Tetrahedron Vol. 49, No. 21, pp. 4677-4698, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00
Pergamon Press Ltd

New Synthetic Applications of Organotin Compounds: Synthesis of Stereodefined 2-Iodo-2-Alkenones, 2-Substituted (E)-2-Alkenones and 2-Methyl-2-Cycloalkenones

Fabio Bellina, Adriano Carpita, Donatella Ciucci, Massimo De Santis[#] and Renzo Rossi[*]

Dipartimento di Chimica e Chimica Industriale – University of Pisa – Via Risorgimento 35, I-56126 Pisa, Italy

(*Received in UK* 16 *February* 1993)

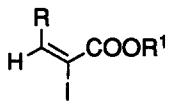
Abstract: Stereoisomeric mixtures of 3-iodo-3-nonen-2-one, **8a**, 2-iodo-1-phenyl-2-octen-1-one, **8b**, 2-iodo-1,3-diphenyl-2-propen-1-one, **8c**, as well as (*Z*)-3-iodo-4-phenyl-3-buten-2-one, **8d**, have been efficiently synthesized by a reaction sequence involving a Pd-catalyzed reaction between the corresponding 1-alkynyl ketones, **10**, and Bu_3SnH followed by iododestannylation. Stereomutation experiments carried out in the presence of daylight and using catalytic amounts of I_2 showed that the *Z* stereoisomers of **8a**, **8b** and **8c**, which could be separated by MPLC on silica gel from the corresponding *E* stereoisomers, as well as compound (*Z*)-**8d** were more stable than their *E* stereoisomers. Compounds **8a-d** underwent Pd-catalyzed cross-coupling reactions with $C_6H_5SnMe_3$, CH_2=CH-$SnBu_3$ and $SnMe_4$ providing an efficient route to the corresponding 2-substituted 2-alkenones, **13**. However, the Pd-catalyzed reaction between (*Z*)-**8c** and $PhSnMe_3$ afforded a mixture of the expected cross-coupled product, (*E*)-**13f** with the compound derived from methyl transfer, (*E*)-**13e**. The couplings involving (*Z*)-**8a**, (*Z*)-**8b**, (*Z*)-**8c** and (*Z*)-**8d** proceeded with clean retention of stereochemistry, but the Pd-catalyzed reaction between (*E*)-**8c** and $SnMe_4$ afforded a stereoisomeric mixture of **13e**. On the contrary, the coupling between (*E*)/(*Z*)-**8b** and $SnMe_4$ produced stereoisomerically pure (*E*)-**13c**. Two 2-iodo-2-cycloalkenones, *i.e.* compounds **18a** and **18b**, also reacted with $SnMe_4$, in the presence of a Pd catalyst, to give the corresponding 2-methyl-2-cycloalkenones, **19a** and **19b** , respectively, in satisfactory yields. Compound **19b** represents a very useful precursor to methylenomycin B, **9**.

Recently we reported that stereoisomerically pure alkyl (*E*)-2-iodo-2-alkenoates, (*E*)-**1**, which are easily prepared by palladium(0)-catalyzed reaction between tributylstannane and alkyl 2-alkynoates followed by treatment with iodine, are useful and direct precursors to stereodefined 2-(hetero)aryl substituted alkyl 2-alkenoates of general formula **2**[1], alkyl (*E*)-2-methyl-2-alkenoates, (*E*)-**3**, having very high stereoisomeric purity[1] as well as to (*Z*)/(*E*)-(1-carbalkoxy-1-alkenyl)zinc iodides, (*Z*)/(*E*)-**4**[2]. Moreover, we showed that reagents (*Z*)/(*E*)-**4**, which represent a new class of unmasked β-substituted acrylate α-anion equivalents, are able to react with functionalized alkenyl or aryl halides, in the presence of a palladium(0) catalyst, to give chemoselectively and in high yields the corresponding cross-coupled products quite rich in the stereoisomers having their trisubstituted double bonds of *E* configuration[2]. Interestingly, the synthetic utility of compounds (*E*)-**1** was also demonstrated by their use in the preparation of three chiral insect pheromone components

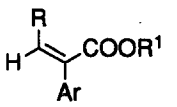
[#] In partial fulfilment of his PhD thesis

[*] To whom correspondence should be addressed

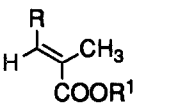
having very high optical purity, *i.e.* (*S*)(*E*)-2,4-dimethyl-2-hexenoic acid, (*S*)(*E*)-**5**[1], a caste-specific substance of male carpenter ants in the genus *Camponotus*, (*S*)(*E*)-4,6-dimethyl-4-octen-3-one, (*S*)(*E*)-**6**[1], an alarm pheromone component of ants in the genus *Manica*, and (*S*)-1-methylbutyl (*E*)-2-methyl-2-pentenoate, (*S*)(*E*)-**7**[3], an aggregation pheromone component of *Rhyzopertha dominica*.



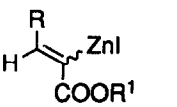
(*E*)-**1**



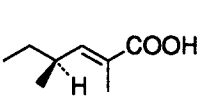
2



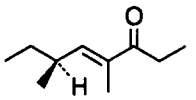
(*E*)-**3**



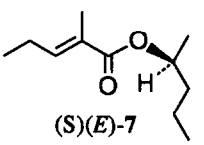
(*E*)/(*Z*)-**4**



(*S*)(*E*)-**5**

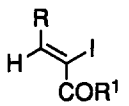


(*S*)(*E*)-**6**

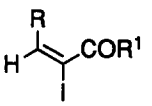


(S)(*E*)-**7**

More recently, in continuation of our studies on 1-alkenylstannanes bearing a functional substituent in the 1-position[4], we turned out our attention to the preparation and the synthetic applications of another class of α-halo-α,β-unsaturated compounds, *i.e.* stereodefined 2-iodo-2-alkenones of general formula (*Z*)- and (*E*)-**8**.



(*Z*)-**8**



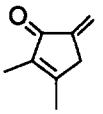
(*E*)-**8**

(R = alkyl, aryl; R^1 = alkyl, aryl)

Our interest was due to the fact that, despite the potential great usefulness of these compounds which, owing to their higher reactivity expecially in transition metal-catalyzed reactions, should be preferred over the corresponding bromo or chloro derivatives, no convenient general procedures for their preparation have been reported. In fact, a previous method, which was based on the reaction of acetylmethyltriphenylarsonium bromide with iodine and potassium carbonate in acetonitrile, followed by treatment with an aldehyde and another portion of potassium carbonate, has been only employed to prepare 3-iodo-4-aryl-3-buten-2-ones quite rich in the corresponding *Z* stereoisomers[5]. Moreover, the recently reported direct preparation of α-iodoenones by treatment of enones with iodine and pyridine in CCl_4 solution[6] turned out to be a practical route for synthesizing 2-iodo-2-cycloalkenones, but unsuitable in the case of acyclic α-iodo-α,β-unsaturated ketones. In fact, besides requiring large amounts of solvent for small scale preparations, the synthesis of these last compounds afforded low or negligible yields.

In this paper we will describe a quite simple new procedure developed to prepare compounds (*Z*)- and (*E*)-**8a** (R = *n*-C_5H_{11}; R^1 = CH_3), (*Z*)- and (*E*)-**8b** (R = *n*-C_5H_{11}; R^1 = C_6H_5), (*Z*)- and (*E*)-**8c** (R = R^1 = C_6H_5) and (*Z*)-**8d** (R = C_6H_5; R^1 = CH_3), as well as the results of an investigation on the

stereomutation of these alkenyl iodides in the presence of daylight and catalytic amounts of iodine. Furthermore, we will report the details of a study concerning the palladium-catalyzed cross-coupling reactions of these stereodefined 2-iodo-2-alkenones with phenyltrimethylstannane, vinyltributylstannane and tetramethylstannane, respectively. Finally, the last part of this paper will be devoted to an extension of these palladium-catalyzed reactions to the efficient synthesis of two 2-methyl-2-cycloalkenones, one of which represents a direct precursor to methylenomycin B, **9**, an antibiotic substance active against both gram-positive and gram-negative bacteria and cytotoxic *in vitro* in the KB assay[7].



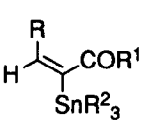
9

RESULTS AND DISCUSSION

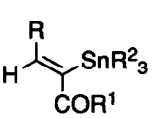
A) Synthesis of (Z)- and (E)-2-iodo-2-alkenones

On the basis of our previous experience on the synthesis of alkyl (*E*)-2-iodo-2-alkenoates, (*E*)-**1**[1], it occurred to us that access to stereodefined 2-iodo-2-alkenones of general formula **8** might be achieved by a regio- and stereoselective palladium-catalyzed reaction between 1-alkynyl ketones, **10**, and Bu_3SnH followed by treatment of the α–tributylstannyl-α,β–unsaturated ketones so obtained with iodine in CH_2Cl_2 solution. However, on examination of the literature we realized that conflicting results were reported as regards the stereochemistry of the palladium-catalyzed hydrostannylation of compounds **10**. In fact, Zhang *et al.* reported that, in the presence of catalytic amounts of $PdCl_2(PPh_3)_2$, the reaction between Bu_3SnH and 3-decyn-2-one, **10a** (R = *n*-C_6H_{13}; R^1 = CH_3) affords stereoisomerically pure (*E*)-3-tributylstannyl-3-decen-2-one, (*E*)-**11a** (R = *n*-C_6H_{13}; R^1 = CH_3; R^2 = *n*-C_4H_9), but the analogous reaction involving 1-phenyl-2-heptyn-1-one, **10b** (R = *n*-C_4H_9; R^1 = C_6H_5) produces a mixture of (*E*)- and (*Z*)-1-phenyl-2-tributystannyl-2-hepten-1-one, (Z)- and (*E*)-**11b** (R = R^2 = *n*-C_4H_9; R^1 = C_6H_5), in a 58:42 ratio, respectively[8]. On the contrary, Cochran *et al.* found that the reaction between 3-hexyn-2-one, **10c** (R = C_2H_5; R^1 = CH_3) and Me_3SnH, in the presence of a catalytic amount of $Pd(PPh_3)_4$, gives (Z)-3-trimethylstannyl-3-hexen-2-one, (*Z*)-**11c** (R = C_2H_5; $R^1 = R^2 = CH_3$)[9].

