Tetrahedron: *Asymmetry* 22 (2011) 893–906

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Enantioselective Friedel–Crafts alkylations catalysed by well-defined iridium and rhodium half-sandwich complexes

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ARTICLE INFO

Article history:
Received 14 April 2011
Accepted 13 May 2011
Available online 15 June 2011

ABSTRACT

Aqua-complexes (S_M,R_C)-[Cp*M{(*R*)-prophos}(H_2O)][SbF_6]$_2$ (M = Rh **1**, Ir **2**) catalysed the alkylation of α,β-unsaturated aldehydes with aromatics and heteroaromatics but in some cases, mixtures of products were obtained. Complexes **1** and **2** were also used to activate nitroalkenes for the Friedel–Crafts alkylation of a variety of aromatics and heteroaromatics, in particular, 1,3,5-trimethoxybenzene. For this substrate, the monoalkylated adduct was obtained in quantitative yield with enantioselectivities of up to 73% ee being achieved. The intermediate catalyst/nitroalkene was isolated and characterized and the complex catalyst/adduct was detected spectroscopically. From these data a plausible catalytic cycle is proposed.

1. Introduction

The catalytic enantioselective Friedel–Crafts reaction of electron-rich aromatic or heteroaromatic substrates with electron-deficient alkenes is one of the most direct methods for introducing a new stereogenic centre on an aromatic or heteroaromatic compound.[1–9] Asymmetric protocols based on both metal-[1–6] and organocatalysed[1–4,6–9] alkylations have been developed.

In particular, the asymmetric alkylation of activated alkenes, carbonyl compounds or imines was shown to take place for a number of (hetero)aromatic compounds and, although the first report of asymmetric Friedel–Crafts reactions involved the alkylation of phenols[10] and naphthols,[11] indoles are by far the most widely employed nucleophiles.[3,4,6,7,9]

We have recently isolated and characterized chiral half-sandwich rhodium or iridium compounds (S_M,R_C)-[Cp*M{(*R*)-prophos}(H_2O)][SbF_6]$_2$ [Cp* = C_5Me_5; M = Rh, Ir; prophos = propane-1,2-diyl-bis(diphenylphosphane)].[12,13] These complexes easily lose water and the resulting unsaturated Lewis-acid cations (Fig. 1) efficiently activate organic substrates, such as enals or α,β-unsaturated nitriles, for Diels–Alder[14–16] or 1,3-dipolar cycloadditions.[12,13,17–19] Quantitative yields and excellent enantioselectivities have been achieved for both types of processes.

Taking into account these results, we envisaged the possibility of applying this metallic fragment as a catalyst for the Friedel–Crafts alkylation of aromatic and heteroaromatic substrates with activated alkenes. Herein we report our results.

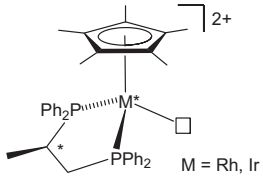

Figure 1. The chiral cations Cp*M{(*R*)-prophos)}.

2. Results and discussion

2.1. Enals as electrophiles

We first examined the homogeneous asymmetric Friedel–Crafts alkylation of a series of activated arenes, pyrroles and indoles (Scheme 1) with enals in the presence of 5 mol % of the catalyst precursors (S_M,R_C)-[Cp*M{(*R*)-prophos}(H_2O)][SbF_6]$_2$ (M = Rh **1**, Ir **2**). Although 2,3-dimethylacrolein **7c** and *trans*-cinnamaldehyde **7d** were tested as enals, most of the reactions were carried out with methacrolein **7a** or *trans*-crotonaldehyde **7b** (Scheme 2). Dichloromethane was used as solvent and reactions were carried out at −10 °C, in the presence of 4 Å molecular sieves (MS). A 1:20:60, catalyst/aromatic/enal molar ratio was employed. According to the NMR data, after 72 h of treatment under these conditions, no reaction was observed between monosubstituted arenes **3a**–**c** and *trans*-crotonaldehyde nor between **3b**,**c** and methacrolein. Under the same conditions, more activated arenes such as 1,3-dimethoxy- or 1,3,5-trimethoxy-benzene do not react either. However, the iridium complex **2** catalysed the reaction between *m*-*N*,*N*-dimethyl anisidine **4a** and *trans*-crotonaldehyde **7b**. After

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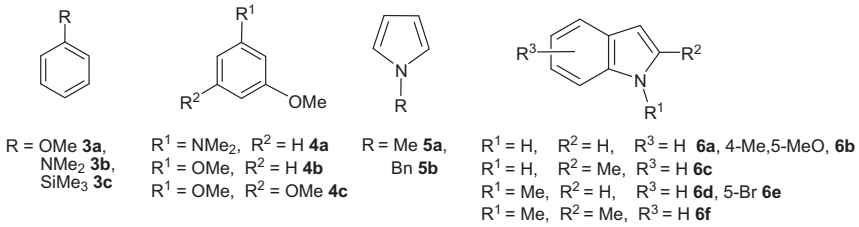
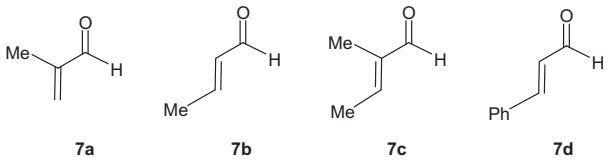
doi:10.1016/j.tetasy.2011.05.003



Scheme 1. Aromatics and heteroaromatics investigated.



Scheme 2. Enals employed.

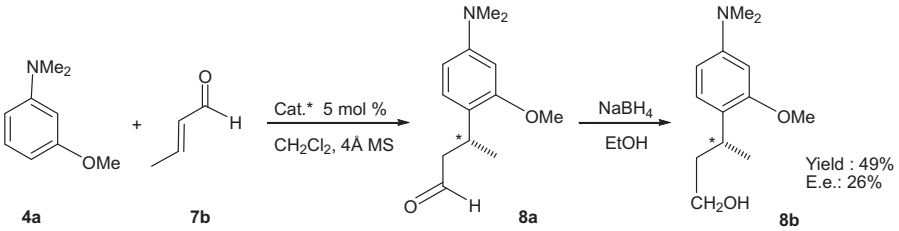
72 h of reaction, the monosubstituted Friedel–Crafts product at the *para*-position with respect to the amine was obtained in 49% isolated yield and in 26% ee, measured on the alcohol obtained by reduction with $NaBH_4$ (Scheme 3). Analogously, complex **2** catalysed the reaction between anisidine **4a** and methacrolein, but a mixture of three compounds was obtained. After reduction with $NaBH_4$, the major product was characterized as alcohol **8c**. The NMR data indicated that the two remaining products were the other two possible monosubstituted Friedel–Crafts adducts **8d** and **8e**. Quantitative conversion was achieved after 72 h of reaction with the product distribution and enantioselectivity, measured on the alcohol derivatives, depicted in Scheme 4.

No reaction was observed between **4a** and the enals 2,3-dimethylacrolein **7c** and *trans*-cinnamaldehyde **7d**. Under the aforementioned conditions, the rhodium complex (S_M,R_C)-[Cp*Rh{(*R*)-prophos}(H_2O)][SbF_6]$_2$ **1** did not catalyse the reaction between anisidine **4a** and enals **7a** and **7b**.

Although poor results were obtained, to the best of our knowledge, this is the first example of the alkylation of activated arenes with enals using metal-based catalysts. In this context, an organocatalysed reaction of anilines and methoxyanilines with α,β-unsaturated aldehydes was recently reported by MacMillan and Paras.[20]

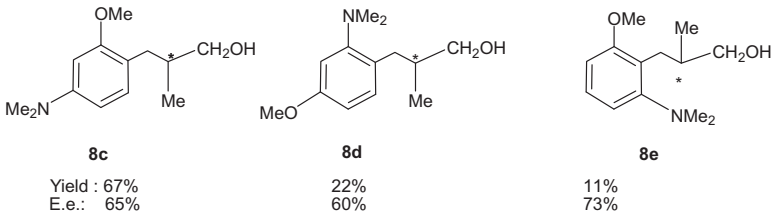
Next, we examined the Friedel–Crafts reaction of pyrroles and indoles with enals. At −10 °C, *N*-methyl pyrrole **5a** reacted with *trans*-crotonaldehyde **7b** to give the corresponding 2-substituted Friedel–Crafts adduct **8f**, with 8% or 12% ee when the rhodium complex **1** or the iridium complex **2** were used as the catalyst precursor, respectively (Scheme 5). No reaction was observed between *N*-benzyl pyrrole **5b** and enals **7a**,**b** in the presence of complexes **1** or **2**.

The reaction of a series of indoles with methacrolein and *trans*-crotonaldehyde was then examined, using iridium complex **2** as a catalyst precursor[†] (Scheme 6). The indole was alkylated at the 3-



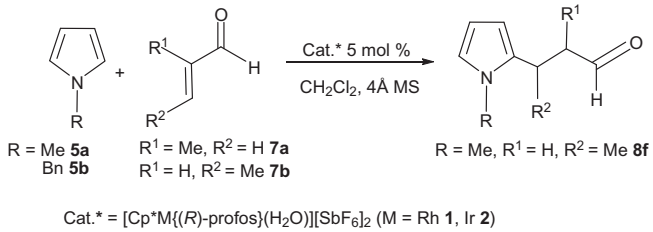
Cat.* = [Cp*Ir{(*R*)-profos}(H_2O)](SbF_6)$_2$ **2**

Scheme 3. Catalytic reaction between *m*-*N*,*N*-dimethylanisidine and *trans*-crotonaldehyde.



