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TETRAHEDRON

A New Synthesis of Fungicidal Methyl (*E*)-3-Methoxypropenoates

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Abstract : Several structural analogues of strobilurin A having general formula (*E*)-**18**, in which the methyl (*E*)-3-methoxypropenoate unit is linked to substituted aromatic, alkenyl or cyclopentenyl substrates, have been efficiently and selectively prepared by Pd-catalyzed cross-coupling reactions between (*Z*)-2-methoxy-1-(methoxycarbonyl)ethenylzinc halides, (*Z*)-**19**, and aryl halides, alkenyl halides or triflates or cyclopentenyl triflates, respectively. Compounds (*Z*)-**19**, which represent a new class of highly functionalized and stereodefined organozinc derivatives, have been synthesized in very high yield by reaction of THF solutions of easily available methyl (*Z*)-2-iodo- or (*Z*)-2-bromo-3-methoxypropenoate, (*Z*)-**8** and (*Z*)-**12**, respectively, with an activated Zn/Ag couple in the presence of TMEDA. Compounds (*E*)-**18** synthesized according to this procedure include substances which are known to be able to control agrochemically important fungi as well as derivatives which are able to inhibit the growth of fungi which deteriorate papery materials.

Strobilurins, **1**, are metabolites isolated from basidiomycetes which inhibit mitochondrial respiration and, as a result, have fungicidal activity.[1] These compounds which cannot be used directly because of insufficient levels of activity, volatility and photochemical instability, served as leads for the development of a new class of fungicides for crop protection which are characterized by direct attachment of the methyl (*E*)-3-methoxypropenoate unit, **2**, to a substituted aromatic or heteroaromatic ring.[1c,2,3] The broad-spectrum systemic fungicide *Azoxystrubin* (formerly ICIA 5504), **3**, to be sold by Zeneca as *Amystar* or *Quadris*, represents one of the most significant examples among the structural analogues of strobilurin A, **1** (X = H), since it is able to control the four major classes of fungi which affect crops.[4] In the last six years several other agrochemical companies have published patent applications which claim double bond locked analogues of strobilurin A, which are characterized by the methyl (*E*)-3-methoxypropenoate unit or the isosteric methyl (*E*)-O-methyloximinoacetate group, **4**, as fungicides for use in agricolture and the research in this very promising area of chemistry is still intense.

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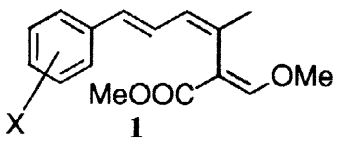
PII: S0040-4020(98)00393-7



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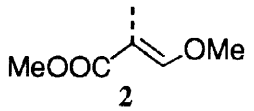

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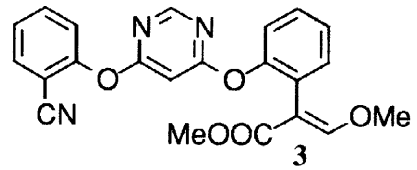

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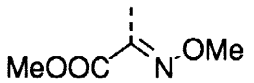
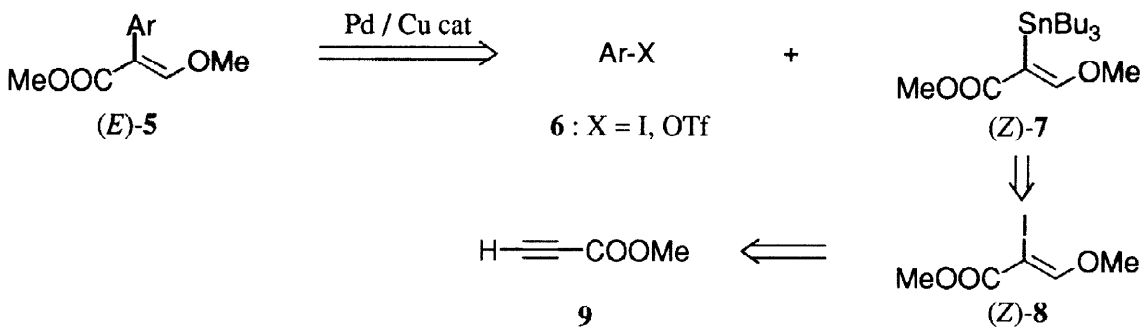


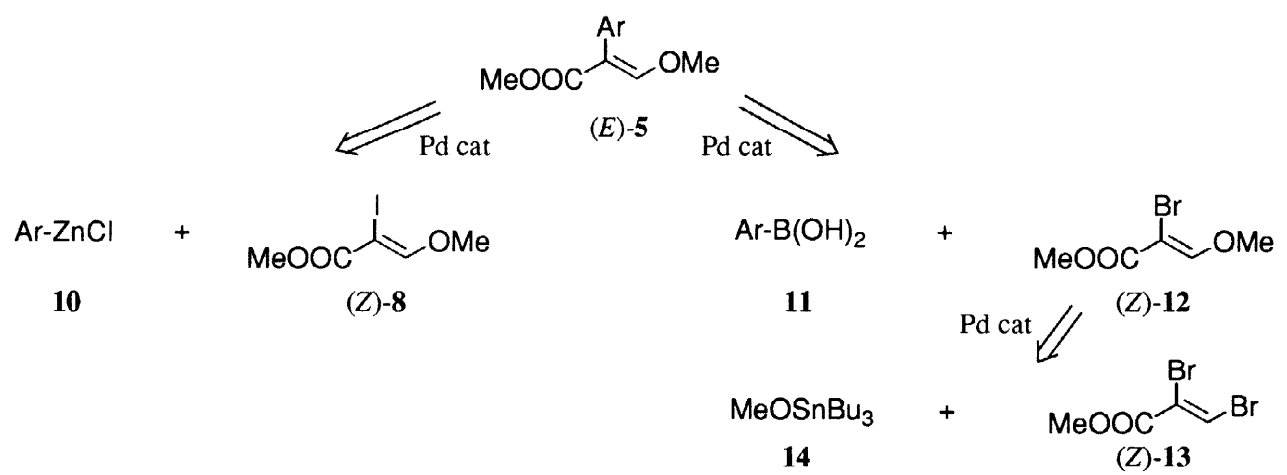
4

Classical methods for introducing the methyl (*E*)-3-methoxypropenoate unit into substrates involve multi-step sequences in which this toxophore is constructed starting from an ester or ketoester precursor.[1c,5,6] Recently, however, three methods for the direct introduction of this key unit have been reported.[7,8] Hodgson's method for the preparation of methyl (*E*)-2-aryl-3-methoxypropenoates, (*E*)-**5**, involves a Pd/Cu co-catalyzed cross-coupling reaction between aryl iodides or triflates, **6**, and methyl (*Z*)-2-tributylstannyl-3-methoxypropenoate, (*Z*)-**7**.[7a] This last compound was synthesized from methyl propiolate, **9**, via conversion of this ester into methyl (*Z*)-2-iodo-3-methoxypropenoate, (*Z*)-**8** (Scheme 1).[7a]



Scheme 1

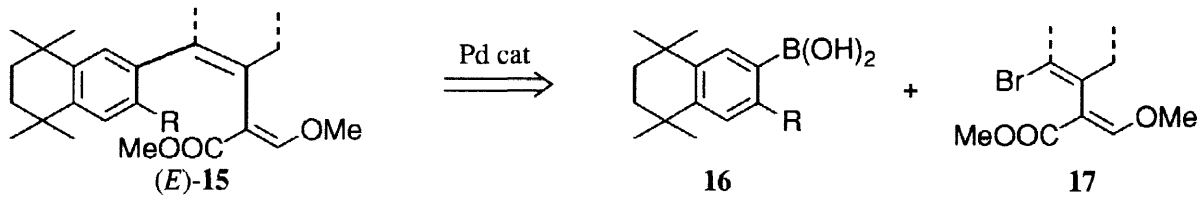
On the other hand, a variety of compounds of general formula (*E*)-**5** has been synthesized by our research group either by Pd-catalyzed cross-coupling reaction between arylzinc chlorides, **10**, and (*Z*)-**8** or by Pd-catalyzed reaction between (hetero)arylboronic acids, **11**, and methyl (*Z*)-2-bromo-3-methoxypropenoate, (*Z*)-**12**, in the presence of potassium phosphate (Scheme 2).[8]



Scheme 2

Compound (*Z*)-**12** was obtained by regioselective and stereospecific Pd-catalyzed reaction of methyl (*Z*)-2,3-dibromopropenoate, (*Z*)-**13**, with methoxytributylstannane, **14** (Scheme 2).[8,9]

More recently, four double bond locked analogues of strobilurin A of general formula (*E*)-**15**, in which the methyl (*E*)-3-methoxypropenoate unit is linked to a cycloalkene or an aromatic ring, have been prepared by synthetic routes which involve Pd-catalyzed reactions between arylboronic acids, **16**, and cycloalkenyl or aryl bromides, **17** (Scheme 3).[10]



(*E*)-**15** **16** **17**

Scheme 3

In connection with ongoing projects relating to the synthesis of photostable compounds to be used for controlling the germination of fungi which deteriorate papery materials,[11] recently we have investigated a new general and versatile procedure for the synthesis of compounds of general formula (*E*)-**18** by direct introduction of the methyl (*E*)-3-methoxypropenoate unit into substituted aromatic, cycloalkenyl or alkenyl derivatives. As shown in Scheme 4, this procedure, which in our expectation had to be more convenient and more scalable up than the previously reported synthetic methods,[1c,7,8,10] is based on the disconnection which involves the use of the organic halides or triflates, **20**, and the highly functionalized organozinc reagent (*Z*)-**19a** or (*Z*)-**19b**.