10



(*E*)-**11**



(*Z*)-**11**

These conflicting results prompted us to start our study by a re-examination of the stereochemistry of the palladium-catalyzed hydrostannylation of compounds **10**. For this purpose we prepared the following 1-alkynyl ketones: 3-nonyn-2-one, **10d**, 1-phenyl-2-octyn-1-one, **10e**, 1,4-diphenyl-2-propyn-1-one, **10f**, and

4-phenyl-3-butyn-2-one, **10g**. In particular, compound **10d** was prepared in 40% yield according to the procedure described by Brown *et al.*[10] which involved the conversion of 1-heptyne, **12a**, into the corresponding lithium (1-alkynyl)trifluoroborate followed by treatment with acetic anhydride [eq. (1)].

$$\underset{\textbf{12a}}{n\text{-}C_5H_{11}-\equiv-H} \xrightarrow[2)\ BF_3{\cdot}Et_2O \\ 3)\ (CH_3CO)_2O]{1)\ BuLi,\ hexane,\ THF,\ -78\ ^\circ C} \underset{\textbf{10d}}{n\text{-}C_5H_{11}-\equiv-COCH_3} \qquad (1)$$

Compounds **10e** and **10f** were prepared in 99 and 95% yields, respectively, according to a modification of the procedure decribed by Tohda *et al*[11] which involved the reaction of a mixture of benzoyl chloride and Et_3N with **12a** and phenylacetylene, **12b**, respectively, in the presence of catalytic amounts of $Pd(PPh_3)_4$ and CuI [eq. (2)].

$$\underset{\begin{array}{l}\textbf{12a}:\ R = n\text{-}C_5H_{11}\\ \textbf{12b}:\ R = C_6H_5\end{array}}{R-\equiv-H} \xrightarrow[Pd(PPh_3)_4,\ CuI]{C_6H_5COCl,\ Et_3N} \underset{\begin{array}{l}\textbf{10e}:\ R = n\text{-}C_5H_{11}\\ \textbf{10f}:\ R = C_6H_5\end{array}}{R-\equiv-COPh} \qquad (2)$$

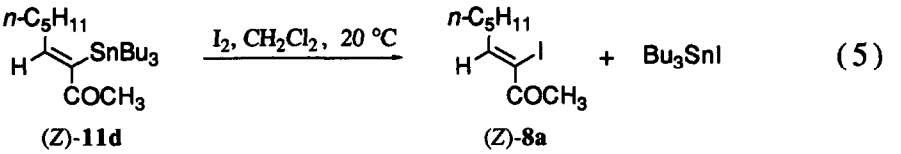
On the other hand, compound **10g** was synthesized in 50% yield according to a procedure[12] which involved treatment of the 1-alkynylzinc chloride derived from **12b** with acetyl chloride, in the presence of a catalytic amount of $Pd(PPh_3)_4$ [eq. (3)].

$$\underset{\textbf{12b}}{C_6H_5-\equiv-H} \xrightarrow[2)\ ZnCl_2,\ 0\ ^\circ C \\ 3)\ Pd(PPh_3)_4 \\ 4)\ CH_3COCl,\ -78\ \text{to}\ 20\ ^\circ C]{1)\ CH_3Li,\ Et_2O,\ THF,\ -78\ ^\circ C} \underset{\textbf{10g}}{C_6H_5-\equiv-COCH_3} \qquad (3)$$

Compound **10d** was then reacted at room temperature with a THF solution of 0.97 equiv of Bu_3SnH, in the presence of *ca.* 2 mol % of $Pd(PPh_3)_4$. The crude reaction product was purified by MPLC on silica gel to give stereoisomerically pure (*Z*)-3-tributylstannyl-3-nonen-2-one, (*Z*)-**11d**, in 38% isolated yield [eq. (4)].

$$\underset{\textbf{10d}}{n\text{-}C_5H_{11}-\equiv-COCH_3} \xrightarrow[2)\ S\ G\ MPLC]{1)\ Bu_3SnH,\ Pd(PPh_3)_4,} \underset{(Z)\textbf{-11d}}{\begin{array}{l}n\text{-}C_5H_{11}\\ H\diagdown\ \diagup SnBu_3\\ \quad\ \ COCH_3\end{array}} \qquad (4)$$

The *Z*-configuration of this compound, which was established by ^1H NMR analysis, was confirmed by its conversion into the corresponding iododestannylation product, (*Z*)-**8a**. In fact, the reaction between **11d** and a CH_2Cl_2 solution of 1.08 equiv of iodine, which was periodically monitored by GLC, produced Bu_3SnI and a stereoisomerically pure compound subsequently identified as (*Z*)-3-iodo-3-nonen-2-one, (*Z*)-**8a** [eq. (5)].



(Z)-**11d** (Z)-**8a** (5)

The reaction mixture was concentrated *in vacuo*, diluted with Et_2O and, in order to eliminate Bu_3SnI, treated with a large excess of a semisaturated aqueous KF solution. The resulting mixture was filtered, extracted with Et_2O and the organic extract was purified by MPLC on silica gel to give stereoisomerically pure (*Z*)-**8a** in 88% yield.

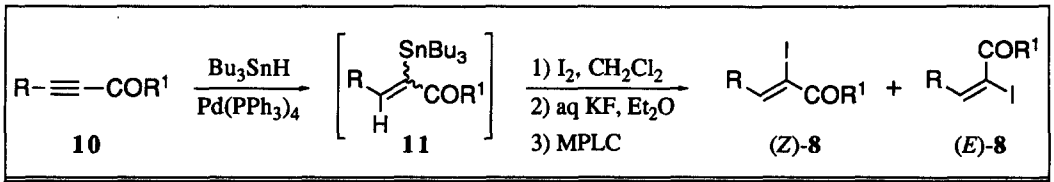
Thus, the result of the palladium-catalyzed hydrostannylation was in agreement with that reported by Cochran *et al.*[9], but the stereochemistry of this reaction resulted to be opposite to that of the palladium-catalyzed hydrostannylation of alkyl 2-alkynoates[9,11]. On the other hand, the low yield of (*Z*)-**11d** could be explained taking into account that a partial protodestannylation occurred during the purification by MPLC on silica gel of the crude reaction product. Therefore, since compound **11d** was very sensitive to acidic conditions and it was probably configurationally unstable, we thought it right to give up our direct investigations on the stereochemistry of the hydrostannylation reaction of compounds **10** and to attempt the preparation in high yields of the desired 2-iodo-2-alkenones, **8**, using without delay the crude hydrostannylation products. Thus, in a model experiment the crude reaction mixture, which was obtained by treatment of **10d** with a THF solution of 0.94 equiv of Bu_3SnH, in the presence of a catalytic quantity of $Pd(PPh_3)_4$, was concentrated *in vacuo* and the residue was diluted with hexane in order to precipitate PPh_3 and part of the catalyst. The mixture was filtered, the filtrate was concentrated *in vacuo* and the residue, which was dissolved in CH_2Cl_2, was treated with a CH_2Cl_2 solution of 0.96 equiv of iodine. After elimination of most of Bu_3SnI formed in this last reaction by treatment with an aqueous KF solution, the crude reaction product was analyzed by GLC/MS and resulted to be constituted of two compounds, subsequently identified as (*E*)- and (*Z*)-**8a** in a 75 : 25 molar ratio, respectively. Purification by MPLC on silica gel allowed to separate these stereoisomerically pure compounds, but during isolation from the chromatographic fractions iodide (*E*)-**8a** underwent stereomutation to give a mixture of (*E*)- and (*Z*)-**8a** in a 59 : 41 ratio, respectively. The overall yield of this reaction sequence was 82% based on Bu_3SnH (entry 1, Table 1).

It is worth mentioning that the result of this reaction sequence gave new informations on the stereochemistry of the palladium-catalyzed hydrostannylation of **10d**. In fact, supposing that the molar ratio between (*E*)- and (*Z*)-**8a** could reflect reasonably that between the corresponding organostannanes, (*E*)- and (*Z*)-**11d**, respectively, this result indicated that *i)* the stereochemistry of the hydrostannylation of **10d** was *cis* leading to (*E*)-**11d** and that *ii)* this last compound underwent easily stereomutation. Moreover, on this basis, the fact that in our attempt to prepare (*E*)-**11d** from **10d** we had obtained (*Z*)-**11d** in a low yield could be explained taking into account the configurational lability of (*E*)-**11d**, which was probably accompanied with its higher chemical fragility to acidic conditions.

The fact that the palladium-catalyzed hydrostannylation of compounds **10** could give rise to stereoisomeric mixtures of compounds **11** was confirmed by ^1H NMR analysis of the crude hydrostannylation product obtained from **10e** after its partial purification from PPh_3 and the catalyst. In fact, this crude reaction

mixture was found to be constituted of (*Z*)- and (*E*)-1-phenyl-2-tributylstannyl-2-octen-1-one, (*Z*)- and (*E*)-**11e**, in a 54 : 46 molar ratio, respectively. Iododestannylation of these crude products gave in 88% yield a mixture of the corresponding iodides, (*Z*)- and (*E*)-**8b** (*Z*/*E* = 69 : 31), which could be separated by MPLC on silica gel (entry 2, Table 1).

Table 1. Synthesis of (*E*)- and (*Z*)-2-Iodoenones of General Formula **8** Starting from 1-Alkynyl Ketones, **10**



10 **11** (*Z*)-**8** (*E*)-**8**

Entry	1-Alkynyl ketone, **10**			Organotin derivative, **11**	2-Iodoenones, **8**		
	Compd.	R	R^1	*Z*/*E* ratio	Compd.	*Z*/*E* ratio[a]	Overall yield (%)[b,c]
1	**10d**	*n*-C_5H_{11}	CH_3	n.d.	(*Z*)/(*E*)-**8a**[d]	25:75	82[d]
2	**10e**	*n*-C_5H_{11}	C_6H_5	54:46	(*Z*)/(*E*)-**8b**[d]	69:31	88[d]
3	**10f**	C_6H_5	C_6H_5	n.d.	(*Z*)/(*E*)-**8c**[d]	27:73	37[d]
4	**10f**	C_6H_5	C_6H_5	n.d.	(*Z*)/(*E*)-**8c**[e]	76:24	95[e]
5	**10g**	C_6H_5	CH_3	n.d.	(*Z*)-**8d**[e]	99: 1	69[e]

a) Referred to crude reaction mixtures. *b)* Referred to compounds (*Z*)- and (*E*)-**8** isolated by MPLC from the crude reaction mixtures. *c)* Based on Bu_3SnH. *d)* Prepared according to Method A. This method involved a partial purification of the crude hydrostannylation products from PPh_3 and the catalyst before iododestannylation. *e)* Prepared according to Method B. This method involved the direct iododestannylation of the crude reaction mixture obtained from the Pd-catalyzed hydrostannylation.

