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# New developments in the Pd-catalysed cyclisation-coupling reaction of alkene-containing carbonucleophiles with organic halides (and triflates). The first examples of asymmetric catalysis.

Didier Bruyère, Nuno Monteiro, Didier Bouyssi, Geneviève Balme *

*Laboratoire de Chimie Organique 1, CNRS UMR 5622, Université Claude Bernard, Lyon 1, CPE. 43, Bd du 11 Novembre 1918, 69622 Villeurbanne, France*

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Dedicated to Professor Jean-Pierre Genêt on the occasion of his 60th birthday with regards and best wishes

**Abstract**

The results of our preliminary investigations directed toward asymmetric catalysis of the cyclocarbopalladation of alkenes bearing a proximate nucleophile with organic halides (or triflates) are disclosed. A series of bidentate phosphine ligands were evaluated in intramolecular versions of this reaction using (*E*)-2-[7-(2-bromophenyl)-hept-4-enyl]-malonic acid dimethyl ester (**1**) and (*Z*)-2-[7-(2-trifluoromethanesulfonyloxy-phenyl)-hept-4-enyl]-malonic acid dimethyl ester (**9**) as model substrates. The highest enantioselective induction was obtained with aryl triflate **9** which produced the corresponding cyclopentylindane as a single diastereomer in 54% chemical yield and 43% ee by using $PdCl_2$[*S*-(−)-TolBINAP] as chiral catalyst and $K_2CO_3$ as base.


*Keywords:* Asymmetric catalysis; Palladium; P ligands; Carbocyclisations

## 1. Introduction

The cyclisation of unsaturated substrates bearing a proximate nucleophile promoted by organopalladium complexes is now well established as a powerful method for the one-step synthesis of various carbo- and heterocyclic systems [1,2].

The mechanistic pathway generally considered for this process is described in Scheme 1. An oxidative addition of the electrophilic substrate RX to palladium (0) gives a $RPdL_2X$ complex. Displacement of one of the ligands L or X and coordination to the insaturation activates it toward the intramolecular attack of the nucleophile from the side opposite to the palladium. Such a mechanism is quite similar to that involved in Wacker-type reactions but in this case an organopalladium complex rather than a palladium salt acts as the electrophilic promotor. Finally, a reductive elimination leads to the expected product and regenerates the catalyst.

In this context, our group has recently developed some efficient intramolecular versions of this methodology for the construction of tricyclic structures [3]. In particular, we have demonstrated that the palladium-mediated cyclisation of linear compounds of type **1** (*Z* or *E*) proceeds with complete retention of the stereochemistry in a stereocontrolled mode since it involves attack of the carbon nucleophile onto the double bond electrophilically activated by the organopalladium species [4a]. Therefore, the reaction was shown to be stereospecific with the stereochemical outcome depending on the geometry of the internal alkene [4b,c]. Moreover, the regiochemistry of the cyclisation (5 *exo* vs. 6 *endo*) can be controlled by the steric bulk of the nucleophilic part (Scheme 2). This transformation occurred with the formation of two new contiguous tertiary carbon stereocenters.

* Corresponding author. Tel.: +33-47-2431-416; fax: +33-47-2431-214.
*E-mail address:* balme@univ-lyon1.fr (G. Balme).

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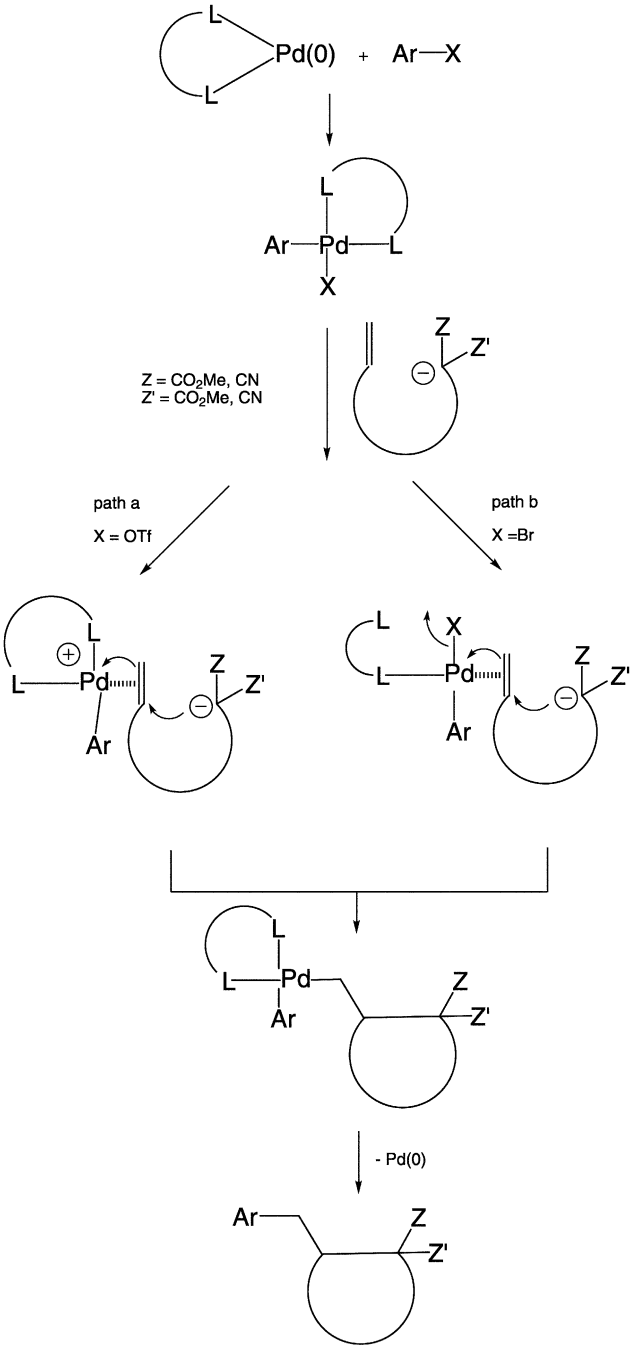



