solution of sodium thiosulfate until discoloration and dried on magnesium sulfate. The solvent was then evaporated and the residue taken up in diethylether for a treatment with KF. After filtration the product was flash chromatographied (deactivated alumina). Yield :1.3g, 78 % . ^{1}H NMR (acetone-d_6) δ : 3.05 (m,4H), 4.10 (s,2H), 5.25 (m,1H) 5.75 (m,1H) .

Preparation of functional cyclohexenyl bromides. To a solution of the functional tributylstannyl-1-cyclohexene (10 mmol) in 30 ml of CH_2Cl_2 at -20°C was slowly added bromine (3.2g, 20 mmol) in 20 ml of the same solvent. Temperature was allowed to reach 20°C. After thiosulfate treatment, drying on magnesium sulfate and evaporation of the solvent the product was bulb to bulb distilled under vacuum (10 mmHg) (oven temperature 130°C). 1-acetyl-2-bromo-1-cyclohexene. ^{1}H NMR : 1.2-2 (m,4H), 2.31 (s,3H), 2.1-2.9 (m,4H). 1-acetyl-2-bromo-6-methyl-1-cyclohexene. ^{1}H NMR : 1.05 (d,3H), 1.5-2.0 (m,4H), 2.35 (s,3H), 2.5-2.8 (m,4H). Methyl 2-bromo-1-cyclohexene-1-carboxylate. ^{1}H NMR : 1.5-1.9 (m,4H), 2.2-2.6 (m,4H), 3.7 (s,3H)

Coupling with acid chlorides (35). A solution of methyl 2-tributylstannyl-6-methyl-1,4-cyclohexadiene-1-carboxylate (2 g, 4.7 mmol) bis(triphenylphosphine)dichloropalladium (70 mg, 0.1 mmol)and benzoyl chloride (1 g, 7 mmol) in chloroform (15 ml) in a sealed tube was heated at 100°C for 40h. After KF treatment (36), drying on magnesium sulfate and column chromatography on silica gel (eluent pentane/diethylether 50/50) 0.85g (70%) of keto-ester was isolated. ^{1}H NMR δ : 1.22 (d,3H), 2.8-3.1 (m,3H), 3.88 (s,3H), 5.6-5.8 (m,2H), 7.3-7.9 (m,5H).

Preparation of sulfides and sulfones(24). A solution of stannylated cyclohexene (10 mmol) and sulfur-containing compound (12 mmol) in toluene (40 ml) was irradiated at 360 nm during 24 hours. The solvent was then evaporated, the residue taken up in ether for a treatment with KF. After filtration the product was flash chromatographied on deactivated alumina. Methyl 2-phenylthio-6-cyclohexene-1-carboxylate. ^{1}H NMR δ : 1.52 (m,4H), 1.95 (m,2H), 2.33 (m,2H), 3.56 (s,3H), 7.25 (m,5H). 1-p-toluenesulfonyl-2-acetyl-3-methyl-1-cyclohexene. ^{1}H NMR δ :1.03 (d,3H), 1.3-2.3 (m,7H), 2.40 (s,3H), 2.49 (s,3H), 7.35 (d,2H), 7.75 (d,2H). Methyl 2-p-toluenesulfonyl-1-cyclohexene-1-carboxylate. ^{1}H NMR δ :1.60 (m,4H), 2.10-2.50 (m,4H), 2.45 (s,3H), 3.78 (s,3H), 7.32 (d,2H).