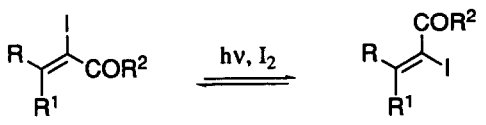
At first, the preparation of (*Z*)- and (*E*)-2-iodo-1,4-diphenyl-2-propen-1-one, (*Z*)- and (*E*)-**8c**, was carried out according to the same procedure employed to prepare compounds **8b** (Method A)(entry 3, Table 1). However, the overall yield (37%) resulted to be lower than that obtained in entries 1 and 2 because of a partial protodestannylation of the crude hydrostannylation product during its partial purification from PPh_3 and the catalyst. Thus, in order to minimize this undesired reaction, the crude reaction mixture obtained from the palladium-catalyzed reaction between a THF solution of Bu_3SnH and **10f** was concentrated *in vacuo*, diluted with CH_2Cl_2 and submitted to iododestannylation. This procedure (Method B) allowed to obtain in 95% yield (based on Bu_3SnH) compounds (*Z*)- and (*E*)-**8c** (*Z*/*E* = 76 : 24), which could be separated by MPLC on silica gel (entry 4, Table 1). Finally, it is interesting to note that, when this same procedure was employed for compound **10g**, only one stereoisomer of 3-iodo-4-phenyl-3-buten-2-one, **8d**, was obtained in a satisfactory yield (69%) (entry 5, Table 1). This compound had spectral properties in good agreement with those previously reported for 95% stereoisomerically pure (*Z*)-**8d**[5,13].

Having established conditions for the preparation of stereodefined 2-iodo 2-alkenones, **8**, attention was

subsequently directed either to evaluate their configurational stability or to check the possibility to convert their stereoisomeric mixtures to one of their possible stereoisomers. Thus, compounds (*E*)/(*Z*)-**8a**, (*E*)/(*Z*)-**8b**, (*Z*)- and (*E*)-**8c** and (*Z*)-**8d** were treated at room temperature with a catalytic amount of iodine, in the presence of daylight, and the corresponding reaction mixtures were periodically monitored by GLC (Table 2).

Some aspects of the results summarized in this table merit comments. Firstly, the *Z* stereoisomers of compounds **8a-d** were found to be more stable, under the conditions employed, than the corresponding *E* stereoisomers. However, whereas for compounds **8a**, **8b** and **8d** the predominance of the *Z* configuration over that *E* was considerable, in the case of compound **8c** the *Z*/*E* ratios of the products obtained by treatment of stereoisomerically pure (*E*)- and (*Z*)-**8c** with a catalytic amount of iodine, in the presence of daylight, for very long reaction times were 74 : 26 and 70 : 30, respectively (entries 6 and 9, Table 2). Secondly, the stereomutation rate of compounds **8a** and **8b** was higher than that of (*Z*)- or (*E*)-**8c**.

Table 2. Stereomutation of (*E*)/(*Z*)-, (*E*)- or (*Z*)-2-Iodo-2-alkenones of General Formula **8**, in the Presence of Daylight and a Catalityc Amount of Iodine.



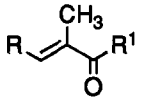
(*Z*)-**8** (*E*)-**8**

Entry	Reagent					Reaction time (h)	Product	
	Compd.	R	R^1	R^2	*E*/*Z* ratio		Compd.	*E*/*Z* ratio
1	(*E*)/(*Z*)-**8a**	*n*-C_5H_{11}	H	CH_3	59 : 41	56 [a]	(*E*)/(*Z*)-**8a**	38 : 62
2	(*E*)/(*Z*)-**8a**	*n*-C_5H_{11}	H	CH_3	38 : 62	24	(*Z*)-**8a**	>1 : 99
3	(*E*)/(*Z*)-**8b**	H	*n*-C_5H_{11}	C_6H_5	26 : 74	20	(*Z*)-**8b**	3 : 97
4	(*E*)-**8c**	H	C_6H_5	C_6H_5	> 99 : 1	8 [b]	(*E*)/(*Z*)-**8c**	91 : 9
5	(*E*)-**8c**	H	C_6H_5	C_6H_5	> 99 : 1	102 [b]	(*E*)/(*Z*)-**8c**	68 : 32
6	(*E*)-**8c**	H	C_6H_5	C_6H_5	> 99 : 1	279 [b]	(*E*)/(*Z*)-**8c**	26 : 74
7	(*Z*)-**8c**	C_6H_5	H	C_6H_5	< 1 : 99	8 [b]	(*E*)/(*Z*)-**8c**	23 : 77
8	(*Z*)-**8c**	C_6H_5	H	C_6H_5	< 1 : 99	102 [b]	(*E*)/(*Z*)-**8c**	30 : 70
9	(*Z*)-**8c**	C_6H_5	H	C_6H_5	< 1 : 99	279 [b]	(*E*)/(*Z*)-**8c**	30 : 70
10	(*Z*)-**8d**	C_6H_5	H	CH_3	< 1 : 99	6	(*E*)/(*Z*)-**8d**	1 : 99
11	(*Z*)-**8d**	C_6H_5	H	CH_3	< 1 : 99	30	(*E*)/(*Z*)-**8d**	1 : 99
12	(*Z*)-**8d**	C_6H_5	H	CH_3	< 1 : 99	170	(*E*)/(*Z*)-**8d**	2 : 98

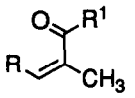
a) This reaction was carried out in the absence of a catalytic amount of iodine. *b)* This reaction was carried out using a 3 M CH_2Cl_2 solution of the solid 2-iodo-2-alkenone.

B) Palladium-catalyzed cross-coupling reactions between 2-iodo-2-alkenones, 8, and organostannanes

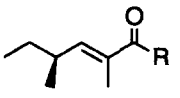
In order to explore the synthetic utility of compounds **8** as equivalents of unsaturated a[2] synthons, we next examined their palladium-catalyzed cross-coupling reactions with organostannanes such as phenyltrimethylstannane, vinyltributylstannane and allyltributylstannane. Nevertheless, our attention was mainly addressed to the preparation of compounds of general formula (*E*)- and/or (*Z*)-**13** by palladium-catalyzed reaction between compounds (*Z*)- and (*E*)-**8** and tetramethylstannane. In fact, compounds **13** include some naturally-occurring substances such as manicone, **14a**, and normanicone, **14b**, which are alarm pheromone components of *Manica* ants[14], as well as lignarenone A, **15**, lignarenone B, **16**, and 3-methyl navenone, **17**, which are alarm pheromone components of the opisthobranch *Navanax inermis*[15,16].



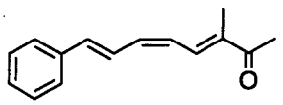
(*E*)-**13**



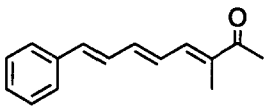
(*Z*)-**13**



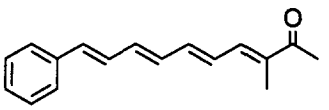
14a : R = C_2H_5
14b : R = CH_3



15



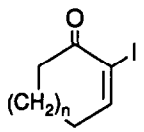
16



17

Moreover, the study of these methylation reactions appeared interesting since in the past years papers dealing specifically with palladium-catalyzed cross-coupling reactions between tetramethylstannane and functionalized alkenyl iodides have not been published[17].

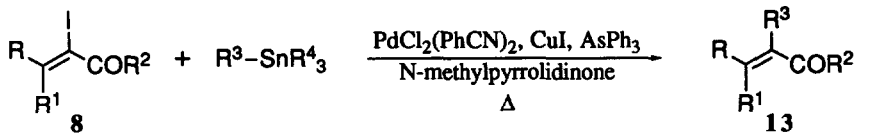
Preliminary experiments showed that the reaction conditions recently employed for alkenylation and arylation of 2-iodo-2-cycloalkenones, **18**[18], were suitable for our substrates.



18

In particular, we used N-methylpyrrolidinone as solvent and a catalyst system which was constituted of bis(benzonitrile)palladium(II) chloride (5 mol %), copper(I) iodide (10 mol %) and triphenylarsine (10 mol %). Moreover, the reactions involving tetramethylstannane were carried out using a large molar excess of this reagent (3 equiv), whereas those involving other organostannanes were performed using a slight excess (1.2 equiv) of these organometallics. The results of the experiments subsequently carried out using these conditions are listed in Table 3.

Table 3. Palladium-Catalyzed Cross-Coupling Reactions between 2-Iodo-2-alkenones, **8**, and Organostannanes.[a]



Entry	2-Iodo-2-alkenone				Organostannane		Reaction time (h/°C)	Product	Isolated yield (%)
	Compd.	R	R^1	R^2	R^3	R^4			
1	(*Z*)-**8a**	*n*-C_5H_{11}	H	CH_3	C_6H_5	CH_3	4.5/55	(*E*)-**13a**	84
2	(*Z*)-**8a**	*n*-C_5H_{11}	H	CH_3	CH_2=CH	C_4H_9	19/45	(*E*)-**13b**	57
3	(*Z*)-**8a**	*n*-C_5H_{11}	H	CH_3	CH_2=CH-CH_2	C_4H_9	[b]	—	–
4	(*Z*)-**8b**	*n*-C_5H_{11}	H	C_6H_5	CH_3	CH_3	19/80	(*E*)-**13c**	70
5	(*Z*)-**8b**	*n*-C_5H_{11}	H	C_6H_5	CH_2=CH	C_4H_9	20/45	(*E*)-**13d**	79
6	(*E*)/(*Z*)-**8b**[c]	H	*n*-C_5H_{11}	C_6H_5	CH_3	CH_3	68/80	(*E*)-**13c**	63[d]
7	(*E*)-**8c**	H	C_6H_5	C_6H_5	CH_3	CH_3	21/80	(*E*)/(*Z*)-**13e**[e]	97
8	(*Z*)-**8c**	C_6H_5	H	C_6H_5	CH_3	CH_3	2.5/80	(*E*)-**13e**	94
9	(*Z*)-**8c**	C_6H_5	H	C_6H_5	C_6H_5	CH_3	22/55	(*E*)-**13f**[f]	50
10	(*Z*)-**8d**	C_6H_5	H	CH_3	CH_3	CH_3	4/80	(*E*)-**13g**	94
11	(*Z*)-**8d**	C_6H_5	H	CH_3	CH_2=CH	C_4H_9	49/45	(*E*)-**13h**[g]	47

a) These reactions were performed in the presence of 5 mol % of $PdCl_2(PhCN)_2$, 10 mol % of CuI and 10 mol % of $AsPh_3$. The reactions involving Me_4Sn were carried out using out using a 3 : 1 molar ratio between this reagent and compounds **8**, but those involving other organostannanes were performed using a 1.2 : 1 molar ratio between these organometallics and compounds **8**. *b)* 1.5/20, 15/55 then 23/80. *c)* *E*/*Z* = 61 : 39. *d)* GLC yield. *e)* *E*/*Z* = 45 : 55. *f)* The crude reaction mixture was constituted of a mixture of (*E*)-**13e** and (*E*)-**13f** in a *ca.* 31 : 69 molar ratio, respectively. *g)* This compound had been previously prepared in 65% yield using this same procedure (see: Ref. *18*).

