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Palladium-catalyzed reaction between aryl or alkenyl halides and (1-carbalkoxy-1-alkenyl)zinc iodides. A new class of unmasked β-substituted acrylate α-anion equivalents *

Renzo Rossi, Adriano Carpita, Fabio Bellina and Paolo Cossi

Dipartimento di Chimica e Chimica Industriale, Università di Pisa, Via Risorgimento 35, I-56126 Pisa (Italy)

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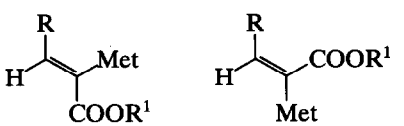
Abstract

Unmasked β-substituted acrylate α-anion equivalents have been directly and very efficiently prepared by insertion of zinc metal into the carbon–iodine bonds of alkyl (*E*)- or (*Z*)-2-iodo-2-alkenoates, (*E*)- or (*Z*)-**4**), respectively. The stereoisomeric composition of these new reagents, **12**, depends on the experimental conditions used for their preparation. Their Pd^0-catalyzed reaction with alkenyl or aryl halides, which can contain functional groups, leads chemoselectively to the corresponding cross-coupled products in high yields. When the reagents **12** are synthesized from compounds (*Z*)-**4** or long reaction times are used for their preparation, their cross-coupled products result are rich in the stereoisomers with trisubstituted double bonds of (*E*)-configuration.

1. Introduction

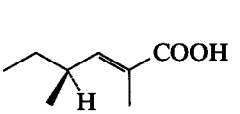
Stereodefined β-substituted α-metallo-α,β-unsaturated esters of general formula (*Z*)- or (*E*)-**1** in which the metal is copper, silicon or tin, form important classes of β-substituted acrylate α-anion equivalents which are very useful in organic synthesis [1].



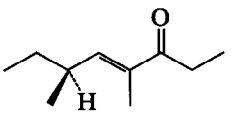
(*Z*)-**1** (*E*)-**1**

Recently, in the course of a study aimed at new synthetic aspects of a class of these organometallic reagents, we reported that alkyl (*E*)-2-tributylstannyl-2-alkenoates, (*E*)-(**2**), which can be prepared in quite good yield by reaction between alkyl 2-alkynoates (**3**) and Bu_3SnH in the presence of a catalytic amount of $[Pd(PPh_3)_4]$, are effective precursors to alkyl (*E*)-2-iodo-2-alkenoates, (*E*)-(**4**), stereodefined 2-(hetero)aryl substituted alkyl 2-alkenoates of general formula **5** as well as alkyl (*E*)-2-methyl-2-alkenoates, (*E*)-(**7**), having very high stereoisomeric purity (Scheme 1) [1i].

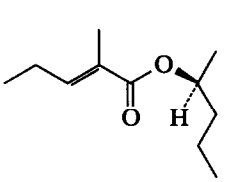
The procedure employed to prepare these last compounds, which involves a configurational inversion, was applied to the synthesis of the (*S*)-enantiomer of (*E*)-2,4-dimethyl-2-hexenoic acid, (*S*)(*E*)-(**8**) [1i], a caste-specific substance of male ants in the genus *Camponotus* [2], 98% optically pure (*S*)(*E*)-4,6-dimethyl-4-octen-3-one, (*S*)(*E*)-(**9**) [3], an alarm pheromone component of ants in the genus *Manica* [4], as well as (*S*)-1-methylbutyl (*E*)-2-methyl-2-pentenoate, (*S*)(*E*)-(**10**) [5], an aggregation pheromone component of the lesser and the greater grain borers [6,7].



(*S*)(*E*)-**8**



(*S*)(*E*)-**9**



(*S*)(*E*)-**10**

Correspondence to: Professor R. Rossi.

* Dedicated to Professor Gian Paolo Chiusoli in recognition of his important contributions to organometallic chemistry and its applications in organic synthesis.

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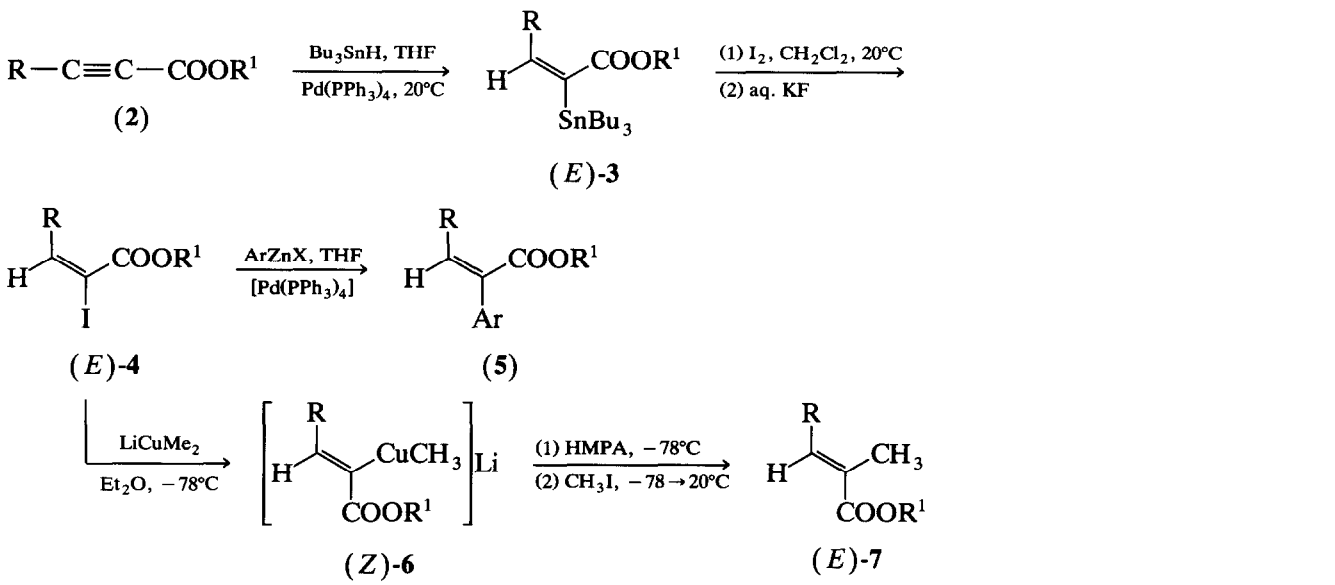
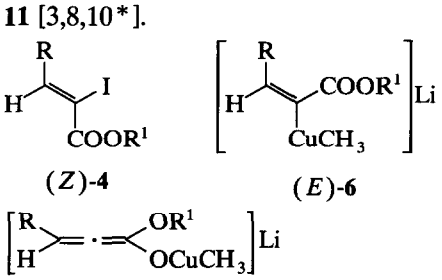


(R = $^{n}C_4H_9$, $^{n}C_5H_{11}$, $C_2H_5CH(CH_3)$, $^{t}BuMe_2SiOCH_2$, Ph; $R^1 = CH_3$, C_2H_5; Ar = Ph, 2-thienyl)

Scheme 1.

More recently we have found that the organometallic derivatives (*Z*)-**6**, which derive from treatment of the iodo derivatives (*E*)-**4** with 3.5 equiv. of lithium dimethylcuprate in Et_2O at −78°C, can also be stereospecifically generated from alkyl (*Z*)-2-iodo-2-alkenoates, (*Z*)-(**4**), using this same procedure [8]. These stereoisomerically pure iodo derivatives could be prepared easily by reaction between alkyl propiolates and lithium dialkylcuprates in Et_2O at −78°C, followed by treatment with iodine [8,9*].

