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TETRAHEDRON

Synthesis of Vinyl Nonaflates Derived from β-Ketoesters, β-Diketones or α-Diketones and Their Palladium-Catalyzed Cross-Coupling Reactions with Organozinc Halides

Fabio Bellina,* Donatella Ciucci, Renzo Rossi* and Piergiorgio Vergamini

Dipartimento di Chimica e Chimica Industriale, University of Pisa, Via Risorgimento 35,
I-56126 Pisa, Italy,[a] and

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Abstract : Cyclic and acyclic β-ketoesters **4**, a typical cyclic α-diketone **5** and a typical cyclic β-diketone **6** were converted to the corresponding vinyl nonaflates of general formula **7**, **8** and **9**, respectively, by reaction with 1.2-1.5 equiv of NaH in DMF at 20-55 °C followed by treatment with 1.15-1.30 equiv of perfluoro-1-butanesulfonyl fluoride at 20 °C. These vinyl nonaflates, which were purified by MPLC on silica gel, proved to be excellent electrophiles in Pd-catalyzed cross-coupling reactions with aryl-, 1-alkynyl- and alkylzinc chlorides. A variety of cyclic and acyclic tetrasubstituted α,β-unsaturated esters which included stereoisomerically pure compounds, a 2-substituted 3-aryl-2-cyclopentenone and naturally-occurring dihydrojasmone were cleanly synthesized by these smooth and selective cross-coupling reactions. © 1999 Elsevier Science Ltd. All rights reserved.

In conjunction with our studies on the synthesis of biologically active natural compounds and their precursors by new procedures based on the use of transition metal-catalyzed reactions between organometallics and highly functionalized and stereodefined C_{sp^2}-electrophiles,[1] recently we became interested in the synthesis of large amounts of highly functionalized substances, which are characterized by tetrasubstituted carbon-carbon double bonds, by palladium-catalyzed reactions of organometallics, which are tolerant of a variety of functional groups, and vinyl perfluoroalkanesulfonates such as those of general formula **1**, **2** and **3**. On the other hand, palladium-catalyzed cross-coupling reactions between organoboron, organoaluminum, organozinc or organotin compounds and vinyl triflates of general formula **1**, **2** or **3** (where C_nF_{2n+1} = CF_3SO_2) have been extensively used in organic synthesis,[2-6] although these reactions, which sometimes are low yielding, do not appear to scale up owing to the high cost of triflic anhydride or N,N-bis(trifluoromethanesulfonyl)-N-phenylimide (N-phenyltriflimide), which are the reagents usually employed for the synthesis of compounds **1**, **2** and **3** from the corresponding β-ketoesters **4**, α-diketones **5** and β-diketones **6**, respectively.[7-9] We now wish to report that vinyl nonaflates of general formula **7**, **8** and **9** represent a convenient alternative to the triflates of general formula **1**, **2** and **3**, respectively. In fact, we found that compounds **7** and **9** can be efficiently prepared by reaction between the sodium enolates derived from compounds **4** and **6**, respectively, and perfluoro-1-butanesulfonyl fluoride, an industrial reagent less expensive than triflic anhydride and, in particular, than N-

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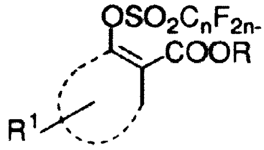
phenyltriflimide. Moreover, a similar procedure allowed us to prepare, although in a modest yield, a typical vinyl nonaflate of general formula **8** starting from the corresponding α-diketone **5**.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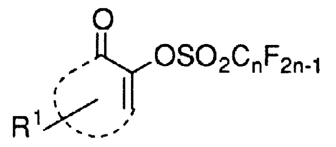
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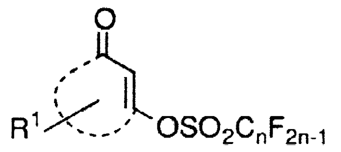
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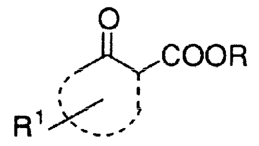
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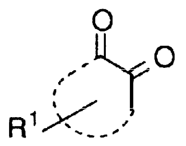
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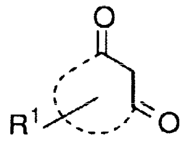
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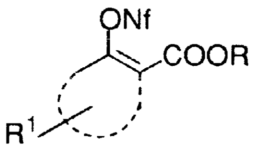
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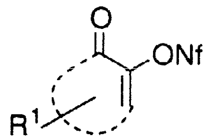
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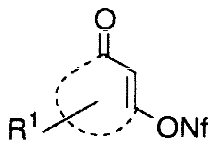
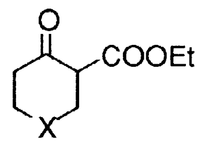
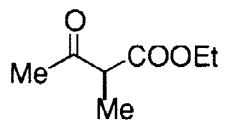