The following observations on these results are worth noting. Firstly, all reactions involving vinyltributylstannane and tetramethylstannane as well as that involving phenyltrimethylstannane and (*Z*)-**8a** (entry 1, Table 3) were quite efficient, but the palladium-catalyzed reaction between compound (*Z*)-**8c** and phenyltrimethylstannane (entry 9, Table 3), which was quite slower than that between (*Z*)-**8a** and this same organometallic reagent (entry 1, Table 3), gave rise to a compound derived from methyl transfer, *i.e.* (*E*)-**13e**, in addition to the expected cross-coupled product, (*E*)-**13f**. On the contrary, the palladium-catalyzed reaction between (*Z*)-**8a** and allyltributylstannane (entry 3, Table 3) did not afford the desired cross-coupled product. Secondly, the couplings involving compounds (*Z*)-**8a-d** proceeded with clean retention of stereochemistry, but a stereoisomeric mixture of 2-methyl-1,4-diphenyl-2-propen-1-one, **13e** (*E*/*Z* = 45 : 55)

was obtained in the palladium-catalyzed reaction between (*E*)-**8c** and tetramethylstannane (entry 7, Table 3). Interestingly, the stereochemistry of this last reaction seemed to be independent of the reaction time, although several hours were necessary to obtain a satisfactory yield of the desired cross-coupled product. On the contrary, the palladium-catalyzed reaction between a stereoisomeric mixture of **8c** (*E*/*Z* = 61:39) with tetramethylstannane afforded stereoisomerically pure (*E*)-**13c** (entry 6, Table 3). Thirdly, a comparison between the coupling experiment involving (*Z*)-**8c** and that in which (*E*)-**8c** was used (entries 7 and 8, Table 3) showed that the *Z*-stereoisomer of this compound coupled more rapidly than the corresponding *E*-isomer.

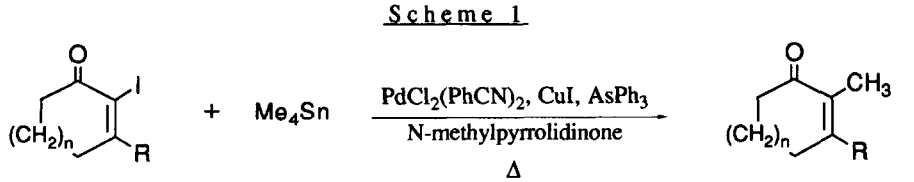
Finally, it must be noted that no attempt was made to optimise the yields of any of the reactions listed in Table 3.

C) Synthesis of 2-methyl-2-cycloalkenones

On the basis of the successful results obtained in the palladium-catalyzed couplings between 2-iodo-2-alkenones, **8**, and tetramethylstannane, we set out to examine whether the procedure employed for these reactions could be used to prepare 2-methyl-2-cycloalkenones, **19**, starting from the corresponding easily available 2-iodo-2-cycloalkenones, **18**[18]. In fact, if successful this methylation reaction might have allowed to obtain in a very simple way compounds **19** which have been so far prepared by methods which in general are not simple nor versatile[19]. Moreover, an easy and efficient access to these substances could allow their use as intermediates for the production of α–methyl-β-(mono- or di-)substituted cycloalkanones through conjugate addition procedures.

Thus, a N-methylpyrrolidinone solution of 2-iodo-2-cyclohexenone, **18a**[18], was treated with 3 equiv of tetramethylstannane at 80-85 °C for 40 h, in the presence of 5 mol % of $PdCl_2(C_6H_5CN)_2$, 10 mol % of CuI and 10 mol % of triphenylarsine, to give the expected cross-coupled product, **19a**[19a,b], in 46% yield (Scheme 1).

Scheme 1



18a : R = H; n = 1
18b : R = CH_3; n = 0

19a : R = H; n = 1
19b : R = CH_3; n = 0

Moreover, 2-iodo-3-methyl-2-cyclopentenone, **18b**[18], was converted to 2,3-dimethyl-2-cyclopentenone[19c-h], **19b**, in 84% yield. This substance represents a direct precursor to methylenomycin B, **9**[20].

However, it must be mentioned that when it was attempted to extend this procedure to the synthesis of other 2-alkyl-2-cycloalkenones, in a model experiment it was found that the palladium catalyzed reaction between **18a** and tetrabutylstannane gave exclusively 2-cyclohexenone, **20**, instead of the desired cross-coupled product.

D) Conclusions

In conclusion, we have shown that stereodefined 2-iodo-2-alkenones, **8**, can be easily and efficiently prepared starting from the corresponding α,β–acetylenic ketones, **10**, and that compounds (*Z*)-**8** are more stable of the corresponding *E*-stereoisomers, in the presence of daylight and catalytic amounts of iodine. Furthermore, we have demonstrated that compounds **8** partecipate in palladium-catalyzed cross-coupling (a^2 reactivity) with phenyltrimethylstannane, vinyltributylstannane and tetramethylstannane providing an efficient route to the corresponding 2-substituted 2-alkenones. The cross-coupling reactions involving compounds (*Z*)-**8a-d** proceed stereospecifically and the reaction involving (*E*)/(*Z*)-**8b** and tetramethylstannane occurs stereoselectively. On the other hand, the coupling between (*E*)-**8c** and tetramethylstannane affords a stereoisomeric mixture of 2-methyl-1,3-diphenyl-2-propen-1-one, **13e**. Finally, the reaction conditions which allow the cross-coupling between compounds **8** and tetramethylstannane have proven to be suitable for the preparation of 2-methyl-2-cycloalkenones, **19**, starting from the corresponding easily available 2-iodo-2-cycloalkenones, **18**. Work is now in hand to demonstrate the synthetic utility of the palladium-catalyzed reaction between stereodefined 2-iodo-2-alkenones and tetramethylstannane in the preparation of some naturally-occurring substances.

EXPERIMENTAL

Precoated silica gel plates Merck F-254 were used for TLC analyses. GLC analyses were performed on a Dani 6500 gas-chromatograph with a PTV injector and equipped with a Perkin-Elmer LCI-100 integrator. Two types of capillary columns were used: a SE-30 bonded FSOT column (30 m x 0.25 mm i.d.) and a AT-35 bonded FSOT column (30 m x 0.25 mm i.d.). Purifications by MPLC were performed on a Büchi instrument, using a Bischoff 8100 differential refractometer as detector. GLC/MS analyses were performed using a Q-mass 910 spectrometer interfaced with a Perkin-Elmer 8500 gas-chromatograph. ^1H NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer using TMS as an internal standard.

All reactions of air and water sensitive materials were performed in flame dried glassware under an atmosphere of argon or nitrogen. Air and water sensitive solutions were transferred with hypodermic syringes or double ended needles.

The following compounds were prepared according to the literature: $Pd(PPh_3)_4$[21], $PdCl_2(C_6H_5CN)_2$[22], 2-iodo-2-cyclohexenone, **18a**[6], 2-iodo-3-methyl-2-cyclopentenone, **18b**[6], phenyltrimethylstannane[23], vinyltributylstannane[24]. Tetramethylstannane, tetrabutylstannane and allyltributylstannane (Aldrich) were used as received.

3-Nonyn-2-one, ***10d***

According to the the general procedure reported in the literature for the synthesis of α,β-acetylenic ketones[10], a 1.74 M hexane solution of *n*-butyllithium (172.4 ml, 300 mmol) was added during 1 h to a cold (-78 °C) solution of 1-heptyne, **12a** (39.3 ml, 300 mmol) in THF (300 ml) which was stirred under argon. Boron trifluoride etherate (36.9 ml, 300 mmol) was then added dropwise and to the resulting mixture, which was stirred for 0.5 h., was added a solution of acetic anhydride (42.5 ml, 450 mmol) in THF (100 ml)

precooled at -78 °C. The reaction was continued for 15 min at -78 °C and the resulting mixture was treated with aqueous 2 N NaOH (500 ml). The reaction mixture was allowed to reach 20 °C and poured into a large excess of Et_2O. The ethereal extract was washed with 4 N NaOH and brine until neutrality, dried and filtered. The filtrate was concentrated under reduced pressure and the residue was fractionally distilled to give compound **10d** (16.7 g, 40% yield): b.p. 85.5-86 °C/5 Torr. ^1H NMR ($CDCl_3$), δ: 2.44-2.35 (2 H, m, H-5), 2.32 (3 H, s , H-1), 1.64-1.30 (6 H, m, H-6, H-7 and H-8), 0.90 ppm (3 H, t, J = 7.1 Hz, H-9). Lit[25] b.p. 65 °C/1.3 Torr.

1-Phenyl-2-octyn-1-one, 10e

To a deareated mixture of Et_3N (160 ml), 1-heptyne, **12a**, (10.5 ml, 80 mmol) and benzoyl chloride (9.3 ml, 80 mmol), cooled at 0 °C, were added $Pd(PPh_3)_4$ (2.0 g, 1.7 mmol) and CuI (1.2 g, 6.3 mmol). The reaction mixture was stirred at room temperature for 15 h under argon. Then, methanol (50 ml) was added, the solvent was removed *in vacuo* and the solid residue was treated with water and extracted with benzene. The organic extract was washed repeatedly with a saturated aqueous NH_4Cl solution and water, dried and concentrated *in vacuo*. The residue was diluted with a mixture of hexane and benzene (7:3 *v/v*) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by MPLC on silica gel, using a mixture of hexane and benzene (7:3 *v/v*) as eluant, to give 99% chemically pure **10e** (14.7 g, 99% yield): ^1H NMR ($CDCl_3$), δ: 8.16-8.12 (2 H, m, H_{arom}), 7.59-7.44 (3 H, m, H_{arom}), 2.49 (2 H, t, J = 7.0 Hz, H-4), 1.69 (2 H, hept, H-5), 1.49-1.38 (4 H, m, H-6 and H-7), 0.93 ppm (3 H, t, J = 6.3 Hz, H-8). MS, *m/z* (%): 200 (M^+, 21), 199 (31), 185 (20), 171 (14), 158 (16), 157 (41), 144 (46), 115 (31), 105 (100), 77 (56), 66 (21), 55 (21), 52 (21), 41 (21). Anal. Calcd. for $C_{14}H_{16}O$: C, 83.91; H, 8.03. Found: C, 83.96; H, 8.05.

1,4-Diphenyl-2-propyn-1-one, 10f

This compound was prepared starting from phenylacetylene, **12b** (8.2 g, 80 mmol) and benzoyl chloride (11.3 g, 80 mmol) according to the same procedure followed for the synthesis of compound **10e**. The crude reaction mixture was concentrated *in vacuo* and the residue was diluted with water and extracted with benzene. The organic extract was washed repeatedly with a saturated aqueous NH_4Cl solution and water, dried, filtered and concentrated *in vacuo*. The residue was diluted with a mixture of benzene and hexane (4:6 *v/v*) and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by MPLC on silica gel, using a mixture of benzene and hexane (4:6 *v/v*) as eluant, to give compound **10f** (15.7 g, 95% yield): m.p. 48 °C. The spectral properties of this compound were in agreement with those previously reported[27].