Scheme 4. Products distribution of the reaction between *m*-*N*,*N*-dimethylanisidine and methacrolein.

[†] When, under similar conditions, rhodium compound **1** was employed as a catalyst precursor instead of iridium compound **2**, for the reactions between *N*-methylindole **6d** and methacrolein or *trans*-crotonaldehyde, the corresponding Friedel–Crafts adducts **8k** and **8l** were obtained in similar yields and enantioselectivities: **8k**, 22% yield, 23% ee; **8l**, 49% yield, 16% ee (yield and ee measured after reduction to the alcohol).



Scheme 5. Catalytic reaction between pyrroles and enals.

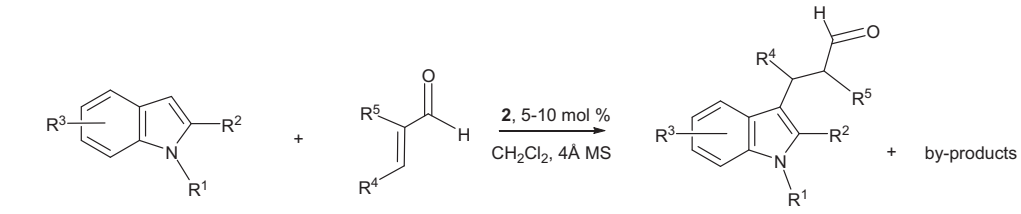
position in all the cases attempted. After 24–48 of reaction at −10 °C, the isolated yield of the alcohol obtained by subsequent reduction of the Friedel–Crafts product, ranged from 15% to 58%. Enantiomeric excesses from 7% to 33% ee were achieved. The low yield was accompanied by the formation of several by-products we were unable to completely characterize. However, when *trans*-crotonaldehyde **7b** was used as the electrophile, together with the expected alkylated indole **8h**, **8j** or **8l**, we detected in the ^{1}H NMR spectra of the crude of the reaction an ABX spin system consistent with the presence of a –C(Me)H–C(H)=C(H) connectivity in one of the by-products in all the three cases. Figure 2 shows the ^{1}H NMR peaks encountered in the crude spectra of compound **8h** and Table 1 collects the chemical shifts and coupling constants detected in the three experiments. It is likely that the formation of this common fragment involves the reaction of both unsaturated enal groups, namely the C=C and C=O double bonds. This fact, along with the generally poor results obtained in the alkylation reaction of enals, prompted us to try the nitrostyrenes as electrophiles. We expected that the nitro group on the one side would provide the substrate with a binding capability and on the other would activate the C=C double bond without interfering in its Friedel–Crafts reactivity.

2.2. *trans*-β-Nitrostyrenes as electrophiles

Examples of homogeneous catalytic enantioselective additions of aromatic and heteroaromatic C–H bonds to nitroolefins have only appeared recently. In 2005, Bandini et al. reported the enantioselective condensation of indole with nitroalkenes catalysed by [AlCl(salen)] (salen = (*R*,*R*)-(−)-*N*,*N*′-bis(3,5-di-*t*-butylsalicylidene)-1,2-cyclohexanediamine).[21] In the same year, Jørgensen et al. developed hydrogen-bond-based organocatalysts for this reaction.[22] Since then, a handful of metal-catalysed,[23–37] and a few organocatalysed,[38–45] examples have been reported. Copper[25,26,31,33,37] and zinc[23,24,27–30,32,34–36] are the only metals that have been employed with nitrogen and/or oxygen donor ligands as the chiral source. The organocatalysts tested were based on thioureas,[38–40,45] phosphoric acids[42–44] or quinolinium amido(thio)amides.[41] Indole alkylation with nitroolefins is by far the most investigated reaction.[21–26,28,29,31–39,41,42] Pyrroles,[28,30,33,43] 4,7-dihydroindoles,[44] phenol[45] and naphthols[40,45] are much less studied, and only one example of the addition of nitroolefins to 2-methoxyfuran[27] has been recently published.

Taking all of the above into account, we decided to investigate the Friedel–Crafts alkylation of nitroolefins, specifically *trans*-β-nitrostyrenes, by introducing catalysts based on two new metals, rhodium and iridium, with a chiral diphosphane ligand namely, (*R*)-prophos, as a chiral source.

First, we examined the reaction of *trans*-β-nitrostyrene as an alkene model, with a series of activated arenes **3c**, **4a–c**, *N*-methyl pyrrole **5a** and indole **6a** using the iridium complex **2** as a catalyst precursor (Scheme 7). Dichloromethane was used as solvent and reactions were carried out at −10 °C, in the presence of 4 Å MS. A 1:20:20, catalyst/aromatic/*trans*-β-nitrostyrene molar ratio was employed. According to spectroscopic and chromatographic data, a quantitative yield was obtained in all cases, except for phenyltri-



R^1 = H, R^2 = H, R^3 = H **6a**,
4-Me,5-MeO **6b**
R^1 = H, R^2 = Me, R^3 = H **6c**
R^1 = Me, R^2 = H, R^3 = H **6d**, 5-Br **6e**
R^1 = Me, R^2 = Me, R^3 = H **6f**

R^4= H, R^5= Me **7a**
R^4= Me, R^5= H **7b**

R^1= H, R^2= H, R^3= H, R^4= H, R^5= Me **8g**
R^1= H, R^2= H, R^3= H, R^4= Me, R^5= H **8h**
R^1= H, R^2= H, R^3= 4-Me,5-MeO, R^4= H, R^5= Me **8i**
R^1= H, R^2= Me, R^3= H, R^4= Me, R^5= H **8j**
R^1= Me, R^2= H, R^3= H, R^4= H, R^5= Me **8k**
R^1= Me, R^2= H, R^3= H, R^4= Me, R^5= H **8l**
R^1= Me, R^2= H, R^3= 5-Br, R^4= H, R^5= Me **8m**
R^1= Me, R^2= Me, R^3= H, R^4= H, R^5= Me **8n**

Scheme 6. Catalytic reaction between indoles and enals.

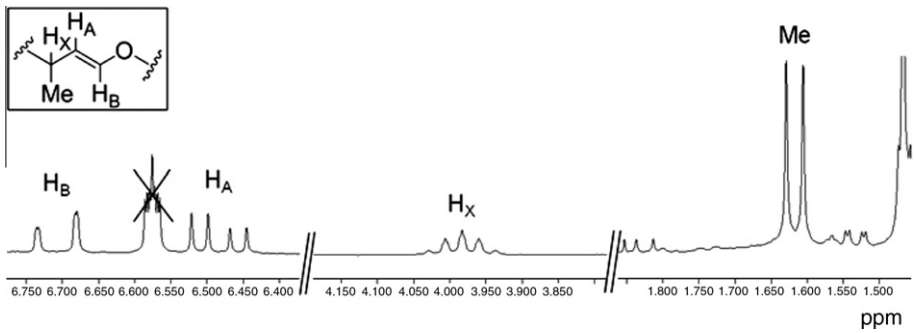


Figure 2. Selected fragments of the ^{1}H NMR spectrum of the crude of the reaction between **6a** and **7b**.

methylsilane **3c** and 1,3-dimethoxybenzene **4b**. No reaction was observed for the monosubstituted arene **3c** after 72 h of treatment while a yield of 17%, with 2% ee, was measured, after the same time of reaction, for **4b**. Reactions were completely regioselective. Only monosubstituted Friedel–Crafts adducts were detected: the arene substituted at the *para*-position with respect to amine **10a**, for *m*-*N*,*N*-dimethyl anisidine **4a** and the 2-substituted pyrrol **10d** or 3-substituted indole **10e** for the heteroaromatic substrates.[‡] Enantiomeric excesses ranging from 3% to 40% ee were achieved.

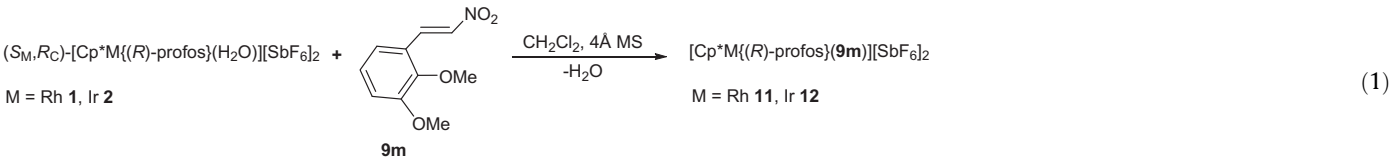
Since the best results were obtained for 1,3,5-trimethoxybenzene **4c** (quantitative yield after 6 h of reaction, 40% ee) and this substrate had not been previously investigated in this type of Friedel–Crafts reaction, we next studied the reactivity between **4c** and a family of *trans*-β-nitrostyrenes. Table 2 lists the results obtained when the catalytic reactions were carried out with complex **2** as a catalyst precursor, under the conditions reported above for unsubstituted *trans*-β-nitrostyrene. The collected results are the average of at least two comparable reaction runs. Reactions are clean: only the monoalkylated adduct was spectroscopically and chromatographically detected.[§] Catalyst precursors have to be treated with the corresponding nitroolefin in the presence of 4 Å MS before the addition of the arene. Under these conditions, $[Cp^*M\{(R)\text{-prophos}\}(\text{nitroolefin})]^{2+}$ were the only metallic complexes present in solution (see below).