9 (Nf = $C_4F_9SO_2$)

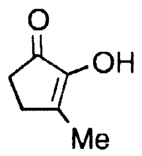
We also found that these vinyl nonaflates, which could be purified by MPLC on silica gel or could be employed as crude products but almost free from the solvent and the reagents used for their preparation or still dissolved in the reaction mixtures derived from their preparation, represent efficient electrophiles in palladium-catalyzed cross-coupling reactions with aryl-, 1-alkynyl- or alkylzinc chlorides.[10]

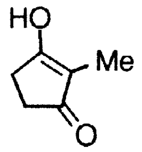
RESULTS AND DISCUSSION

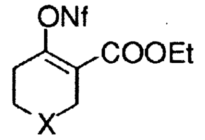
Two cyclic β-ketoesters, *i.e.* compounds **4a** and **4b**, the acyclic β-ketoester **4c**, the cyclic α-diketone **5a** and the cyclic β-diketone **6a** were used as starting materials for the preparation of the corresponding vinyl nonaflates, *i.e.* compounds **7a**, **7b**, (*E*)-**7c**, **8a** and **9a**, respectively.

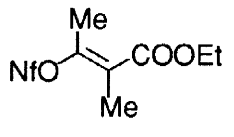

4a : X = CH_2
4b : X = NMe

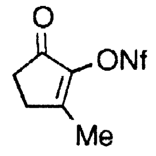

4c

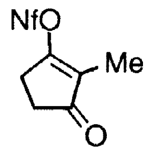

5a


6a


7a : X = CH_2
7b : X = NMe


(*E*)-**7c**

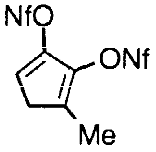

8a


9a

Compounds **4a**, **4c**, **5a** and **6a** were commercially available and compound **4b** was synthesized by cyclization of bis[2-(ethoxycarbonyl)ethyl]methylamine with NaH[11] or $TiCl_4$.[12] Reaction of **4a**, **4b** and **4c** with

1.2 equiv of NaH in dry DMF at room temperature for 1.5-6 h followed by treatment of the resulting sodium enolates with 1.15 equiv of freshly distilled perfluoro-1-butanesulfonyl fluoride allowed to obtain crude **7a**, **7b** and stereoisomerically pure (*E*)-**7c** in 92-100 % yield and chemical purity higher than 95 %. Crude **7a** and (*E*)-**7c** were then purified by MPLC on silica gel and were fully characterized. On the contrary, no attempt was made to purify crude **7b**, which was directly used as electrophile in Pd-catalyzed cross-coupling reactions with organozinc chlorides. Interestingly, the procedure used to prepare compounds **7a**, **7b** and (*E*)-**7c** also allowed to synthesize very efficiently, starting from **6a**, a solution of crude **9a** in the reaction mixture derived from its preparation. However, an attempt to isolate pure **9a** proved to be unsuccessful owing to the instability of this nonaflate at room temperature in the absence of solvents. Therefore, the DMF solution of **9a**, which was obtained in the preparation of this compound from **6a**, was directly used in a subsequent Pd-catalyzed cross-coupling reaction with an aryl zinc chloride.