Scheme 1.

The synthetic utility of this new process would be enhanced if optically active products were to be produced. Indeed, although this new palladium-mediated cyclisation process has received considerable attention since its discovery, asymmetric catalysis of this reaction has not been investigated to date [5]. In this regard, we envisioned that the use of a palladium complex containing chiral phosphine ligands would offer an opportunity for enantioselective induction when the reaction is applied to alkene substrates. We would like to report herein our preliminary results in this field.

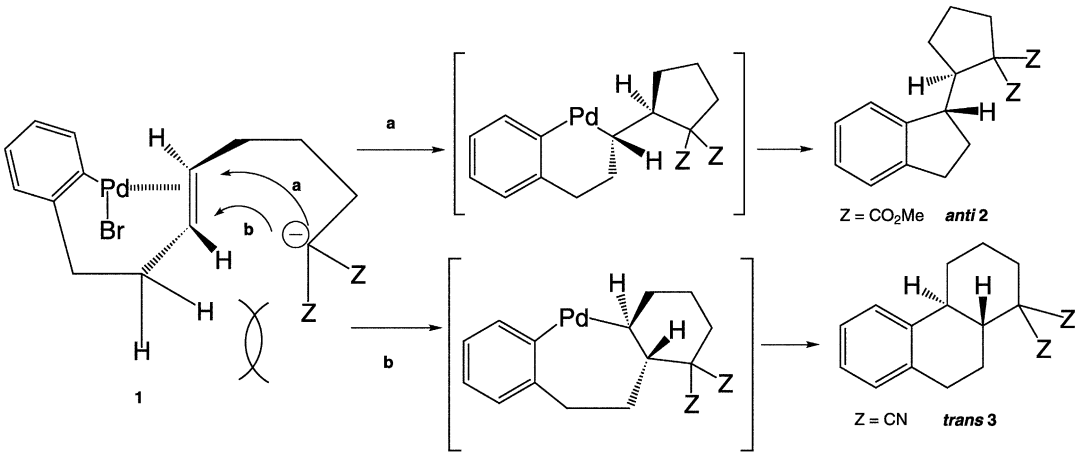
## 2. Results and discussion

With regard to the enantioselectivity, the key steps in the catalytic cycle seems to be complexation of the organopalladium intermediate to the alkene (identical to that of the Heck reaction) and attack of the carbon nucleophile onto this activated alkene. It is not very easy to determine which of these two elementary steps is the more important for the resulting enantioselectivity, however, it appeared to us that to maximize the asymmetric induction, as for the Heck reaction, both phosphines of the diphosphine ligand have to be coordinated to palladium during the enantioselective step. Cabri and Hayashi have demonstrated that a high level of asymmetric induction can be obtained in Heck reactions when aryl or vinyltriflates were used as substrates 6a,b. In this case, the reaction follows a cationic pathway and the chiral bidentate ligand is strongly associated to the palladium atom in the complexation step (Scheme 1, path a). In marked contrast, a low enantioselectivity was observed in the presence of the corresponding halides. This was attributed to the reaction mechanism involving here a neutral organopalladium intermediate via a partial dissociation of the chiral ligand (Scheme 1, path b). However, it was shown that addition of silver salts regenerates a cationic pathway by scavenging the halide [7].

### 2.1. Cyclisation of (*E*)-2-[7-(2-bromophenyl)-hept-4-enyl]-malonic acid dimethyl ester (**1**)

The linear substrate (*E*)-**1** prepared previously [4a] was selected for our preliminary study of the enantioselective intramolecular biscyclisation reaction. The effect of varying the chiral auxiliary was studied and the enantiomeric purity determined by $^1$H-NMR in the presence of the chiral shift reagent (+)-Eu(hfc)$_3$. In this case, it is not possible to add silver salts to the reaction so as to sequestre the halide because they would oxidize the metal malonate enolates to give homocoupling products [8].