The fact that either compound (*Z*)-**4** or (*E*)-**4** affords the cuprates (*Z*)-**6** has been rationalized on the basis that: (i) these organometallic reagents are thermodynamically more stable than the corresponding (*E*)-vinylcuprates, (*E*)-**6**, which are formed initially in the reaction between compounds (*E*)-**4** and lithium dimethylcuprate [8]; (ii) the conversion of the cuprates (*E*)-**6** to the corresponding (*Z*)-stereoisomers involves the formation of allenoate species of general formula **11** [3,8,10*].

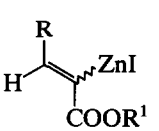


(*Z*)-**4** (*E*)-**6**

(**11**)

* Reference number with asterisk indicates a note in the list of references.

We have now carried out some investigations on a new class of unmasked β-substituted acrylate α-anion equivalents, *i.e.* (1-carbalkoxy-1-alkenyl)zinc iodides of general formula **12**, and we describe herein the synthesis of these new organometallic reagents by direct insertion of zinc metal into the carbon–iodine bond of compounds (*Z*)- or (*E*)-**4**. Furthermore, we report that the stereoisomeric composition of these organometallic compounds depends on the experimental conditions used for their preparation. Finally, we demonstrate their utility by a palladium(0)-catalyzed reaction with aryl and alkenyl halides, which can contain functional groups. This reaction leads efficiently and chemoselectively to the corresponding cross-coupled products.

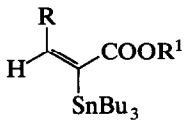


(**12**)

2. Results and discussion

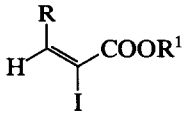
The following stereoisomerically pure alkyl 2-iodo-2-alkenoates (**4**) were used for the present study: ethyl (*Z*)-2-iodo-2-heptenoate, (*Z*)-(**4a**), methyl (*Z*)- and (*E*)-2-iodo-2-octenoate, (*Z*)-(**4b**) and (*E*)-(**4b**), respectively, and ethyl (*E*)-2-iodo-3-phenyl-2-propenoate, (*E*)-(**4c**). Compounds (*E*)-**4b** and (*E*)-**4c** were synthesized by reaction of methyl (*E*)-2-tributylstannyl-2-octenoate (*E*)-(**3a**) and ethyl (*E*)-2-tributylstannyl-3-phenyl-2-propenoate (*E*)-(**3b**), each with an equimolar

amount of iodine in CH_2Cl_2 solution at room temperature, followed by treatment of the resulting reaction mixtures with a semisaturated aqueous KF solution [1i,3] (Scheme 1).



(*E*)-**3a** R = $^nC_5H_{11}$; $R^1 = CH_3$

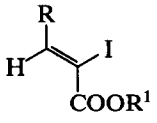
(*E*)-**3b** R = C_6H_5; $R^1 = C_2H_5$



(*E*)-**4b** R = $^nC_5H_{11}$; $R^1 = CH_3$

(*E*)-**4c** R = C_6H_5; $R^1 = C_2H_5$

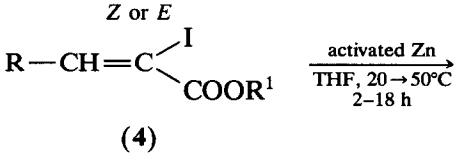
In contrast, compounds (*Z*)-**4a** and (*Z*)-**4b** were prepared by reaction of the corresponding alkyl propiolates with lithium dibutylcuprate and lithium dipentylcuprate, respectively, in Et_2O at −78°C, followed by treatment with iodine [8,9*]



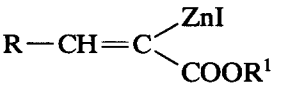
(*Z*)-**4a** R = $^nC_4H_9$; $R^1 = C_2H_5$

(*Z*)-**4b** R = $^nC_5H_{11}$; $R^1 = CH_3$

All these iodo derivatives, like several β-halo unsaturated carbonyl derivatives [11], were found to undergo a very efficient insertion of zinc metal into their carbon–iodine bonds, provided that the metal had been first activated with *ca.* 3.7 mol% of 1,2-dibromoethane and then with *ca.* 3.0 mol% of chlorotrimethylsilane [12] (eqn. (1) and Table 1).

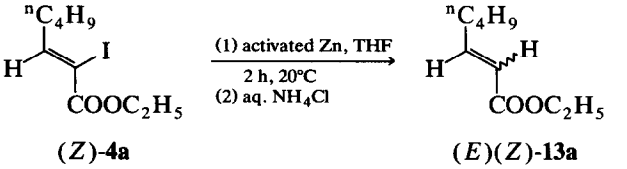


(**4**)



(*Z*)/(*E*)-**12** (1)

Thus, dropwise addition of a THF solution of compound (*Z*)-**4a** to a suspension of activated zinc dust (3 equiv.) at room temperature led to an exothermic reaction (the reaction temperature rose to *ca.* 45°C). After 2 h of stirring at room temperature, a GLC analysis of a hydrolyzed reaction aliquot showed that the iodo derivative had been completely consumed and also showed the presence of two compounds, subsequently identified as ethyl (*E*)- and (*Z*)-2-heptenoate, (*E*)- and (*Z*)-(**13a**), in a 79:21 molar ratio. We assumed that this ratio reflected the *Z*/*E* ratio of the organozinc reagent (*Z*)/(*E*)-(**12a**) formed in the insertion reaction (Entry 1, Table 1). The reaction mixture was then hydrolyzed to give compound (*E*)/(*Z*)-**13a** in 89.8% isolated yield (eqn. (2)).



(*Z*)-**4a** (*E*)(*Z*)-**13a** (2)

However, a stereoisomeric mixture of the organozinc reagent **12a**, in which the *Z*/*E* ratio was 76:24, was almost quantitatively obtained by reaction of a THF solution of (*Z*)-**4a** with activated zinc dust for 1.5 h at 20°C, followed by a period of 1 h to settle the reaction mixture (Entry 4, Table 1).

In a like manner, the other alkyl (*Z*)- or (*E*)-2-iodo-2-alkenoates, compounds (*Z*)-**4b**, (*E*)-**4b** and (*E*)-**4c** can be easily and quantitatively converted to stereoisomeric mixtures of the corresponding organozinc derivatives **12**. As shown in Table 1, the *Z*/*E* ratio of these reagents was found to be dependent on the experimental conditions employed for their preparation. In fact, the reaction between (*E*)-**4b** and activated zinc dust at 20°C for 2 h, followed by a period of 1 h to settle the excess of zinc, afforded (*Z*)- and (*E*)-(1-carbomethoxy-1-heptenyl)zinc iodide (**12b**) in a 49:51 molar ratio (Entry 2, Table 1). On the other hand, on increasing the reaction time between zinc dust and (*E*)-**4b** to 16 h, the *Z*/*E* ratio of the stereoisomeric mixture of **12b** was found to be 76:24 (Entry 3, Table 1). Moreover, when **12b** was obtained by reaction of (*Z*)-**4b** with activated zinc dust for 1 h at 40°C and then for 14 h at 20°C, it was a stereoisomeric mixture in which the *Z*/*E* ratio was still higher (87:13) (Entry 7, Table 1).

These last results show that when *Z*/*E* stereoisomeric mixtures of the reagents **12** are prepared from compounds (*Z*)-**4**, they are quite rich in the (*Z*)-stereoisomers and that when short reaction times are used, the stereochemistry of compounds (*E*)-**4** is determined in part by the stereochemistry of the corresponding organozinc derivatives.