In general, high yields were obtained after a few hours of reaction at −10 °C. Enantiomeric excesses of up to 73% were achieved. similar trend by plotting the obtained ee's versus the reported Hammet parameter σ values for a series of nitroalkenes (Fig. 3).

2.3. Isolation and characterization of the catalyst/electrophile intermediate

In spite of the fact that several metal-based catalytic systems have already been applied to the Friedel–Crafts reaction between aromatic or heteroaromatic substrates and nitroalkenes,[21,23–37] to the best of our knowledge, no experimental data regarding the metallic intermediates involved in the catalytic reaction have been reported to date. In some cases, the stereochemical outcome of the catalytic reactions has been explained by assuming that activation of the nitroalkene occurs through monodentate[35,37] or bidentate[23,24,28,31] coordination to copper[31,37] or zinc[23,24,28,35] accompanied[24,28,35,37] or not[23,28,31] by additional interactions between the catalyst and the nucleophilic partner.

To gain an insight into the catalytic mechanism, we studied the reaction between the catalyst precursors (S_M,R_C)-$[Cp^*M\{(R)\text{-prophos}\}(H_2O)][SbF_6]_2$ (M = Rh **1**, Ir **2**) and nitroalkene **9m**, as a model. When 3 equiv of **9m** were added to dichloromethane solutions of complexes **1** or **2**, in the presence of 4 Å MS, the complex cations $[Cp^*M\{(R)\text{-prophos}\}(\mathbf{9m})]^{2+}$ are instantaneously and quantitatively formed. From the solution solids of formula $[Cp^*M\{(R)\text{-prophos}\}(\mathbf{9m})][SbF_6]_2$ (M = Rh **11**, Ir **12**) can be isolated in around 80% yield (Eq. 1).



(1)

Both, electron donating and electron withdrawing groups generate less active systems (compare, e.g., entry 1 with entries 3 and 6 or with entries 17 and 18). Only the 3-methoxy and the 2-fluoro substituted substrates (entries 4 and 16, respectively) gave a catalytic rate comparable to that of the unsubstituted nitroolefin. In this line, the lowest rates corresponded to nitroolefins with two substituents on the aromatic ring. This trend is probably caused by the increase in steric hindrance of the alkylation reagent.

Electronic factors strongly affect the enantioselectivity of the system. Thus, while electron donating substituents located at the 2- or 4-positions of the aromatic ring improve ee (compare entry 1 with entries 3 and 5 or 6 and 8), it decreases when substituents of this type are placed at the 3-position (compare entry 1 with entries 4 or 7). However, two donor substituents situated at 2- and 4-positions do not produce further improvement on the ee (compare entries 3 and 5 with entry 10). Conversely, lower ee's were obtained with electron withdrawing substituents. The 2,6-disubstituted nitroolefin **9ac**, which gives a 47% ee (entry 24), is the only exception to this trend. In this context, Bandini et al. found a good degree of correlation between the enantiomeric excess of the products and the Hammet parameter[46] associated with the nitroalkene substituent, for the Friedel–Crafts reaction between indoles and nitroalkenes, catalysed by aluminium–salen complexes.[21] With regard to the influence of the electronic factors on the ee, we found a

Complexes **11** and **12** were characterized by microanalysis and by IR, ^1H, ^{13}C and ^{31}P NMR spectroscopies (see Section 4). The reaction is completely diastereoselective; from −50 °C to rt only one set of sharp signals was observed in the NMR spectra of the three nuclei investigated. The assignment of the NMR peaks was carried out by a combination of mono- and bi-dimensional, homo- and hetero-nuclear experiments. The ^1H NMR spectrum showed the presence of the Cp*, (*R*)-prophos and **9m** ligands in a 1:1:1 molar ratio. This technique unambiguously establishes the presence of coordinated **9m**. Thus, for example for complex **11**, two doublets centred at 7.31 (H_b, see Fig. 4) and 7.47 (H_a) ppm, with a coupling constant of 13.9 Hz, could be attributed to the olefinic protons of the nitroalkene and the two methoxy substituents of the aromatic ring resonate as singlets at 3.87 (OMe_a) and 3.89 (OMe_b) ppm.

The ^{31}P NMR spectrum of the rhodium complex **11** consisted of two double doublets centred at 75.99 ($J(Rh,P^1)$ = 130.8 Hz, $J(P^2,P^1)$ = 38.3 Hz) and at 51.52 ppm ($J(Rh,P^2)$ = 133.1 Hz) while that of the iridium compound **12** comprised of two doublets centred at 49.04 (P^1) and 27.71 (P^2) ppm with a coupling of 10.7 Hz.

Important stereochemical conclusions can be drawn from the NMR experiments (Fig. 4). Notably, the strong NOE relationship between the protons H_{21} and H_{11} and the methyl protons of one of the methoxy groups (OMe_a) support the (*S*)-configuration at the metal for both complexes. Thus, the reaction depicted in Eq. 1 takes place with retention of the configuration at the metal atom. Furthermore, from the assignment of the resonances for the *ortho* protons of the phenyl rings of the (*R*)-prophos ligand, a λ conformation can be inferred for the M–P^1–C–C–P^2 five-membered metallacycle.

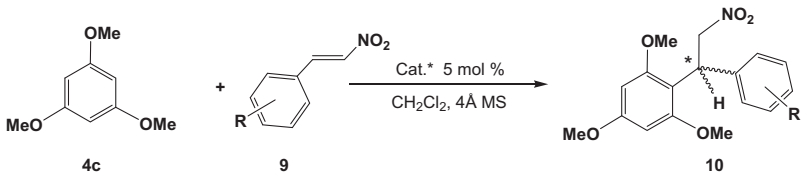
[‡] The low yield did not allow the complete NMR characterization of adduct **10b**.

[§] The low yield did not allow the complete NMR characterization of adducts **10ab** and **10ad**.

Table 1
Chemical shifts and coupling constants for the detected –C(Me)H–C(H)=C(H) moieties

Indole	H_A		H_B		H_X		Me
	δ (ppm)	J_{XA} (Hz)	δ (ppm)	J_{AB} (Hz)	δ (ppm)	J_{MeX} (Hz)	δ (ppm)
6a	6.48	6.9	6.71	16.0	3.98	7.0	1.62
6c	6.55	5.6	6.64	16.4	4.01	7.1	1.64
6d	6.44	6.9	6.69	15.9	3.97	6.5	1.73

Table 2
Reactions between 1,3,5-trimethoxybenzene and *trans*-β-nitrostyrenes



Entry	R	t (h)	Yield (%)	ee (%)	Adduct
1	H **9c**	6	>99	40	**10c**
2	4-Me **9f**	14	>99	54	**10f**
3	2-OMe **9g**	16	94	73	**10g**
4	3-OMe **9h**	7	>99	18	**10h**
5	4-OMe **9i**	15	>99	51	**10i**
6	2-OBn **9j**	17	69	69	**10j**
7	3-OBn **9k**	21	83	15	**10k**
8	4-OBn **9l**	17	98	43	**10l**
9	2,3-$(OMe)_2$ **9m**	24	89	70	**10m**[a]
10	2,4-$(OMe)_2$ **9n**	22	22	51	**10n**
11	2,5-$(OMe)_2$ **9o**	24	95	40	**10o**
12	3,4-$(OMe)_2$ **9p**	22	92	67	**10p**
13	3,4-$(OBn)_2$ **9q**	25	96	20	**10q**
14	3,5-$(OBn)_2$ **9r**	18	>99	9	**10r**
15	3-OBn,4-OMe **9s**	18	97	35	**10s**
16	2-F **9t**	4	>99	22	**10t**
17	2-Cl **9u**	22	92	31	**10u**
18	2-Br **9v**	25	89	21	**10v**
19	4-Cl **9w**	22	>99	9	**10w**
20	4-Br **9x**	16	>99	9	**10x**
21	2,3-$(Cl)_2$ **9y**	40	95	0	**10y**
22	2,4-$(Cl)_2$ **9z**	17	60	0	**10z**
23	2,6-$(Cl)_2$ **9ab**	49	2.5	3	**10ab**
24	2-Cl,6-F **9ac**	118	50	47	**10ac**
25	2-CF_3 **9ad**	96	22	9	**10ad**

[a] Enantiopure samples (>99.9% ee) of **10m** can be obtained by crystallization from CH_2Cl_2/*n*-hexane.