Preparation of 1(3H)-dihydro-4,7-isobenzofuranones. To a solution of stannylated cyclohexadiene (7 mmol) in 50 ml of diethylether at -50°C was added 10 ml of a solution of diisobutylaluminium hydride (1.0 M, 10 mmol) in hexanes. Temperature was raisen to -20°C, the mixture hydrolyzed with a saturated solution of ammonium chloride, dried with magnesium sulfate, and the solvents evaporated. The crude alcohol was then diluted in 20 ml of THF at -90°C. Butyllithium (1.5 mmol, 9.5 ml of a 1,6 M solution in hexanes) was slowly added and the temperature raisen at -60°C for 30 mn. Dry ice (3g, 70 mmol) was added and the temperature allowed to reach -20°C. After hydrolysis, 1N NaOH was added until the pH be strongly basic. The organic phase was discarded and 1N HCl was added until the pH reached 3. Ether extraction, drying with magnesium sulfate, evaporation of the solvent gave the pure lactones as oils. 1(3H)-4,7-dihydro-3,5,6-trimethyl-isobenzofuranone, ^{1}H NMR (acetone-d_6) δ : 1.35 (d,3H), 1.71 (s,6H), 2.7-3.2, (m,4H), 4.8 (m,1H). 1(3H)-dihydro-3,4-dimethyl-isobenzofuranone, ^{1}H NMR (acetone-d_6) δ : 1.32 (d,3H), 1.53 (d,3H), 2.87 (m,2H), 3.34 (m,1H), 4.95 (m,1H), 5.75 (m,2H). 1(3H)-4,7-dihydro-3-phenyl-4-methyl-isobenzofuranone, ^{1}H NMR (acetone-d_6) δ : 0.55 (d,3H), 2.7-3.5 (m,3H), 5.7 (m,2H), 6.12 (m,1H), 7.58 (s,5H). 1(3H)-4,7-dihydro-4-methyl-isobenzofuranone, ^{1}H NMR (acetone-d_6) δ : 1.22 (d,2H), 2.75 (m,3H), 3.25 (m,1H), 4.80 (m, $^2J_{3-3'}$=17.2 Hz, $^4J_{3-4}$=0.5 Hz, $^5J_{3-7}$ = $^5J_{3-7'}$=2.1 Hz,1H), 4.95 (m,1H), 5.78 (m,2H).

Preparation of 1,4-cyclohexadienediols. The procedure was the same as for the preparation of isobenzofuranone except that a solution of aldehyde or ketone (10 mmol) in 10 ml of THF was added instead of dry ice. After hydrolysis and partition (37) in pentane/acetonitrile, pure diols were obtained by column chromatography on deactivated (6%) alumina. Eluent : pentane/diethylether (50/50). 2-(2-ethanol-3-methyl-1,4-cyclohexadienyl)-2-propanol, ^{1}H NMR (acetone-d_6) δ : 1.1-1.4 (m,12H), 2.4-3.0 (m,3H), 4.1-4.6 (m,2H), 5.02 (m,1H) 5.75 (m,2H). 1-(2-ethanol-3-methyl-1,4-cyclohexadienyl)-1-phenylethanol, ^{1}H NMR (acetone-d_6) δ : 1.0-1.3 (m,6H), 1.65 (m,3H), 2.4-3.0 (m,3H), 3.72 (m,2H), 4.87 (m,1H), 5.74 (m,2H), 7.2-7.5 (m,5H). 1-(2-ethanol-3-methyl-1,4-cyclohexadienyl)-1-butanol, ^{1}H NMR (acetone-d_6) δ : 0.9-1.8 (m,11H), 2.6-3.0 (m,3H), 4.88 (m,1H), 5.75 (m,2H). (2-ethanol-3-methyl-1,4-cyclohexadienyl)phenylmethanol, ^{1}H NMR (acetone-d_6) δ : 1.1-1.6 (m,6H), 2.5-3.3 (m,3H), 3.9-4.5 (m,2H), 5.02 (m,1H), 5.57 (m,2H), 6.08 (m,1H), 7.1-7.5 (m,5H). 2-(2-phenylmethanol-3-methyl-1,4-cyclohexadienyl)-2-propanol, ^{1}H NMR (acetone-d_6) δ : 0.72 (m,3H), 1.53 (m,6H), 2.3-3.1 (m,3H), 4.12 (m,2H), 5.67 (m,2H), 6.48 (m,1H), 7.1-7.7 (m,5H). 1-(2-phenylmethanol-3-methyl-1,4-cyclohexadienyl)-1-phenyl-1-ethanol, ^{1}H NMR (acetone-d_6) δ : 0.67 (m,3H), 1.36 (m,3H), 2.6-3.2 (m,3H), 4.88 (m,2H), 5.71 (m,2H), 6.08 (m,1H), 6.39 (m,1H), 7-7.5 (m,10H). 1-(2-phenylmethanol-3-methyl-1,4-cyclohexadienyl)-1-butanol, ^{1}H NMR (acetone-d_6) δ : 0.50-1.8 (m,8H), 2.70-3.30 (m,3H), 3.74 (m,2H), 4.77 (m,1H),