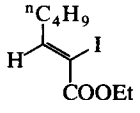
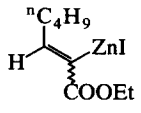
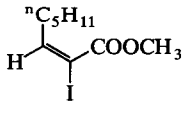
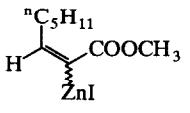
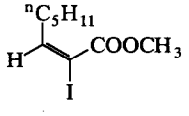
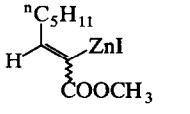
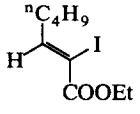
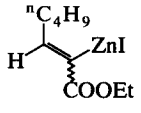
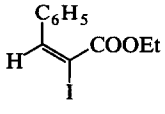
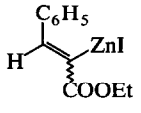
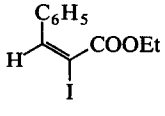
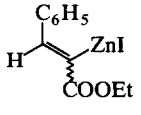
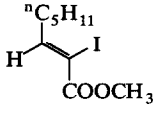
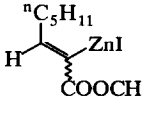
Finally, it was observed that the *Z*/*E* ratio for (1-carbethoxy-2-phenyl-1-ethenyl)zinc iodide (**12c**), which was prepared from (*E*)-**4c** using a long reaction time was 90:10 (Entries 5 and 6, Table 1).

All these results thus indicate that (*Z*)-(1-carbalkoxy-1-alkenyl)zinc iodides, (*Z*)-(**12**), like lithium (*Z*)-(1-carbalkoxy-1-alkenyl)methylcuprates, (*Z*)-(**6**) [8], are thermodynamically more stable than the corresponding (*E*)-stereoisomers.

With these new organozinc reagents, we next investigated their use in carbon–carbon bond-forming reactions and we found that compounds **12**, in the presence of 2 mol% of bis(dibenzylideneacetone)palladium(0), [$Pd(dba)_2$] [13], and 8 mol% of PPh_3, reacted with alkenyl or aryl bromides or iodides, which could contain alkoxycarbonyl, acetoxymethyl, methoxy or carbonyl groups, to give the corresponding cross-coupled products in quite good yields (Table 2) [14].

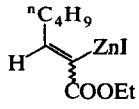
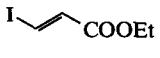
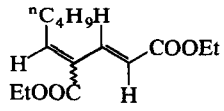
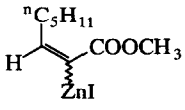
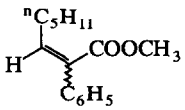
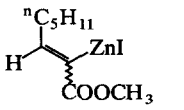
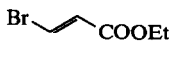
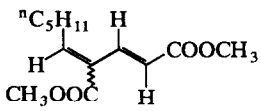
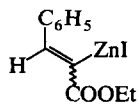
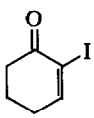
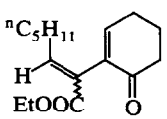
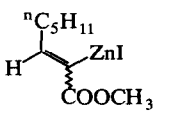
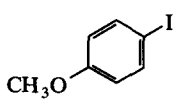
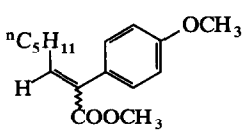
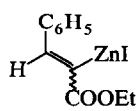
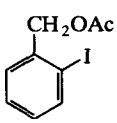
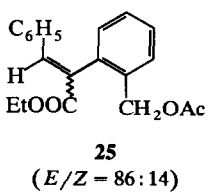
Thus, the reaction of a THF solution of the organozinc reagent (*Z*)/(*E*)-**12a** (*Z*/*E* = 76:24) with 0.8

TABLE 1. Preparation of (*Z*)/(*E*)(1-carbalkoxy-1-alkenyl)zinc iodides, (*Z*)/(*E*)-(**12**), from alkyl (*E*)- or (*Z*)-2-iodo-2-alkenoates, (*E*)- or (*Z*)-(**4**)[a]

Entry	Alkyl 2-iodo-2-alkenoate (**4**)	Reaction time/temperature (h/°C)	Organozinc derivative, (*Z*)/(*E*)-**12**	*Z*/*E* ratio [b]
1	 (*Z*)-**4a**	2/20	 (*Z*)/(*E*)-**12a**	79:21
2	 (*E*)-**4b**	2 + 1 [c]/20	 (*Z*)/(*E*)-**12b**	49:51
3	 (*E*)-**4b**	16 + 1 [c]/20	 (*Z*)/(*E*)-**12b**	76:24
4	 (*Z*)-**4a**	1.5 + 1 [c]/20	 (*Z*)/(*E*)-**12a**	76:24
5	 (*E*)-**4c**	17 + 1 [c]/20	 (*Z*)/(*E*)-**12c**	90:10
6	 (*E*)-**4c**	0.5/50, then 17 + 1 [c]/20	 (*Z*)/(*E*)-**12c**	90:10
7	 (*Z*)-**4b**	1/40, then 14 + 1 [c]/20	 (*Z*)/(*E*)-**12b**	87:13

[a] All reactions were carried out in THF, using 3 equiv. of activated zinc dust. The yields of these reactions, which were evaluated by GLC of hydrolyzed aliquots of the reactions mixtures, were almost quantitative. [b] It was assumed that the *Z*/*E* ratio of compounds **12** reflects the *E*/*Z* ratio of the corresponding alkyl 2-alkenoates, **13**, which were obtained by hydrolysis of **12**. [c] Time required to allow the reaction mixture to settle.

TABLE 2. Products obtained by the palladium(0)-catalyzed reaction of the organozinc reagents (*E*)/(*Z*)-**12** with alkenyl or aryl halides [a]

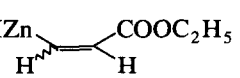
Entry	Organozinc reagent, **12**	Organic halide	Reaction time/temperature (h/°C)	Product [b]	Isolated yield [c]
1	 (*Z*)/(*E*)-**12a** (*Z*/*E* = 76:24)	 **14**	15/20	 **20** (2*E*,4*E*/2*E*,4*Z* = 77:23)	98.3
2	 (*Z*)/(*E*)-**12b** (*Z*/*E* = 49:51)	 **15**	4/20, then 12/20	 **21** (*E*/*Z* = 52:48)	99.2
3	 (*Z*)/(*E*)-**12b** (*Z*/*E* = 76:24)	 **16**	0.5/0, then 12/20	 **22** (2*E*,4*E*/2*E*,4*Z* = 78:22)	87.2
4	 (*Z*)/(*E*)-**12c** (*Z*/*E* = 90:10)	 **17**	20/20	 **23** (*E*/*Z* = 90:10)	63.7
5	 (*Z*)/(*E*)-**12b** (*Z*/*E* = 87:13)	 **18**	16/20	 **24** (*E*/*Z* = 92:8)	94.5
6	 (*Z*)/(*E*)-**12b** (*Z*/*E* = 90:10)	 **19**	16/20	 **25** (*E*/*Z* = 86:14)	96.0

[a] The reaction between the organozinc reagents **12** and the organic halides **14**–**19** (0.8 equiv.) was performed in the presence of 2 mol% of [$Pd(dba)_2$] and 8 mol% of PPh_3. [b] All *E*/*Z* ratios reported in parentheses are referred to crude reaction products. [c] Based on the amount of the organic halide used.