Finally, several attempts were made to prepare selectively compound **8a** from **5a** either using experimental conditions similar to those employed for the synthesis of **7a**, **7b**, (*E*)-**7c** and **9a** or by modifications of these conditions. Nevertheless, GLC/MS analyses of the reaction mixtures obtained in these attempts showed that in any case they contained the desired vinyl nonaflate **8a** contaminated by significant amounts of unreacted **5a** and a compound, which presumbly corresponded to the dinonaflate **10**.

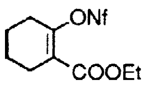
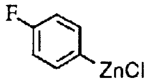
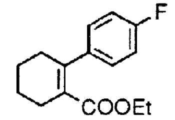
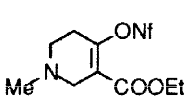
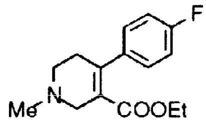
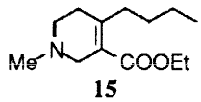
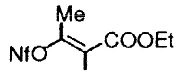
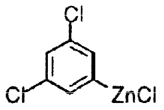
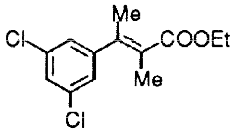
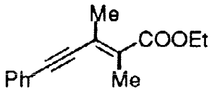
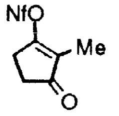
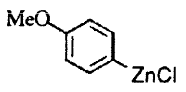
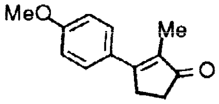
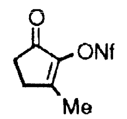
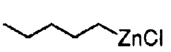
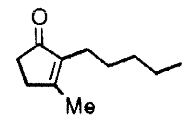


10

The best result was obtained when **5a** was reacted with 1.5 equiv of NaH in DMF at 55 °C for 1.5 h and the resulting deep violet reaction mixture was treated with 1.3 equiv of perfluoro-1-butanesulfonyl fluoride at 20 °C for 3 h. The so obtained reaction mixture proved to contain compounds **5a**, **8a** and **10** in a 9.5 : 77.1 : 13.4 molar ratio, respectively, the ratio being determined by GLC analyses. Purification of this mixture of compounds by MPLC on silica gel allowed to obtain compound **8a** in 33 % yield.

We next examined the palladium-catalyzed cross-coupling reactions between a variety of organozinc halides **12**, which included aryl-, 1-alkynyl- and alkylzinc chlorides, and the chemically pure vinyl nonaflates **7a**, (*E*)-**7c** and **8a**, crude compound **7b** as well as crude **9a**, which was dissolved in the DMF solution derived from its preparation. These reactions were carried out in THF solution (or in a mixture of THF and DMF when compound **9a** was used) at 65 °C for 5-28 h using 1.5 equiv of organozinc chlorides **12** and in the presence of 2 mol % bis(dibenzylideneacetone)palladium(0) [$Pd(dba)_2$] and 2 mol % bis(diphenylphosphino)ferrocene (dppf). As shown in the Table, where the results of these smooth and clean cross-couplings are summarized, these reactions, although not optimized, afforded the desired cross-coupled products **13**-**19** in satisfactory to good yields. As expected the lower yield (38 %) was obtained when the above mentioned DMF solution of crude **9a** was employed (entry 6, Table). As regards the reactions involving the vinyl nonaflates **7a**, **7b** and stereoisomerically pure (*E*)-**7c**, it must be noted that they allowed to prepare selectively and very efficiently a variety of tetrasubstituted α,β-unsaturated esters which are not easily available by other methods (entries 1-5, Table) and that the esters derived from (*E*)-**7c**, *i.e.* (*E*)-**16** and (*E*)-**17**, were stereoisomerically pure. Finally, it is worthwhile mentioning that by the palladium-catalyzed reaction between **8a** and the alkylzinc chloride **12f** (entry 7, Table) it was possible to prepare in a satisfactory yield dihydrojasmone, **19**, a naturally-occurring substance used as a perfume ingredient. Thus, the experimentally very simple two-step synthesis of this compound from commercially available **5a** represents an attractive alternative to the existing literature procedures.[13]