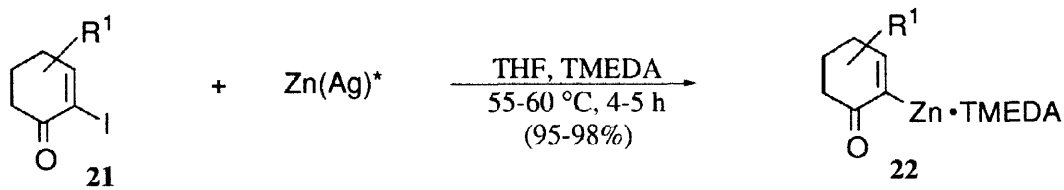
(*E*)-**18** : Y = aryl, (cyclo)alkenyl (*Z*)-**19a** : X = I; (*Z*)-**19b** : X =Br **20** : Y = aryl, (cyclo)alkenyl; Z = Br, I, OTf

Scheme 4

Herein we wish to report the preparation of these unpreviously described organometallic reagents as well as their use in the efficient and stereocontrolled Pd-catalyzed synthesis of a large variety of compounds of general formula (*E*)-**18**. Preliminary data on the bioactivity of some of these 2-substituted methyl (*E*)-3-methoxypropenoates against fungi which deteriorate papery materials will also be briefly mentioned.

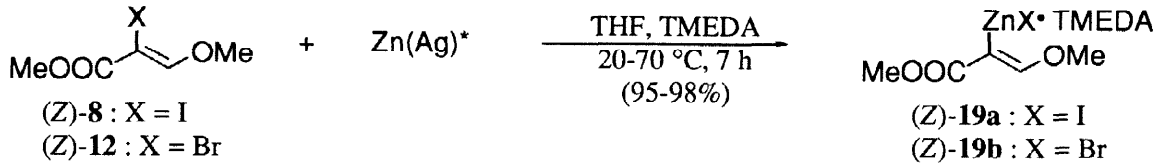
RESULTS AND DISCUSSION

Very recently we reported that 3-oxo-2-cyclohexen-2-ylzinc iodides, **22**, can be prepared in high yield by direct reaction of 2-iodo-2-cyclohexen-1-ones, **21**, with a large molar excess of an activated Zn/Ag couple in the presence of tetramethylenediamine (TMEDA) [Eq. (1)].[12]



21 **22** (1)

It seemed likely that a similar procedure could be extended to the preparation of (Z)-2-methoxy-1-(methoxycarbonyl)ethenylzinc iodide, (Z)-**19a**, and (Z)-2-methoxy-1-(methoxycarbonyl)ethenylzinc bromide, (Z)-**19b**, starting from easily available (Z)-**8**[7a] and (Z)-**12**[8,9], respectively. In fact, we found that (Z)-**19a** could be prepared in 96-98 % yield by the following optimized protocol [Eq. (2)].



(Z)-**8** : X = I
(Z)-**12** : X = Br

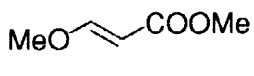
(Z)-**19a** : X = I
(Z)-**19b** : X = Br

(2)

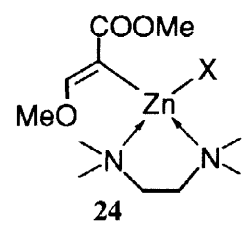
Chlorotrimethylsilane (0.14 eq) was added to a THF suspension of a Zn/Ag couple (2.5 equiv) containing 0.4 % Ag, which was prepared from chemically pure zinc dust (< 10 micron) according to the literature.[13] After the mixture was vigorously stirred under argon at room temperature for 10 min, a deareated solution of (Z)-**8** (1 equiv) and TMEDA (1 equiv) in THF was added and the resulting mixture was stirred for 7.5 h at room temperature. After this period a GLC/MS analysis of an aliquot of the settled reaction mixture, which was hydrolyzed with a saturated aqueous NH_4Cl solution, showed the presence of a compound which corresponded to methyl (E)-3-methoxypropenoate, (E)-**23**,[14] derived from hydrolysis of the desired TMEDA-complexed organozinc derivative, (Z)-**19a**. Interestingly, only a small amount (1-2 %) of unreacted (Z)-**8** was also present.

In a similar way, compound (Z)-**19b** was prepared in 98 % yield by reaction of a THF solution of (Z)-**12** and TMEDA (1 equiv) with a molar excess of a chlorotrimethylsilane-activated Zn/Ag couple containing 1.5 % Ag, which was prepared according to the procedure described by Clark and Heathcock.[15] The reaction, which occurred at 70 °C for 7 h, afforded stereoisomerically pure (Z)-**19b** contaminated by less than 2 % of (Z)-**12**.

It is worth mentioning that the TMEDA-complexed organozinc halides (Z)-**19a** and (Z)-**19b** so prepared, for which we assume a chelate structure such as **24**, were quite stable in THF solution and they could be stored at room temperature or at 70 °C for several days in the absence of air or moisture showing no sign of decomposition.

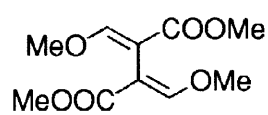


(E)-**23**



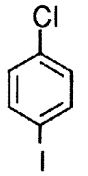
24

It must also be noted that the presence of TMEDA was very important for the selective preparation of compounds (Z)-**19a** and (Z)-**19b** in mild experimental conditions and using short reaction times. In fact, in an attempt to prepare (Z)-**19a** according to the above mentioned protocol but in the absence of TMEDA it was observed that compound (Z)-**8**, which was used as starting material, was completely consumed only after 22 h at 60 °C. Moreover, as shown by GLC and GLC/MS analyses of an aliquot of the final reaction mixture, which was hydrolyzed with an aqueous NH_4Cl solution, this mixture contained (Z)-**19a** and a new compound, to which we tentatively assigned the structure **25**, in a *ca.* 56 : 44 molar ratio, respectively.

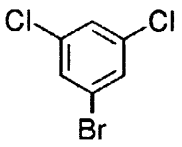


25

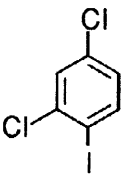
With an efficient route to compounds (*Z*)-**19a** and (*Z*)-**19b** established, we examined the use of these organometallic derivatives for the synthesis of compounds (*E*)-**18** by Pd-catalyzed cross-coupling reactions with aryl halides, alkenyl halides or triflates and cycloalkenyl triflates. Among the organic halides or triflates employed, *i.e.* **20a-o**, compounds **20a**, **20b**, **20c** and **20i** were commercially available, whereas the following compounds were prepared according to the literature: **20d**,[16] **20e**,[9] **20g**, [17] **20j**[9] and **20k**.[9]



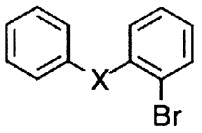
20a



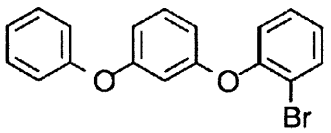
20b



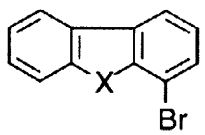
20c



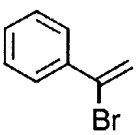
20d : X = O
20e : X = S



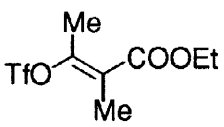
20f



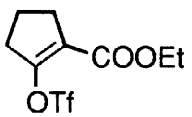
20g : X = O
20h : X = S



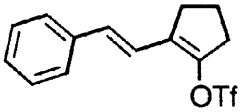
20i



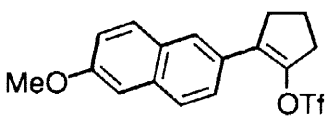
(*E*)-**20j**



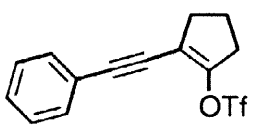
20k



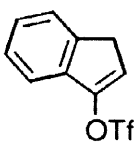
(*E*)-**20l**



20m

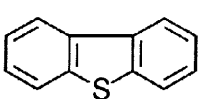


20n



20o

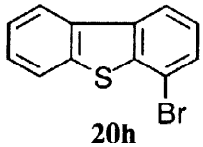
On the other hand, compound **20h** was synthesized in 71 % yield by metallation of dibenzothiophene, **26**, dissolved in THF, with an hexane solution of 1.04 equiv of butyllithium at - 40 - 0 °C, treatment of the resulting solution of aryllithium derivative with a large molar excess of 1,2-dibromoethane at - 78 °C and allowing the reaction mixture to warm up to room temperature [Eq. (3)].



26

1) BuLi, THF, hexane, -40 → 0 °C
2) $BrCH_2CH_2Br$, -78 → 20 °C

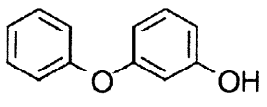
(71%)



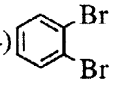
20h

(3)

Compound **20f** was synthesized starting from 3-phenoxyphenol, **27**, which was easily available from 3-phenoxyaniline.[16] The Ullmann reaction of the sodium salt of **27** with 1.3 equiv of 1,2-dibromobenzene, **28**, in refluxing pyridine, in the presence of 18 mol % CuBr, afforded **20f** in 52 % yield [Eq. (4)].