equiv. of a THF solution of ethyl (*E*)-3-iodo-2-propenoate (**14**) [15] at room temperature, in the presence of the above-mentioned catalyst system, gave in 98.3% isolated yield ethyl (2*E*,4*E*)- and (2*E*,4*Z*)-4-carbethoxy-2,4-nonadienoate (**20**) in a 77:23 molar ratio (Entry 1, Table 2). Moreover, under similar experimental conditions the organozinc reagent (*Z*)/(*E*)-**12b** was coupled with iodobenzene (**15**), methyl (*E*)-3-bromo-

2-propenoate (**16**) [16] and 4-methoxy-1-iodobenzene (**18**) to give stereoisomeric mixtures of the products **21**, **22** and **24** in 99.2, 87.2 and 94.5% isolated yields, respectively (Entries 2, 3 and 5, Table 2). Finally, the Pd^0-catalyzed reactions of compound (*Z*)/(*E*)-**12c** with 2-iodo-2-cyclohexenone (**17**) [17] and 2-acetoxymethyl-1-iodobenzene (**19**) [18] gave chemoselectively ethyl (*E*)/(*Z*)-2-(3-oxo-2-cyclohexen-2-yl)-3-phenyl-2-propenoate (**23**) [19] and ethyl (*E*)/(*Z*)-2-(2-acetoxymethylphenyl)-3-phenyl-2-propenoate (**25**) in 63.7 and 96.0% isolated yields, respectively (Entries 4 and 6, Table 2).

The collected data at Table 2 show several interesting features. First, the reactions between compounds **12a** and **12b** with the stereodefined alkenyl halides **14** and **16**, respectively, result in the cross-coupled products, **20** and **22**, respectively, which derive from retention of configuration with respect to the alkenyl–halogen bond. Second, although the Pd^0-catalyzed reaction summarized in Table 2 was carried out using a molar excess of compound (*Z*)/(*E*)-**12**, no data indicate a significantly higher reactivity of one of the stereoisomers of the compounds **12** towards the organic halides **14–18** in the reaction conditions employed. In fact, the stereoisomeric composition of the products **20–25** is similar to the initial *Z*/*E* ratio of the organozinc compounds from which they were derived. Thus, the behaviour of the reagents **12** is quite different from that observed for a stereoisomeric mixture of (2-carbethoxy-1-ethenyl)zinc iodide (**26**) in an analogous Pd^0-catalyzed cross-coupling reaction [11]. In fact, the reaction between (*E*)-1-iodo-1-octene and a molar excess of (*E*)/(*Z*)-**26** (*E*/*Z* = 11:89) in THF solution, in the presence of catalytic amounts of [$Pd(dba)_2$] and PPh_3 leads to stereoisomerically pure ethyl (2*Z*,4*E*)-2,4-nonadienoate, indicating a higher reactivity for the zinc organometallic (*Z*)-**26** [11].



(**26**)

In conclusion, a very efficient procedure for the preparation of (*Z*)/(*E*)(1-carbalkoxy-1-alkenyl)zinc iodides (**12**) has been developed. This is a new class of unmasked β-substituted acrylate α-anion equivalents. Moreover, it has been found that these reagents are able to react chemoselectively with various electrophiles in the presence of a Pd^0-catalyst system to give in high yields highly functionalized molecules containing trisubstituted double bonds. Unfortunately, this cross-coupling reaction lacks stereoselectivity. However, there is some compensation to this because when the organozinc reagents **12** were prepared from iodo derivatives **4** having (*Z*)-configuration, or when long reaction times were employed, their cross-coupled products are quite rich in the stereoisomers having trisubstituted double bonds of (*E*)-configuration.

3. Experimental details

Precoated silica gel plates Merck F-254 were used for thin-layer analytical chromatography. GLC analyses were performed on a Dani 6500 gas-chromatograph equipped with a Perkin-Elmer LCI-100 integrator. Two types of capillary column were used: a SE-30 bonded FSOT column (30 m × 0.25 mm i.d.) and a SRL-300 bonded FSOT column (30 m × 0.25 mm i.d.). Purifications by MPLC were performed on a Büchi 681 instrument, using a Bischoff 8100 differential refractometer as detector. GLC/MS analyses were performed using a VG 70-70E spectrometer interfaced with a Dani gas-chromatograph. ^1H NMR spectra were recorded in $CDCl_3$ solution 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 dinitrogen or argon. Air- and water-sensitive solutions were transferred with syringes or cannulas.

The following compounds were prepared according to the literature: ethyl (*E*)-3-iodo-2-propenoate (**14**) [15], methyl (*E*)-3-bromo-2-propenoate (**16**) [16], 2-acetoxymethyl-1-iodobenzene (**19**) [18], ethyl 3-phenyl-2-propynoate [20], $Pd(dba)_2$ [13], and $Pd(PPh_3)_4$ [21].

3.1. Methyl (E)-2-tributylstannyl-2-octenoate (E)(3a)

A de-areated solution of Bu_3SnH (18.85 g, 64.86 mmol) in THF (55 ml) was added during 2 h to a solution of methyl 2-octynoate (10.0 g, 64.86 mmol) and [$Pd(PPh_3)_4$] (1.49 g, 1.29 mmol) in THF (55 ml), which was stirred at room temperature under argon. After stirring for 4 h, THF was removed *in vacuo* and the residue was diluted with hexane (800 ml). After 1 h the mixture was filtered through Celite and the filtrate was concentrated *in vacuo*. GLC/MS analysis of the residue showed the presence of two compounds in a *ca* 92:8 molar ratio. This residue was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (99:1) as eluant, to give compound (*E*)-**3a** (24.5 g, 85% yield) as a colourless liquid. ^1H NMR: δ 6.05 (1H, t, *J* = 7.1 Hz, H-3); 3.69 (3H, s, OCH_3); 2.41 (2H, *pseudo*-q, *J* = 7.1 Hz, H-4); 1.65–1.13 (18H, m, H-2′, H-3′, H-5, H-6 and H-7); 1.10–0.75 (18H, m, H-4′, H-1′ and H-8). MS: *m*/*z* (%) 393 (16), 391 (15), 390 (16), 389 (100), 388 (40), 387 (74), 385 (40), 357 (15), 265 (9), 179 (13), 151 (20), 121 (6). Anal. Found: C, 56.74; H, 9.70. $C_{21}H_{42}O_2Sn$ calc.: C, 56.64; H, 9.51%. GLC and ^1H NMR analyses showed that compound (*E*)-**3a** had chemical and stereoisomeric purity higher than 99%.

By comparison of the ^1H NMR spectrum of this compound with that of the above residue it was possible to obtain the ^1H NMR parameters of the minor component of the reaction mixture. This corresponded to methyl (*E*)-3-tributylstannyl-2-octenoate. ^1H NMR: δ 5.94 (1H, t, $J = 1.2$ Hz, H-2); 3.68 (3H, s, OCH_3); 2.87 (2H, br t, $J = 6.9$ Hz, H-4); 1.68–1.16 (18H, m, H-2′, H-3′, H-5, H-6, and H-7); 1.13–0.77 (18H, m, H-4′, H-1′, and H-8). MS: *m/z* (%) 393 (17), 391 (16), 390 (18), 389 (100), 388 (40), 387 (73), 385 (42), 333 (15), 277 (13), 177 (9), 151 (11).