Table. Palladium-catalyzed reactions between organozinc chlorides, **12**, and vinyl nonaflates **7a**, **7b**, (*E*)-**7c**, **8a** and **9a**, respectively.[a]

Entry	Vinyl nonaflate	Organozinc chloride	Solvent	Reaction conditions (h / °C)	Product	Isolated Yield (%)
1	 **7a**	 **12a**	THF	5 / 65	 **13**	91
2[b]	 **7b**	**12a**	THF	11 / 65 then 14 / 20	 **14**	57
3[b,c]	**7b**	 **12b**	THF	17 / 65	 **15**	72
4	 (*E*)-**7c**	 **12c**	THF	28 / 65	 (*E*)-**16**	77
5	(*E*)-**7c**	Ph—≡—ZnCl **12d**	THF	22 / 65	 (*E*)-**17**	85
6[d]	 **9a**	 **12e**	DMF-THF	15 / 65	 **18**	38
7	 **8a**	 **12f**	THF	20 / 65	 **19**	62

(a) Unless otherwise reported these reactions were carried out in the presence of 2 mol % Pd(dba)$_2$ and 2 mol % dppf. b) This reaction was carried out using crude compounds **7b**. c) This reaction was carried out using a catalyst system constituted of 4 mol % Pd(dba)$_2$ and 4 mol % dppf. d) This reaction was carried out using the DMF solution of crude compound **9a** which derived from treatment of **6a** with a suspension of NaH in DMF followed by addition of perfluoro-1-butanesulfonyl fluoride.

In summary, we have shown that cyclic and acyclic β-ketoesters and cyclic α- and β-diketones can be easily and, in general, conveniently converted into the corresponding vinyl nonaflates. Moreover, we have demonstrated that these last compounds represent efficient electrophiles in palladium-catalyzed cross-coupling reactions with a variety of organozinc derivatives. In fact, these smooth reactions allow to prepare efficiently and selectively a variety of tetrasubstituted α,β-unsaturated esters, which include stereoisomerically pure compounds, 2-substituted 3-aryl-2-cyclopentenones such as compound **18**, as well as 3-substituted 2-alkyl-2-cyclopentenones such as naturally-occurring dihydrojasmone, **19**. Thus, it is possible to conclude that the vinyl nonaflates derived from β-ketoesters, α- and β-diketones represent an excellent alternative to the corresponding triflates.

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-35 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. ^{1}H 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. 2-Ethoxycarbonylcyclohexanone **4a**, ethyl 2-methylacetoacetate **4c**, 3-methyl-1,2-cyclopentanedione **5a** and 2-methyl-1,3-cyclopentanedione **6a** were commercially available. 1-Methyl-3-ethoxycarbonyl-4-piperidone **4b** was synthesized by cyclization of bis[2-(ethoxycarbonyl)ethyl]methylamine with NaH[10] or $TiCl_4$.[11] Pd(dba)$_2$ and dppf were commercially available. 4-Fluorophenylzinc chloride **12a**, 1-butylzinc chloride **12b**, 3,5-dichlorophenylzinc chloride **12c**, phenylethynylzinc chloride **12d**, 4-methoxyphenylzinc chloride **12e** and 1-pentylzinc chloride **12f** were prepared by reaction of THF solutions of the corresponding Grignard reagents with a THF solution of 1.3 equiv of dry $ZnCl_2$.