BINAP [2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] has been used widely as chiral ligand in catalytic Heck reactions [9] and the asymmetric reaction of linear substrate (*E*)-**1** was first investigated with this ligand. Bromide **1** was subjected to the conditions that had been determined optimum for the cyclisation of the linear homologous substrates [4]. The reaction was carried out by heating the substrate in *N*-methylpyrrolidinone (NMP) at 60 °C in the presence of 5 mol% Pd(*R*-(+)-BINAP), 1.1 equivalents of KH and 0.2 equivalents of 18-crown-6. These conditions gave the expected regioi-




Scheme 2.

somer *anti* **2** in 50% chemical yield but with low enantioselectivity (7%) (Table 1, entry 1). Other chiral phosphines including (−)-DIOP (2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane) and (−)-CHIRAPHOS [(2*S*,3*S*)-bis(diphenylphosphino)butane] resulted in an increase of the optical yield of the reaction to 16 and 21% ee, respectively (Table 1, entries 2 and 3). When *S*-(−)TolBINAP [2,2′-bis(di-*p*-tolylphosphino)-1,1′-binaphtyl] was used as asymmetric ligand, more satisfactory results were obtained. The expected product was formed in 42% chemical yield (73% conversion) and in 35% ee (Table 1, entry 4).

### 2.2. Cyclisation of (*Z*)-2-[7-(2-trifluoromethanesulfonyloxy-phenyl)-hept-4-enyl]-malonic acid dimethyl ester (**9**)

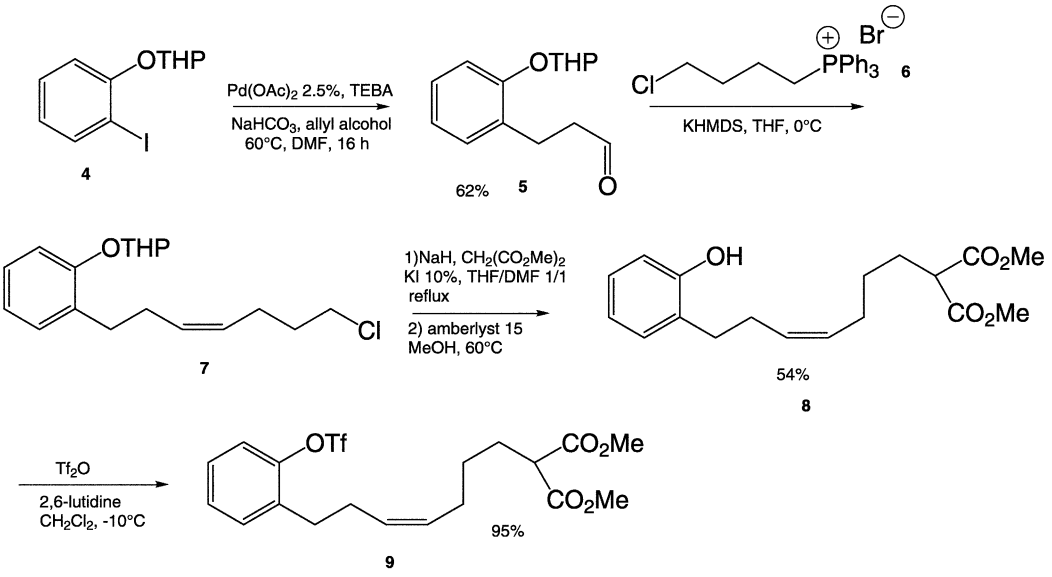
This last result encouraged us to develop the same reaction on the corresponding aryltriflate. However, aryltriflates are reported to be ineffective substrates for similar intermolecular palladium-mediated cyclisation processes [10]. Therefore, it was necessary to first investigate their utilisation in this intramolecular cyclisation reaction in the racemic version. In order to carry out these preliminary studies, we decided to prepare the readily available linear substrate (*Z*)-**9**. Indeed, this cyclisation precursor was accessible in only four steps from the known 2-(2-iodophenoxy)-tetrahydropyran (**4**) [11]. Thus, treatment of **4** with allylic alcohol according to the procedure published by Jeffery [12] afforded aldehyde **5** in 62% yield. Wittig olefination of the latter with the ylide derived from phosphonium salt **6** [13] proceeded smoothly at 0 °C to provide chloride **7** in 70% yield. Substitution of chloride group by the sodium salt of dimethylmalonate and subsequent removal of the THP protecting group provided the phenolic derivative **8** which was converted to the triflate **9** using standard conditions (Scheme 3).