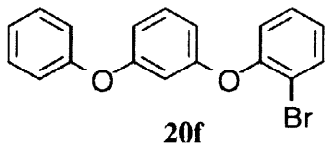


27

1) NaH, benzene
2) - benzene
3) + pyridine, Δ
4) 

(**28**), CuBr, Δ

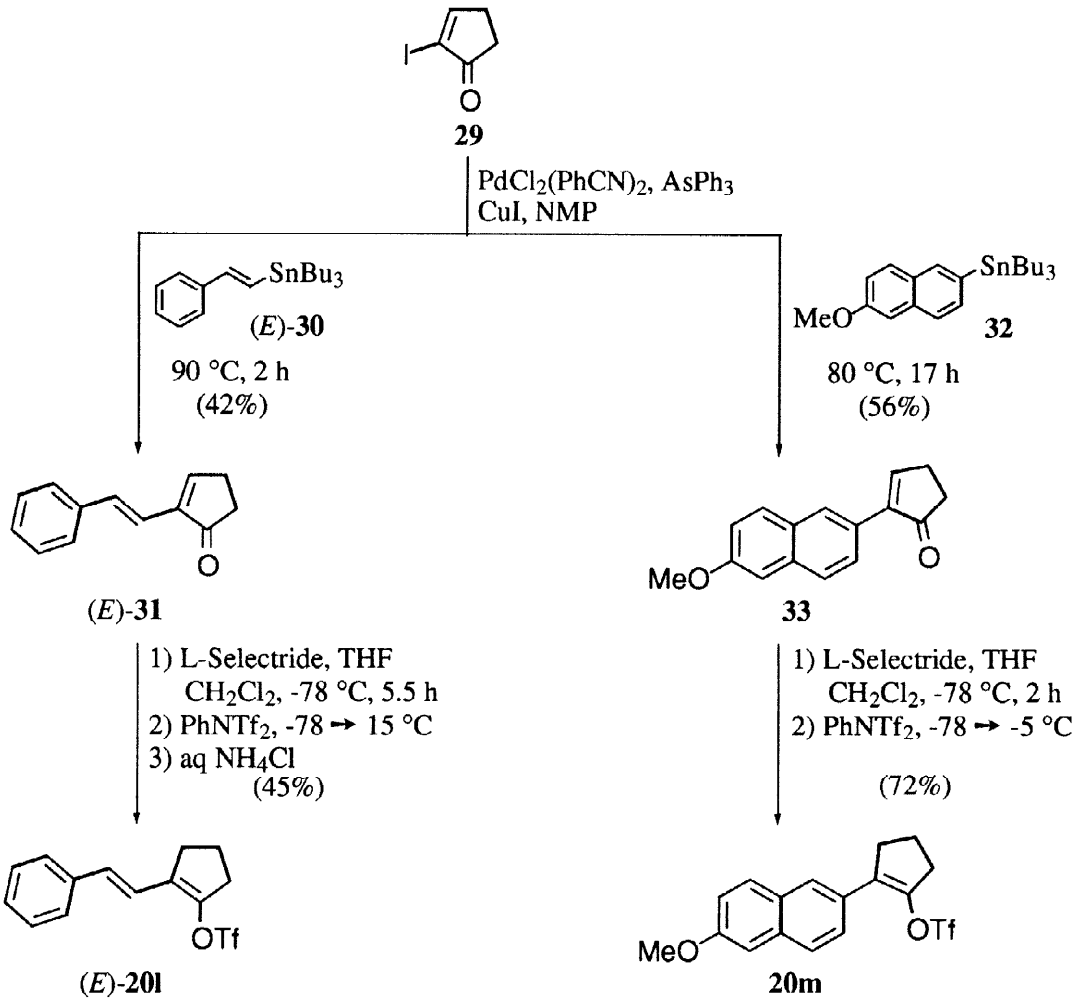
(52%)



20f

(4)

Compounds (*E*)-**20l** and **20m** were selectively synthesized from 2-iodo-2-cyclopenten-1-one, **29**,[12] according to the reaction sequences illustrated in Scheme 5. In particular, treatment of a NMP solution of **29** with 1.2 equiv of (*E*)-2-(tributylstannyl)-1-phenylethene, (*E*)-**30**, which was easily available by reaction of phenylacetylene with tributyltin hydride in the presence of a catalytic amount of azobisisobutyronitrile,[18] at 90 °C for 2 h in the presence of 5 mol % $PdCl_2(PhCN)_2$, 10 mol % $AsPh_3$ and 10 mol % CuI, allowed to obtain (*E*)-2-(2-phenylethenyl)cyclopenten-1-one, (*E*)-**31** in 42 % yield.



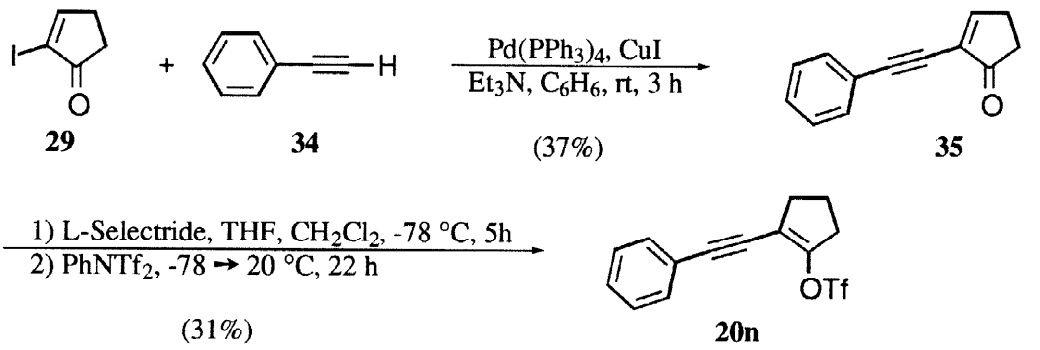
Scheme 5

Finally, reaction of a solution of (*E*)-**31** in a mixture of THF and CH_2Cl_2 with 1 equiv of a 1M THF solution of L-Selectride at - 78 °C for 5.5 h, followed by treatment of the resulting reaction mixture with 1 equiv of N-phenyltrifluoromethanesulfonimide at - 78 °C for 3 h and then at 0 - 15 °C for 14 h, gave (*E*)-2-(2-phenylethenyl)-1-[(trifluoromethyl)sulfonyloxy]cyclopentene, (*E*)-**20l**, in 45 % yield.

In a similar way, the Pd/Cu co-catalyzed cross-coupling reaction between **29** and 6-methoxy-2-(trimethylstannyl)naphthalene, **32**,[19] afforded 2-(6-methoxy-2-naphthyl)cyclopenten-1-one, **33**, in 56 % yield. This last compound was then converted in 72 % yield to **20m** (Scheme 5) by a procedure very similar to that used to prepare (*E*)-**20l** from (*E*)-**31**.

The synthesis of 2-(phenylethynyl)-1-[(trifluoromethyl)sulfonyloxy]cyclopentene, **20n**, was accomplished starting from **29** by a reaction sequence (Scheme 6) in which the first step was the Pd(0)- and Cu(I)-catalyzed

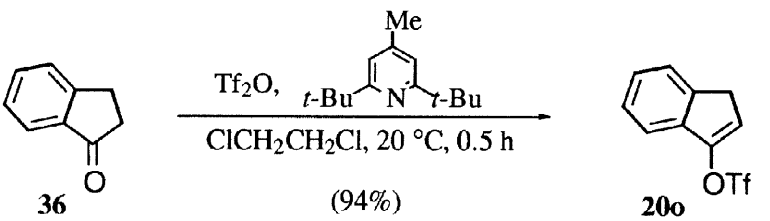
reaction of this cycloalkenyl iodide with phenylacetylene, **34**, under the Sonogashira conditions.[20] Treatment of a CH_2Cl_2 solution of 2-(phenylethynyl)cyclopenten-1-one, **35**, which was so obtained in 37 % yield, with a 1M THF solution of L-Selectride at - 78 °C, followed by reaction of the resulting reaction mixture with N-phenyltrifluoromethanesulfonimide, gave 90 % chemically pure **20n** in 31 % yield.



29 34 35 20n

Scheme 6

Finally, 1-[(trifluoromethyl)sulfonyloxy]indene, **20o**, was prepared in 94 % yield by a procedure previously employed by Farina[21] which involved treatment of a 1,2-dichloroethane solution of 1-indanone, **36**, with equimolar amounts of triflic anhydride and 2,6-di-*t*-butyl-4-methylpyridine at 40 °C for 0.5 h [Eq. (5)].



36 20o (5)

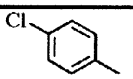
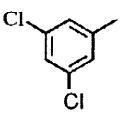
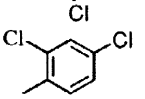
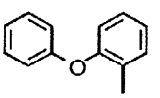
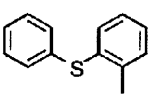
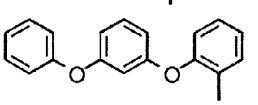
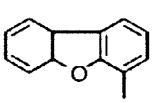
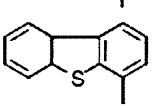
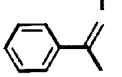
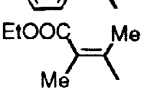
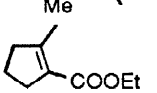
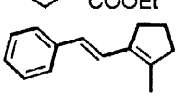
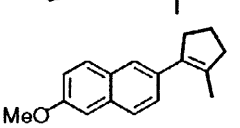
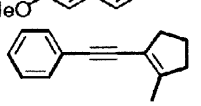
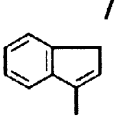
Table 1 lists the results obtained in the synthesis of methyl (*E*)-2-aryl-, (*E*)-2-alkenyl- and (*E*)-2-cyclopentenyl-3-methoxypropenoates of general formula (*E*)-**18**, which have been prepared by cross-coupling reactions between (*Z*)-**19a** or (*Z*)-**19b** and the organic halides or triflates **20a-o** in THF solution in the presence of 5 mol % $Pd(PPh_3)_4$. These results deserve the following comments. Firstly, the Pd-catalyzed reactions, which were carried out at 60 - 65 °C using a *ca.* 1.5 : 1 organozinc halide/electrophile molar ratio, proved to be clean and allowed the synthesis of a large variety of compounds of general formula (*E*)-**18**, some of which were highly functionalized. In these coupling reactions aryl iodides, aryl bromides, alkenyl bromides, alkenyl triflates as well as cyclopentenyl triflates proved to be viable electrophilic substrates. The *E* stereochemistry of the cross-coupled products at the 3-methoxypropenoate unit was assigned on the basis of the chemical shift of the alkenyl proton of this unit which was close to 7.5 ppm and therefore diagnostic for the *E* configuration.[1c] Secondly, in general these Pd-catalyzed reactions were stereospecific. Nevertheless, GLC and GLC/MS analyses of the crude reaction mixtures, which were obtained in the preparation of (*E*)-**18d** (Entry 4, Table 1) and (*E*)-**18f** (Entry 6, Table 1), showed the presence of small amounts of compounds having MS spectra very similar to those of the desired cross-coupled products. However, purification by MPLC on silica gel of the crude reaction products allowed to obtain chemically and stereoisomerically pure (*E*)-**18d** and (*E*)-**18f**. Thirdly, the yields of the cross-coupling reactions examined were generally good or excellent and those which were obtained in the Pd-catalyzed reactions involving aryl halides (Entries 1-8, Table 1) were comparable to those previously obtained by Pd-catalyzed reaction between arylzinc halides and (*Z*)-**8**.[8]