Ethyl 2-(perfluoro-1-butanesulfonyloxy)-1-cyclohexene carboxylate, 7a. A dispersion of NaH (60 %, 0.72 g, 18.0 mmol) in mineral oil was washed with pentane and the residue was diluted with DMF (33 ml). To the resulting suspension stirred at room temperature was added dropwise a solution of **4a** (2.55 g, 15.0 mmol) in DMF (9 ml). After stirring for 1.5 h, perfluoro-1-butanesulfonyl fluoride (5.21 g, 17.25 mmol) was added dropwise and the resulting mixture, which was periodically monitored by TLC and GLC analyses, was stirred for an additional 6 h. It was then poured into a large excess of a cold saturated aqueous NH_4Cl solution and extracted repeatedly with Et_2O. The collected organic extracts were washed with water, dried and concentrated *in vacuo* to give crude **7a** (7.47 g) as a colourless oil. GLC/MS analysis showed that this compound had 95 % chemical purity. Crude **7a** was then purified by MPLC on silica gel, using a mixture of hexane and THF (97 : 3) as eluant, to give **7a** (6.50 g, 96 % yield) as an oil, which had chemical purity higher than 99 %. MS, *m/z* (%): 452 (0.4), 407 (8), 219 (5), 169 (39), 123 (100), 99 (23), 96 (42), 79 (20), 55 (26). IR (film): ν 1728, 1426, 1287, 1240, 1202, 1145, 1045 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.28 (2H, q, J = 7.2 Hz), 2.52-2.37 (4H, br m), 1.82-1.62 (4H, br m), 1.33 ppm (3H, t, J = 7.2 Hz). Anal. Calc for $C_{13}H_{13}F_9O_5S$: C, 34.52; H, 2.90. Found: C, 34.80; H, 2.60.

*Ethyl 4-(perfluoro-1-butanesulfonyloxy)-1-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate, **7b**.* This crude compound, having 99 % chemical purity, was prepared in 92 % yield starting from **4b** by the same procedure employed in the synthesis of crude **7a**. Crude **7b** was obtained as a pale yellow oil. MS, *m/z* (%): 467 (0.5), 422 (45), 218 (28), 184 (98), 168 (24), 137 (88), 11 (100), 84 (71), 69 (98). IR (film): ν 1724, 1429, 1280, 1241, 1202, 1144, 1034 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.29 (2H, q, J = 7.0 Hz), 3.34 (2H, t, J = 2.5 Hz), 2.70-2.50 (4H, br m), 2.42 (3H, s), 1.33 ppm (3H, t, J = 7.0 Hz). Anal. Calc for $C_{13}H_{14}F_9NO_5S$: C, 33.41; H, 3.02. Found: C, 33.72; H, 2.70. This compound was used in the next step without any further purifiction.

Ethyl (E)-2-methyl-3-(perfluoro-1-butanesulfonyloxy)-2-butenoate, (E)-7c. Compound **4c** was converted into crude (*E*)-**7c** by the same procedure used for the synthesis of crude **7a** and **7b**. This crude product, which had 94.5 % chemical purity, was purified by MPLC on silica gel, using a mixture of hexane and benzene (80 : 20) as eluant, to give chemically and stereoisomerically pure (*E*)-**7c** (6.10 g, 83.5 % yield) as a colourless oil. MS, *m/z* (%): 381 (75), 380 (62), 131 (28), 127 (34), 98 (80), 87 (61), 83 (24), 70 (72), 69 (100). IR (film): ν 1728, 1422, 1282, 1241, 1205, 1146, 1081 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 4.26 (2H, q, J = 7.1 Hz), 2.42 (3H, br s), 2.01 (3H, br s), 1.33 ppm (3H, t, J = 7.1 Hz).Anal. Calc for $C_{11}H_{11}F_9O_5S$: C, 30.99; H, 2.60. Found: C, 31.24; H, 2.75.