Initial attempts to effect the palladium-catalysed cyclisation of the triflate **9** under conditions similar to those reported for bromide **1** ($Pd(OAc)_2$, dppe, KH, 75°C) proved disappointing, the desired tricyclic compound *syn* **2** being formed in poor yields (<20%). Several reaction parameters were varied such as the nature of the base (*t*-BuOK and KH), the solvent (DMF, THF, DMSO), but no improvement in the yield of *syn* **2** was observed. The best results were obtained by using 5 mol% $Pd(OAc)_2$ as the palladium source with 10

Table 1
Cyclisation of aryl bromide **1**

| Entry | Phosphine | Solvent | *T* (°C) | Time (h) | Yield (%) [a] | Ee (%) [b] |
|---|---|---|---|---|---|---|
| 1 | *R*-(+)-BINAP | NMP | 60 | 16 | 50 | 7 |
| 2 | (−)-DIOP | NMP | 60 | 3 | 50 | 16 |
| 3 | (−)-Chiraphos | NMP | 60 | 3 | 48 | 21 |
| 4 | *S*-(−)-TolBINAP | NMP | 60 | 3 | 42 | 35 [c] |
| 5 | *R*-(+)-BINAP | NMP–toluene | 60 | 16 | 50 | 0 |
| 6 | *S*-(−)-TolBINAP | NMP–toluene | 60 | 16 | 50 | 0 |

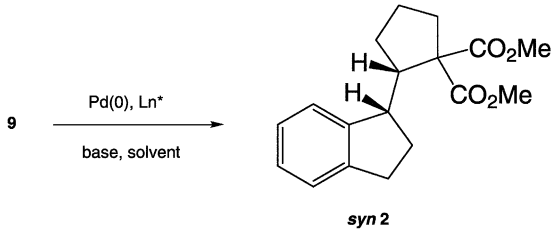
All reactions were run in the presence of 5 mol% $Pd(OAc)_2$, 1.1 equivalents KH, 0.2 equivalents 18-crown-6 and 10 mol% of the ligand.
[a] Isolated yield.
[b] Determined by $^1$H-NMR using (+)-Eu(hfc)$_3$ as shift reagent.
[c] $[\alpha]_D^{20} = -16.7$ ($c = 2.4\ 10^{-3}$, $CHCl_3$).




Scheme 3.

mol% of dppb or dppf [14] as ligand in DMSO at room temperature. These conditions afforded *syn* **2** in 52 and 53% yield, respectively (Scheme 4).

Having established satisfactory conditions for the palladium-mediated intramolecular cyclisation of the linear triflate (*Z*)-**9**, we turned our attention to the asymmetric version using different chiral ligands and the results of these studies are reported in Table 2. With chiral biphosphine such as (−)-BPPFA ((*R*)-*N*,*N*-dimethyl-1-[(*S*)-1′,2-bis(diphenylphosphino)ferrocenyl] ethylamine), cyclisation of **9** afforded the desired adduct in 45% yield and in 17% ee (Table 2, entry 1). When DIOP ligand was used, improved yields were observed (64%) but enantioselectivities were not improved (16%) (Table 2, entry 2). When $Pd(OAc)_2$ was used as a precursor of the catalyst, the highest enantiomeric excess observed (26%) was obtained with BINAP as chiral ligand but the chemical yield was rather modeste (Table 2, entry 3). As the palladium(0) catalyst generated in situ by reduction of $PdCl_2(PPh_3)_2$ with *n*-BuLi has been found particularly effective in related carbopalladation reactions [15] we decided to test the biscyclisation reaction with the preformed catalyst $PdCl_2$[(*S*)-TolBINAP] prepared by the reaction of dichlorobis (acetonitrile) palladium with one equivalent of [(*S*)-TolBINAP] according to the procedure reported by Hayashi and coworkers [16]. To our delight, when the reaction was performed in DMSO at 35 °C, a remarkable improvement was achieved since *syn* **2** was isolated in 62% chemical yield and 37% ee (Table 2, entry 5). When the same reaction was performed in the presence of BINAPAs (2-diphenylarsino-2′-diphenylphosphino-1,1′binaphtyl) as an asymmetric ligand [17], a low enantioselectivity was observed and the chemical yield dropped to 36% (Table 2, entry 6).




Scheme 4.

In order to improve the enantioselectivity and the chemical yield of this palladium-mediated biscyclisation reaction using $PdCl_2$[(*S*)-TolBINAP] as catalytic system, we further examined the effect of the temperature and of the nature of the base. The results of this investigation are compiled in Table 3. When the reaction was conducted at lower temperature (Table 3, entry 2) the yield (50%) and ee (18%) were inferior compared to the value obtained at 35 °C (Table 3, entry 1).