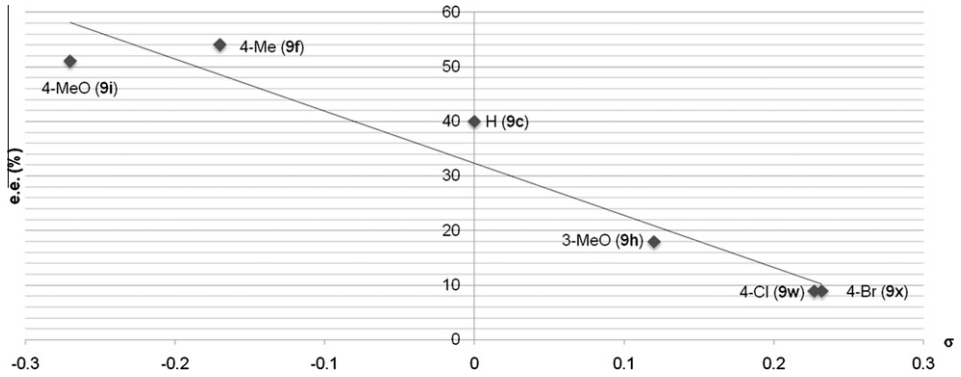
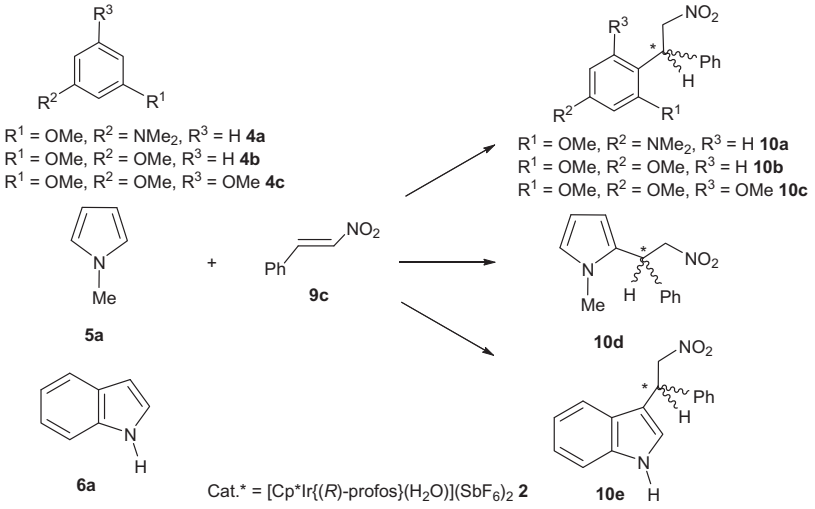


Figure 3. Plot of the ee obtained in the reaction of the nitroolefins **9c**, **9f**, **9h**, **9i**, **9w**, and **9x**, versus the Hammet parameter σ.

2.4. The catalyst/electrophile/1,3,5-trimethoxybenzene system

After the formation of the diastereopure electrophile containing species (S_M,R_C)-[Cp*M{(*R*)-prophos}(**9m**)][SbF_6]$_2$ (M = Rh **11**, Ir **12**), the next step of the catalytic process most likely should involve their interaction with the nucleophilic species 1,3,5-trimethoxybenzene **4c**. For this reason, we monitored, by NMR, the system generated by the addition of **4c** to the rhodium complex **11**. Figure 5 shows the evolution of the region of the ^{31}P NMR spectra where the double doublets corresponding to the P^2 nucleus appear (see Fig. 4). Each double doublet in this zone is related to one Rh{(*R*)-prophos} containing complex. Trace **A** corresponds to



Scheme 7. Reaction of several aromatics and heteroaromatics with *trans*-β-nitrostyrene.

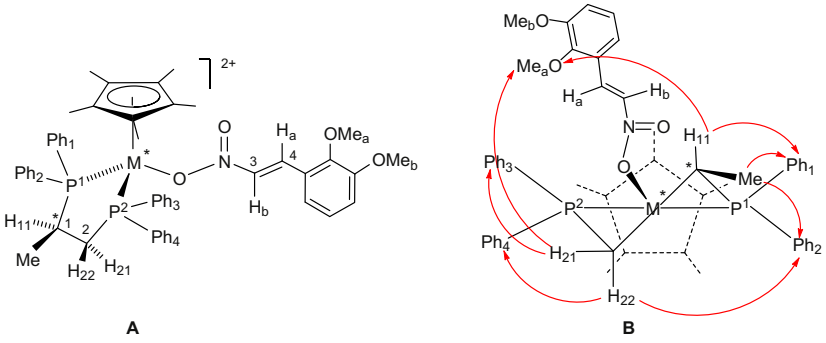


Figure 4. (A) Cation of the complexes **11** (M = Rh) and **12** (M = Ir) showing the NMR labelling scheme. (B) NOE pattern measured for these cations.

complex **11**, formed *in situ* by the addition of 2 equiv of nitroalkene **9m** to a CD_2Cl_2 solution of the aqua complex (S_{Rh},R_C)-[Cp*Rh{(*R*)-prophos}(H_2O)][SbF_6]$_2$, in the presence of 4 Å MS, according to Eq. 1. At −50 °C, two double doublets (labelled as complexes **I** and **II**, trace **B**) emerged when one equivalent of arene **4c** was added. These doublets correlate with two Cp* proton peaks at 1.30, (**I**) and 1.32 (**II**) ppm. At this temperature, the concentration of **I** and **II** increases with time at the expense of complex **11** (trace **C**) while the formation of Friedel–Crafts adduct was not detected by ^{1}H NMR spectroscopy. Heating up to −25 °C produces a decrease in the concentration of **II** and also the slow formation of the Friedel–Crafts adduct (trace **D**). Finally, at −10 °C, the Fri-

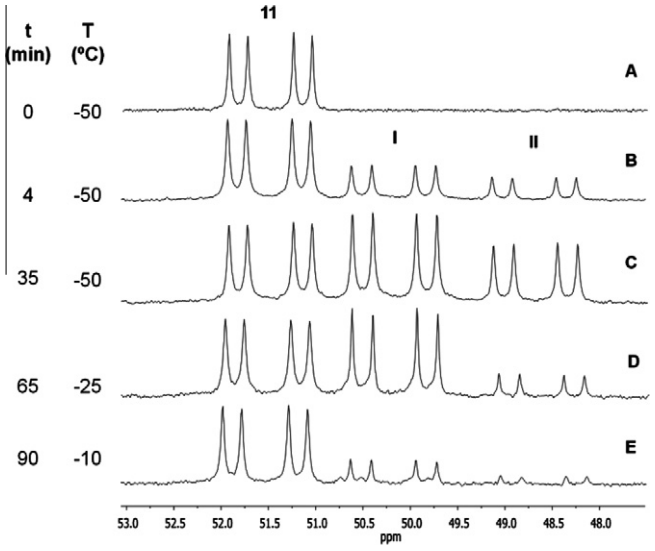


Figure 5. Fragment of the ^{31}P NMR spectra for the reaction between the rhodium complex **11** and 1,3,5,-trimethoxybenzene (see text).

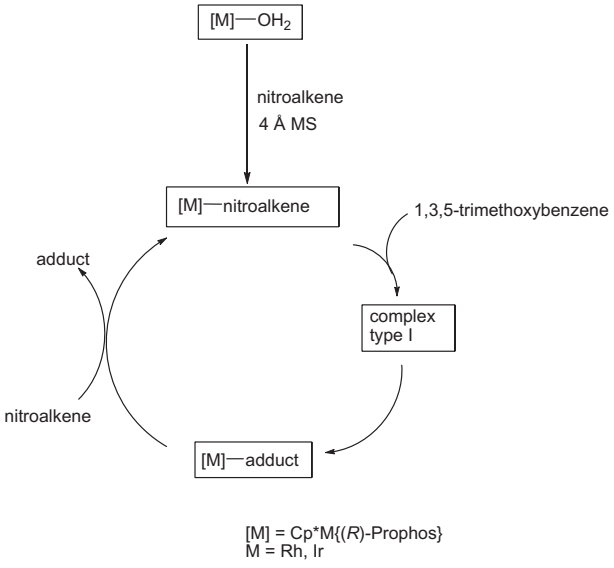
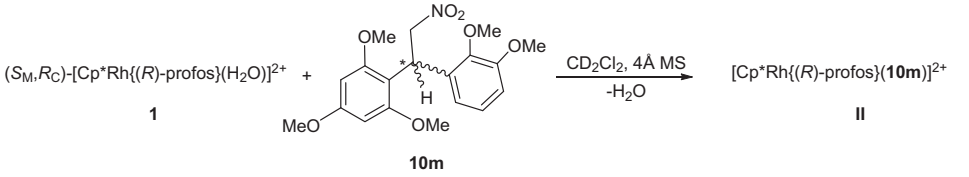


Figure 6. Proposed catalytic cycle.

edel–Crafts alkylation was quickly completed with concomitant decrease of the concentrations of **I** and **II** (trace **E**).