4-Phenyl-3-butyn-2-one, 10g

According to a procedure reported in the literature[12], a 1.67 M Et_2O solution of methyllithium (76.4 ml, 127.5 mmol) was dropwise added to a cold (-23 °C) solution of freshly distilled phenylacetylene, **12b** (13.0 g, 127.5 mmol) in THF (150 ml) and the reaction mixture was stirred under argon at -78 °C for 1 h. This solution was added by a double ended needle to a solution of anhydrous $ZnCl_2$ (18.4 g, 135 mmol) in THF (140 ml) maintained at 0 °C and the resulting mixture was stirred for 0.5 h at 0 °C. $Pd(PPh_3)_4$ (4.3 g, 3.7 mmol) was then added and the mixture was cooled to -78 °C and treated within 0.5 h with a solution of acetyl chloride (8.8 ml, 123 mmol) in THF (25 ml). The resulting mixture was stirred for 2 h at -78 °C, for 18 h at -10 °C and for 9

h at room temperature. It was then poured into a large excess of a saturated aqueous NH_4Cl solution and extracted with Et_2O. The organic extract was washed with water until neutrality, dried, filtered and concentrated *in vacuo*. The residue was dissolved in a mixture of hexane and Et_2O (95:5 *v/v*) and filtered on Celite. The filtrate was concentrated *in vacuo* and the residue was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (95:5 *v/v*) as eluant, to give compound **10g** (8.9 g, 50% yield): b.p. 60-61 °C/0.20 Torr. ^1H NMR ($CDCl_3$), δ: 7.59-7.38 (5 H, br m, H_{arom}), 2.45 ppm (3 H, s, CH_3). The physical and spectroscopic properties of this compound were in agreement with those previously reported[25].

It is interesting to note that a preparation carried out according to a procedure very similar to that used for the synthesis of **10d** gave compound **10g** in a low yield (12%).

*(Z)-3-Tributylstannyl-3-nonen-2-one, (Z)-**11d***

A deareated solution of Bu_3SnH (17.2 ml, 63.6 mmol) in THF (105 ml) was added during 1 h to a solution of 3-nonyn-2-one, **10d**, (9.0 g, 65.2 mmol) and $Pd(PPh_3)_4$ (1.5 g, 1.3 mmol) in THF (105 ml) which was stirred at room temperature under argon. Upon completion of the addition the mixture was stirred for additional 4 h, THF was removed under reduced pressure and the residue was diluted with hexane (600 ml). The mixture was allowed to settle and filtered. The filtrate was concentrated under reduced pressure, the residue was diluted with hexane (500 ml), filtered on Celite and the filtrate was again concentrated *in vacuo*. The new residue was purified by MPLC on silica gel, using a mixture of hexane and benzene (75:25 *v/v*) as eluant, to give compound (Z)-**11d** (10.2 g, 38% yield). ^1H NMR ($CDCl_3$), δ: δ 7.17 (1 H, t, J = 7.3 Hz, H-4), 2.27 (3H, s, H-1), 2.24-2.15 (2H, m, H-5), 1.55-1.20 (18 H, br m, H-6, H-7, H-8, H-2' and H-3'), 1.10-0.76 ppm (18 H, br m, H-8, H-1' and H-4'). Anal. Calcd. for $C_{21}H_{42}OSn$: C, 58.76; H, 9.86. Found: C, 58.64; H, 9.90.

*(Z)-3-Iodo-3-nonen-2-one, (Z)-**8a***

A solution of iodine (4.4 g, 17. 3 mmol) in dry CH_2Cl_2 (200 ml) was added during 3 h to a solution of compound (Z)-**11d** (6.9 g, 16.0 mmol) in dry CH_2Cl_2 (120 ml) which was stirred at room temperature under argon. Upon completion of the addition the reaction mixture was stirred for additional 2 h and concentrated *in vacuo*. The residue was dissolved in Et_2O (500 ml) and stirred with a semisaturated aqueous KF solution (500 ml) at room temperature for 2 h. The reaction mixture was filtered and the filtrate was extracted with Et_2O. The organic extract was washed with a dilute aqueous $Na_2S_2O_3$ solution and water, dried, filtered and concentrated *in vacuo*. The residue was purified by MPLC on silica gel, using a mixture of hexane and benzene (7:3 *v/v*) as eluant, to give chemically and stereoisomerically pure (Z)-**8a** (3.8 g, 88% yield). ^1H NMR ($CDCl_3$), δ: 7.01 (1 H, t, J = 6.9 Hz, H-4), 2.51 (3 H, s, H-1), 2.43 (2 H, *pseudo*-q, J = 7.2 Hz, H-5), 1.65-1.25 (6 H, m, H-6, H-7 and H-8), 0.91 ppm (3 H, t, J = 6.9 Hz, H-9). MS, *m/z* (%): 266 (M^+, 44), 223 (24), 210 (18), 197 (55), 196 (16), 181 (18), 139 (19), 97 (21), 96 (59), 95 (34), 82 (23), 81 (21), 71 (27), 69 (18), 68 (18), 55 (37), 53 (25), 43 (100), 41 (64), 39 (57). Anal. Calcd. for $C_9H_{15}IO$: C, 40.62; H, 5.68. Found: C, 40.42; H, 5.68.

*(Z)- and (E)-3-Iodo-3-nonen-2-one, (Z)- and (E)-**8a***

A deareated solution of Bu_3SnH (13.6 ml, 50.3 mmol) in THF (85 ml) was added during 2 h to a solution of compound **11d** (7.4 g, 53.4 mmol) and $Pd(PPh_3)_4$ (1.3 g, 1.1 mmol) in THF (85 ml), which was

stirred at room temperature under argon. Upon completion of the addition the mixture was stirred for additional 4 h and concentrated *in vacuo*. The residue was diluted with hexane (700 ml) and the mixture was allowed to settle for 1 h. It was then filtered and the filtrate was concentrated *in vacuo* to afford an oily residue (21.4 g). A solution of iodine (13.0 g, 51.3 mmol) in dry CH_2Cl_2 (600 ml) was added during 2 h to a solution of this residue in dry CH_2Cl_2 (300 ml). Upon completion of the addition the reaction mixture was stirred for additional 2 h and concentrated *in vacuo*. The residue was dissolved in Et_2O (500 ml), treated with a semisaturated aqueous KF solution (500 ml) and the resulting mixture was stirred for 2 h at room temperature. It was then filtered and the filtrate was extracted with Et_2O. The organic extract was washed with a dilute aqueous $Na_2S_2O_3$ solution and water, dried, filtered and concentrated *in vacuo*. GLC/MS analysis of the residue showed the presence of two compounds, subsequently identified as (*Z*)- and (*E*)-**8a**, in a 25:75 molar ratio, respectively. This residue was purified by MPLC on silica gel, using a mixture of hexane and benzene (7:3 *v/v*) as eluant. GLC analyses of the first eluted fractions showed that they contained chemically and stereoisomerically pure (*E*)-**8a**. However, concentration of these fractions under reduced pressure gave a mixture of (*E*)- and (*Z*)-**8a** (7.64 g) in a 59:41 ratio, respectively. ^{1}H NMR analysis of this mixture allowed to determine the ^{1}H NMR parameters of (*E*)-**8a**. ^{1}H NMR ($CDCl_3$), δ: 6.58 (1 H, t, J = 7.8 Hz, H-4), 2.49 (3H, s, H-1), 2.29 (2 H, *pseudo*-q, J = 7.6 Hz, H-5), 1.43-1.26 (6 H, m, H-6, H-7, and H-8), 0.89 ppm (3 H, t, H-9). Moreover, GLC/MS of the stereoisomeric mixture allowed to establish that the MS spectrum of (*E*)-**8a** was very similar to that of compound (*Z*)-**8a**.

Concentration of the last eluted chromatographic fractions allowed to obtain compound (*Z*)-**8a** (3.38 g). The spectroscopic properties of this substance were in very good agreement with those of (*Z*)-**8a** prepared from compound (*Z*)-**11d**. The overall yield of iodides **8a** was 82% based on Bu_3SnH.

*(Z)- and (E)-2-Iodo-1-phenyl-2-octen-1-one, (Z)- and (E)-**8b***

A deareated solution of Bu_3SnH (19.2 ml, 71.2 mmol) in THF (115 ml) was added during 1.5 h to a solution of 1-phenyl-2-octyn-1-one, **10e**, (14.7 g, 73.4 mmol) and $Pd(PPh_3)_4$ (1.7 g, 1.5 mmol) in THF (115 ml), which was stirred at room temperature under argon. Upon completion of the addition the reaction mixture was stirred for additional 4 h and concentrated under reduced pressure. The residue was diluted with hexane (900 ml) and the mixture, after settling for 2 h, was filtered on Celite. The filtrate was concentrated *in vacuo* to afford a residue (36.1 g). ^{1}H NMR analysis of this crude reaction product showed that it was essentially constituted of (*Z*)- and (*E*)-1-phenyl-2-tributylstannyl-2-octen-1-one, **11e**, in a 54:46 molar ratio, respectively. Compound (Z)-**11e** had: ^{1}H NMR ($CDCl_3$), δ: 7.78 (2 H, dt, J = 6.6 and 1.6 Hz, $H_{arom(orto)}$), 7.56-7.36 (3 H, br m, $H_{arom(meta\ and\ para)}$), 6.68 (1 H, t, J = 7.3 Hz, H-3), 2.24 (2 H, *pseudo*-q, J = 7.3 Hz, H-4), 1.60-0.72 ppm (36 H, br m, H-5, H-6, H-7, H-8, H-1', H-2', H-3' and H-4'). Compound (*E*)-**11e** had: ^{1}H NMR ($CDCl_3$), δ: 7.92 (2H, dt, J = 6.6 and 1.6 Hz, $H_{arom(orto)}$), 7.56-7.36 (3 H, br m, $H_{arom(meta\ and\ para)}$), 5.92 (1 H, t, J = 7.1 Hz, H-3), 1.99 (2 H, *pseudo*-q, J = 7.1 Hz, H-4), 1.60-0.72 ppm (36 H, br m, H-5, H-6, H-7, H-8, H-1', H-2', H-3' and H-4').