Table 1. Synthesis of Methyl (*E*)-2-Aryl-, (*E*)-2-Alkenyl- and (*E*)-2-Cycloalkenyl-3-methoxypropenoates of General Formula (*E*)-**18** by Pd-Catalyzed Cross-Coupling Reactions between Compounds (*Z*)-**19** and **20**.[a]

(*Z*)-**19a** : X = I
(*Z*)-**19b** : X =Br

20a-o : Y = aryl, (cyclo)alkenyl; Z = Br, I, OTf

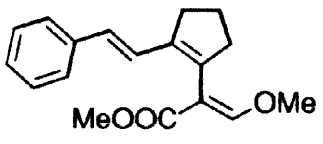
(*E*)-**18a-o**

Entry	Organozinc derivative	Organic electrophile	Reaction conditions	Product		Yield
	(*Z*)-**19a**	**20**	(°C / h)	(*E*)-**18**	Y	(%)
1	(*Z*)-**19a**	**20a**	65 / 30	(*E*)-**18a**		70
2	(*Z*)-**19b**	**20b**	60 / 20	(*E*)-**18b**		80
3	(*Z*)-**19b**	**20c**	60 / 20	(*E*)-**18c**		79
4	(*Z*)-**19a**	**20d**	60 / 21	(*E*)-**18d**		76
5	(*Z*)-**19a**	**20e**	65 / 54	(*E*)-**18e**		71
6	(*Z*)-**19a**	**20f**	60 / 50	(*E*)-**18f**		80
7	(*Z*)-**19b**	**20g**	65 / 24	(*E*)-**18g**		70
8	(*Z*)-**19a**	**20h**	65 / 26	(*E*)-**18h**		71
9	(*Z*)-**19a**	**20i**	65 / 6	(*E*)-**18i**		98
10	(*Z*)-**19a**	(*E*)-**20j**	50 / 7	(*E,E*)-**18j**		70
11	(*Z*)-**19a**	**20k**	50 / 7	(*E*)-**18k**		90
12	(*Z*)-**19b**	(*E*)-**20l**	65 / 29	(*E,E*)-**18l**		65
13	(*Z*)-**19a**	**20m**	60 / 7	(*E*)-**18m**		72
14	(*Z*)-**19a**	**20n**	65 / 24	(*E*)-**18n**		31
15	(*Z*)-**19a**	**20o**	65 / 8	(*E*)-**18o**		20

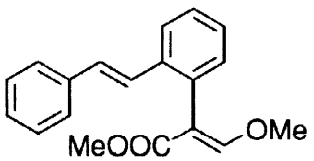
(a) All these reactions were carried out in the presence of 5 mol% $Pd(PPh_3)_4$ using a *ca.* 1.5 : 1 organozinc derivative / organic electrophile molar ratio.

However, unexpectedly, the yields obtained in the synthesis of (*E*)-**18n** (Entry 14, Table 1) and (*E*)-**18o** (Entry 15, Table 1) were low.

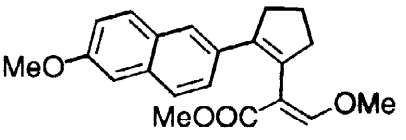
Some comments must also be deserved to the lipophilic backbones of some of the analogues of strobilurin A prepared by these Pd-catalyzed cross-coupling reactions. In fact, compound (*E,E*)-**18l**, which was obtained in 65 % yield from (*Z*)-**19b** and **20l** (Entry 12, Table 1), is a new analogue of **1** in which the *Z* double bond of this natural substance is locked into a 1,2-disubstituted cyclopentene ring instead of into a 1,2-disubstituted benzene ring as for (*E,E*)-**37**.[1a,1c] This last compound was found to be a strong inhibitor of mitochondrial respiration and highly active against a range of fungi growing in plants in the glasshouse.[1c] Compound (*E*)-**18m**, which was prepared in 72 % yield from (*Z*)-**19a** and **20m** (Entry 13, Table 1), is another new analogue of **1** in which the *Z* double bond of this substance and the *E* double bond linked to the aromatic ring of **1** are locked into a 1,2-disubstituted cyclopentene ring and into an aromatic ring, respectively.



(*E,E*)-**18l**

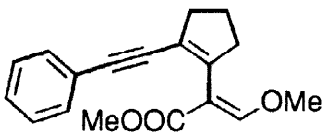


(*E,E*)-**37**

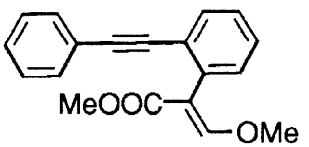


(*E*)-**18m**

Moreover, compound (*E*)-**18n**, which was prepared in 31 % yield from (*Z*)-**19a** and **20n** (Entry 14, Table 1), similarly to (*E*)-**38**, which was found to be fungicidal,[22] is characterized by a phenylethynyl unit, which in this case is linked to a 1,2-disubstituted cyclopentene ring.



(*E*)-**18n**



(*E*)-**38**

On the other hand, the Pd-catalyzed reactions between compunds (*Z*)-**19** and aryl halides (Entries 1 - 8, Table 1) allowed the efficient and stereocontrolled synthesis of a variety of methyl (*E*)-2-aryl-3-methoxypropenoates, (*E*)-**18**, which included two previously described compounds, *i.e.* (*E*)-**18d**[1a,1c,22] and (*E*)-**18f**,[1a] which are known to be fungicidal. In fact, it has been reported that (*E*)-**18d** is a systemic and photochemically stable fungicide able to control the growth of a variety of commercially important fungi in the field, although it produces unacceptable crop damage.[1a,1c,22] On the other hand, (*E*)-**18f**, although it is not systemic, has fungicidal activity higher than (*E*)-**18d**.[1a,3]

Finally, it must be mentioned that in connection with our ongoing studies relating to the identification of compounds to be used for controlling the germination of conidia and spores and the fungal growth of fungal strains isolated from deteriorated papers, very recently we undertook a study aimed at evaluating the bioactivity of some substances, among those of general formula (*E*)-**18** reported in Table 1, against *Aspergillus terreus* Thom, *Penicillium chrysogenum* Thom, *Stachibotriys atra* Corda and *Chaetomium elatum* Kunze, which had been isolated from deteriorated papery materials.[23] The bioactivity tests, which were performed using synthetic culture media as well as strips of different types of paper, were carried out keeping in mind either the structures of the 2-aryl substituted methyl (*E*)-3-methoxypropenoates which are known to be active against

agrochemically important fungi or that the systemic activity is not a fundamental requirement for compounds able to control fungi which damage papery materials.

The following compounds have been tested so far: (*E*)-**18a**, (*E*)-**18c**, (*E*)-**18d**, (*E*)-**18e**, (*E*)-**18g**, (*E,E*)-**18l** and (*E*)-**18m**. In the experiments involving synthetic culture media (*in vitro* experiments), which were carried out using 0.5 x 10^5 conidia or spores of the above mentioned fungal strains, all the compounds were tested at 27 °C at concentrations as low as 0.5 x 10^{-4} M for periods of time of incubation until 10 days and the effect of the different compounds was measured as percentage of inhibition of germination of the conidia and/or spores.

In a second series of experiments all the above mentioned compounds were tested on germinated conidia and/or spores and the fungal growth was assaied by evaluation of the ergosterol content. All the tested substances were found to be bioactive, but compounds (*E*)-**18a**, (*E*)-**18c** and (*E*)-**18d** proved to be the most effective in inhibiting the germination of the fungal conidia and/or spores as well as the fungal growth. On the other hand, in the experiments which were carried out using strips of paper, the effect of the most *in vitro* effective compounds was evaluated for 20 days on paper strips incubated at 27 °C and 85 % relative humidity, which had been inoculated with conidia or spores as in the *in vitro* experiments. Also in these tests compounds (*E*)-**18a**, (*E*)-**18c** and (*E*)-**18d** proved to be the most effective in inhibiting the fungal growth and the germination of conidia and/or spores. The other strobilurin analogues were found to be less effective; moreover, it was observed that, in some cases, compounds (*E,E*)-**18l** and (*E*)-**18m** enhanced the fungal growth and the germination of conidia and spores of the fungal strains.

In conclusion, a new general and efficient procedure for the synthesis of 2-aryl, 2-alkenyl and 2-cyclopentenyl substituted methyl (*E*)-3-methoxypropenoates of general formula (*E*)-**18** has been developed. This procedure involves Pd-catalyzed cross-coupling reactions between a new type of highly functionalized and stereodefined organozinc derivatives, *i.e.* (*Z*)-2-methoxy-1-(methoxycarbonyl)ethenylzinc halides, (*Z*)-**19**, and aryl halides, alkenyl halides or triflates or cyclopentenyl triflates, respectively. Compounds (*Z*)-**19** are easily available in high yield by reaction of THF solutions of the corresponding organic halides, (*Z*)-**8** or (*Z*)-**12**, with an activated Zn/Ag couple in the presence of TMEDA. Interestingly, compounds (*E*)-**18** obtained by these Pd-catalyzed reactions include substances which are able to control agrochemically important fungi and/or fungi which damage papery materials.