To obtain more information on the nature of the species **I** and **II**, in an independent experiment, we added 1 equivalent of enantiopure Friedel–Crafts adduct **10m** (see footnote, in Table 2) to a CD_2Cl_2 solution of the aqua complex (S_{Rh},R_C)-[Cp*Rh{(*R*)-prophos}(H_2O)][SbF_6]$_2$, in the presence of 4 Å MS (Eq. 2). At −50 °C, a new compound was formed, which was characterized as **II** by comparison of its ^{1}H and ^{31}P NMR spectra with those recorded in the preceding experiment.



(2)

Similarly, the reaction between the aqua complex **1** and a sample of **10m** of 70% ee was also monitored. As expected, two new complexes appeared. The major one was complex **II** and the minor, complex **III**, presented a P^2 double doublet centred at 51.11 ppm that in the spectra of Figure 5 could be overlapped by the corresponding signal of complex **11**. Thus, complex **III** has to be the isomer of complex **II** in which the less abundant enantiomer of the Friedel–Crafts adduct **10m** is coordinated to the [Cp*Rh{(*R*)-prophos} moiety and the structure of the intermediate **I** remains unclear. We currently do not have data enough to propose a structure for it. However, from the evolution of the spectra shown in Figure 5, it seems that complex **I** is an intermediate formed by the interaction between **11** and the nucleophile 1,3,5-trimethoxybenzene **4c** before the catalyst/adduct complexes **II** and **III** are formed.

2.5. Proposed catalytic cycle

Taking into account all of the above observations, we proposed the catalytic cycle shown in Figure 6. Nitroalkenes displace the coordinated molecule of water from the catalysts precursors (S_M,R_C)-[Cp*M{(*R*)-prophos}(H_2O)][SbF_6]$_2$ (M = Rh **1**, Ir **2**), in the presence of 4 Å MS, affording the corresponding nitroalkene complex, which is the true catalyst. These complexes reacted with free 1,3,5-trimethoxybenzene to give catalyst-adduct complexes probably via intermediates of the type **I**, which we have not been able to characterize. The adduct is dissociated by a new molecule of nitroalkene with concomitant regeneration of the metal-nitroalkene complex which restarts a new catalytic cycle.

3. Conclusions

The chiral fragments Cp*M{(*R*)-prophos} (M = Rh, Ir) efficiently activate α,β-unsaturated aldehydes and nitroalkenes for the Friedel–Crafts alkylation of a variety of aromatics and heteroaromatics. Clean reactions to the monoalkylated Friedel–Crafts product were observed in most of the cases investigated. In particular, quantitative and regioselective conversion to the monoalkylated adduct was obtained in the reaction between 1,3,5-trimethoxybenzene and nitroalkenes. The intermediates (S_M,R_C)-[Cp*M{(*R*)-prophos}(**9m**)][SbF_6]$_2$ (M = Rh **11**, Ir **12**) have been isolated and characterized. The catalyst/adduct complexes formed by the reaction of complex **11** with 1,3,5-trimethoxybenzene have been spectroscopically detected. A catalytic cycle that includes these two types of intermediates is proposed.

4. Experimental

4.1. General

All solvents were treated in a PS-400-6 Innovative Technologies Solvent Purification System (SPS) and degassed prior to use. All preparations were carried out under argon. Infrared spectra were obtained as KBr pellets with a Perkin–Elmer 1330 spectrophotometer. Carbon, hydrogen and nitrogen analyses were performed using a Perkin–Elmer 2400 CHNS/O microanalyser. NMR spectra were recorded on Brucker Avance-300, 400 or 500 MHz spectrometers; unless otherwise stated all NMR measurements were carried at rt. ^{1}H (300.13, 400.16, 500.13 MHz), ^{31}P{^{1}H} (161.96 MHz) and ^{13}C{^{1}H} (75.48, 100.61, 125.77 MHz) NMR chemical shifts are reported in ppm relative to tetramethylsilane and referenced to partially deuterated solvent resonances for ^{1}H and ^{13}C and H_3PO_4 (85%) for ^{31}P. Coupling constants (*J*) are given in Hertz. NOEDIFF and ^{1}H correlation spectra were obtained using standard procedures. Analytical high performance liquid chromatography (HPLC) was performed on an Alliance Waters (Waters 2996 PDA detector) instrument using the chiral columns Chiralcel OD-H (0.46 × 25 cm) and OD-H guard (0.46 × 5 cm) or Chiralpak AD-H (0.46 × 25 cm) or AS-H (0.46 × 25 cm).

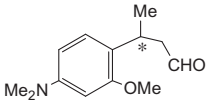
The complexes (S_M,R_C)-[Cp*M{(*R*)-Prophos}(H_2O)](SbF_6)$_2$ (M = Rh **1**, Ir **2**) were prepared using literature procedures[13] with the following small modifications: to a suspension of [(Cp*MCl)$_2$(μ-Cl)$_2$] (0.400 mmol) in acetone (20 mL) 549.9 mg (1.6 mmol) of $AgSbF_6$ were added. The resulting suspension was stirred for 15 h and the precipitate was filtered off and washed with acetone (3 × 1 mL). The filtrate was vacuum-concentrated until ca. 5 mL and cooled down to −25 °C (Rh) or −50 °C (Ir). Under argon, at the corresponding temperature, 330.4 mg (0.800 mmol) of (*R*)-prophos was added and the solution was stirred for 30 min. The addition of *n*-hexane (20 mL) and subsequent stirring gave orange (Rh) or yellow (Ir) solids. The solution was poured off and the solid washed with *n*-hexane (3 × 20 mL) and then vacuum-dried. The solids were recrystallized three times at −25 °C (Rh) or −50 °C (Ir) from CH_2Cl_2/*n*-hexane, 1:5, v/v. Yield: 92.3% (Rh), 88.7% (Ir).

4.2. General procedure for the reaction between aromatics or heteroaromatics and enals

At −10 °C, in a thermostatic bath, a Schlenk flask equipped with a magnetic stirrer was introduced. Under argon, 0.03 mmol of (S_M,R_C)-[Cp*M{(*R*)-Prophos}(H_2O)](SbF_6)$_2$, CH_2Cl_2 (4 mL), the corresponding enal (0.60 mmol) and approximately 100 mg of 4 Å MS were added. The mixture was stirred for 15 min and then the corresponding aromatic or heteroaromatic reagent (1.80 mmol) was added. The reaction was monitored by TLC. After the appropriate reaction time, the suspension was vacuum-concentrated until dryness. The residue was extracted with Et_2O (3 × 5 mL) and the solution vacuum-evaporated until dryness. In some cases, the resulting oils were analysed and characterized by NMR and HPLC techniques. The residue was dissolved in ethanol (4 mL) and 68.1 mg (1.80 mmol) of $NaBH_4$ were added. After 15 min of reaction, 1 mL of a saturated solution of Na_2CO_3 in water was added. The mixture

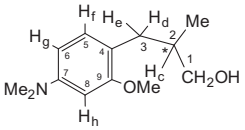
was extracted with CH_2Cl_2 (3 × 10 mL) and the organic phase was dried over $MgSO_4$. The resulting solution was vacuum-evaporated to dryness and purified by column chromatography (SiO_2; AcEt/*n*-hexane, 40:60). Evaporation of the solvent gives pale oils that were analysed and characterized by NMR and HPLC techniques.

4.2.1. 3-(4-(Dimethylamino)-2-methoxyphenyl)butanal 8a



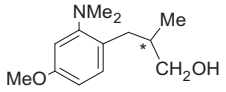
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[20] Yield: 49%. Ee: 26% (*S*).

4.2.2. 3-(4-(Dimethylamino)-2-methoxyphenyl)-2-methylpropan-1-ol 8c



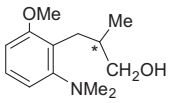
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 6.98 (pt, 1H, H_f), 6.34 (br d, 1H, H_g), 6.33 (s, 1H, H_h), 3.86 (s, 3H, OMe), 3.40, 3.45 (m, 2H, CH_2OH), 2.96 (s, 6H, NMe_2), 2.61, 2.50 (dd, J = 21.2, 7.3 Hz, 2H, $H_d + H_e$), 1.92 (m, 1H, H_c), 0.97 (d, J = 7.3 Hz, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 158.16 (C^9), 150.51 (C^7), 133.14 (C^5), 117.09 (C^4), 105.25, 96.61 (C^6, C^8), 66.88 (C^1), 55.39 (OMe), 40.99 (NMe_2), 36.87 (C^2), 28.84 (C^3), 17.05 (Me). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol; 1.0 mL/min); t_R, min: 10.9 (minor), 12.7 (major). Yield: 67%. Ee: 65%.

4.2.3. 3-(2-(Dimethylamino)-4-methoxyphenyl-2-methylpropan-1-ol 8d



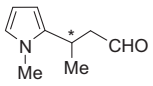
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 3.88 (s, 3H, OMe), 2.98 (s, 6H, NMe_2), 0.99 (br d, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 55.60 (OMe), 40.81 (NMe_2), 20.43 ppm (Me). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 15.25 (minor), 16.31 (major). Yield: 22%. Ee: 60%.