3-Methyl-2-(perfluoro-1-butanesulfonyloxy)-2-cyclopenten-1-one, 8a. A dispersion of NaH (60 %, 1.50 g, 37.5 mmol) in mineral oil was washed with pentane and the residue was diluted with DMF (40 ml). To the resulting suspension stirred at room temperature was added dropwise a solution of **5a** (2.80 g, 25.0 mmol) in DMF (30 ml) and the mixture was stirred for 1.5 h at 55 °C. The resulting reaction mixture, which was quite viscous and deep violet coloured, was then cooled to 0 °C and perfluoro-1-butanesulfonyl fluoride (9.82 g, 32.5 mmol) was slowly added. The resulting mixture, which became more fluid and brown coloured, was stirred at room temperature for 3 h. GLC and GLC/MS analyses of an its small sample showed that it contained a mixture of **5a**, the expected vinyl nonaflate **8a** and another compound, which presumably corresponded to the dinonaflate **10**, in a 9.6 : 77.1 : 13.3 molar ratio, respectively. The reaction mixture was then poured into a large excess of cold saturated aqueous NH_4Cl solution and extracted with Et_2O. The organic extract was washed with water, dried and concentrated *in vacuo*. The resultant oil was purified by MPLC on silica gel, using a mixture of hexane and CH_2Cl_2 (50 : 50) as eluant, to give pure **8a** (3.24 g, 32.8 % yield) as a colourless solid. M.p. 33-34 °C. MS, *m/z* (%): 394 (9), 315 (12), 302 (18), 159 (11), 131 (17), 83 (40), 69 (100), 55 (94), 41 (89). IR (KBr): ν 1729, 1260, 1239, 1202, 1144, 799 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.72-2.63 (2H, br m), 2.55-2.47 (2H, br m), 2.17 ppm (3H, s). Anal. Calc for $C_{10}H_7F_9O_4S$: C, 30.47; H, 1.78. Found: C, 30.83; H, 1.60.

2-Methyl-3-(perfluoro-1-butanesulfonyloxy)-2-cyclopenten-1-one, 9a. A dispersion of NaH (60 %, 0.96 g, 23.0 mmol) in mineral oil was washed with pentane and the residue was diluted with DMF (44 ml). To the resulting mixture stirred at room temperature was added dropwise a solution of **6a** (2.24 g, 20.0 mmol) in DMF (10 ml). After stirring for 4 h at room temperature and for 45 min at 45 °C, perfluoro-1-butanesulfonyl fluoride (6.95 g, 23.0 mmol) was added dropwise and the resulting mixture, which was periodically monitored by GLC analysis, was stirred at room temperature for 3.5 h. After this period a GLC/MS analysis of a sample of the reaction mixture, which was poured into water and extracted with Et_2O, showed that **6a** had been completely consumed and the presence of a new compound which had MS spectrum corresponding to that of **9a**. MS, *m/z* (%): 394

(18), 219 (14), 131 (43), 119 (17), 111 (100), 100 (22), 83 (52), 69 (79), 55 (33). The so obtained DMF solution of crude **9a** was used directly in the next step. In fact, owing to the instability of **9a** in the absence of solvents, an attempt to isolate **9a** from this DMF solution was unsuccessful.

*General procedure for the palladium-catalyzed cross-coupling rections between organozinc chlorides **12** and the vinyl nonaflates **7a**, **7b**, (E)-**7c**, and **8a**.* A THF slurry of an organozinc chloride **12** in THF was prepared by addition of a 0.50 M THF solution of the corresponding Grignard reagent (40 ml, 20.0 mmol) to a solution of dry $ZnCl_2$ (3.54 g, 26.0 mmol) in THF (30 ml), which was stirred at 0 °C. After stirring for an additional 40 min, $Pd(dba)_2$ (0.23 g, 0.40 mmol), dppf (0.22 g, 0.40 mmol) and a solution of a vinyl nonaflate (13.3 mmol) in THF (25 ml) were sequentially added. The resulting mixture was allowed to warm up to room temperature and then heated to 65 °C for the period of time reported in the Table. After usual aqueous workup, the crude reaction product 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 *in vacuo* and the residue was purified by MPLC on silica gel. Compounds **13**, **14**, **15**, (*E*)-**16**, (*E*)-**17** and **19** (entries 1-5 and 7, Table) were prepared according to this procedure.

*Ethyl 2-(4-fluorophenyl)-1-cyclohexene-1-carboxylate, **13**.* The crude reaction product, which was obtained from the palladium-catalyzed reaction between **7a** and 4-fluorophenylzinc chloride, **12a**, according to the above mentioned procedure (entry 1, Table), was purified by MPLC on silica gel, using a mixture of hexane and Et_2O (95 : 5) as eluant, to give in 91 % yield compound **13** as a colourless liquid. MS, *m/z* (%): 248 (42), 219 (14), 202 (70), 175 (49), 174 (51), 147 (61), 133 (40), 109 (100), 79 (15). IR (film): ν 1708, 1509, 1286, 1254, 1244, 1051 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.09-6.98 (4H, br m), 3.89 (2H, q, J = 7.1 Hz), 2.42-2.35 (4H, dd, J = 11.9 and 2.1 Hz), 1.73 (4H, t, J = 7.1 Hz), 0.89 ppm (3H, t, J = 7.1 Hz). Anal. Calc for $C_{15}H_{17}FO_2$: C, 72.56; H, 6.90. Found: C, 73.01; H, 6.75.