EXPERIMENTAL

All boiling and melting points are uncorrected. Precoated plastic silica gel sheets Merck 60 F_{254} were used for TLC analyses. GLC analyses were performed on a Dani GC 1000 instrument with a PTV injector, which was equipped with a Dani data station 86.01. Two types of capillary columns were used: an Alltech AT-1 bonded FSOT column (30 m × 0.25 mm i.d.) and an Alltech AT-WAX bonded FSOT column (30 m × 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 and ^{13}C NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer using TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer 1725-X FT-IR spectrophotometer. 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. Solvents were dried and distilled before use. The following compounds were

prepared according to the literature: $Pd(PPh_3)_4$;[24] methyl (Z)-2-iodo-3-methoxypropenoate (Z)-**8**;[7a] methyl (Z)-2-bromo-3-methoxypropenoate, (Z)-**12**;[9] 1-bromo-2-phenoxybenzene, **20d**;[16] 1-bromo-2-(phenylthio)benzene, **20e**;[9] 4-bromodibenzofuran, **20g**;[17] ethyl (*E*)-2-methyl-3-[(trifluoromethyl)sulfonyloxy]-2-butenoate, **20j**;[9] ethyl 2-[(trifluoromethyl)sulfonyloxy]-1-cyclopentene-1-carboxylate, **20k**;[9] 3-phenoxyphenol, **27**;[16] 2-iodo-2-cyclopenten-1-one, **29**;[12] (E)-2-(tributylstannyl)-1-phenylethene, **30**;[18] $PdCl_2(PhCN)_2$;[25] 6-methoxy-2-trimethylstannyl)naphthalene, **32**.[19]

*TMEDA-Complexed (Z)-2-methoxy-1-(methoxycarbonyl)ethenylzinc iodide, (Z)-**19a***. According to the literature,[13] commercially available 98 % chemically pure zinc dust (< 10 micron) (50 g, 0.76 mol) was added to a stirred suspension of silver acetate (50 mg, 0.3 mmol) in glacial acetic acid (100 ml) which was maintained under reflux. After 1 min the mixture was quickly cooled to 10 °C and allowed to settle. The clear supernatant solution was eliminated by siphoning and the solid residue was washed with Et_2O (5 x 50 ml) and dried for 20 h at 0.05 Torr. The Zn/Ag couple so obtained was stored in the dark under argon. Chlorotrimethylsilane (0.37 ml, 4.28 mmol) was added to a suspension of this Zn/Ag couple (4.90 g, 75.0 mmol) in THF (24 ml) and the mixture was stirred under argon for 25 min at room temperature. A degassed solution of TMEDA (4.52 ml, 30.0 mmol) and (Z)-2-iodo-3-methoxypropenoate, (Z)-**8**, (7.26 g, 30.0 mmol) in THF (10 ml) was quickly added to this stirred mixture; 2-3 min after the addition was completed a remarkable exothermic effect was observed. After the heat evolution ceased the mixture was stirred at 20 °C for 7 h and finally it was allowed to settle. A GLC/MS analysis of an aliquot of the clear supernatant solution, which was hydrolyzed with a saturated aqueous NH_4Cl solution, showed the presence of a compound which was identified as stereoisomerically pure methyl (*E*)-3-methoxypropenoate, (*E*)-**23**, by comparison with an authentic sample of this substance.[14] Compound (*E*)-**23** derived from hydrolysis of the organozinc iodide (*Z*)-**19a**. Interestingly, only a very small amount (< 2 %) of unreacted (*Z*)-**8** was present in the reaction mixture. The clear supernatant solution of (*Z*)-**19a** was then transferred via syringe to a new reaction flask.

*TMEDA-Complexed (Z)-2-methoxy-(1-methoxycarbonyl)ethenylzinc bromide, (Z)-**19b***. According to the literature,[15,26] 85 % chemically pure zinc dust (< 325 mesh) (50 g, 0.76 mol) was added to 10 % aqueous HCl (350 ml) and the mixture was stirred for 5 min at 20 °C. It was then filtered and the solid was sequentially washed with dry acetone (3 x 200 ml) and Et_2O (2 x 200 ml) and dried *in vacuo*. It was then added to a stirred suspension of silver acetate (2.0 g, 12 mmol) in glacial acetic acid (330 ml) which was maintained under reflux. After 1 min the mixture was quickly cooled to 10 °C and allowed to settle. The clear supernatant solution was eliminated by siphoning and the solid residue was sequentially washed with glacial acetic acid (170 ml) and Et_2O (5 x 250 ml). It was then dried for 20 h at 0.05 Torr and stored in the dark under argon. According to a procedure similar to that previously employed for the preparation of a TMEDA-complexed trifluoroisopropenylzinc reagent,[27] chlorotrimethylsilane (160 µl, 0.06 mmol) was added to a suspension of this Zn/Ag couple (2.28 g, 34.8 mmol) in THF (14 ml) and the mixture was stirred under argon for 15 min at room temperature. A degassed solution of methyl (Z)-2-bromo-3-methoxypropenoate, (Z)-**12**, (2.74 g, 14.08 mmol) and TMEDA (2.12 ml, 14.08 mmol) in THF (10 ml) was quickly added and the resulting mixture was stirred under argon at 70 °C for 7 h, then cooled to room temperature and allowed to settle. A GLC/MS analysis of an aliquot of the clear supernatant solution, which was hydrolyzed with a saturated NH_4Cl solution, showed the presence of stereoisomerically pure (*E*)-**23** and unreacted (*Z*)-**12** in a molar ratio higher than 98 : 2. The clear

solution of (Z)-**19b** so obtained was then transferred via syringe to a new reaction flask.

*1-Bromo-2-(3-phenoxyphenoxy)benzene, **20f**.* A 60 % dispersion of NaH in mineral oil (2.34 g, 58.5 mmol) was washed with dry pentane and the solid residue was suspended in dry benzene (65 ml). To this suspension, which was stirred under argon, was added over 0.5 h a solution of 3-phenoxyphenol, **27** (10.7 g, 57.4 mmol) in dry benzene (65 ml) and the resulting mixture was refluxed for 1.5 h. It was then cooled to room temperature and concentrated *in vacuo*. The residue, which was maintained under argon, was diluted with dry pyridine (96 ml) and the mixture was stirred under reflux. 1,2-Dibromobenzene, **28**, (17.6 g, 74.6 mmol) and CuBr (1.48 g, 10.3 mmol) were sequentially added and the resulting mixture was refluxed under stirring for 7 h. It was then cooled to 5 °C, poured into a large excess of cold 6N HCl and the mixture was repeatedly extracted with Et_2O. The collected organic extracts were washed with water, dried and concentrated *in vacuo*. The residue was purified by MPLC on silica gel, using a mixture of benzene and Et_2O (90 : 10) as eluant, to give **20f** (10.6 g, 54 % yield) as an oil. MS, *m/z* (%): 342 (10), 341 (5), 340 (8), 339 (7), 261 (8), 169 (13), 168 (100), 139 (10), 77 (10). ^{1}H NMR ($CDCl_3$): δ 7.66 (1H, d, J = 7.8 Hz), 7.50 - 7.24 (4H, m), 7.22 - 6.96 (5H, m), 6.86 - 6.62 ppm (3H, m). Anal. Calc for $C_{18}H_{13}BrO_2$: C, 63.36; H, 3.84. Found: C, 63.45; H, 4.01.

*4-Bromodibenzothiophene, **20h*** To a stirred solution of dibenzothiophene, **26**, (25.20 g, 136.8 mmol) in dry THF (230 ml) at - 40 °C was added a 2.5M hexane solution of butyllithium (56.7 ml, 141.8 mmol) and the mixture was allowed to warm to 0 °C and stirred at this temperature for 6 h. It was then cooled to - 78 °C and a solution of 1,2-dibromoethane (51.1 g, 272 mmol) in THF (20 ml) was added dropwise with stirring. The reaction mixture was allowed to warm to room temperature and stirred for 14 h. The solvent was evaporated and the residue was dissolved in CH_2Cl_2, washed with water, dried and concentrated *in vacuo*. The residue was recrystallized from a mixture of CH_2Cl_2 and hexane to give **20g** (25.6 g, 71 % yield) as white crystals. M.p. 78 - 80 °C. MS, *m/z* (%): 265 (11), 264 (100), 262 (97), 183 (50), 139 (70), 132 (16), 131 (10), 91 (68), 69 (18). ^{1}H NMR ($CDCl_3$): δ 8.25 - 8.00 (2H, m), 7.94 - 7.80 (1H, m), 7.60 (1H, d, J = 7.8 Hz), 7.55 - 7.40 (2H, m), 7.34 ppm (1H, t, J = 7.8 Hz). Anal. Calc for $C_{12}H_7BrS$: C, 54.77; H, 2.68. Found: C, 54.99; H, 2.57.

*(E)-2-(2-Phenylethenyl)cyclopenten-1-one, (E)-**31***. A dried flask flushed with argon was charged with $PdCl_2(PhCN)_2$ (0.55 g, 1.44 mmol), $AsPh_3$ (0.88 g, 2.88 mmol), CuI (0.55 g, 2.88 mmol) and a degassed solution of 2-iodo-2-cyclopenten-1-one, **29**, (6.0 g, 28.86 mmol) in dry NMP (40 ml). A degassed solution of (*E*)-2-(tributylstannyl)phenylethene, (*E*)-**30**, (13.6 g, 34.63 mmol) in dry NMP (30 ml) was then added and the mixture was stirred under argon at 90 °C for 2 h. After this period a GLC analysis of an aliquot of the reaction mixture, which was poured into water and extracted with CH_2Cl_2, showed that compound **29** had completely reacted. The reaction mixture was cooled to room temperature and poured into a large excess of a saturated aqueous NH_4Cl solution. After stirring for 0.5 h in the air the mixture was repeatedly extracted with CH_2Cl_2. The collected organic extracts were concentrated *in vacuo* and the residue was diluted with Et_2O (200 ml), stirred for 12 h with a large molar excess of a 50 % aqueous KF solution and filtered over Celite. The filtrate was repeatedly extracted with Et_2O and the collected organic extracts were washed with brine, filtered over Celite and concentrated under reduced pressure. The residue was purified by MPLC on silica gel, using a mixture of CH_2Cl_2 and hexane (60 : 40) as eluant, to give stereoisomerically pure (*E*)-**31** (2.22 g, 41.8 % yield) as a crystalline solid. M.p. 95 - 97 °C. MS, *m/z* (%): 184 (58), 165 (19) 155 (34), 1451 (100), 128 (71), 115 (68), 103 (38), 91 (32), 51 (88). ^{1}H NMR ($CDCl_3$): δ 7.65 -7.20 (7H, m, C_6H_5, H-3 and H-2'), 6.81 (1H, d, J =

16.5 Hz, H-1'), 2.75 - 2.60 (2H, m, H-5), 2.60 - 2.45 ppm (2H, m, H-4). Anal. Calc for $C_{13}H_{12}O$: C, 84.75; H, 6.56. Found: C, 84.53; H, 6.61.