5.73 (m,2H), 6.01 (m,1H), 7-7.5 (m,5H). (2-phenylmethanol-2-methyl-1,4-cyclohexadienyl)phenylmethanol, ^{1}H NMR (acetone-d_6) δ : 0.97 (m,3H), 2.31-3.30 (m,3H), 4.67 (m,2H), 5.66 (m,2H), 6.10-6.38 (m,2H), 7.10-7.95 (m,10 H). 2-(2-methanol-3-methyl-1,4-cyclohexadienyl)-2-propanol, ^{1}H NMR (acetone-d_6) δ : 1.08 (d,3H), 1.35 (d,6H), 2.40-3.20 (m,3H), 4.10-4.50 (m,2H), 5.57 (m,2H). 1-(2-methanol-3-methyl-1,4-cyclohexadienyl)-1-phenyl-1-ethanol, ^{1}H NMR (acetone-d_6) δ : 0.97 (d,3H), 1.62 (s,3H), 2.51-3.05 (m,3H), 3.5-4.18 (m,2H), 5.27 (m,1H), 5.61 (m,2H), 7-7.65 (m,5H). 1-(2-methanol-3-methyl-1,4-cyclohexadienyl)-1-butanol, ^{1}H NMR (acetone-d_6) δ : 0.81-1.70 (m,8H), 2.55-2.95 (m,3H), 3.54-4.48 (m,6H), 5.64 (m,2H). (2-methanol-3-methyl-1,4-cyclohexadienyl)phenylmethanol, ^{1}H NMR (acetone-d_6) δ : 1.05 (d,3H), 2.21-3.15 (m,3H), 3.97 (t,1H), 4.32 (m,2H), 4.45 (d,1H), 5.57 (m,2H), 5.98 (d,1H), 7-7.60 (m,5H).

ACKNOWLEDGEMENT. We are indebted to M-C. Rascle for her skilled assistance and to Schering-France for a generous gift of chemicals.