4.2.4. 3-(2-(Dimethylamino)-5-methoxyphenyl-2-methylpropan-1-ol 8e



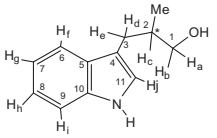
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 3.85 (s, 3H, OMe), 2.95 (s, 6H, NMe_2), 1.03 (d, J = 6.6 Hz, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 55.56 (OMe), 40.85 (NMe_2), 19.66 (Me). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 19.57 (minor), 20.63 (major). Yield: 11%. Ee: 73%.

4.2.5. 3-(1-Methyl-1*H*-pyrrol-2-yl)butanal 8f



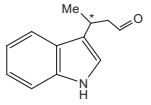
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[47] (Cat.* **1**: Yield: 82%, Ee: 8% (*S*). Cat.* **2**: Yield: 50%, Ee: 12% (*S*).

4.2.6. Characterization of the alcohol derived from 8g



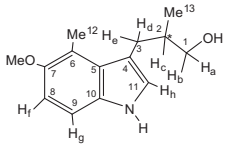
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.96 (br s, 1H, NH), 7.55 (d, J = 7.8 Hz, 1H, H_f), 7.29 (d, J = 8.1 Hz, 1H, H_i), 7.12 (pt, 1H, H_h), 7.04 (pt, 1H, H_g), 6.93 (d, J = 2.3 Hz, 1H, H_j), 3.52, 3.45 (dd, J = 10.5, 5.9 Hz, 2H, $H_a + H_b$), 2.80, 2.56 (dd, J = 14.4, 6.6 Hz, 2H, $H_d + H_e$), 2.01 (oc, 1H, J = 6.8 Hz, H_c), 1.29 (br s, 1H, OH), 0.91 (d, J = 6.8 Hz, 3H, Me). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 137.00 (C^{10}), 128.23, 113.50 (C^4, C^5), 126.98 (C^{11}), 121.44 (C^7), 119.13 (C^9), 118.62 (C^8), 111.09 (C^6), 68.06 (C^1), 36.87 (C^2), 28.84 (C^3), 17.05 (Me). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 53.8 (minor), 64.5 (major). Yield: 26%. Ee: 22%.

4.2.7. 3-(1*H*-Indole-3-yl)butanal 8h



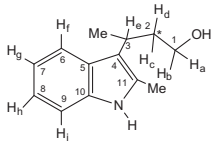
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[48] Yield: 15%. Ee: 7%.

4.2.8. Characterization of the alcohol derived from 8i



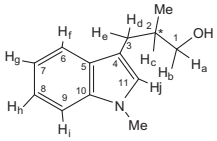
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 8.00 (br s, 1H, NH), 7.15, 6.92 (d, J = 8.6 Hz, 1H, $H_f + H_g$), 6.93 (s, 1H, H_h), 3.87 (s, 3H, OMe), 3.66, 3.55 (dd, J = 10.6, 5.4 Hz, 2H, $H_a + H_b$), 3.00, 2.70 (dd, J = 14.7, 6.6 Hz, 2H, $H_d + H_e$), 2.61 (s, 3H, Me^{12}), 2.05 (ps, 1H, J = 6.7 Hz, H_c), 1.30 (br s, 1H, OH), 1.02 (d, J = 6.7 Hz, 3H, Me^{13}). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 151.40 (C^7), 132.88, 126.93, 118.65, 115.39 (C^4, C^5, C^6, C^{10}) 124.10 (C^{11}), 110.18, 108.72 (C^8, C^9), 67.98 (C^1), 58.26 (OMe), 37.44 (C^2), 31.11 (C^3), 16.96 (Me^{13}), 12.01 (Me^{12}). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 50.8 (major), 61.4 (minor). Yield: 16%. Ee: 26%.

4.2.9. Characterization of the alcohol derived from 8j



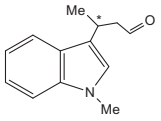
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.91 (br s, 1H, NH), 7.62 (d, J = 7.9 Hz, 1H, H_f), 7.30 (d, J = 7.9 Hz, 1H, H_i), 7.09 (pt, 1H, H_h), 7.03 (pt, 1H, H_g), 3.53 (m, 2H, $H_a + H_b$), 3.17 (m, 2H, $H_c + H_d$), 2.41 (s, 3H, $C^{11}Me$), 2.06 (m, 1H, J = 6.8 Hz, H_c), 1.45 (d, J = 7.1 Hz, 3H, C^3Me). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 135.60, 130.63, 127.42, 115.22 (C^4, C^5, C^{10}, C^{11}), 120.50 (C^8), 119.11 (C^6), 118.64 (C^7), 110.28 (C^9), 61.68 (C^1), 39.52 (C^2), 27.77 (C^3), 21.11 (Me). HPLC: Chiralpak AD-H (90:10, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 14.5 (minor), 19.2 (major). Yield: 16%. Ee: 5%.

4.2.10. Characterization of the alcohol derived from 8k



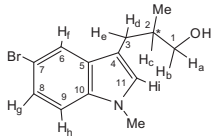
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.60 (d, J = 7.9 Hz, 1H, H_f), 7.28 (d, J = 8.2 Hz, 1H, H_i), 7.22 (pt, 1H, H_h), 7.12 (pt, 1H, H_g), 6.84 (s, 1H, H_j), 3.74 (s, 1H, NMe), 3.58, 3.50 (dd, J = 10.5, 5.9 Hz, 2H, $H_a + H_b$), 2.84, 2.60 (dd, J = 14.4, 6.5 Hz, 2H, $H_d + H_e$), 2.05 (ps, 1H, J = 6.8 Hz, H_c), 1.61 (br s, 1H, OH), 0.97 (d, J = 6.5 Hz, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 137.00 (C^{10}), 128.24, 113.05 (C^4, C^5), 126.98 (C^{11}), 121.45 (C^7), 119.15 (C^9), 118.64 (C^8), 109.16 (C^6), 68.06 (C^1), 32.60 (NMe), 36.87 (C^2), 28.84 (C^3), 17.05 (Me). HPLC: Chiralpak AS-H (95:5, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 14.4 (minor), 15.9 (major). Yield: 25%. Ee: 28%.

4.2.11. 3-(1-Methyl-1*H*-indole-3-yl)butanal 8l



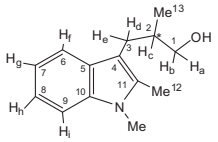
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[48] Yield: 58%. Ee: 21% (*S*).

4.2.12. Characterization of the alcohol derived from 8m



^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.72 (s, 1H, H_f), 7.17 (br d, 2H, $H_g + H_h$), 6.88 (s, 1H, H_i), 3.77 (s, 3H, NMe), 3.56 (m, 2H, $H_a + H_b$), 2.83, 2.57 (dd, J = 14.3, 6.7 Hz, 2H, $H_d + H_e$), 2.04 (m, 1H, H_c), 1.27 (br s, 1H, OH), 0.99 (d, J = 6.7 Hz, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 135.67, 129.92, 112.82, 112.13 (C^4, C^5, C^7, C^{10}), 128.15 (C^{11}), 124.22, 110.66 (C^8, C^9), 121.69 (C^6), 67.88 (C^1), 36.77 (C^2), 32.83 (NMe), 28.62 (C^3), 16.95 (Me). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 22.3 (major), 24.2 (minor). Yield: 11%. Ee: 19%.

4.2.13. Characterization of the alcohol derived from 8n

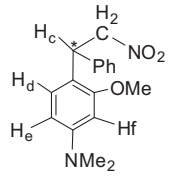


^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.42 (br d, 1H, H_f), 7.29 (br d, 1H, H_i), 7.19 (pt, 1H, H_h), 7.08 (pt, 1H, H_g), 3.69 (s, 3H, NMe), 3.61, 3.51 (m, 2H, $H_a + H_b$), 2.85, 2.59 (m, 2H $H_d + H_e$), 2.40 (s, 3H, Me^{12}), 2.05 (m, 1H, J = 6.8 Hz, H_c), 0.91 (d, J = 6.8 Hz, 3H, Me^{13}). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 136.56–107.15 (aromatic carbons), 68.20 (C^1), 37.63 (C^2), 29.56 (NMe), 28.84 (C^3), 17.10 (Me^{13}), 10.46 (Me^{12}). HPLC: Chiralpak AS-H (97:3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 13.6 (minor), 16.1 (major). Yield: 33%. Ee: 33%.

4.3. General procedure for the reaction between aromatics or heteroaromatics and *trans*-β-nitrostyrenes

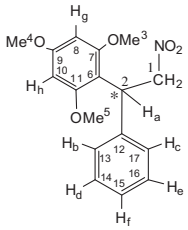
A Schlenk flask equipped with a magnetic stirrer was introduced in a thermostatic bath at −10 °C. Under argon, 0.03 mmol of (S_M,R_C)-[Cp*M{(*R*)–Prophos}(H_2O)](SbF_6)$_2$, CH_2Cl_2 (4 mL), the corresponding *trans*-β-nitrostyrene (0.60 mmol) and about 100 mg of 4 Å MS were added. The resulting red mixture was stirred for 15 min and then the corresponding aromatic or heteroaromatic reagent (0.60 mmol) was added. The reaction was monitored by TLC. After the appropriate reaction time, the suspension was vacuum-concentrated until dryness. The residue was extracted with Et_2O (3 × 5 mL) and the solution vacuum-evaporated until dryness rendering a white or pale yellow solid that was analysed and characterized by NMR and HPLC techniques.