2-(6-Methoxy-2-naphthyl)cyclopenten-1-one, 33. A deareated solution of 6-methoxy-2-(trimethylstannyl)-naphthalene, **32**, (5.0 g, 15.59 mmol) in dry NMP (20 ml) was added to a mixture of $PdCl_2(PhCN)_2$ (0.237 g, 0.56 mmol), $AsPh_3$ (0.39 g, 1.25 mmol), CuI (0.25 g, 1.25 mmol) and 2-iodo-2-cyclopenten-1-one, **29**, (2.70 g, 12.99 mmol) in dry NMP (16 ml), which was stirred under argon. The resulting mixture was stirred at 80 °C for 17 h, then cooled to room temperature and poured into a large excess of a saturated aqueous NH_4Cl solution. After stirring for 0.5 h in the air the mixture was repeatedly extracted with CH_2Cl_2. The collected organic extracts were washed with water, dried and concentrated *in vacuo*. The residue was purified by MPLC on silica gel, using a mixture of CH_2Cl_2 and hexane (70 : 30) as eluant, to give compound **33** (1.73 g, 56 % yield) as a colourless crystalline solid. M.p. 177 - 178 °C. MS, *m/z* (%): 239 (17), 238 (100), 209 (17), 195 (15), 182 (14), 179 (11), 167 (13), 152 (11), 139 (20). IR (KBr): 1627, 1615, 1599, 1258, 1167, 1028, 858, 819, 479 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.29 (1H, s, Harom), 7.89 (1H, t, J = 2.8 Hz, H-3), 7.82 - 7.55 (3H, m, Harom), 7.21 - 6.98 (2H, m, Harom), 3.91 (3H, s, OCH_3), 2.82 2.50 ppm (4H, m, H-4 and H-5). Anal. Calc for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 81.06; H, 5.64.

2-Phenylethynylcyclopenten-1-one, 35. A dried reaction flask flushed with argon was charged with $Pd(PPh_3)_4$ (1.39 g, 1.20 mmol), CuI (0.55 g, 2.89 mmol) and 2-iodo-2-cyclopenten-1-one, **29**, (5.0 g, 24.05 mmol). Deareated bry benzene (40 ml), Et_3N (6.67 ml, 48.1 mmol) and phenylacetylene, **34**, (2.46 g, 24.05 mmol) were sequentially added to the stirred mixture. A remarkable exothermic reaction occurred and, after the heat evolution ceased, the mixture was stirred at room temperature for 3 h. After this period a GLC analysis of an aliquot of the reaction mixture, which was hydrolyzed with a saturated aqueous NH_4Cl solution and extracted with Et_2O, showed that compounds **29** and **34** had been completely consumed. The reaction mixture was diluted with benzene and poured into a large excess of a saturated aqueous NH_4Cl solution. The resulting mixture was stirred in the air for 0.5 h and extracted repeatedly with benzene. The collected organic extracts were washed with water, dried, filtered over Celite and concentrated *in vacuo*. The residue was purified by MPLC on silica gel, using a mixture of CH_2Cl_2 and hexane (80: 20) as eluant, to give **35** (1.62 g, 37.0 % yield) as a colourless crystalline solid. M.p. 61 - 63 °C. MS, *m/z* (%): 183 (15), 182 (100), 154 (28), 153 (62), 126 (43), 115 (11), 74 (25), 63 (31), 51 (56). ^1H NMR ($CDCl_3$): δ 7.84 (1H, t, J = 2.9 Hz, H-3), 7.60 - 7.40 (2H, br m, Harom), 7.40 - 7.20 (3H, br m, Harom), 2.72 (2H, *pseudo*-quint, J = 4.3 Hz, H-4), 2.49 ppm (2H, t, J = 4.3 Hz, H-5). Anal. Calc for $C_{13}H_{10}O$: C, 85.69; H, 5.53. Found: C, 85.85; H, 5.31.

(E)-2-(2-Phenylethenyl)-1-[(trifluomethyl)sulfonyloxy]cyclopentene, (E)-20l. A 1M THF solution of L-Selectride (12.8 ml, 12.80 mmol) was added over 10 min to a stirred solution of (*E*)-**31** (2.12 g, 11.52 mmol) in THF (70 ml) which was maintained at - 78 °C under argon and the resulting heterogeneous mixture was stirred for 5.5 h at - 78 °C and then diluted with CH_2Cl_2 (10 ml). A solution of N-phenyltrifluoromethanesulfonimide (4.48 g, 12.56 mmol) in CH_2Cl_2 (50 ml) was added and the resulting mixture was stirred for 3 h at - 78 °C. It was then allowed to warm to room temperature within 14 h, poured into a large excess of water, extracted with an aqueous NH_4Cl solution, dried and concentrated *in vacuo* at room temperature. The residue was purified by MPLC on silica gel, using a mixture of hexane and CH_2Cl_2 (85 : 15) as eluant, to give (*E*)-**20l** (1.64 g, 44.7 % yield) as an oil. ^1H NMR ($CDCl_3$): δ 7.46 - 7.26 (5H, br m, Harom), 6.98 (1H, d, J = 16.0 Hz, H-1' or H-2'),

6.53 (1H, d, J = 16.0 Hz, H-2' or H-1'), 2.77 (2H, t, J = 7.3 Hz, H-3 or H-5), 2.64 (2H, t, J = 6.8 Hz, H-5 or H-3), 2.06 ppm (2H, quint, J = 7.3 Hz, H-4). This compound, which on the basis of GLC analyses had chemical purity higher than 98 %, was used in the next step without any further characterization and purification.

2-(6-Methoxy-2-naphthyl)-1-[(trifluoromethyl)sulfonyloxy]cyclopentene, ***20m***. According to a procedure similar to that employed for the synthesis of (*E*)-**20l**, a 1M THF solution of L-Selectride (15.7 ml, 125.7 mmol) was added to a stirred solution of **33** (3.60 g, 15.11 mmol) in CH_2Cl_2 (200 ml), which was maintained at - 78 °C under argon, and the resulting mixture was stirred at - 78 °C for 2 h. N-Phenyltrifluoromethanesulfonimide (5.40 g, 15.11 mmol) was then added and the resulting mixture was stirred at - 65 °C for 3 h, at - 30 °C for 1 h, the allowed to warm to - 5 °C within 17 h and finally stirred at room temperature for 24 h. It was then diluted with CH_2Cl_2 and washed repeatedly with water. The organic phase was dried and concentrated *in vacuo* at room temperature. The residue was purified by MPLC on silica gel, using a mixture of hexane and CH_2Cl_2 (60 : 40) as eluant, to give **20m** (4.06 g, 72.2 % yield) as a colourless crystalline solid. M.p. 64- 66 °C (dec). ^{1}H NMR ($CDCl_3$): δ 7.82 - 7.60 (4H, m, Harom), 7.20-7.10 (2H, m, Harom), 3.91 (3H, s, OCH_3), 2.89 (4H, *pseudo*-t, J = 7.3 Hz, H-3 and H-5), 2.11 ppm (2H, quint, J = 7.3 Hz, H-4). This substance, which on the basis of GLC analyses had chemical purity higher than 93 %, was used in the next step without any further purification and characterization.

2-(Phenylethynyl)-1-[(trifluoromethyl)sulfonyloxy]cyclopentene, ***20n***. The crude reaction mixture, which was obtained by sequential reaction of a CH_2Cl_2 solution of **35** (4.20 g, 23.05 mmol) with a 1M THF solution of L-Selectride and N-phenyltrifluoromethanesulfonimide according to the same procedure used for the preparation of **20l**, was purified by MPLC on silica gel, using a mixture of hexane and CH_2Cl_2 (90 : 10) as eluant, to give **20n** (2.25 g, 31 % yield) as a waxy solid. ^{1}H NMR ($CDCl_3$): δ 7.55 - 7.32 (5H, br m, Harom), 2.77 - 2.59 (4H, br m, H-3 and H-5), 2.07 ppm (2H, quint, J = 7.6 Hz, H-4). This substance, which on the basis of GLC analyses had chemical purity higher than 89 %, was used in the next step without any further purification and characterization.

1-[(Trifluoromethyl)sulfonyloxy]indene, ***20o***. Triflic anhydride (6.49 g, 23.02 mmol) was added to a solution of 1-indanone, **36**, (2.90 g, 21.92 mmol) in dry 1,2-dichloroethane (120 ml) which was stirred under Argon at room temperature. 2,6-Di-*t*-butyl-4-methylpyridine (4.84 g, 23.57 mmol) was added to the reaction mixture in one portion. The solution warmed up to about 40 °C. After stirring for 0.5 h at room temperature the reaction mixture was diluted with 1,2-dichloroethane, washed with 1N HCl and water, dried and concentrated under reduced pressure at room temperature. The residue was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (99 :1) as eluant, to give **20o** (5.45 g, 94 % yield) as a colourless oil. ^{1}H NMR ($CDCl_3$): δ 7.60 - 7.25 (4H, m, Harom), 6.37 (1H, br s, H-2), 3.47 ppm (2H, br s, H-3). This substance, which on the basis of GLC analyses had chemical purity higher than 98 %, was used in the next step without further characterization. It must also be noted that **20o** was quite unstable; in fact, when maintaned for few days at - 20 °C under argon, in part it decomposed.