The moderate yields generally observed during the cyclisation of the triflate substrate when compared to the same reaction effected on the corresponding bromide (90%) [4c] can be attributed to the cleavage of the triflate by attack of the strong base. The same problem was observed by Buchwald during a coupling reaction between aryl triflates and amines in the presence of *t*-BuOK as base [18]. The use of a weaker base such as $Cs_2CO_3$ was a solution to this problem. However, while strong bases such as KH or *t*-BuOK had previously been used to promote this palladium-mediated cyclisation reaction, a competitive Heck reaction was generally observed with weaker bases [19]. The cyclisation of **9** was then attempted in the presence of two equivalents of $Cs_2CO_3$ as base in place of *t*-BuOK. Remarkably, the isolated yield of *syn* **2** was noticeably improved to 85%

Table 2
Cyclisation of aryl triflate **9**

| Entry | Phosphine | $T$ (°C) | Time (h) | Yield (%) [b] | Ee (%) [c] | $[\alpha]_D^{20}$ [d] |
|---|---|---|---|---|---|---|
| 1 | (−)-BPPFA | 25 | 20 | 45 | 17 | −8 |
| 2 | (−)-DIOP | 25 | 22 | 64 | 16 | −6 |
| 3 | *R*-(+)-BINAP | 25 | 20 | 48 | 26 | – |
| 4 | *S*-(−)–TolBINAP | 25 | 23 | 53 | 11 | +4.4 |
| 5 [a] | $PdCl_2$[*S*-(−)-TolBINAP] | 35 | 3 | 62 | 37 | +15.8 |
| 6 [a] | $PdCl_2$[*R*-BINAPAs] | 40 | 15 | 36 | 9 | – |

All reactions were run in DMSO in the presence of 5 mol% $Pd(OAc)_2$, 1.1 equivalents of base, 0.2 equivalents of 18-crown-6 and 10 mol% of the ligand or 5 mol% of catalyst (entries 5, 6).
[a] In this case the catalyst was reduced with *n*-BuLi prior to use.
[b] Isolated yield.
[c] Determined by $^1$H-NMR using (+)-Eu(hfc)$_3$ as shift reagent.
[d] *deg*, $CHCl_3$.

and the enantiomeric purity was 21% (Table 3, entry 3). The best enantioselectivity (43%) was obtained when the reaction was carried out in the presence of $K_2CO_3$ as base (Table 3, entry 4). Quite surprisingly, while using a single enantiomer of the TolBINAP ligand, the opposite enantiomer of *syn* **2** was obtained by changing the nature of the inorganic base [20] (Table 3, entries 3 and 4).

In conclusion, enantioenriched cyclopentylindanes were obtained through asymmetric catalysis of the palladium-mediated biscyclisation reaction developed on an aryl bromide or triflate tethered to an alkene bearing a stabilized carbonucleophile. The best combination of chemical yields (54%) and enantioselectivity (43%) was realized on the aryltriflate substrate. $PdCl_2$[(*S*)-TolBINAP] prepared from $PdCl_2(PPh_3)_2$ as the precatalyst and [(*S*)-TolBINAP] as the chiral biphosphine was found to be the optimal palladium system, the reaction beeing performed at 35 °C in DMSO using $K_2CO_3$ as base. Unexpectedly, the enantioselectivity can be reversed in the cyclisation of this aryl triflate by simply changing the nature of the inorganic base, the opposite enantiomer being formed in 85% chemical yield and 21% ee.

## 3. Experimental

### 3.1. General

Infrared spectra were recorded on a Perkin–Elmer 298 or Perkin–Elmer FT-IR PARAGON 500. Proton magnetic resonance ($^1$H-NMR) and carbon magnetic resonance ($^{13}$C-NMR) spectra were measured at 300 MHz with a Bruker AM 300 and ALS 300 spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane ($\delta$ scale). The multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, number of protons and coupling constants (reported in Hz)) are indicated in parentheses.

Table 3
Effect of base in the cyclisation of aryl triflate **9**

| Entry | Base | Solvent | $T$ (°C) | Time (h) | Yield (%) | Ee (%) [a] | $[\alpha]_D^{20}$ [b] |
|---|---|---|---|---|---|---|---|
| 1 | *t*-BuOK | DMSO | 35 | 3 | 62 | 37 | +15.5 |
| 2 | *t*-BuOK | DMSO | 25 | 24 | 50 | 18 | – |
| 3 | $Cs_2CO_3$ | DMSO | 40 | 4 | 85 | 21 | +11.4 |
| 4 | $K_2CO_3$ | DMSO | 40 | 24 | 54 | 43 | −21.6 |

All reactions were run using 5% of $PdCl_2$[*S*-(−)-TolBINAP] as catalyst
[a] Determined by $^1$H-NMR using (+)-Eu(hfc)$_3$ as shift reagent
[b] *deg*, $CHCl_3$.