3.2. *Ethyl (E)-3-phenyl-2-tributylstannyl-2-propenoate (E)-(**3b**)*

Bu_3SnH (20.04 g, 68.96 mmol) and ethyl 3-phenyl-2-propynoate (12.0 g, 68.96 mmol) were reacted in THF solution, in the presence of $[Pd(PPh_3)_4]$ (1.66 g, 1.44 mmol) using the procedure employed for the synthesis of compound (*E*)-**3a**. The crude reaction product was analyzed by GLC/MS analysis and showed the presence of two compounds in a *ca.* 90:10 molar ratio. Purification by MPLC on silica gel, using a mixture of benzene and hexane (70:30) as eluant yielded the main component, (*E*)-**3b** (22.7 g, 71% yield) as a colourless liquid. ^1H NMR: δ 7.48–7.13 (5H, m, C_6H_5); 6.71 (1H, s, H-3); 4.18 (2H, q, $J = 7.1$ Hz, OCH_2); 1.78–1.26 (12H, m, H-2′ and H-3′); 1.22 (3H, t, $J = 7.1$ Hz, O–C–CH_3); 1.07 (6H, t, $J = 8.1$ Hz, H-1′); 0.91 (9H, t, $J = 7.1$ Hz, H-4′). MS: *m/z* (%) 409 (100), 407 (73), 406 (33), 405 (44), 365 (17), 295 (27), 293 (20), 251 (48), 249 (40), 247 (24), 237 (26), 235 (19), 179 (93), 178 (26), 177 (91), 176 (32), 175 (62), 165 (96), 163 (73), 161 (46), 121 (66), 91 (38), 57 (29). Anal. Found: C, 59.60; 8.36. $C_{23}H_{38}O_2Sn$ calc.: C, 59.40; H, 8.23%. GLC showed that compound (*E*)-**3b** had chemical purity higher than 98%.

By comparison of its ^1H NMR spectrum with that of the crude reaction mixture, it was possible to obtain the ^1H NMR parameters of the minor component. This corresponded to ethyl (*E*)-3-tributylstannyl-3-phenyl-2-propenoate. ^1H NMR: δ 7.43–6.85 (5H, m, C_6H_5); 6.12 (1H, s, H-3); 3.98 (2H, q, $J = 7.1$ Hz, OCH_2); 1.65–1.15 (12H, m, H-2′ and H-3′); 1.04 (3H, t, $J = 7.1$ Hz, O–C–CH_3); 1.00–0.70 (15H, m, H-1′ and H-4′). MS: *m/z* (%) 409 (62), 408 (27), 407 (49), 406 (17), 405 (25), 353 (6), 291 (13), 267 (16), 223 (20), 221 (15), 179 (72), 177 (90), 175 (66), 147 (46), 137 (38), 135 (29), 133 (23), 131 (23), 121 (64), 120 (54), 116 (38), 103 (100), 102 (30), 91 (26), 77 (20), 57 (15).

3.3. *Methyl (E)-2-iodo-2-octenoate (E)-(**4b**)*

A solution of iodine (10.37 g, 40.8 mmol) in dry CH_2Cl_2 (400 ml) was added during 3.5 h to a solution of compound (*E*)-**3a** (18.17 g, 40.8 mmol) in dry CH_2Cl_2 (250 ml), which was stirred at room temperature under argon. Upon completion of the addition, the reaction mixture was stirred for an additional 2 h and concentrated *in vacuo*. The residue was diluted with Et_2O (300 ml) and stirred with a semisaturated aqueous KF solution (300 ml) at room temperature for 2.5 h. The reaction mixture was filtered and the filtrate was extracted with Et_2O. The organic extract was dried and concentrated *in vacuo* and the residue was purified by MPLC on silica gel, using a mixture of hexane and benzene (85:15) as eluant to give stereoisomerically pure (*E*)-**4b** (8.40 g, 73% yield) as a pale yellow liquid. ^1H NMR: δ 6.92 (1H, t, $J = 7.7$ Hz, H-3); 3.79 (3H, s, OCH_3); 2.46 (2H, *pseudo*-q, $J = 7.7$ Hz, H-4); 1.50–1.20 (6H, m, H-5, H-6 and H-7); 0.89 (3H, t, $J = 6.4$ Hz, H-8). MS: *m/z* (%) 283 ($M^+ + 1$, 11), 282 (M^+, 100), 239 (67), 213 (40), 211 (20), 181 (20), 155 (15), 112 (22), 95 (78), 81 (25). Anal. Found: C, 38.59; H, 5.56. $C_9H_{15}IO_2$ calc.: C, 38.32; H, 5.36%.

3.4. *Ethyl (E)-2-iodo-3-phenyl-2-propenoate (E)-(**4c**)*

This stereoisomerically pure compound was synthesised in 89% yield starting from compound (*E*)-**3b**, *via* a procedure very similar to that employed for the preparation of (*E*)-**4b**. ^1H NMR: δ 7.49 (1H, s, H-3); 7.45–7.12 (5H, m, C_6H_5); 4.19 (2H, q, $J = 7.1$ Hz, OCH_2); 1.17 (3H, t, $J = 7.1$ Hz, CH_3). MS: *m/z* (%) 303 ($M^+ + 1$, 17), 302 (M^+, 50), 257 (21), 175 (65), 147 (93), 129 (20), 103 (33), 102 (100), 77 (20), 76 (21), 51 (20). Anal. Found: C, 44.07; H, 3.85. $C_{11}H_{11}IO_2$ calc.: C, 43.73; H. 3.67%.

3.5. *Ethyl (Z)-2-iodo-2-heptenoate (Z)-(**4a**)*

A 1.76 M hexane solution of BuLi (227 ml, 0.40 mol) was added slowly to a suspension of CuI (38.09 g, 0.20 mol) in THF (700 ml) cooled to −10°C. The reaction mixture was then cooled to −78°C and a solution of ethyl propiolate (18.6 g, 0.19 mol) in THF (70 ml) was added. After stirring for 4 h at −78°C, iodine (101.5 g, 0.40 mol) was added and the resulting mixture was stirred for 1 h at −78°C and then allowed to warm to −20°C during 14 h. Triethyl phosphite (20 ml, 0.12 mol) and a saturated aqueous NH_4Cl solution (150 ml) were added consecutively and the resulting mixture was poured into a large excess of stirred water. This caused the precipitation of a white solid. The mixture was filtered and the filtrate was extracted with Et_2O. The organic extract was washed with water, dried, filtered and concentrated *in vacuo*. The residue was purified by MPLC on silica gel, using a mixture of hexane and benzene (90:10) as eluant, to give compound (*Z*)-**4a** (39.02 g, 72.8% yield) as a pale yellow liquid. ^1H NMR: δ 7.20 (1H, t, $J = 7.1$ Hz, H-3); 4.26 (2H, q, $J = 7.1$ Hz, OCH_2); 2.32 (2H, *pseudo*-q, $J = 7.1$

Hz, H-4); 1.55–1.40 (4H, m, H-5 and H-6); 1.33 (3H, t, $J = 7.1$ Hz, O–C–CH_3); 0.94 (3H, t, $J = 7.1$ Hz, H-7). MS: *m/z* (%) 283 ($M^+ + 1$, 11), 282 (M^+, 100), 254 (12), 253 (15), 239 (24), 227 (44), 226 (15), 225 (29), 211 (16), 199 (37), 198 (30), 181 (20), 127 (16), 109 (19), 84 (12), 81 (46), 68 (17), 56 (19), 55 (14), 53 (12), 41 (14). Anal. Found: C, 38.17; H, 5.42. $C_9H_{15}IO_2$ calc.: C, 38.32; H, 5.36%.

*3.6. Methyl (Z)-2-iodo-2-octenoate (Z)-(**4b**)*

This compound was prepared in 70% yield from lithium dipentylcuprate and methyl propiolate using a procedure very similar to that employed to prepare compound (*Z*)-**4a**. ^1H NMR: δ 7.22 (1H, t, $J = 7.1$ Hz, H-3); 3.82 (3H, s, OCH_3); 2.31 (2H, *pseudo*-q, $J = 7.1$ Hz, H-4); 1.65–1.41 (2H, m, H-5); 1.43–1.25 (4H, m, H-6 and H-7); 0.91 (3H, t, $J = 6.7$ Hz, H-8). The MS spectrum of this substance, which had chemical and stereoisomerical purity higher than 99%, was very similar to that of (*E*)-**4b**. Anal. Found: C, 38.48; H, 5.40. $C_9H_{15}IO_2$ calc.: C, 38.32; H, 5.36%.