*General procedure for the synthesis of 2-substituted methyl (E)-3-methoxypropenoates, (E)-****18***. In a typical experiment a 0.79 M THF solution of TMEDA-complexed (Z)-2-methoxy-1-(methoxycarbonyl)ethenylzinc iodide, (Z)-**19a**, (28.4 ml, 22.5 mmol) or a 0.54M THF solution of TMEDA-complexed (Z)-2-methoxy-1-

(methoxycarbonyl)ethenylzinc bromide, (*Z*)-**19b**, (41.7 ml, 22.5 mmol) was added to a solution of an aryl halide, an alkenyl halide or triflate or a cycloalkenyl triflate, **20**, (15.0 mmol) and $Pd(PPh_3)_4$ (0.87 g, 0.75 mmol) in THF (30 ml), which was prepared immediately prior to use, and the resulting mixture was stirred at the temperature and for the period of time reported in Table 1. The mixture was periodically monitored by GLC/MS analysis of its aliquots, which were hydrolyzed with a saturated aqueous NH_4Cl solution, until compound **20** was consumed. The reaction mixture was then cooled to room temperature, poured into a large excess of a saturated aqueous NH_4Cl solution and repeatedly extracted with Et_2O. The collected organic extracts were washed with water, filtered over Celite, dried and concentrated under reduced pressure. The residue, which was analyzed by GLC and GLC/MS analyses was diluted with the solvent which was subsequently used for its purification by MPLC on silica gel, and filtered over Celite. The filtrate was concentrated under reduced pressure and the residue was purified by MPLC on silica gel. Compounds (*E*)-**18a-o** were prepared according to this procedure (Table 1). The isolation and characterization of these compounds by MS spectrometry, by IR, ^1H and ^{13}C NMR spectroscopy as well as by elemental analysis is reported below. As regards the ^{13}C NMR spectra of compounds (*E*)-**18a**, (*E*)-**18b**, (*E*)-**18d**, (*E*)-**18e**, (*E*)-**18f**, (*E*)-**18i**, (*E*)-**18l**, (*E*)-**18m** and (*E*)-**18n** which were registered at 50 MHz, it must be noted that the number of the detected signals did not correspond to the number of their carbon atoms. In fact, for all these compounds some aromatic carbon atoms present in their skeleton had very similar chemical shifts. In these compounds the values of chemical shift corresponding to two different aromatic carbon atoms are marked by an asterisk.

*Methyl (E)-2-(4-chlorophenyl)-3-methoxypropenoate, (E)-**18a***. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 4-iodo-chlorobenzene, **20a** (Entry 1, Table 1), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (70 : 30) as eluant, to give in 70 % yield stereoisomerically pure (*E*)-**18d** as a colourless crystalline solid. M.p. 59 - 61 °C. MS, *m/z* (%): 228 (7), 227 (4), 226 (24), 195 (4), 154 (5), 152 (12), 89 (12), 76 (4), 75 (100). IR (KBr): 1706, 1625, 1271, 1259, 1137, 1089 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.56 (1H, s, H-3), 7.35 - 7.24 (4H, m, Harom), 3.86 (3H, s, OCH_3), 3.74 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.7, 159.9, 132.9, 131.5*, 130.9, 127.9; 110.5, 62.1, 51.6 ppm. Anal. Calc for $C_{11}H_{11}ClO_3$: C, 58.29; H, 4.89. Found: C, 58.40; H, 4.82.

*Methyl (E)-2-(3,5-dichlorophenyl)-3-methoxypropenoate, (E)-**18b***. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 3,5-dichloro-bromobenzene, **20b** (Entry 2, Table 1), was purified by MPLC on silica gel, using a mixture of benzene and hexane (80 : 20) as eluant, to give in 80 % yield stereoisomerically pure (*E*)-**18b** as a colourless crystalline solid. M.p. 127 - 129 °C. MS, *m/z* (%): 262 (26), 261 (5), 260 (41), 231 (9), 229 (13), 188 (22), 186 (34), 123 (23), 75 (100). IR (KBr): 1708, 1621, 1259, 1197, 1132, 1121 cm^{-1}.^1H NMR ($CDCl_3$): δ 7.59 (1H, s, H-3), 7.40 - 7.15 (3H, br m, Harom), 3.90 (3H, s, OCH_3), 3.75 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.1, 160.7, 135.4, 134.1*, 128.6*, 121.1, 109.3 62.4, 51.8 ppm. Anal. Calc for $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86. Found: C, 50.81; H, 3.95.

*Methyl (E)-2-(2,4-dichlorophenyl)-3-methoxypropenoate, (E)-**18c***. The crude reaction product, which was obtained from the Pd-catalyyzed reaction between (*Z*)-**19b** and 2,4-dichloro-iodobenzene, **20c** (Entry 3, Table 1), was purified by MPLC on silica gel, using benzene as eluant, to give in 79 % yield stereoisomerically pure (*E*)-**18c** as a colourless crystalline solid. M.p. 74 - 76 °C. MS, *m/z* (%): 260 (5), 227 (33), 226 (12), 225 (100), 188 (19), 186 (27), 158 (10), 123 (27), 75 (93). IR (KBr): 1703, 1621, 1265, 1128, 1104, 1078 cm^{-1}. ^1H NMR

($CDCl_3$): δ 7.57 (1H, s, H-3), 7.43 (1H, d, J = 1.9 Hz, H-3'), 7.35 - 7.10 (2H, m, H-5' and H-6'), 3.85 (3H, s, OCH_3), 3.71 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.1, 160.6, 135.3, 134.0, 133.0, 130.6, 129.2, 126.7, 108.8, 62.1, 51.7 ppm. Anal. Calc for $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86. Found: C, 50.37; H, 3.78.

Methyl (E)-2-(2-phenoxyphenyl)-3-methoxypropenoate, (E)-18d. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19b** and 1-bromo-2-phenoxybenzene, **20d** (Entry 4, Table 1), was purified by MPLC on silica gel, using a mixture of hexane and ethyl acetate (85 : 15) as eluant, to give in 76 % yield stereoisomerically pure (*E*)-**18d** as a viscous oil. MS, *m/z* (%): 285 (17), 284 (92), 239 (60), 191 (48), 181 (66), 165 (18), 152 (20), 77 (20), 75 (100). IR (film): 1713, 1636, 1489, 1253, 1235, 1129 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.48 (1H, s, H-3), 7.37 - 6.87 (9H, br m, Harom), 3.76 (3H, s, OCH_3), 3.61 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.8, 159.9, 157.5, 154.7, 132.3, 129.3*, 128.9, 124.8, 123.1, 122.6, 119.0, 118.2*, 108.0, 61.6, 51.3 ppm. Anal. Calc for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 72.10; H, 5.54.

Methyl (E)-2-(2-phenythiophenyl)-3-methoxypropenoate, (E)-18e. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 1-bromo-2-(phenylthio)benzene, **20e** (Entry 5, Table 1), was purified by MPLC on silica gel, using benzene as eluant, to give in 71 % yield stereoisomerically pure (*E*)-**18e** as a viscous oil. MS, *m/z* (%): 300 (25), 210 (22), 197 (26), 192 (17), 191 (100), 176 (21), 165 (20), 121 (13), 77 (17). IR (film): 1709, 1635, 1288, 1249, 1193, 1130 cm^{-1}.^1H NMR ($CDCl_3$): δ 7.48 (1H, s, H-3), 7.40 - 7.09 (9H, br m, Harom), 3.73 (3H, s, OCH_3), 3.64 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.8, 160.1, 136.9, 135.9, 135.5, 133.0, 131.6, 130.4*, 128.8*, 128.5, 127.4, 126.3, 111.1, 61.7, 51.5 ppm. Anal. Calc for $C_{17}H_{16}O_3S$: C, 67.98; H, 5.37. Found: C, 68.02; H, 5.51.

Methyl (E)-2-[2-(3-phenoxyphenoxy)phenyl]-3-methoxypropenoate, (E)-18f. The crude reaction pruduct, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 1-bromo-2-(3-phenoxyphenoxy)benzene, **20f** (Entry 6, Table 1), was purified by MPLC on silica gel, using CH_2Cl_2 as eluant, to give in 80 % yield stereoisomerically pure (*E*)-**18f** as a viscous oil. MS, *m/z* (%): 376 (3), 331 (34), 330 (19), 273 (8), 191 (14), 181 (13), 152 (7), 77 (16), 75 (100). IR (film): 1713, 1636, 1479, 1291, 1219, 1127 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.47 (1H, s, H-3), 7.42 - 6.91 (10H, br m, Harom), 6.66 - 6.56 (3H, m, Harom), 3.73 (3H, s, OCH_3), 3.58 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.8, 160.0, 158.9, 158.3, 156.8, 154.3, 132.4, 129.9, 129.7*, 129.0, 124.9, 123.42, 123.37, 119.3, 118.9*, 112.9, 109.1, 107.9, 61.7, 51.4 ppm. Anal. Calc for $C_{23}H_{20}O_5$: C, 73.39; H, 5.36. Found: C, 73.45; H, 5.50.

Methyl (E)-2-(4-dibenzofuranyl)-3-methoxypropenoate, (E)-18g. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19b** and 4-bromodibenzofuran, **20g** (Entry 7, Table 1), was purified by MPLC on silica gel, using a mixture of benzene and hexane (60 : 40) as eluant, to give in 70 % yield stereoisomerically pure (*E*)-**18g** as a crystalline solid. M.p. 123 - 125 °C. MS, *m/z* (%): 282 (21), 208 (10), 180 (8), 179 (4), 152 (8), 151 (4), 150 (4), 76 (7), 75 (100). IR (KBr): 1719, 1634, 1288, 1140, 1121, 758 cm^{-1}. ^1H NMR ($CDCl_3$): δ8.08 -7.83 (2H, m, Harom), 7.74 (1H, s, H-3), 7.54 (1H, d, J = 8.1 Hz, Harom), 7.51 - 7.22 (4H, m, Harom), 3.85 (3H, s, OCH_3), 3.73 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.8, 161.0, 156.0, 154.0, 129.1, 126.9, 124.4, 124.2, 122.5, 122.4, 120.6, 120.0, 117.2, 111.6, 106.5, 62.1, 51.7 ppm. Anal. Calc for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.52; H, 4.98.

Methyl (E)-2-(4-dibenzothienyl)-3-methoxypropenoate, (E)-18h. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 4-bromodibenzothiophene, **20h** (Entry 8, Table 1), was purified by MPLC on silica gel, using benzene as eluant, to give in 71 % yield stereoisomerically pure (*E*)-**18h** as a crystalline solid. M.p. 164 - 165 °C. MS, *m/z* (%): 299 (9), 298 (48), 224 (14), 208 (7), 196 (11), 195 (16), 163 (5), 152 (16), 75 (100). IR (KBr): 1702, 1621, 1264, 1114, 1103, 755 cm^{-1}. ^1H NMR ($CDCl_3$): δ 8.20 - 8.05 (2H, m, Harom), 7.88 - 7.76 (1H, m, Harom), 7.53 (1H, s, H-3), 7.56 - 7.27 (4H, m, Harom), 3.86 (3H, s, OCH_3), 3.71 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 167.6, 161.1, 140.5, 139.4, 136.0, 135.6; 128.7, 127.9, 126.6, 124.4, 124.2, 122.6, 121.6, 120.8, 110.2, 62.1, 51.8 ppm. Anal. Calc for $C_{17}H_{14}O_3S$: C, 68.44; H, 4.73. Found: C, 68.59; H, 4.95.