### 3.2. Synthesis of triflate **9**

#### 3.2.1. 3-[2-(Tetrahydropyran-2-yloxy)-phenyl]-propionaldehyde (**5**)

2-(2-Iodo-phenoxy)-tetrahydropyran (9.7 g, 32 mmol), allyl alcohol (6.72 g, 96 mmol), $Pd(OAc)_2$ (180 mg, 0.8 mmol), triethylbenzylammonium chloride (7.3 g, 32 mmol), $NaHCO_3$ (6.72 g, 80 mmol) were successively added to 225 ml of DMF and the resulting solution was stirred at 65 °C for 22 h. The reaction mixture was quenched with 300 ml of water and extracted with $Et_2O$ ($2 \times 250$ ml) and washed with brine (200 ml). The organic phase was dried ($MgSO_4$) and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (eluent: PE:$Et_2O$:$Et_3N$ 87:10:3) yielded **5** as a yellow oil (4.8 g, 64%).

IR (film): 3060, 2940, 2880, 2720, 1730, 1680, 1600, 1495, 1240, 1130, 930, 880, 760 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 300 MHz): $\delta$ 1.60–1.90 (m, 6H), 2.77 (m, 2H), 3.00 (t, $J = 7$ Hz, 2H), 3.63 (m, 1H), 3.87 (m, 1H), 5.43 (t, $J = 3$ Hz, 1H), 6.91 (t, $J = 7.5$ Hz, 1H), 7.00–7.20 (m, 3H), 9.83 (s, 1H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): $\delta$ 19.1, 23.7, 30.6, 30.7, 44.2, 62.2, 96.4, 114.3, 121.5, 127.8, 129.1, 130.0, 154.9, 202.4. Microanalysis Found: C, 71.98; H, 7.78. Calc. for $C_{14}H_{18}O_3$: C, 71.80; H, 7.70%.

#### 3.2.2. Synthesis of phenol **8**

The phenol was prepared from **5** by a two-step procedure: Wittig reaction with phosphonium salt **6** as described in Ref. [4] followed by reaction of the resulting chloride **7** with dimethyl malonate and subsequent deprotection of the tetrahydropyranlyloxy protecting group.

*3.2.2.1. (Z)-2-[2-(7-Chloro-hept-3-enyl)-phenoxy]-tetrahydropyran (**7**).* A mixture of (4-chloro-butyl)-triphenyl phosphonium bromide **6** (7.32 g, 16.8 mmol) and KHMDS (3.43 g, 16.8 mmol) was dissolved in THF (72 ml) at 0 °C. The resulting red solution was stirred for 15 min. Aldehyde **5** (1.98 g, 8.46 mmol) in 18 ml of THF was added to the above solution which was stirred for a further 15 min at 0 °C and 1 h at 25 °C. The reaction mixture was poured into 300 ml of petroleum ether, and filtrated through a pad of silica gel. The filtrate was concentrated in vacuo and the crude product **7** directly engaged in the next step.

*3.2.2.2. 2-[7-(2-Hydroxy-phenyl)-hept-4-enyl]-malonic acid dimethyl ester (**8**).* Dimethyl malonate (1.6 ml, 14 mmol) was added slowly to a suspension of sodium hydride (washed previously by pentane) (288 mg, 12 mmol) in THF (80 ml). The resulting solution was stirred at room temperature (r.t.) for 30 min at which time chloride **7** (3 g, 9.7 mmol) in DMF (80 ml) and KI (161 mg, 0.97 mmol) were added. The solution was warmed to 80 °C and stirred for 6 h. After usual work-up the crude product was directly treated with amberlyst IR-15 (0.5 g) in 130 ml of MeOH for 1 h at 45 °C. After filtration on Celite and evaporation, the crude product was purified by flash chromatography on silica gel (eluent: PE:$Et_2O$ 80:20) yielding **8** as a yellow oil (1.67 g, 54%).

IR (film): 3460, 3000, 2950, 1735, 1610, 1590, 1500, 1460, 1440, 1150, 760 $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 300 MHz): $\delta$ 1.30 (m, 2H), 1.89 (m, 2H), 2.00 (m, 2H), 2.37 (m, 2H), 2.67 (t, $J = 7.5$ Hz, 2H), 3.37 (t, $J = 7.5$ Hz, 1H), 3.75 (s, 6H), 5.3–5.5 (m, 2H), 6.7–7.0 (m, 4H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): $\delta$ 26.7, 27.3, 27.5, 28.5, 30.7, 51.7, 52.6, 115.3, 120.3, 127.1, 128.3, 129.4, 130.0, 130.4, 154.1, 170.2. Microanalysis Found: C, 67.11; H, 7.60. Calc. for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55%.