A solution of iodine (10.6 g, 41.6 mmol) in dry CH_2Cl_2 (500 ml) was added during 2 h to a solution of part of the above mentioned residue (19.6 g, *ca.* 40 mmol) in dry CH_2Cl_2 (200 ml). Upon completion of the addition the mixture was stirred at room temperature for additional 3 h and then worked up using the same procedure followed for the preparation of (*Z*)-**8a**. GLC/MS analysis of the crude reaction product showed that

it was constituted of two compounds, subsequently identified as (Z)- and (*E*)-**8b**, in a 69:31 molar ratio, respectively. This crude product was purified by MPLC on silica gel, using a mixture of hexane and benzene (75:25 *v/v*) as eluant. Concentration of the first eluted chromatographic fractions allowed to isolate 98% stereoisomerically pure (*E*)-**8b** (3.6 g). ^{1}H NMR ($CDCl_3$), δ: 7.98 (2 H, dt, J = 6.8 and 1.6 Hz, $H_{arom(orto)}$), 7.63-7.40 (3 H, m, $H_{arom(meta\ and\ para)}$), 6.59 (1 H, t , J = 7.8 Hz, H-3), 1.99 (2 H, *pseudo*-q, J = 7.8 Hz, H-4), 1.45-1.10 (6 H, br m, H-5, H-6 and H-7), 0.82 ppm (3 H, t, J = 6.4 Hz, H-8). MS, *m/z* (%): 328 (M^+, 5), 285 (3), 271 (7), 201 (5), 158 (27), 157 (12), 145 (14), 144 (26), 141 (6), 131 (7), 129 (6), 128 (21), 127 (12), 117 (6), 116 (7), 115 (21), 106 (8), 105 (100), 91 (7), 77 (30), 55 (11), 53 (13), 51 (28), 43 (11), 41 (32), 39 (30). Anal. Calcd.. for $C_{14}H_{17}IO$: C, 51.23; H, 5.22. Found: C, 51.66; H, 5.37.

Concentration of the last eluted chromatographic fractions allowed to obtain compound (Z)-**8b** (5.1 g) having stereoisomeric purity higher than 98%. ^{1}H NMR ($CDCl_3$), δ: 7.69 (2 H, dt, J = 6.7 and 1.5 Hz, $H_{arom(orto)}$), 7.59-7.35 (3 H, br m, $H_{arom(meta\ and\ para)}$), 6.63 (1 H, t, J = 7.0 Hz, H-3), 2.45 (2 H, *pseudo*-q, J = 7.0 Hz, H-4),1.60-1.28 (6 H, br m, H-5, H-6 and H-7), 0.90 ppm (3 H, t, J = 6.9 Hz, H-8). MS, *m/z* (%): 328 (M^+, 2), 285 (1), 271 (3), 257 (6), 201 (5), 159 (5), 158 (11), 157 (7), 145 (7), 144 (13), 128 (13), 127 (7), 115 (13), 106 (8), 105 (100), 77 (23), 55 (6), 53 (8), 51 (19), 41 (22), 39 (20). Anal. Calcd. for $C_{14}H_{17}IO$: C, 51.23; H, 5.22. Found: C, 51.45; H, 5.48.

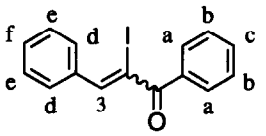
Moreover, concentration of the intermediate chromatographic fractions allowed to obtain a mixture of (*E*)- and (Z)-**8b** (2.4 g) in a 26:74 molar ratio, respectively, which was subsequently separated into its components by a further MPLC. Therefore, compounds (*E*)- and (Z)-**8b** were prepared in 88% overall yield based on Bu_3SnH.

(Z)- and (E)-2-Iodo-1,4-diphenyl-2-propen-1-one, (Z)- and (E)-8c

Method A (entry 3, Table 1). 1,4-Diphenyl-2-propyn-1-one, **10f**, (13.1 g, 63.7 mmol) underwent a reaction with Bu_3SnH (18 g, 61.8 mmol), in the presence of $Pd(PPh_3)_4$ (1.5 g, 1.3 mmol) under experimental conditions very similar to those employed to synthesize crude (Z)-and (*E*)-**11e**. The crude reaction mixture was concentrated under reduced pressure and the residue was diluted with hexane. The resulting mixture was allowed to settle for 12 h, filtered on Celite and the filtrate was concentrated *in vacuo*. ^{1}H NMR analysis of the residue (29.8 g) showed the presence of three components in a *ca.* 12:38:50 molar ratio, respectively. The first two of these substances were identified as (Z)-and (*E*)-1,4-diphenyl-2-propen-1-one, respectively, while the third compound, which had higher retention time, very probably corresponded to a steroisomeric mixture of 1,4-diphenyl-2-tributylstannyl-2-propen-1-one, **11f**. This residue, which was kept at -15 °C under nitrogen for 9 days, was subsequently dissolved in dry CH_2Cl_2 (400 ml) and reacted under argon with a solution of iodine (15.2 g, 60 mmol) in dry CH_2Cl_2 (700 ml), using experimental conditions very similar to those employed to prepare (Z)- and (*E*)-**8b**. After usual work up the crude reaction products were purified by MPLC on silica gel, using a mixture of hexane and benzene (6:4 *v/v*) as eluant. Whereas the last eluted chromatographic fractions contained (Z)- and (*E*)-1,4-diphenyl-2-propen-1-one, concentration of the first chromatographic fractions allowed to obtain 99% stereoisomerically pure (*E*)-**8c** (5.1 g): m.p. 46-47 °C. ^{1}H NMR ($CDCl_3$), δ: 8.05-7.94 (2 H, m, H_a), 7.53 (1 H, s, H-3), 7.53-7.34 (3 H, m, H_b and H_c), 7.14 ppm (5 H, br s, H_d, H_e and H_f). MS, *m/z* (%): 334 (M^+, 4), 207 (12), 129 (6), 106 (8), 105 (100), 103 (6),

77 (66), 76 (15), 75 (6), 63 (8), 52 (10), 51 (55), 50 (22), 43 (10), 39 (14). Anal. Calcd. for $C_{15}H_{11}IO$: C, 53.92; H, 3.32. Found: C, 54.38; H, 3.43.

Moreover, concentration of the intermediate eluted chromatographic fractions allowed to obtain a mixture of (*Z*)- and (*E*)-**8c** in a 58:42 molar ratio, respectively. MPLC on silica gel of this mixture allowed to obtain either stereoisomerically pure (*E*)-**8c** (0.9 g) or compound (*Z*)-**8c** (1.5 g) having stereoisomeric purity higher than 99%. Compound (*Z*)-**8c** had: m.p. 42-44°C. ^{1}H NMR ($CDCl_3$): δ 7.86-7.73 (4H, m, H_a and H_d), 7.63 (1 H, s, H-3), 7.60-7.40 (6 H, m, H_b, H_e, H_c and H_f). MS, *m/z* (%): 334 (M^+, 4), 207 (11), 129 (8), 106 (8), 105 (100), 102 (20), 77 (64), 76 (15), 75 (7), 52 (10), 51 (52), 50 (21), 39 (14). Anal. Calcd. for $C_{15}H_{11}IO$: C, 53.92; H, 3.32. Found: C, 54.11; H, 3.23. Compounds (*E*)- and (*Z*)-**8c** were so obtained in 37% overall yield based on Bu_3SnH.



Method B (entry 4, Table 1). A deareated solution of Bu_3SnH (19.8 ml, 73.7 mmol) in THF (100 ml) was added during 40 minutes to a solution of compound **10f**, (15.7 g, 76.0 mmol) and $Pd(PPh_3)_4$ (1.8 g, 1.5 mmol) in THF (100 ml). Upon completion of the addition the reaction mixture was stirred for additional 4.5 h at room temperature and for 11 h at 0 °C. It was then concentrated under reduced pressure and the residue was diluted with dry CH_2Cl_2 (300 ml). This solution was reacted under an atmosphere of argon with a solution of iodine (20.2 g, 79.5 mmol) in dry CH_2Cl_2 (700 ml) using experimental conditions similar to those employed to prepare compounds (*Z*)-and (*E*)-**8b**. After usual work up, the crude reaction product was analyzed by GLC and showed the presence of compounds (*Z*)- and (*E*)-**8c** in a 76:24 molar ratio, respectively. Purification by MPLC on silica gel, using a mixture of hexane and benzene (6:4 *v/v*) as eluant, allowed to obtain 97% stereoisomerically pure (*E*)-**8c** (1.8 g), a mixture of chemically pure (*E*)- and (*Z*)-**8c** (14.5 g) as well as 97% stereoisomerically pure (*Z*)-**8c** (7.1 g). Therefore, compounds **8c** were obtained in 95% overall yield based on Bu_3SnH.

(Z)-3-Iodo-4-phenyl-3-buten-2-one (Z)-8d

This compound was prepared using a procedure very similar to method B employed to synthesize compounds (*Z*)- and (*E*)-**8c**. In particular, a deareated solution of Bu_3SnH (22.0 ml, 81.8 mmol) in THF (100 ml) was added under argon during 0.5 h to a solution of 4-phenyl-3-butyn-2-one, **10g** (12.1 g, 84.1 mmol) and $Pd(PPh_3)_4$ (1.9 g, 1.7 mmol) in THF (100 ml). Upon completion of the addition the reaction mixture was stirred at room temperature for additional 5 h and for 16 h at 0 °C. It was then concentrated *in vacuo* and the residue was diluted with dry CH_2Cl_2 (200 ml). This solution was then reacted under argon with a solution of iodine (22.5 g, 88.6 mmol) in dry CH_2Cl_2 (800 ml) using experimental conditions similar to those employed to prepare compounds (*Z*)- and (*E*)-**8b**. After usual work up the crude reaction product was analyzed by GLC and showed the presence of a main product which was subsequently identified as (*Z*)-**8d**. This crude product was purified by MPLC on silica gel, using a mixture of benzene and hexane (6:4 *v/v*) as eluant, to give 99% stereoisomerically pure (*Z*)-**8d** (15.3 g, 69% yield based on Bu_3SnH). ^{1}H NMR ($CDCl_3$), *δ*: 8.03 (1 H, s, H-4), 7.88-7.72 (2 H, m, $H_{arom(orto)}$), 7.53-7.40 (3 H, m, $H_{arom(meta\ and\ para)}$),

2.66 ppm (3 H, s, H-1). The spectral properties of this compound were in good agreement with those previously reported for 95% stereoisomerically pure (Z)-**8d**[5].

General procedure for the stereomutation of (E)/(Z)-, (E)- or (Z)-2-iodo-2-alkenones of general formula 8 induced by iodine and daylight

In a typical experiment, a mixture of compound (*E*)/(*Z*)-, (*E*)- or (*Z*)-**8** (3.0 mmol) and iodine (0.3 mmol) was magnetically stirred at room temperature, in the presence of daylight, for the period of time reported in Table 2. The reaction, which was periodically monitored by GLC, was interrupted after a GLC analysis showed that no change of the stereoisomeric composition of compound **8** was observed. Then, the reaction mixture was diluted with Et_2O, washed with a dilute aqueous $Na_2S_2O_3$ solution and water, dried, filtered and concentrated *in vacuo* at room temperature. The residue was analyzed by GLC and ^1H NMR. Table 2 summarizes the results obtained in the stereomutation reactions of (*E*)/(*Z*)-**8a**, (*E*)/(*Z*)-**8b**, (*E*)- and (*Z*)-**8c** and (*Z*)-**8d**. As shown in this table (entry 1), a partial stereomutation of (*E*)/(*Z*)-**8a** also occurred after exposure of this stereoisomeric mixture (*E*/*Z* = 59 : 41) at the daylight for 56 h, in the absence of iodine.