Methyl (E)-2-(1-phenylethenyl)-3-methoxypropenoate, (E)-18i. The crude reaction product which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and α-bromostyrene, **20i** (Entry 9, Table 1), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (70 : 30) as eluant, to give in 98 % yield stereoisomerically pure (*E*)-**18i** as a crystalline solid. M.p. 53.5 - 55 °C. MS, *m/z* (%): 218 (60), 203 (91), 145 (30), 116 (23), 115 (100), 103 (16), 91 (28), 77 (29), 75 (69). IR (KBr): 1699, 1640, 1289, 1233, 1111, 786 cm^{1}. ^1H NMR ($CDCl_3$): δ 7.57 (1H, s, H-3), 7.45 - 7.17 (5H, m, Harom), 5.81 (1H, s, (*E*)-H-2'), 5.24 (1H, s, (*Z*)-H-2'), 3.83 (3H, s, OCH_3), 3.62 ppm (3H, s, OCH_3). ^{13}C NMR ($CDCl_3$): δ 168.0, 160.2, 139.7, 139.6, 128.2*, 127.4, 125.7*, 117.2, 111.7, 61.8, 51.5 ppm. Anal. Calc for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46. Found: C, 71.62; H, 6.54.

Methyl (E)-2-[(E)-2-ethoxycarbonyl-2-buten-2-yl]-3-methoxypropenoate, (E,E)-18j. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and ethyl (*E*)-2-methyl-3-[(trifluoromethyl)sulfonyloxy]-2-butenoate, (*E*)-**20j** (Entry 10, Table 1), was purified by MPLC on silica gel, using a mixture of hexane and ethyl acetate (80 : 20) as eluant, to give in 70 % yield stereoisomerically pure (*E,E*)-**18j** as an oil. MS, m/z (%): 242 (33), 197 (70), 183 (84), 169 (74), 155 (98), 153 (87), 139 (73), 110 (65), 75 (100). IR (film): 1713, 1631, 1251, 1199, 1142, 1112 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.29 (1H, s, H-3), 4.21 (2H, q, J = 7.1 Hz, OCH_2), 3.86 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.09 (3H, s, H1' or H-4'), 1.75 (3H, s, H-4' or H-1'), 1.31 ppm (3H, t, J = 7.1 Hz, O-C-CH_3). ^{13}C NMR ($CDCl_3$): δ 168.9, 167.0, 157.8, 137.8, 127.1, 112.9, 61.8, 60.1, 51.4, 20.8, 17.0, 14.2 ppm. Anal. Calc for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.72; H, 7.90.

Methyl (E)-2-[2-(ethoxycarbonyl)-1-cyclopentenyl]-3-methoxypropenoate, (E)-18k. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and ethyl 2-(trifluoromethyl)sulfonyloxy--1-cyclopentene-1-carboxylate, **20k** (Entry 11, Table 1), was purified by MPLC on silica gel, using a mixture of hexane and ethyl acetate (75 : 25) as eluant, to give in 90 % yield stereoisomerically pure (*E*)-**18k** as a viscous oil. MS, *m/z* (%): 254 (14), 223 (25), 222 (100), 209 (31), 208 (69), 195 (34), 194 (71), 162 (46), 75 (55). IR (film): 1713, 1646, 1333, 1256, 1199, 1117 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.28 (1H, s, H-3), 4.12 (2H, q, J = 8.0 Hz, OCH_2), 3.83 (3H, s, OCH_3), 3.68 (3H, s, OCH_3), 2.70 (4H, br t, J = 7.5 Hz, H-3' and H-5'), 1.92 (2H, *pseudo*-quint, J = 7.5 Hz, H-4'), 1.22 ppm (3H, t, J = 8.0 Hz, C-CH_3). ^{13}C NMR ($CDCl_3$): δ 167.0, 165.3, 158.4, 146.2, 132.3, 108.6, 61.7, 59.7, 51.3, 37.6, 33.3, 21.8, 14.0 ppm. Anal. Calc for $C_{13}H_{18}O_5$: C, 61.40; H, 7.19. Found: C, 61.13; H, 7.36.

*Methyl (E)-[(E)-2-phenylethenyl-1-cyclopentenyl]-3-methoxypropenoate, (E,E)-**18l***. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19b** and (*E*)-2-(2-phenylethenyl)-1-[(trifluomethyl)sulfonyloxy]cyclopentene, (*E*)-**20l** (Entry 12, Table 1), was purified by MPLC on silica gel, using a mixture of benzene and hexane (80 : 20) as eluant, to give in 65 % yield stereoisomerically pure (*E,E*)-**18l** as a crystalline solid. M.p. 125 - 127 °C. MS, *m/z* (%): 284 (5), 263 (19), 262 (99), 261 (18), 193 (18), 184 (24), 183 (100), 108 (44), 107 (21). IR (KBr): 1698, 1623, 1284, 1246, 965, 755 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.46 (1H, s, H-3), 7.43 - 7.10 (5H, m, Harom), 6.77 (1H, d, J = 16.0 Hz, H-2" or H-1"), 6.44 (1H, d, J = 16.0 Hz, H-1" or H-2"), 3.82 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.67 (4H, *pseudo*-q, J = 7.6 Hz, H-3' and H-5'), 1.98 ppm (2H, *pseudo*-quint, J = 7.6 Hz, H-4'). ^{13}C NMR ($CDCl_3$): δ 168.1, 159.3, 138.9, 138.1, 134.1, 128.8, 128.5*, 127.0, 126.3*, 124.6, 107.8, 61.8, 51.5, 37.2, 32.5, 22.1 ppm. Anal. Calc for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.20; H, 7.39.

*Methyl (E)-2-[2-(6-methoxy-2-naphthyl)-1-cyclopentenyl]-3-methoxypropenoate, (E)-**18m***. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 2-(6-methoxy-2-naphthyl)-1-[(trifluoromethyl)sulfonyloxy]cyclopentene, **20m** (Entry 13, Table 1), was purified by MPLC on silica gel, using a mixture of hexane and ethyl acetate (75 : 25) as eluant, to give in 72 % yield (*E*)-**18m** as a crystalline solid. M.p. 129 - 131 °C. MS, *m/z* (%): 338 (39), 306 (38), 307 (100), 291 (16), 279 (15), 275 (26), 248 (42), 247 (22), 165 (17). IR (KBr): 1703, 1623, 1282, 1250, 1127, 1094 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.74 - 7.43 (4H, m, Harom), 7.25 (1H, s, H-3), 7.15 - 7.03 (2H, m, Harom), 3.90 (3H, s, OCH_3), 3.62 (3H, s, OCH_3), 3.53 (3H, s, OCH_3), 2.94 (2H, t, J = 7.3 Hz, H-3' or H-5'), 2.73 (2H, t, J = 7.3 Hz, H-5' or H-3'), 2.04 ppm (2H, *pseudo*-quint, J = 7.3 Hz, H-4'). ^{13}C NMR ($CDCl_3$): δ 168.1, 159.2, 157.4, 139.8, 134.0, 133.2, 129.6, 129.5, 128.7, 125.9*, 125.1, 118.4, 109.4, 105.5, 61.4, 55.2, 51.3, 38.0, 36.8, 22.2 ppm. Anal. Calc for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.19; H, 6.41.

*Methyl (E)-(2-phenylethynyl-1-cyclopentenyl)-3-methoxypropenoate, (E)-**18n***. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 2-phenylethynyl-1-[(trifluoromethyl)sulfonyloxy]cyclopentene, **20n** (Entry 14, Table 1), was purified by MPLC on silica gel, using benzene as eluant, to give in 31 % yield stereoisomerically pure (*E*)-**18n** as a viscous oil. MS, *m/z* (%): 282 (50), 251 (100), 223 (75), 192 (71), 191 (81), 179 (59), 178 (85), 165 (56), 75 (52). IR (film): 1709, 1627, 1256, 1142, 1120, 758 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.43 -7.21 (6H, br m, Harom and H-3), 3.86 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 2.68 (4H, br t, J = 7.5 Hz, H-3' and H-5'), 1.98 ppm (2H, *pseudo*-quint, J = 7.5 Hz, H-4'). ^{13}C NMR ($CDCl_3$): δ 167.9, 159.5, 141.8, 131.3*, 120.2*, 127.7, 123.9, 122.9, 108.0, 94.7, 86.9, 61.9, 51.5, 36.9, 36.4, 23.0 ppm. Anal. Calc for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found, C, 76.85; H, 5.60.

*Methyl (E)-2-(1-indenyl)-3-methoxypropenoate, (E)-**18o***. The crude reaction product, which was obtained from the Pd-catalyzed reaction between (*Z*)-**19a** and 1-[(trifluoromethyl)sulfonyloxy]indene, **20o** (Entry 15, Table 1), was purified by MPLC on silica gel, using benzene as eluant, to give in 20 % yield stereoisomerically pure (*E*)-**18o** as a crystalline solid. M.p. 77 - 79.5 °C. MS, *m/z* (%): 230 (100), 198 (29), 170 (40), 155 (50), 142 (29), 141 (32), 127 (53), 115 (31), 75 (74). IR (KBr): 1698, 1645, 1284, 1258, 1134, 780 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.63 (1H, s, H-3), 7.50 - 7.05 (4H, br m, Harom), 6.50 (1H, br s, H-2'), 3.83 (3H, s, OCH_3), 3.71 (3H, s, OCH_3), 3. 49 ppm (2H, br s, H-3'). ^{13}C NMR ($CDCl_3$): δ 168.0, 160.6, 144.4, 143.5, 135.5, 134.3, 125.8, 124.4, 123.6, 120.3, 105.9, 61.9, 51.5, 38.4 ppm. Anal. Calc for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.37;

H, 6.32.

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