*Ethyl 4-(4-fluorophenyl)-1-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate, **14**.* The crude reaction product, which was obtained from the palladium-catalyzed rection between **7b** and **12a** (entry 2, Table) according to the above mentioned procedure, was purified by MPLC on silica gel, using a mixture of hexane, AcOEt and Et_3N (75 : 20 : 5) as eluant, to give in 57 % yield chemically pure **14** as a pale yellow oil. MS, *m/z* (%): 263 (20), 234 (92), 218 (11), 191 (13), 190 (89), 175 (14), 147 (60), 109 (29), 42 (100). IR (film): ν 1703, 1509, 1295, 1227, 1132 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.15-6.96 (4H, m), 3.92 (2H, q, J = 7.0 Hz), 3.29 (2H, br s), 2.65-2.51 (5H, br m), 2.46 (3H, s), 0.92 ppm (3H, t, J -= 7.0 Hz). Anal. Calc for $C_{15}H_{18}FNO_2$: C, 68.42; H, 6.89. Found: C, 69.00; H, 7.50.

*Ethyl 4-butyl-1-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate, **15**.* The crude reaction product, which was obtained from the palladium-catalyzed reaction between **7b** and 1-butylzinc chloride, **12b**, according to the above mentioned procedure (entry 3, Table), was purified by MPLC on silica gel, using a mixture of CH_2Cl_2 and hexane (70 : 30) as eluant, to give in 72 % yield chemically pure **15** as a colourless liquid. MS, *m/z* (%): 225 (10), 196 (100), 180 (11), 178 (13), 168 (30), 152 (35), 140 (26), 109 (12), 108 (11). IR (film): ν 1714, 1465, 1385, 1294, 1274, 1239, 1091 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.18 (2H, q, J = 7.1 Hz), 3.13 (2H, br s), 2.50-2.40 (6H, br m), 2.38 (3H, s), 1.46-1.30 (4H, br m), 1.29 (3H, t, J = 7.1 Hz), 0.90 ppm (3H, t, J = 7.1 Hz). Anal.

Calc for $C_{13}H_{23}NO_2$: C, 69.29; H, 10.29. Found: C, 69.67; H, 10.60.

Ethyl (E)-2-methyl-3-(3,5-dichlorophenyl)-2-butenoate, (E)-16. The crude reaction product, which was obtained from the palladium-catalyzed reaction between (*E*)-**7c** and 3,5-dichlorophenylzinc chloride, **12c**, according to the above mentioned procedure (entry 4, Table), was purified by MPLC on silica gel, using a mixture of hexane and benzene (75 : 25) as eluant, to give in 77 % yield chemically and stereoisomerically pure (*E*)-**16** as a colourless solid. M.p. 64.5-65.5 °C. MS, *m/z* (%): 274 (20), 272 (36), 227 (73), 226 (100), 199 (20), 198 (22), 191 (25), 149 (20), 128 (50). IR (KBr): ν 1716, 1557, 1291, 1260, 1150, 1089, 800 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.28 (1H, s), 7.04 (2H, s), 4.26 (2H, q, J = 7.0 Hz), 2.20 (3H, s), 1.75 (3H, s), 1.34 ppm (3H, t, J = 7.0 Hz). Anal. Calc for $C_{13}H_{14}Cl_2O_2$: C, 57.16; H, 5.16. Found: C, 57.14; H, 4.97.