4.3.1. 3-Methoxy-*N*,*N*-dimethyl-4-(2-nitro-1-phenilethyl)aniline 10a



^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.45–7.36 (m, 5H, Ph), 6.78 (d, J = 9.4 Hz, H_e), 6.14–6.13 (m, 2H, $H_d + H_f$), 5.06 (dd, J = 8.3, 6.1 Hz, H_c), 4.82–4.93 (m, 2H, CH_2), 3.73 (s, 3H, OMe), 2.84 ppm (s, 6H, NMe_2). HPLC: Chiralcel AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 27.3 (minor), 28.4 min (major). Ee: 5%.

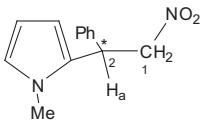
4.3.2. 2-(1-Phenyl-2-nitroethyl)-1,3,5-trimethoxybenzene 10c



^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.33 (d, J = 7.8 Hz, 2H, $H_b + H_c$), 7.28 (pt, J = 6.8 Hz, 2H, $H_d + H_e$), 7.21 (pt, J = 6.8 Hz, 1H, H_f), 6.15 (s, 2H, $H_g + H_h$), 5.52 (pt, J = 7.95 Hz, 1H, H_a), 5.26, 5.16 (dd, J = 12.7, 7.9 Hz, 2H, C^1H_2), 3.82 (s, 9H, OMe). ^{13}C NMR

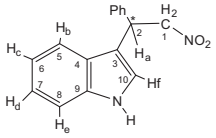
(100.61 MHz, $CDCl_3$) δ, ppm: 160.52, (C^9), 158.91 (C^7, C^{11}), 140.46 (C^6), 128.78, 128.74 (C^{13}, C^{17}), 128.67, 128.06 (C^{16}, C^{14}), 125.94 (C^{15}), 108.58 (C^{12}), 91.17 (C^8, C^{10}), 78.10 (C^1), 55.16–55.78 (C^3, C^4, C^5), 38.55 (C^2). HPLC: Chiralpak AD-H (90:10, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 14.3 (minor), 15.0 (major).

4.3.3. 2-(1-Phenyl-2-nitroethyl)-pyrrole 10d



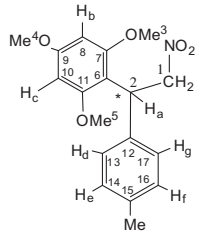
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.07–7.21 (m, 5H, Ph), 6.43 (s, 1H, H_{py}), 6.01–6.06 (m, 2H, H_{py}), 4.52–4.76 (m, 3H, $CH_2 + H_a$), 3.05 (s, 3H, NMe). HPLC: Chiralcel OD-H (80:20, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 22.8 (minor), 29.5 (major).

4.3.4. 3-(1-Phenyl-2-nitroethyl)-indole 10e



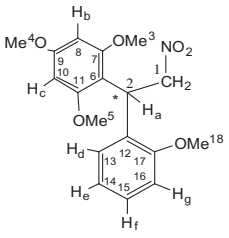
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[23] Ee: 3% (*R*).

4.3.5. 2-(1-(4-Methylphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10f



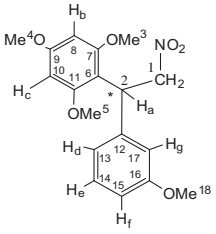
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.11 (d, J = 8.0 Hz, 2H, $H_d + H_g$), 6.97 (d, J = 7.7 Hz, 2H, $H_e + H_f$), 6.04 (s, 2H, $H_b + H_c$), 5.37 (pt, J = 7.8 Hz, 1H, H_a), 5.13, 5.04 (dd, J = 12.9, 7.8 Hz, 2H, C^1H_2), 3.72 (s, 6H, $OMe^3 + OMe^5$), 3.71 (s, 3H, OMe^4), 2.21 (s, 3H, Me). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.67, (C^9), 158.97, (C^7, C^{11}), 137.62 (C^6), 136.46 (C^{15}), 129.04 (C^{13}, C^{17}) 127.51 (C^{14}, C^{16}), 109.04 (C^{12}), 91.17 (C^8, C^{10}), 78.52 (C^1), 55.80, 55.32 (C^3, C^4, C^5), 38.32 (C^2), 21.04 (Me). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 16.5 (minor), 18.2 (major).

4.3.6. 2-(1-(2-Methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10g



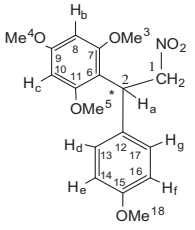
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.24 (pt, 1H, H_f), 7.03 (d, J = 8.5 Hz, 1H, H_d), 6.87 (d, J = 8.5 Hz, 1H, H_g), 6.83 (pt, 1H, H_e), 6.19 (s, 2H, $H_b + H_c$), 5.80 (pt, J = 6.1 Hz, 1H, H_a), 5.20, 5.07 (dd, J = 18.6, 6.1 Hz, 2H, C^1H_2), 3.89, 3.84, 3.79 (s, 12H, OMe). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.59 (C^9), 159.17 (C^7, C^{11}), 157.16, (C^{17}), 129.14 (C^{13}), 127.96 (C^{15}), 127.48 (C^6), 120.33 (C^{14}), 110.43 (C^{16}), 107.39 (C^{12}), 91.24 (C^8, C^{10}), 77.31 (C^1), 55.82, 55.44, 55.30 (C^3, C^4, C^5, OMe^{18}), 34.10 (C^2). HPLC: Chiralpak AD-H (98:2, *n*-hexane/2-propanol, 0.25 mL/min); t_R, min: 78.0 (minor), 80.3 (major).

4.3.7. 2-(1-(3-Methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10h



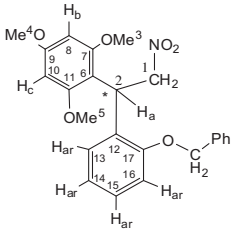
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.19 (pt, 1H, H_e), 6.92 (d, J = 8.5 Hz, 1H, H_d), 6.90 (t, J = 1.9 Hz, 1H, H_g), 6.74 (dd, J = 8.5, 1.9 Hz, 1H, H_f), 6.14 (s, 2H, $H_b + H_c$), 5.48 (pt, J = 7.7 Hz, 1H, H_a), 5.23, 5.13 (dd, J = 20.3, 7.7 Hz, 2H, C^1H_2), 3.79 (s, 3H, OMe^4); 3.82, 3.81, 3.78 (s, 12H, OMe). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.61, (C^9), 159.51, (C^{16}), 159.00 (C^7, C^{11}), 142.15 (C^6), 129.21 (C^{14}), 120.03 (C^{13}), 113.97 (C^{17}), 111.54 (C^{15}), 108.58 (C^{12}), 91.24 (C^8, C^{10}), 78.35 (C^1), 55.80, 55.30, 55.10 (C^3, C^4, C^5, OMe^{18}), 38.58 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 13.4 (minor), 14.7 (major).

4.3.8. 2-(1-(4-Methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10i



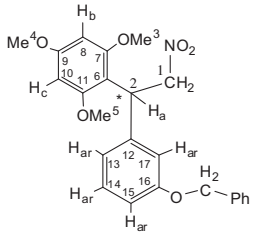
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.21 (d, J = 8.6 Hz, 2H, $H_d + H_g$), 6.76 (d, J = 8.6 Hz, 2H, $H_e + H_f$), 6.10 (s, 2H, $H_b + H_c$), 5.39 (pt, J = 7.7 Hz, 1H, H_a), 5.16, 5.06 (dd, J = 20.1, 7.7 H, 2H, C^1H_2), 3.77 (s, 6H, $OMe^3 + OMe^5$), 3.76, 3.73 (s, 6H, $OMe^4 + OMe^{18}$). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 160.55 (C^9), 158.53 (C^7, C^{11}), 158.21, (C^{15}), 132.60 (C^6), 128.69 (C^{14}, C^{16}), 113.69 (C^{13}, C^{17}), 108.83 (C^{12}), 91.15 (C^8, C^{10}), 78.78 (C^1), 55.80, 55.29, 55.18 (C^3, C^4, C^5, OMe^{18}), 38.02 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 28.8 (minor), 33.8 min (major).

4.3.9. 2-(1-(2-Benzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10j



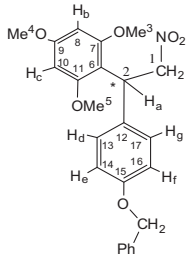
^{1}H NMR (400.16 MHz, CD_3COCD_3) δ, ppm: 7.52–6.82 (m, 9H, H_{ar}), 6.27 (s, 2H, $H_b + H_c$), 5.93 pt, J = 7.2 Hz, 1H, H_a), 5.22–5.05 (m, 4H, $C^1H_2 + CH_2Ph$), 3.82 (s, 3H, OMe^4), 3.74 (s, 6H, $OMe^3 + OMe^5$). ^{13}C NMR (100.61 MHz, CD_3COCD_3) δ, ppm: 160.90, 159.75, 156.22 (C^7, C^9, C^{11}, C^{17}), 137.62 (C^6), 129.14–112.11 (C^{13}, C^{14}, C^{15}, C^{16}, C^{12}, and C, Ph), 91.35 (C^8, C^{10}), 76.85 (C^1), 69.77 (CH_2Ph), 55.20, 54.70 (C^3, C^4, C^5), 33.86 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.25 mL/min); t_R, min: 75.2 (minor), 77.3 (major).