General procedure for the palladium-catalyzed cross-coupling reactions of 2-iodo-2-alkenones, 8, with organostannanes

A dried flask flushed with argon was charged with $PdCl_2(C_6H_5CN)_2$ (0.17 g, 0.45 mmol), CuI (0.17 g, 0.91 mmol), $AsPPh_3$ (0.28 g, 0.91 mmol) a 2-iodo-2-alkenone, **8**, (9.07 mmol) and N-methylpyrrolidinone (14 ml). A degassed solution of an organostannane in N-methylpyrrolidinone (3 ml) was then added and the mixture was stirred at the temperature and for the period of time reported in Table 3. The reactions involving tetramethylstannane (entries 4, 6-8, 10) were carried out using a 3 : 1 molar ratio between such organometallic reagent and compound **8**, but the coupling reactions involving other organostannanes were performed using a 1.2 : 1 molar ratio between such organometallics and compounds **8**. After completion of the reaction, which was periodically monitored by GLC, the reaction mixture was allowed to cool to room temperature and poured into a large excess of a saturated aqueous NH_4Cl solution. After stirring for 0.5 h the mixture was extracted with Et_2O. The crude Et_2O extracts derived from the reactions involving vinyltributylstannane were stirred for 2 h with a large excess of a semisaturated aqueous KF solution, filtered and the filtrate was extracted with Et_2O. The organic extract was washed with brine, dried, filtered, concentrated under reduced pressure and the residue was analyzed by GLC/MS and TLC. It was then diluted with the solvent (150 ml) used for the TLC analysis and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by MPLC on silica gel.

Compounds (*E*)-**13a**, (*E*)-**13b**, (*E*)-**13c**, (*E*)-**13d**, (*E*)-**13e**, (*E*)/(*Z*)-**13e**, (*E*)-**13f**, (*E*)-**13g** and (*E*)-**13h** were prepared according to this general procedure.

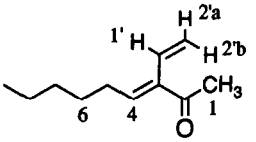
(E)-3-Phenyl-3-nonen-2-one, (E)-13a

The crude reaction product, which was obtained from the palladium-catalyzed reaction between (*Z*)-**8a** and phenyltrimethylstannane (entry 1, Table 3), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (92 : 8 *v*/*v*) as eluant, to give (*E*)-**13a** in 84% yield. ^1H NMR ($CDCl_3$), δ: 7.50-7.18 (3 H, m, H_{arom}), 7.11-7.06 (2H, m, H_{arom}), 6.89 (1 H, t, J = 7.6 Hz, H-4), 2.27 (3 H, s, H-1), 2.06 (2 H,

pseudo-q, J = 7.6 Hz, H-5), 1.49-1.16 (6 H, br m, H-6, H-7 and H-8), 0.85 ppm (3 H, t, J = 6.5 Hz, H-9). MS, *m/z* (%): 216 (M^+, 22), 173 (18), 155 (13), 131 (10), 129 (7), 128 (6), 117 (27), 116 (6), 115 (19), 103 (6), 91 (18), 43 (100), 41 (20), 39 (11). Anal. Calcd. for $C_{15}H_{20}O$: C, 83.29; H, 9.32. Found: C, 83.28; H, 9.48. GLC analysis showed that (*E*)-**13a** had chemical and stereoisomeric purity higher than 99%.

(E)-3-Vinyl-3-nonen-2-one, (E)-13b

The crude reaction product, which was obtained from the palladium-catalyzed reaction between (*Z*)-**8a** and vinyltributylstannane (entry 2, Table 3), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (98:2 *v/v*) as eluant, to give (*E*)-**13b** in 57% yield. ^1H NMR ($CDCl_3$), δ: 6.57 (1 H, t , J = 7.4 Hz, H-4), 6.44 (1 H, dd, J = 18.4 and 10.9 Hz, H-1'), 5.46-5.36 (2H, m, H-2'a and H-2'b), 2.36-2.29 (2 H, m, H-5), 2.33 (3 H, s, H-1), 1.55-1.43 (2 H, m, H-6), 1.35-1.30 (4 H, m, H-7 and H-8), 0.90 ppm (3 H, t, J = 6.6 Hz, H-9). MS, *m/z* (%): 166 (M^+, 1), 151 (1), 137 (1), 123 (5), 109 (10), 97 (6), 95 (5), 81 (10), 67 (10), 55 (5), 43 (100), 41 (16), 39 (10). Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.68; H, 11.01. GLC analysis showed that (*E*)-**13b** had stereoisomeric purity higher than 99%.



(E)-2-Methyl-1-phenyl-2-octen-1-one, (E)-13c

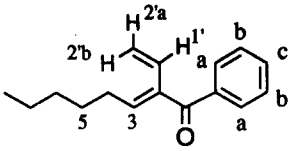
The crude reaction product, which was obtained from the palladium-catalyzed reaction between (*Z*)-**8b** and tetramethylstannane (entry 4, Table 3), was purified by MPLC on silica gel, using a mixture of hexane and benzene (7:3 *v/v*) as eluant, to give (*E*)-**13c** in 70% yield. ^1H NMR ($CDCl_3$), δ: 7.64-7.36 (5 H, m, C_6H_5), 6.30 (1 H, t, J = 7.2 Hz, H-3), 2.27 (2 H, *pseudo*-q, J = 7.2 Hz, H-4), 1.96 (3 H, s, CH_3), 1.60-1.15 (6 H, m, H-5, H-6 and H-7), 0.89 ppm (3 H, t, J = 6.4 Hz, H-8). MS, *m/z* (%): 216 (M^+, 4), 173 (6), 159 (19), 145 (19), 105 (69), 91 (9), 77 (31), 55 (39), 54 (7), 53 (18), 51 (44), 50 (8), 43 (57), 42 (9), 41 (100), 40 (8), 39 (55). Anal. Calcd. for $C_{15}H_{20}O$: C, 83.29; H, 9.32. Found: C, 83.34; H, 9.50. GLC analysis showed that compound (*E*)-**13c** was stereoisomerically pure and had chemical purity higher than 98%.

This same stereoisomerically pure compound was obtained in 63% GLC yield by palladium-catalyzed reaction between a stereoisomeric mixture of **8b** (*E/Z* = 61:39) and tetramethylstannane (entry 6, Table 3).

(E)-1-Phenyl-2-vinyl-2-octen-1-one, (E)-13d

The crude reaction product, which was obtained from the palladium-catalyzed reaction between (*Z*)-**8b** and vinyltributylstannane (entry 5, Table 3), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (97:3 *v/v*) as eluant, to give (*E*)-**13d** in 79% yield. ^1H NMR ($CDCl_3$), δ: 7.86-7.81 (2 H, m, H_a), 7.58-7.42 (3H, m, H_b and H_c), 6.70 (1 H, ddd, J = 17.1, 10.8 and 1.0 Hz, H-1'), 5.94 (1 H, dt, J = 7.5 and 1.0 Hz, H-3), 5.34 (1H, d, J =17.1 Hz, H-2'b), 5.33 (1H, d, J = 10.8 Hz, H-2'a), 2.37 (2 H, *pseudo*-q, J = 7.5 Hz, H-4), 1.51-1.20 (6 H, m, H-5, H-6 and H-7), 0.90 ppm (3 H, t, J = 7.1 Hz, H-8). MS, *m/z* (%): 228 (M^+, 3), 185 (7), 171 (7), 106 (7), 105 (100), 81 (7), 79 (8), 77 (60), 55 (7), 51 (13), 41

(25), 39 (13). Anal. Calcd. for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 83.83; H, 8.92. GLC analysis showed that (*E*)-**13d** was stereoisomerically pure.

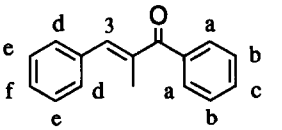


(E)- and (E)/(Z)-2-Methyl-1,3-diphenyl-2-propen-1-one, (E)- and (E)/(Z)-13e

The crude reaction product, which was obtained from the palladium-catalyzed reaction between (*Z*)-**8c** and tetramethylstannane (entry 8, Table 3), was purified by MPLC on silica gel, using a mixture of benzene and hexane (6:4 *v/v*) as eluant, to give stereoisomerically pure (*E*)-**13e** in 94% yield. ^{1}H NMR ($CDCl_3$), δ: 7.77-7.73 (2 H, m, H_a), 7.60-7.25 (8 H, m, H_b, H_c, H_d, H_e and H_f), 7.18 (1H, q, J = 1.4 Hz, H-3), 2.27 ppm (3 H, d, J = 1.4 Hz, CH_3). MS, *m/z* (%): 222 (M^+, 18), 221 (14), 145 (7), 131 (6), 117 16), 116 (13), 115 (38), 106 (7), 105 (86), 96 (11), 91 (21), 89 (7), 78 (9), 77 (100), 76 (7), 65 (14), 63 (11), 51 (41), 50 (12), 39 (23). Anal. Calcd. for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.21; H, 6.11.

On the other hand, the palladium-catalyzed reaction between (*E*)-**8c** and tetramethylstannane (entry 7, Table 3) afforded a crude product which was constituted of (*E*)- and (*Z*)-**13e** in a 45:55 ratio, respectively. This crude product was purified by MPLC on silica gel, using a mixture of benzene and hexane (6:4 *v/v*) as eluant, to give (*Z*)- and (*E*)-**13e** in 97% yield. Concentration of the first eluted cromatographic fractions allowed to obtain (*Z*)-**13e** having stereoisomeric purity higher than 98%. ^{1}H NMR ($CDCl_3$), δ: 7.91-7.86 (2 H, m, H_a), 7.55-7.25 (3 H, m, H_b and H_c), 7.12-7.06 (5 H, m, H_d, H_e and H_f), 6.74 (1 H, q, J = 1.6 Hz, H-3), 2.16 ppm (3 H, d, J = 1.6 Hz, CH_3). MS, *m/z* (%): 222 (M^+, 21), 221 (15), 207 (6), 117 (17), 116 (12), 115 (35), 106 (7), 105 (82), 91 (20), 78 (10), 77 (100), 65 (12), 63 (11), 51 (46), 50 (13), 39 (29). Anal. Calcd. for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.20; H, 6.10.

Concentration of the last eluted chromatographic fractions allowed to isolate 98% stereoisomerically pure (*E*)-**13e**. This compound had spectral properties in very good agreement with those of the compound obtained in entry 8.