*3.7. 2-Iodo-2-cyclohexenone (**17**)*

A solution of iodine (5.07 g, 20 mmol) in a mixture of CCl_4 and pyridine (1 : 1) (40 ml) was dropwise added under argon to a solution of 2-cyclohexenone (0.96 g, 10 mmol) in a mixture of CCl_4 and pyridine (1 : 1) (35 ml) maintained at 0°C. The mixture was stirred for 2 h at room temperature, diluted with Et_2O and washed successively with water, 1 N HCl, water and 20% aqueous $Na_2S_2O_3$. It was then dried, filtered and concentrated *in vacuo*. The colourless solid residue was crystallized from a mixture of pentane and Et_2O to give 99% chemically pure **17** (1.99 g, 89.6% yield); m.p. 47.5–48°C (Lit. [17] m.p. 48–48.5°C). ^1H NMR: δ 7.78 (1H, t, $J = 4.5$ Hz, H-3); 2.67 (2H, t, $J = 6.8$ Hz, H-6); 2.45 (dt, $J = 5.8$ and 4.5 Hz, H-4); 2.20–2.00 (2H, m, H-5).

*3.8. General procedure for the preparation of (Z) / (E)-(1-carbalkoxy-1-alkenyl)zinc iodides (Z) / (E)-(**12**)*

A suspension of zinc dust (3.47 g, 53.1 mmol) in THF (4 ml) containing 1,2-dibromoethane (0.38 g, 2.0 mmol) was heated with stirring to 65°C for 1 min and cooled to room temperature. Chlorotrimethylsilane (0.2 ml, 1.6 mmol) was then added. After 15 min at 20°C, a solution of an alkyl (*Z*)- or (*E*)-2-iodo-2-alkenoate, (*Z*)- or (*E*)-(**4**) (17.7 mmol) in THF (15 ml) was added dropwise and the mixture was stirred at the temperature and for the time reported in Table 1. THF (50 ml) was then added and the mixture was allowed to settle for 1 h. Finally, the clear solution of the organozinc derivative (*Z*)/(*E*)-**12** so obtained was transferred *via* syringe to a new reaction flask. GLC/MS analysis of a hydrolyzed aliquot of this solution showed that compounds (*Z*)- or (*E*)-**4** had been completely consumed and allowed to determine the *Z*/*E* ratio of compounds **12**. Moreover, a comparison between the retention times and the MS spectra of alkyl (*E*)- and (*Z*)-2-alkenoates (**13**) present in this aliquot with those of authentic samples of these esters confirmed the structure and stereochemistry of these compounds.

The stereoisomeric composition of compounds (*Z*)/(*E*)-**12a–c** prepared according to this general procedure is reported in Table 1.

*3.9. Ethyl (E) / (Z)-2-heptenoate (E)(Z)-(**13a**)*

A THF solution of ethyl (*Z*)-2-iodo-2-heptenoate, (*Z*)-(**4a**) (17.7 mmol) was allowed to react with activated zinc dust by the general procedure reported above. After stirring for 2 h the mixture, which contained (*Z*)/(*E*)(1-carbethoxy-1-hexenyl)zinc iodide (**12a**), was poured into an excess of a cold saturated aqueous NH_4Cl solution and extracted with Et_2O. The organic phase was dried, filtered and concentrated *in vacuo*. Fractional distillation of the residue gave compound (*E*)/(*Z*)-**13a** (2.48 g, 89.8% yield), b.p. 84–85°C/10 Torr (Lit. [22] 58–58.8°C/3 Torr). ^1H NMR analysis of the fractions of the distillation allowed elucidation of the ^1H NMR parameters of the two stereoisomers. Compound (*Z*)-**13a** had: ^1H NMR: δ 6.21 (1H, dt, $J = 11.5$ and 7.4 Hz, H-3); 5.75 (1H, dt, $J = 11.5$ and 1.6 Hz, H-2); 4.17 (2H, q, $J = 7.1$ Hz, OCH_2); 2.65 (2H, *pseudo*-qd, $J = 7.4$ and 1.6 Hz, H-4); 1.52–1.28 (4H, m, H-5 and H-6); 1.29 (3H, t, $J = 7.1$ Hz, O–C–CH_3); 0.91 (3H, t, $J = 7.0$ Hz, H-7). Compound (*E*)-**13a** had: ^1H NMR: δ 6.97 (1H, dt, $J = 15.6$ and 7.1 Hz, H-3); 5.81 (1H, dt, $J = 15.6$ and 1.5 Hz, H-2); 4.18 (2H, q, $J = 7.1$ Hz, OCH_2); 2.23 (2H, *pseudo*-qd, $J = 7.1$ and 1.5 Hz, H-4); 1.52–1.28 (4H, m, H-5 and H-6); 1.29 (3H, t, $J = 7.1$ Hz, O–C–CH_3); 0.91 (3H, t, $J = 7.0$ Hz, H-7).

*3.10. Ethyl (2E,4E)- and (2E,4Z)-4-carbethoxy-2,4-nonadienoate, (2E,4E)- and (2E,4Z)-(**20**)*

A solution of ethyl (*E*)-3-iodo-2-propenoate (**14**) (5.95 g, 26.32 mmol), [Pd(dba)$_2$] (378 mg, 0.66 mmol) and PPh_3 (690 mg, 2.63 mmol) in THF (15 ml), which was prepared immediately prior to use, was added to a 0.25 M THF solution of (*Z*)/(*E*)(1-carbethoxy-1-hexenyl)zinc iodide (**12a**) (32.9 mmol) (*Z*/*E* = 76 : 24) and the resulting mixture was stirred at room temperature for 15 h (Entry 1, Table 2). It was then diluted with Et_2O and washed with an aqueous NH_4Cl solution. The organic phase was dried, filtered, and concentrated *in vacuo*. GLC/MS analysis of the residue showed the presence of two compounds, subsequently identified as (2E,4E)- and (2E,4Z)-**20** in a 77 : 23 molar