Ethyl (E)-2-methyl-3-phenylethynyl-2-butenoate, (E)-17. The crude reaction product, which was obtained from the palladium-catalyzed reaction between (E)-**7c** and phenylethynylzinc chloride, **12d**, according to the above mentioned procedure (entry 5, Table), was purified by MPLC on silica gel, using a mixture of hexane and benzene (70 : 30) as eluant, to give in 85 % yield chemically and stereoisomericallly pure (*E*)-**17** as a pale yellow liquid. MS, *m/z* (%): 228 (58), 200 (56), 199 (50), 183 (54), 155 (34), 153 (45), 143 (73), 128 (49), 115 (100). IR (film): ν 1710, 1323, 1267, 1184, 1098, 757, 691 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.49-7.32 (5H, m), 4.23 (2H, q, J = 7.1 Hz), 2.26 (3H, s), 2.19 (3H, s), 1.32 ppm (3H, t, J = 7.1 Hz). Anal. Calc for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.08; H, 7.21.

3-Methyl-2-pentyl-2-cyclopenten-1-one (dihydrojasmone), 19. The crude reaction product, which was obtained from the palladium-catalyzed reaction between **8a** and pentylzinc chloride, **12f**, according to the above mentioned procedure (entry 7, Table), was purified by MPLC on silica gel, using a mixture of CH_2Cl_2 and hexane (80 : 20) as eluant, to give 97 % chemically pure **19** as a colourless liquid. B.p. 121-122/14 Torr. Lit[13f] b.p. 110-112 °C/10 Torr. MS, *m/z* (%): 166 (4), 151 (68), 137 (17), 123 (20), 110 (100), 95 (28), 81 (27), 67 (23). IR (film): ν 1702, 1650, 1386, 1178, 1074 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.60-1.90 (6H, m), 2.05 (3H, s), 1.45-1.15 (6H, br m), 0.87 ppm (3H, t, J = 6.9 Hz). The physical and spectral properties of this compound matched those previously reported.[13f]

3-(4-Methoxyphenyl)-2-methyl-2-cyclopenten-1-one, 18. Pd(dba)$_2$ (0.23 g, 0.40 mmol) and dppf (0.22 g, 0.40 mmol) were added to a slurry of 4-methoxyphenylzinc chloride **12e** in THF, which was prepared by reaction of a 0.47 M THF solution of 4-methoxyphenylmagnesium bromide (63.8 ml, 30.0 mmol) and a solution of dry $ZnCl_2$ (5.31 g, 39.0 mmol) in THF at 0 °C. To this mixture, which was maintained under stirring at 0°C, was slowly added a DMF solution of crude **9a**, which, as described above, had been obtained by reaction of a solution of **6a** (2.24 g, 20.0 mmol) in DMF (10 ml) with suspension of NaH (24.0 mmol) in DMF (44 ml) followed by treatment with perfluoro-1-butanesulfonyl fluoride (23.0 mmol). The resulting mixture was allowed to warm up to room temperature and then heated to 65 °C for 15 h. After this period a GLC/MS analysis of a sample of the reaction mixture, which was hydrolyzed with a cold saturated aqueous NH_4Cl solution and extracted with Et_2O, showed that **9a** had been completely consumed and the presence of three compounds in a *ca.* 48 : 49 : 3 molar ratio, which were identified as anisole, compound **18** and 4,4'-dimethoxybiphenyl, respectively. After usual workup the crude reaction mixture was purified by MPLC on silica gel, using a mixture of benzene and Et_2O (90 : 10) as eluant, to give chemically pure **18** (1.54 g, 38 % yield) as a solid (entry 6, Table). M.p. 58-61 °C. MS, *m/z* (%): 202 (100), 201 (78), 171 (61), 159 (19), 146 (9), 131 (9), 115 (12). IR (KBr): ν 1691, 1680, 1607, 1512, 1294, 1258, 1182, 1027, 837 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.54 (2H, d, J = 8.8 Hz), 6.98 (2H, d, J = 8.8 Hz), 3.86 (3H, s), 2.90-2.86 (3H, br m), 2.52 (3H, br m), 1.99 ppm (3H, s). Anal. Calc for $C_{13}H_{14}O_2$: C, 77.13; H, 6.92. Found: C, 77.25; H, 7.02.

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