#### 3.2.3. (Z)-2-[7-(2-Trifluoromethanesulfonyloxy-phenyl)-hept-4-enyl]-malonic acid dimethyl ester (**9**)

2,6-Lutidine (0.97 ml, 7.8 mmol) was added slowly to a cooled solution ($-10$ °C) of phenol **8** (5.2 mmol, 1.67 g) in $CH_2Cl_2$ (10 ml), followed by the addition of $Tf_2O$ (0.98 ml, 5.7 mmol). After 1 h at this temperature, the reaction mixture was quenched by a solution of sat. $NH_4Cl$–1 N HCl 3/1 (5 ml). The organic phase was separated and the aqueous layer extracted with $CH_2Cl_2$ (10 ml). The combined organic phases were washed with water and brine, dried over $Na_2SO_4$, and concentrated in vacuo. The crude oil was purified by flash chromatography on silica gel (eluent: PE:$Et_2O$ 90:10) yielding **9** as a yellow oil (2.23 g, 95%).

$^1$H-NMR ($CDCl_3$, 300 MHz): $\delta$ 1.32 (m, 2H), 1.85 (m, 2H), 1.96 (m, 4H), 2.35 (m, 2H), 2.75 (t, $J = 7.7$ Hz, 2H), 3.32 (t, $J = 7.7$ Hz, 1H), 3.75 (s, 6H), 5.3–5.5 (m, 2H), 7.2–7.4 (m, 4H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): $\delta$ 26.7, 27.2, 27.6, 28.4, 30.0, 51.7, 52.4, 117.0, 121.3, 127.9, 128.3, 128.4, 130.0, 130.4, 131.4, 134.6, 148.1, 169.9. Microanalysis Found: C, 50.47; H, 5.10. Calc. for $C_{19}H_{23}O_7SF_3$: C, 50.50; H, 5.10%.

### 3.3. Palladium-catalysed cyclisation of bromide **1** or triflate **9**

#### 3.3.1. 2-Indan-1-yl-cyclopentane-1,1-dicarboxylic acid dimethyl ester (**2**)

Bromide **1** or triflate **9** (1 equivalent) were treated in DMSO with the appropriate base (1.1 equivalents or two equivalents for inorganic bases). The palladium source was added and the resulting solution heated for the indicated time (see tables). The crude mixture was directly purified by flash-chromatography on silica gel (eluent: PE:$Et_2O$ 80:20) yielding the corresponding cyclisation product *anti* **2** or *syn* **2**, respectively (yield: see text).

*Anti* **2** colourless solid. M.p.: 50–52 °C. $^1$H-NMR (300 MHz, $CDCl_3$) $\delta$ 1.45 (1H, ddd, $J = 3.6$, 8.7, 17.5

Hz), 1.65 (1H, ddd, $J = 7.9$, 11.2, 14.2 Hz), 1.85 (2H, m), 2.1 (3H, m), 2.56 (1H, dt, $J = 8.1$, 13.6 Hz), 2.75 (2H, m), 3 (1H, dt, $J = 2.8$, 10 Hz), 3.1 (1H, ddd, $J = 7.1$, 9.7, 23.8 Hz), 3.75 (6H, s), 7.1 to 7,53 (4H, m). $^{13}$C-NMR (75 MHz, $CDCl_3$) $\delta$ 23.5, 30.9, 31.6, 31.9, 37.32, 47.6, 49.9, 52.2, 52.6, 63, 124.6, 125.5, 125.6, 126.6, 144.7, 146.6, 172.3, 174. IR (KBr): 3060, 2940, 2840, 1740. Anal. Calc. for $C_{18}H_{22}O_4$: C, 71.5; H, 7.33. Found: C, 71.29; H, 7.68%. *Syn* **2** yellow oil $^1$H-NMR ($CDCl_3$, 300 MHz): $\delta$ 1.50 (m, 3H), 1.75 (m, 2H), 2.00 (m, 2H), 2.50 (ddd, $J = 7.1$, 8.5, 13.6 Hz, 1H), 2.85 (m, 2H), 3.0 (dt, $J = 2.9$, 7.2 Hz, 1H), 3.60 (dt, $J = 2.9$, 10 Hz, 1H), 3.75 (s, 6H), 7.10–7.34 (m, 4H). $^{13}$C-NMR ($CDCl_3$, 75 MHz): $\delta$ 22.9, 26.4, 29.9, 32.2, 34.8, 44.7, 50.1, 52.6, 62.9, 123.9, 124.3, 126.4, 126.6, 143.7, 146.9, 173.0. Microanalysis Found: C, 71.45; H, 7.54. Calc. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33%.

### 3.4. Determination of enantiomeric excess of **2**

Enantiomeric excesses were measured by adding 1.2 equivalents of (+) Eu(hfc)$_3$ to **2** (8–10 mg) in 1 ml of $CDCl_3$ to the NMR tube and the methyl esters at 3.75 ppm split into four singlets (4.2–4.5 ppm) which could be integrated.