ratio. This residue was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (93:7) as eluant, to give chemically pure (2*E*,4*E*)- and (2*E*,4*Z*)-**20** (6.58 g, 98.3% yield). Compound (2*E*,4*E*)-**20** was present mainly in the first eluted chromatographic fractions. ^1H NMR: δ 7.54 (1H, d, J = 16.1 Hz, H-3); 7.03 (1H, t, J = 7.8 Hz, H-5); 6.51 (1H, d, J = 16.1 Hz, H-2); 4.26 (2H, q, J = 7.1 Hz, OCH_2); 4.24 (2H, q, J = 7.1 Hz, OCH_2); 2.42 (2H, *pseudo*-q, J = 7.8 Hz, H-6); 1.60–1.20 (4H, m, H-7 and H-8); 1.33 (3H, t, J = 7.1 Hz, O–C–CH_3); 1.31 (3H, t, J = 7.1 Hz, O–C–CH_3); 0.93 (3H, t, J = 7.1 Hz, H-9). MS: m/z (%) 254 (M^+, 22), 209 (53), 208 (54), 197 (48), 180 (35), 153 (39), 138 (58), 125 (68), 123 (49), 107 (70), 79 (81), 77 (43), 68 (58), 65 (63), 53 (42), 41 (100). Anal. Found: C, 66.21; H, 8.95. $C_{14}H_{22}O_4$ calc.: C, 66.12; H, 8.72%. Compound (2*E*,4*Z*)-**20** was mainly present in the last eluted chromatographic fractions. ^1H NMR: δ 7.27 (1H, d, J = 15.9 Hz, H-3); 6.30 (1H, t, J = 7.8 Hz, H-5); 6.02 (1H, d, J = 15.9 Hz, H-2); 4.31 (2H, q, J = 7.1 Hz, OCH_2); 4.21 (2H, q, J = 7.1 Hz, OCH_2); 2.39 (2H, *pseudo*-q, J = 7.8 Hz, H-6); 1.50–1.23 (4H, m, H-7 and H-8); 1.35 (3H, t, J = 7.1 Hz, O–C–CH_3); 1.29 (3H, t, J = 7.1 Hz, O–C–CH_3); 0.91 (3H, t, J = 7.0 Hz, H-9). MS: m/z (%) 254 (M^+, 40), 209 (93), 208 (100), 197 (66), 180 (50), 179 (45), 153 (52), 151 (49), 137 (76), 125 (81), 123 (55), 107 (72), 97 (51), 79 (77), 67 (49), 65 (52), 55 (48), 41 (80). Anal. Found: C, 65.80; H, 9.01. $C_{14}H_{22}O_4$ calc.: C, 66.12; H, 8.72%.

3.11. Methyl (E)- and (Z)-2-phenyl-2-octenoate, (E)- and (Z)-(21)

Iodobenzene (**15**) (0.95 ml, 8.50 mmol) was allowed to react with a 0.25 M THF solution of (*Z*)/(*E*)(1-methoxycarbonyl-1-heptenyl)zinc iodide (**12b**) (10.63 mmol) (*Z*/*E* = 49:51) using experimental conditions similar to those employed for the synthesis of (2*E*,4*E*)- and (2*E*,4*Z*)-**20** (Entry 2, Table 2). After the usual work-up, a GLC/MS analysis of the crude reaction mixture showed the presence of two compounds, subsequently identified as (*Z*)- and (*E*)-**21**, in a 48:52 molar ratio. This mixture was purified by MPLC on silica gel, using a mixture of hexane and benzene (70:30) as eluant. Concentration of the first fractions yielded compound (*Z*)-**21** (0.96 g, 48.6% yield). ^1H NMR: δ 7.35–7.23 (5H, m, C_6H_5); 6.18 (1H, t, J = 7.6 Hz, H-3); 3.79 (3H, s, OCH_3); 2.44 (2H, *pseudo*-q, J = 7.6 Hz, H-4); 1.60–1.20 (6H, m, H-5, H-6 and H-7); 0.90 (3H, t, J = 6.9 Hz, H-8). MS: m/z (%) 233 (M^+ + 1, 18), 232 (M^+, 95), 201 (11), 189 (19), 163 (18), 162 (100), 158 (58), 129 (45), 115 (70), 104 (40), 91 (32), 77 (10), 59 (8). Anal. Found: C, 77.87; H, 8.75. $C_{15}H_{20}O_2$ calc.: C, 77.55; H, 8.68%. Concentration of the last fractions allowed the isolation of 99% stereoisomerically pure (*E*)-**21** (1.0 g, 50.6% yield). ^1H NMR: δ 7.45–7.05 (5H, m, C_6H_5); 7.08 (1H, t, J = 7.7 Hz, H-3); 3.72 (3H, s, OCH_3); 2.07 (2H, *pseudo*-q, J = 7.7 Hz, H-4); 1.50–1.15 (6H, m, H-5, H-6 and H-7); 0.84 (3H, t, J = 6.6 Hz, H-8). MS: m/z (%) 233 (M^+ + 1, 5), 232 (M^+, 28), 189 (6), 162 (39), 157 (20), 129 (38), 117 (33), 116 (32), 115 (100), 103 (41), 91 (36), 77 (18), 63 (11), 41 (34). Anal. Found: C, 77.77; H, 8.90. $C_{15}H_{20}O_2$ calc.: C, 77.55; H, 8.68%.

3.12. Methyl (2E,4E)- and (2E,4Z)-4-methoxycarbonyl-2,4-decadienoate, (2E,4E)- and (2E,4Z)-(22)

Methyl (*E*)-3-bromo-2-propenoate (**16**) (2.33 g, 14.17 mmol) was allowed to react with a 0.26 M THF solution of (*Z*)/(*E*)(1-methoxycarbonyl-1-heptenyl)zinc iodide (**12b**) (17.72 mmol) (*Z*/*E* = 76:24) using experimental conditions similar to those employed for the synthesis of (2*E*,4*E*)- and (2*E*,4*Z*)-**20** (Entry 3, Table 2). After the usual work-up, a GLC/MS analysis of the crude reaction mixture showed the presence of two compounds, subsequently identified as (2*E*,4*Z*)- and (2*E*,4*E*)-**22**, in a 22:78 molar ratio. Purification by MPLC on silica gel, using a mixture of hexane and Et_2O (93:7) as eluant gave chemically pure (2*E*,4*E*)- and (2*E*,4*Z*)-**22** (2.97 g, 87.2% yield). Compound (2*E*,4*E*)-**22** was mainly in the first fractions. ^1H NMR: δ 7.54 (1H, d, J = 16.1 Hz, H-3); 7.06 (1H, t, J = 7.7 Hz, H-5); 6.52 (1H, d, J = 16.1 Hz, H-2); 3.79 (3H, s, OCH_3); 3.78 (3H, s, OCH_3); 2.41 (2H, *pseudo*-q, J = 7.7 Hz, H-6); 1.60–1.20 (6H, m, H-7, H-8 and H-9); 0.90 (3H, t, J = 6.8 Hz, H-10). MS: m/z (%) 240 (M^+, 42), 209 (50), 208 (73), 169 (64), 153 (41), 140 (33), 139 (100), 137 (38), 111 (48), 79 (36), 59 (49), 41 (29). Anal. Found: C, 64.68; H, 8.69. $C_{13}H_{20}O_4$ calc.: C, 64.98; H, 8.39%.

Compound (2*E*,4*Z*)-**22** was mainly in the last fractions. ^1H NMR: δ 7.29 (1H, d, J = 15.9 Hz, H-3); 6.35 (1H, t, J = 7.8 Hz, H-5); 6.03 (1H, d, J = 15.9 Hz, H-2); 3.83 (3H, s, OCH_3); 3.76 (3H, s, OCH_3); 2.40 (2H, *pseudo*-q, J = 7.8 Hz, H-6); 1.60–1.20 (6H, m, H-7, H-8 and H-9); 0.89 (3H, t, J = 6.2 Hz, H-10). The MS spectrum of this compound is very similar to that of the corresponding (2*E*,4*E*)-stereoisomer. Anal. Found: C, 64.88; H, 8.41. $C_{13}H_{20}O_4$ calc.: C, 64.98; H, 8.39%.