REFERENCES

(1) D. Seyferth, M.A. Weiner, J.Am.Chem.Soc., 83, 3583, (1961).
(2) M. Pereyre, J.P. Quintard, A. Rahm, Tin in Organic Synthesis, Butterworths, London, (1987).
(3) A.G. Davies, P.J. Smith, Comprehensive Organometallic Chemistry, G. Wilkinson, F.G.A. Stone, E.W. Abel Eds., Pergamon Press, Oxford, 591, (1982). M. Gielen, J. Nasielski, Organotin Compounds, A.K. Sawyer Ed., M. Dekker Inc., New York, 625, (1972). W.P. Neumann, The Organic Chemistry of Tin, Wiley-Interscience, New York, (1970).
(4) E. Piers, J.M. Chong, J. Chem.Soc. Chem. Communs, 934, (1983), H. Westmijze, K. Ruitenberg, J. Meijer, P. Vermeer, Tetrahedron Lett., 23, 2793, (1982), T. Mitchell, A. Amamria, H. Killing, D. Rutschow, J. organometal.Chem., 241, C45, (1983), M. Ochiai, T. Ukita, E. Fujita, Tetrahedron Lett., 24, 4025, (1983).
(5) D.E. Seitz, S.H. Lee, Tetrahedron Lett., 22, 4909, (1981).
(6) E. Piers, H.L.A. Tse, Tetrahedron Lett., 26, 3155, (1984).
(7) M.P. Cooke, J. Org. Chem., 47, 4963, (1982).
(8) C. Minot, A. Laporterie, J. Dubac, Tetrahedron, 32, 1523, (1976).
(9) A.B. Evnin, D. Seyferth, J. Am. Chem. Soc., 89, 952 and 1468, (1967).
(10) A. Rahm, M. Degueil-Castaing, Synth. React. Inorg. Met. Org. Chem., 12, 243, (1982).
(11) Z. Djeghaba, B. Jousseaume, M. Ratier, J.G. Duboudin, J. Organometal. Chem., 304, 115, (1986).
(12) W.P. Neumann, F.G. Kleiner, Tetrahedron Lett., 5, 3779, (1964).
(13) M.W. Logue, K. Teng, J. Org. Chem., 47, 2549, (1982).
(14) B. Jousseaume, J. Chem. Soc. Chem. Commun., 1452, (1984).
(15) E. Kataev, M. Mat'kova, Uchenye Zapiski Kakan. Gosudarst. Univ. im. V. I. Ul'yanovalenina, Khim., 115, 21, (1955), Chem. Abst., 52, 1976b, (1958).
(16) J. Sauer, Angew. Chem., Internat, Edit. Eng., 5, 211, (1966). J. Sauer, R.Sustmann, Angew. Chem. Internat. Edit. Eng., 19, 779, (1979).
(17) P.J. Smith, A.P. Tupciauskas, Ann. Rep. N.M.R. Spectrosc., 8, 291, (1978). B. Wrackmeyer, Ann. Rep. N.M.R. Spectrosc., 14, 73, (1986).
(18) D. Walker and J.D. Hiebert, Chem. Rev., 67, 153, (1967).
(19) J. March, Advanced Organic Chemistry, 3rd ed., Wiley, New York, 692, (1985).
(20) J.K. Stille, Angew. Chem. Internat. Edit. Eng., 25, 508, (1986).
(21) F.K. Sheffy, J.K Stille, J. Am. Chem. Soc., 105, 7173, (1983).
(22) S.Y. Delavarenne, H.G. Viehe, Chemistry of Acetylenes, H.G. Viehe Ed., M. Dekker, New York, 651, (1969).
(23) B. Jousseaume, P. Villeneuve, J. Chem. Soc., Chem. Commun., 513, (1987).
(24) G.A. Russel, P. Ngoviwatchai, H. Tashtoush, J. Hershberger, Organometallics, 6, 1414, (1987).
(25) E. Piers, J.M. Chong, J. Org. Chem., 47, 1602, (1982).
(26) P. Collins, C.J. Jung, A. Graseski, R. Rappo, Tetrahedron Lett., 19, 3187, (1978).
(27) S.M.L. Chem, R.E. Schanis, C.V. Grundzinkas, J. Org. Chem., 43, 3460, (1978).
(28) B. Jousseaume, P. Villeneuve, M. Dräger, S. Roller, J.M. Chezeau, J. Organometal. Chem. 346, C1, (1988).
(29) E. Piers, H.E. Morton, J. Org. Chem., 45, 4263, (1980).
(30) E. Vedejs, D.A. Engler, Tetrahedron Lett., 17, 3487, 1976.
(31) H. Nishiyama, M. Sasaki, K. Itoh, Chem. Lett., 1363, (1981), L.P.J. Burton, J.D. White, J. Am. Chem. Soc., 103, 3226, (1981).
(32) Y.S. Rao, Chem. Rev., 76, 625, (1976), T.K. Chakraborty, S. Chandrasekaran, Tetrahedron Lett., 25, 2891, (1984).
(33) O. Eisenstein, J.M. Lefour, N.T. Anh, R.F. Hudson, Tetrahedron, 33, 523, (1977).
(34) Y. Ikeda, J. Ukai, N. Ikeda, H. Yamamoto, Tetrahedron, 43, 723, (1987).
(35) D. Milstein,J.K. Stille, J. Am. Chem. Soc., 100, 3636, (1978)
(36) J.E. Leibner, J. Jacobus, J. Org. Chem., 44, 449, (1979)
(37).J.M. Berge, S.M. Roberts, Synthesis, 471, (1979)