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## References

[1] For reactions involving carbon nucleophiles see;
(a) G. Balme, D. Bouyssi, T. Lomberget, N. Monteiro, Synthesis, in press;
(b) G. Balme, N. Monteiro, D. Bouyssi, in: E.-I. Negishi (Ed.), Handbook of Organopalladium Chemistry for Organic Synthesis, WileyNew York, 2002, pp. 2245–2265

[2] For reactions involving oxygen nucleophiles see:
(a) S. Cacchi, A. Arcadi, in: E.-I. Negishi (Ed.), Handbook of Organopalladium Chemistry for Organic Synthesis, Wiley, New York, 2002, pp. 2193–2210;
(b) For reactions involving nitrogen nucleophiles see:
(b) S. Cacchi, F. Marinelli, E.-I. Negishi (Ed.), Handbook of Organopalladium Chemistry for Organic Synthesis, Wiley, New York, 2002, 2227–2244.

[3] (a) G. Balme, D. Bouyssi, Tetrahedron 50 (1994) 403;
(b) M. Cavicchioli, S. Decortiat, D. Bouyssi, J. Goré, G. Balme, Tetrahedron 52 (1996) 11463;
(c) I. Coudanne, G. Balme, Synlett (1998) 998.

[4] (a) D. Bruyere, G. Gaignard, D. Bouyssi, G. Balme, J.-M. Lancelin, Tetrahedron Lett. 38 (1997) 827;
(b) C. Bressy, D. Bruyere, D. Bouyssi, G. Balme, ARKIVOC (Gainesville, FL, United States) [online computer file] 5 (2002) 127;
(c) D. Bruyere, D. Bouyssi, G. Balme, to be published.

[5] N. Monteiro, Asymmetric catalysis of the intermolecular version of this process was however briefly investigated in our laboratories soon after its discovery but with little success, PhD dissertation, Lyon, 1992.

[6] (a) W. Cabri, I. Candiani, Acc. Chem. Res. 28 (1995) 2;
(b) F. Ozawa, A. Kubo, T. Hayashi, J. Am. Chem. Soc. 113 (1991) 1417.

[7] F. Miyazaki, K. Uotsu, M. Shibasaki, Tetrahedron 54 (1998) 13073.

[8] Z. Wrobel, M. Makosza, Liebigs Ann. Chem. 7 (1990) 619.

[9] (a) M. Shibasaki, F. Miyazaki, in: E-I. Negishi (Ed.), Handbook of Organopalladium Chemistry for Organic Synthesis, Wiley, New York, 2002, 1283–1315;
(b) For review see: M. Shibasaki, C.D.J. Boden, A. Kojima, Tetrahedron 53 (1997) 7371.

[10] (a) G. Balme, M. Bottex, D. Bouyssi, T. Lomberget, N. Monteiro, Unpublished results;
(b) A. Arcadi, A. Burini, S. Cacchi, M. Delmastro, F. Marinelli, B.R. Pietroni, J. Org. Chem. 57 (1992) 976.

[11] G.T. Crisp, T.P. Bubner, Tetrahedron 53 (1997) 11881.

[12] T. Jeffery, Tetrahedron Lett. 32 (1991) 2121.

[13] W.H. Pearson, H. Suga, J. Org. Chem. 63 (1998) 9910.

[14] Examples of Heck reactions involving aryl or vinyltriflates and using dppf, dppb and/or dppp as ligands
(a) S. Laschat, F. Narjes, L.E. Overman, Tetrahedron 50 (1994) 347;
(b) W. Cabri., I. Candiani, A. Bedeschi, R. Santi, J. Org. Chem. 57 (1992) 3558.

[15] (a) M. Bottex, M. Cavicchioli, B. Hartmann, N. Monteiro, G. Balme, J. Org. Chem. 63 (2001) 175;
(b) T. Lomberget, D. Bouyssi, G. Balme, Synlett (2002) 1439.

[16] (a) Y. Matsumoto, T. Hayashi, Y. Ito, Tetrahedron 50 (1994) 335;
(b) M. Tinkl, S. Evans, P. Nesvadba, Preparation of 3-arylbenzofuranones via carbonylation of arylmethylidenecyclohexadienones, PCT Int. Appl., WO 9967232 A2 19991229 (1999).

[17] Recently BINAPAs was found to be more effective chiral ligand than BINAP in asymmetric Heck reactions that use aryl triflates, see: S.Y. Cho, M. Shibasaki, Tetrahedron Lett. 39 (1998) 1773.

[18] J. Ahman, S.L. Buchwald, Tetrahedron Lett. 38 (1997) 6363.

[19] I. Coudanne, J. Castro, G. Balme, Synlett (1998) 995.

[20] A similar result was recently reported. In this case, either enantiomer of a Heck product was formed using a single enantiomer of the BINAP ligand depending on the presence of tertiary amine or silver salts in the mixture. see:
(a) A. Ashimori, L.E. Overman, J. Org. Chem. 57 (1992) 4571;
(b) A. Ashimori, B. Bachand, L.E. Overman, D.J. Poon, J. Am. Chem. Soc. 120 (1998) 6477.