(E)-1,2,3-Triphenyl-2-propen-1-one, (E)-13f

GLC analysis of the crude reaction product, which was obtained from the palladium-catalyzed reaction between (*Z*)-**8c** and phenyltrimethylstannane (entry 9, Table 3), showed that it was constituted of a mixture of two compounds in a *ca.* 31:69 molar ratio, which were subsequently identified as (*E*)-**13e** and (*E*)-1,2,3-triphenyl-2-propen-1-one, (*E*)-**13f**, respectively. This crude product was purified by MPLC on silica gel, using a mixture of hexane and benzene (6:4 *v/v*) as eluant. Concentration of the first eluted fractions allowed to isolate a mixture of (*E*)-**13e** and (*E*)-**13f** (1.6 g) in a *ca.* 28:62 molar ratio, respectively, which was subsequently purified by crystallyzation from a mixture of benzene and hexane to give 98% chemically

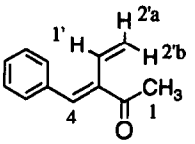
pure (*E*)-**13f** (0.9 g): m.p. 100.5-101.5 °C (Lit[27] m.p. 100.5-101.5 °C; Lit[28] m.p. 103-103.5 °C). On the other hand, concentration of the last eluted chromatographic fractions allowed to isolate 95% chemically pure compound (*E*)-**13f** (0.1 g). ^{1}H NMR ($CDCl_3$), δ: 7.86 (2 H, dd, J = 6.7 and 1.6 Hz, $H_{(arom)}$), 7.60-7.15 ppm (14 H, br m, $H_{(arom)}$ and H-3). Thus, compound (*E*)-**13f** was obtained in 50% yield.

*(E)-3-Methyl-4-phenyl-3-buten-2-one, (E)-**13g***

The crude reaction product, which was obtained from the palladium-catalyzed reaction between 99% stereoisomerically pure (*Z*)-**8d** and tetramethylstannane (entry 10, Table 3), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (92:8 *v/v*) as eluant, to give 99% chemically pure (*E*)-**13g** in 94% yield. ^{1}H NMR ($CDCl_3$), δ: 7.52 (1 H, br s, H-4), 7.43-7.32 (5 H, m, C_6H_5), 2.46 (3 H, s, H-1), 2.05 ppm (3 H, d, J = 1.4 Hz, =C-CH_3). The spectral properties of this compound were in agreement with those previously reported[29].

*(E)-4-phenyl-3-vinyl-3-buten-2-one, (E)-**13h***

The crude reaction product, which was obtained from the palladium-catalyzed reaction between 99% stereoisomerically pure (*Z*)-**8d** and vinyltributylstannane (entry 11, Table 3), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (94:6 *v/v*) as eluant, to give (*E*)-**13h** in 47% yield. ^{1}H NMR ($CDCl_3$), δ: 7.48-7.32 (5 H, br m, C_6H_5), 7.30 (1 H, br s, H-4), 6.58 (1H, ddd, J = 17.9, 11.6 and 1.2 Hz, H-1'), 5.63 (1 H, ddd, J = 17.9, 1.7 and 0.5 Hz, H-2'b), 5.48 (1 H, ddd, J = 11.6, 1.7 and 1.2 Hz, H-2'a), 2.46 ppm 3H, s, H-1). Anal. Calcd. for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.59; H, 6.89.



*2-Methyl-2-cyclohexenone, **19a***

The palladium-catalyzed reaction between 2-iodo-2-cyclohexenone, **18a**, and tetramethylstannane was carried out at 80 °C for 40 h according to the same procedure followed to prepare compounds (*E*)-**13c**, (*E*)/(*Z*)- and (*E*)-**13e** and (*E*)-**13g**. After usual work up the crude reaction product was purified by MPLC on silica gel, using a mixture of pentane and Et_2O (9:1 *v/v*) as eluant, to give **19a** in 46% isolated yield. B.p. 100-101 °C/77 Torr. Lit[19a] b.p. 98-101 °C/77 Torr. ^{1}H NMR ($CDCl_3$), δ: 6.75 (1 H, tq, J = 4.2 and 1.6 Hz, H-3), 2.43 (2 H, t, J = 6.4 Hz, H-6), 2.38-2.28 (2 H, m, H-4), 1.99 (2 H, *pseudo*-quint, J = 6.4 Hz, H-5), 1.78 ppm (3 H, *pseudo*-q, J = 1.6 Hz, CH_3). The spectral properties of this compound were in good agreement with those previously reported[19b].

*2,3-Dimethyl-2-cyclopentenone, **19b***

The palladium-catalyzed reaction between 2-iodo-3-methyl-2-cyclopentenone, **18b**, and tetramethylstannane was carried out at 80 °C for 40 h according to the same procedure followed to prepare compound **19a**. After usual work up the crude reaction product was purified by MPLC on silica gel, using a mixture of pentane and Et_2O (7:3 *v/v*) as eluant, to give 96% chemically pure **19b** in 84% yield. ^{1}H NMR ($CDCl_3$), δ:

2.56-2.45 (2 H, m, H-4), 2.39-2.34 (2 H, m, H-5), 2.06 (3 H, br s, H-2'), 1.70-1.68 (3 H, m, H-3'). The spectral properties of this compound were in good agreement with those previously reported[19g,20].

Acknowledgements: We thank the Consiglio Nazionale delle Ricerche (CNR, Roma), Progetto Finalizzato *Chimica Fine* and the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST) for funding this work.

REFERENCES AND NOTES

1. Rossi, R.; Carpita, A.; Cossi, P. *Tetrahedron* **1992**, *48*, 8801.
2. Rossi, R.; Carpita, A.; Bellina, F.; Cossi, P. *J. Organomet. Chem.*, in press.
3. Rossi, R.;Carpita, A.; Cossi, P. *Synth. Commun.*, in press.
4. For previous studies on this subject, see: *a)* Ref. *1*; *b)* Ref. *3*; *c)* Rossi, R. Carpita, A.; Bellina, F.; De Santis, M.; Veracini, C. A. *Gazz. Chim. Ital.* **1990**, *120*, 457; *d)* Rossi, R.; Carpita, A.; Bellina, F.; De Santis, M. *Gazz. Chim. Ital.* **1991**, *121*, 261; *e)* Rossi, R.; Carpita, A.; Messeri, T. *Synth. Commun.* **1991**, *21*, 1875; *f)* Rossi, R.; Carpita, A.; Messeri, T. *Synth. Commmun.* **1992**, *22*, 603.
5. Huang, Y-Z.; Shi, L-L.; Li, S-W.; Huang, R. *Synth. Commun.* **1989**, *19*, 2639.
6. Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W.; Wovkulich, P. M.; Uskokovic, M. R. *Tetrahedron Lett.* **1992**, *33*, 917.
7. *a)* Haneishi,T.; Kitahara, N.; Takiguchi, Y.; Arai, M.; Sugawara, S. *J. Antibiot.* **1974**, *27*, 386; *b)* Tius, M. A.; Patterson, G. M.; Astrab, D. P. *J. Antibiot.* **1985**, *38*, 1061.
8. Zhang, H. X.; Guibé, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857.
9. Cochran, J. C.; Bronk, B. S.; Terrence, K. M.; Phillips, H. K. *Tetrahedron Lett.* **1990**, *31*, 6621.
10. Brown, H. C.; Raeherla, U. S.; Singh, S. M. *Tetrahedron Lett.* **1984**, *25*, 2411.
11. Thoda, Y., Sonogashira, K.; Hagihara, N. *Synthesis*, **1977**, 777.
12. Negishi, E.; Bagheri, V.; Chatterjee, S.; Luo, F-T.; Miller, J. A.; Stoll, A. T. *Tetrahedron Lett.* **1983**, *24*, 5181.
13. This same compound had been previously prepared in 38% yield by iodination of the corresponding α,β-unsaturated ketone, in the presence of pyridine (see: Ref. *6*).
14. Bestmann, H. J.; Attygalle, A. B.; Glassbrenner, J.; Reimer, R.; Vostrowsky, O.; Constantino, M. G.; Melikian, G.; Morgan, E. D. *Liebigs Ann. Chem.* **1988**, 55.
15. Cimino, G.; Spinella, A.; Sodano, G. *Tetrahedron Lett.* **1989**, *30*, 5003.
16. *a)* Sleeper, H. L.; Paul, V. J.; Fenical, W. *J. Chem. Ecol.* **1980**, *6*, 57; *b)* Clelland, J.; Knox, G.

R. *J. Chem. Soc. Chem. Commun.* **1983**, 1219.

17. For a recent review on the palladium-catalyzed reactions of organotin compounds, see: Mitchell, T. N. *Synthesis* **1992**, 803.
18. Johnson, C. R.; Adams, J. P.; Braun, M. P.; Senanayake, C. B. W. *Tetrahedron Lett.* **1992**, *33*, 919.
19. For previous syntheses of 2-methyl-2-cycloalkenones, see: *a)* Waruhoff, E. W.; Johnson, W. S. *J. Am. Chem. Soc.* **1953**, *75*, 494; *b)* Danishefsky, S.; Cain, P. *J. Org. Chem.* **1975**, *40*, 3607; *c)* Berkowitz, W. F.; Ozorio, A. A. *J. Org. Chem.* **1971**, *36*, 3787; *d)* Jernow, J.; Tautz, W.; Rosen, P.; Williams, T. H. *J. Org. Chem.* **1979**, *44*, 4213; *e)* Sum, F-W.; Weiler, L. *Can. J. Chem.* **1979**, *57*, 1431; *f)* Mikolcyczyk, M.; Grzejszczak, S.; Lyzwa, P. *Tetrahedron Lett.* **1982**, *23*, 2237; *g)* Hendrickson, J. B.; Palumbo, P. S. *J. Org. Chem.* **1985**, *50*, 2110; *h)* Liotta, D.; Saindane, M.; Barnum, C.; Zima, G. *Tetrahedron Lett.* **1985**, *21*, 4881.
20. Newton, R. F.; Reynolds, D. P.; Eyre, T. *Synth. Commun.* **1981**, *11*, 527.
21. Coulson, D. R. *Inorg. Synth.* **1971**, *13*, 121.
22. Doyle, J. R.; Slade, P. E.; Jonassen, H. B. *Inorg. Synth.* **1960**, *6*, 216.
23. Eaborn, C.; Waters, J. A. *J. Chem. Soc.* **1962**, 1131.
24. Seyferth, D.; Stone, F. G. A. *J. Am. Chem. Soc.* **1957**, *79*, 515.
25. Yamaguchi, M.; Shibato, K.; Fujiwara, S.; Hirao, I. *Synthesis* **1966**, 421.
26. Iman, M.; Bouyssou, P.; Chenault, J. *Synthesis* **1990**, 631.
27. Newkome, G. R.; Robinson, J. M. *J. Org. Chem.* **1976**, *41*, 2536.
28. Black, W. B.; Lutz, R. E. *J. Am. Chem. Soc.* **1953**, *75*, 5990.
29. Roustan, J. L.; Guinot, A.; Cadiot, P. *J. Organomet. Chem.* **1980**, *194*, 367.