3.13. Ethyl (E)- and (Z)-2-(3-oxo-2-cyclohexen-2-yl)-3-phenyl-2-propenoate, (E)- and (Z)-(23)

2-Iodo-2-cyclohexenone (**17**) (2.25 g, 9.48 mmol) was allowed to react with a 0.33 M THF solution of (*Z*)/(*E*)(1-carbethoxy-2-phenyl-1-ethenyl)zinc iodide (**12c**) (11.85 mmol) (*Z*/*E* = 90:10) using experimental conditions similar to those employed for the synthesis of (2*E*,4*E*)- and (2*E*,4*Z*)-**20** (Entry 4, Table 2). GLC/MS analysis of the crude reaction product

showed the presence of two compounds, subsequently identified as (*E*)- and (*Z*)-**23**, in a 90:10 molar ratio. This crude product was purified by MPLC on silica gel using a mixture of hexane and Et_2O (70:30) as eluant to give chemically pure (*E*)- and (*Z*)-**23** (1.63 g, 63.8% yield). Stereoisomerically pure (*E*)-**23** was isolated from the first fractions. ^1H NMR: δ 7.78 (1H, s, H-3); 7.24–7.06 (5H, m, C_6H_5); 6.73 (1H, t, $J = 4.2$ Hz, H-1′); 4.21 (2H, q, $J = 7.1$ Hz, OCH_2); 2.56 (2H, t, $J = 6.7$ Hz, H-4′); 2.38 (2H, *pseudo*-q, $J = 5.4$ Hz, H-6′); 2.09–2.00 (2H, m, H-5′); 1.28 (3H, t, $J = 7.1$ Hz, O–C–CH_3). MS: *m/z* (%) 271 ($M^+ + 1$, 19), 270 (M^+, 100), 241 (11), 225 (25), 197 (92), 169 (25), 141 (34), 115 (26), 91 (15), 77 (12), 55 (15), 41 (16). Anal. Found: C, 75.39; H, 6.90. $C_{17}H_{18}O_3$ calc.: C, 75.54; H, 6.71%.

Compound (*Z*)-**23** was present in the last fractions. ^1H NMR: δ 7.29 (5H, br s, C_6H_5); 7.12 (3H, t, $J = 4.3$ Hz, H-1′); 6.94 (1H, s, H-3); 4.14 (2H, q, $J = 7.1$ Hz, OCH_2); 2.60–2.40 (4H, m, H-4′ and H-6′); 2.15–1.96 (2H, m, H-5′); 1.10 (3H, t, $J = 7.1$ Hz, O–C–CH_3). MS: *m/z* (%) 271 ($M^+ + 1$, 19), 270 (M^+, 100), 241 (11), 225 (28), 197 (94), 169 (26), 141 (36), 115 (28), 86 (52), 84 (82), 69 (18), 47 (19). Anal. Found: C, 75.82; H, 6.91. $C_{17}H_{18}O_3$ calc.: C, 75.54; H, 6.71%.

3.14. Methyl (E)- and (Z)-2-(4-methoxyphenyl)-2-octenoate, (E)- and (Z)-24

4-Methoxy-1-iodobenzene (**18**) (2.94 g, 12.56 mmol) was allowed to react with a 0.4 M THF solution of (*Z*)/(*E*)(1-carbomethoxy-1-heptenyl)zinc iodide (**12b**) (15.57 mmol) (*Z*/*E* = 87:13) using experimental conditions similar to those employed for the synthesis of (2*E*,4*E*)- and (2*E*,4*Z*)-**20** (Entry 5, Table 2). GLC analysis of the crude reaction product showed the presence of two compounds, subsequently identified as (*E*)- and (*Z*)-**24**, in a 92:8 molar ratio. This crude product was purified by MPLC on silica gel, using benzene and hexane (70:30) as eluant, to give chemically pure (*E*)- and (*Z*)-**24** (3.11 g, 94.5% yield). Compound (*Z*)-**24** was present in the first fractions. ^1H NMR: δ 7.23 (2H, d, $J = 8.8$ Hz, H-2′ or H-3′); 6.85 (2H, d, $J = 8.8$ Hz, H-3′ or H-2′); 6.10 (1H, t, $J = 7.6$ Hz, H-3); 3.79 (6H, s, OCH_3 and $COOCH_3$); 2.40 (2H, *pseudo*-q, $J = 7.6$ Hz, H-4); 1.58–1.10 (6H, m, H-5, H-6 and H-7); 0.90 (3H, t, $J = 6.8$ Hz, H-8). MS: *m/z* (%) 263 ($M^+ + 1$, 18), 262 (M^+, 100), 230 (8), 203 (30), 192 (70), 187 (15), 173 (12), 159 (20), 147 (25), 145 (61), 133 (25), 121 (30).

Concentration of the last fractions yielded stereoisomerically pure (*E*)-**24** (2.39 g). ^1H NMR: δ 7.10 (d, 2H, $J = 8.9$ Hz, H-2′ or H-3′); 7.04 (1H, t, $J = 7.6$ Hz, H-3); 6.91 (d, 2H, $J = 8.9$ Hz, H-3′ or H-2′); 3.81 (3H, s, OCH_3 or $COOCH_3$); 3.72 (3H, s, $COOCH_3$ or OCH_3); 2.09 (2H, *pseudo*-q, $J = 7.6$ Hz, H-4); 1.52–1.14 (6H, m, H-5, H-6 and H-7); 0.85 (3H, t, $J = 6.8$ Hz, H-8). MS: *m/z* (%) 263 ($M^+ + 1$, 18), 262 (M^+, 100), 230 (8), 203 (30), 192 (73), 187 (17), 173 (12), 159 (18), 147 (25), 145 (62), 133 (27), 121 (30). Anal. Found: C, 72.85; H, 8.11. $C_{16}H_{22}O_3$ calc.: C, 73.25; H, 8.45%.

3.15. Ethyl (E)- and (Z)-2-(2-acetoxymethylphenyl)-3-phenyl-2-propenoate, (E)- and (Z)-(25)

2-Acetoxymethyl-1-iodobenezene (**19**) (2.62 g, 9.48 mmol) was allowed to react with a 0.33 M THF solution of (*Z*)(*E*)-(1-carbethoxy-2-phenyl-1-ethenyl)zinc iodide (**12c**) (11.85 mmol) (*Z*/*E* = 90:10) using experimental conditions similar to those employed for the synthesis of (2*E*,4*E*)- and (2*E*,4*Z*)-**20** (Entry 6, Table 2). GLC/MS analysis of the crude reaction product showed the presence of two compounds, subsequently identified as (*E*)- and (*Z*)-**25**, in a 86:14 molar ratio. This crude product was then purified by MPLC on silica gel, using a mixture of hexane and Et_2O (80:20) as eluant, to give chemically pure (*E*)- and (*Z*)-**25** (2.95 g, 96% yield). Compound (*Z*)-**25** was in the first fractions. ^1H NMR: δ 7.55–7.20 (9H, m, aromatic protons); 6.85 (1H, s, H-3); 5.21 (2H, s, Ar–CH_2–OCO); 4.14 (2H, q, $J = 7.1$ Hz, =C–COO–CH_2); 2.06 (3H, s, $COCH_3$); 1.11 (3H, t, $J = 7.1$ Hz, O–C–CH_3). MS: *m/z* (%) 234 (M^+, 7), 264 (43), 236 (22), 191 (100), 165 (12), 135 (7), 115 (10), 91 (18), 43 (56).

Compound (*E*)-**25** was in the last fractions. ^1H NMR: δ 7.90 (1H, s, H-3); 7.54–6.92 (9H, m, aromatic protons); 4.94 (2H, d, $J = 4.0$ Hz, Ar–CH_2–OCO); 4.24 (2H, q, $J = 7.1$ Hz, =C–COO–CH_2); 1.80 (3H, s, $COCH_3$); 1.26 (3H, t, $J = 7.1$ Hz, O–C–CH_3). MS: *m/z* (%) 324 (M^+, 8), 264 (54), 236 (24), 191 (100), 165 (10), 115 (8), 91 (12), 43 (43). Anal. Found: C, 73.78; H, 6.14. $C_{20}H_{20}O_4$ calc.: C, 74.06; H, 6.21%.

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