4.3.10. 2-(1-(3-Benzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10k



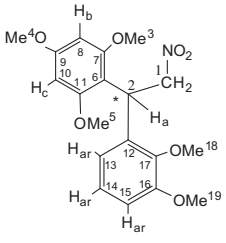
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.50–6.81 (m, 9H, H_{ar}), 6.14 (s, 2H, $H_b + H_c$), 5.47 (pt, J = 7.8 Hz, 1H, H_a), 5.23, 5.12 (dd, J = 12.8, 7.8 Hz, 2H, C^1H_2), 5.03 (s, 2H, CH_2Ph), 3.81 (s, 3H, OMe^4),3.79 (s, 6H, $OMe^3 + OMe^5$). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 161.94, 160.59, 158.98, 158.76 (C^7, C^9, C^{11}, C^{16}), 142.17 (C^6), 137.04–108.47 (C^{13}, C^{14}, C^{15}, C^{17}, C^{12}, and C, Ph), 92.90 (C^8, C^{10}), 76.85 (C^1), 69.77 (CH_2Ph), 55.20, 54.70 (C^3, C^4, C^5), 33.86 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 34.6 (minor), 38.4 (major).

4.3.11. 2-(1-(4-Benzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10l



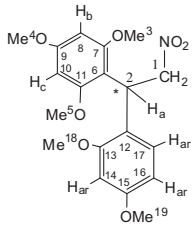
^{1}H NMR (500.13 MHz, $CDCl_3$) δ, ppm: 7.44–7.32 (m, 5H, H_{ar}), 7.27 (d, J = 13.7 Hz, 2H, $H_d + H_g$), 6.77 (d, J = 13.7 Hz, 2H, $H_e + H_f$), 6.04 (s, 2H, $H_b + H_c$), 5.46 (pt, J = 7.8 Hz, 1H, H_a), 5.22, 5.12 (dd, J = 19.76, 7.40, 2H, C^1H_2), 5.04 (CH_2Ph), 3.83 (s, 6H, $OMe^3 + OMe^5$), 3.82 (s, 3H, OMe^4). ^{13}C NMR (125.77 MHz, $CDCl_3$) δ, ppm: 160.52, 158.93, 157.54 (C^7, C^9, C^{11}, C^{15}), 137.13 (C^6), 132.93, 128.76, 128.59, 127.95, 127.49, 114.65, 108.93 (C^{13}, C^{14}, C^{16}, C^{17}, C^{12}, and C, Ph), 91.22 (C^8, C^{10}), 78.68 (C^1), 70.01 (CH_2Ph), 55.83, 55.33 (C^3, C^4, C^5), 38.07 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 32.4 (minor), 36.5 (major).

4.3.12. 2-(1-(2,3-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10m



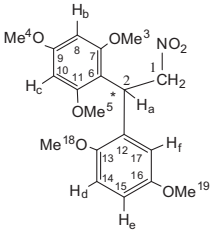
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 6.95, 6.81, 6.80 (3H, H_{ar}), 6.14 (s, 2H, $H_b + H_c$), 5.78 (pt, J = 6.9 Hz, 1H, H_a), 5.01, 5.18 (dd, J = 19.5, 6.9, 2H, C^1H_2), 3.88, 3.86, 3.81, 3.79 (s, 15H, OMe). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm): 160.67, (C^9), 159.52, 152.68 (C^7, C^{11}), 147.1, 133.49 (C^{16}, C^{17}), 123.49 (C^6), 120.86 (C^{13}), 111.11 (C^{14}), 125.94 (C^{15}), 107.73 (C^{12}), 91.26 (C^8, C^{10}), 77.34 (C^1), 60.44–55.28 (C^3, C^4, C^5, C^{18}, C^{19}), 33.94 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 34.3 (minor), 35.9 (major).

4.3.13. 2-(1-(2,4-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10n



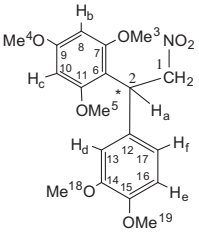
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 6.95–6.80 (m, 3H, H_{ar}), 6.14 (s, 2H, $H_b + H_c$), 5.30 (pt, J = 7.0 Hz, 1H, H_a), 4.80, 4.64 (dd, J = 11.8, 7.0 Hz, 2H, C^1H_2), 3.58 (s, 6H, $OMe^3 + OMe^5$), 3.57, 3.55, 3.52 ppm (s, 9H, $OMe^4 + OMe^{18} + OMe^{19}$). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 36.8 (minor), 38.4 (major).

4.3.14. 2-(1-(2,5-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10o



^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 6.71 (d, J = 8.8 Hz, 1H, H_d), 6.63 (dd, J = 8.8, 3.0 Hz, 1H, H_e), 6.56 (d, J = 3.0 Hz, 1H, H_f), 6.07 (s, 2H, $H_b + H_c$), 5.67 (pt, J = 8.6 Hz, 1H, H_a), 5.10, 4.94 (dd, J = 12.4, 8.5 Hz, 2H, C^1H_2), 3.77, 3.73, 3.59 (s, 9H, $OMe^4 + OMe^{18} + OMe^{19}$), 3.70 (s, 6H, $OMe^3 + OMe^5$). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 31.2 (minor), 34.3 (mayor).

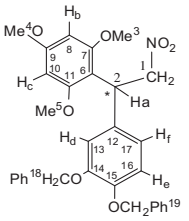
4.3.15. 2-(1-(3,4-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10p



^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 6.92 (d, J = 1.9 Hz, 1H, H_d), 6.89 (dd, J = 8.3, 1.9 Hz, 1H, H_f), 6.77 (d, J = 8.3 Hz, 1H, H_e), 6.14 (s, 2H, H_b+ H_c), 5.44 (pt, J = 7.8 Hz, 1H, H_a), 5.22, 5.11 (dd, J = 12.7, 7.8 Hz, 2H, C^1H_2), 3.85 (s, 6H, $OMe^3 + OMe^5$), 3.84 (s, 6H, $OMe^{18} + OMe^{19}$), 3.81 (s, 3H, OMe^4). ^{13}C NMR (100.61 MHz, $CDCl_3$)

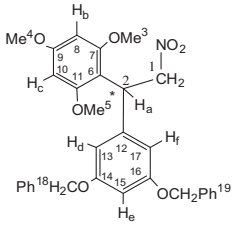
δ, ppm: 161.55, 160.53, 158.91, 148.68, 147.79 (C^7, C^9, C^{11}, C^{14}, C^{15}), 133.10 (C^6), 119.77 (C^{17}), 11.33 (C^{13}), 111.01 (C^{16}), 108.84 (C^{12}), 91.26 (C^8, C^{10}), 78.77 (C^1), 55.81–55.32 (C^3, C^4, C^5, C^{18}, C^{19}), 38.48 (C^2). HPLC: Chiralpak AD-H (90:10, *n*-hexane/2-propanol, 1 mL/min); t_R, min = 35.5 (minor), 53.4 (major).

4.3.16. 2-(1-(3,4-Dibenzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10q



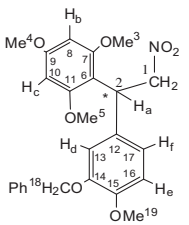
^{1}H NMR (500.13 MHz, $CDCl_3$) δ, ppm: 7.44–7.28 (m, 10H, Ph^{18} + Ph^{19}), 6.94 (br d, 1H, H_d), 6.83 (m, 2H, H_e + H_f), 6.12 (s, 2H, H_b + H_c), 5.38 (pt, J = 7.8 Hz, 1H, H_a), 5.16–4.98 (m, 6H, C^1H_2 + CH_2Ph^{18} + CH_2Ph^{19}), 3.81 (s, 3H, OMe^4), 3.75 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (125.77 MHz, $CDCl_3$) δ, ppm: 160.52, 158.88, (C^7, C^9, C^{11}, C^{14}, C^{15}), 137.46 (C^6), 148.58–108.78 (C^{13}, C^{16}, C^{17}, C^{12}, and C, Ph), 91.25 (C^8, C^{10}), 78.60 (C^1), 71.42, 71.31 (CH_2Ph^{18}, CH_2Ph^{19}), 55.77, 55.31 (C^3, C^4, C^5), 38.25 (C^2). HPLC: Chiralpak AD-H (80:20, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 20.5 (minor), 34.2 (major).

4.3.17. 2-(1-(3,5-Dibenzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10r



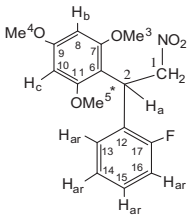
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.32–7.21 (m, 10H, Ph^{18} + Ph^{19}), 6.48 (d, J = 2.0 Hz, 2H, H_d + H_f), 6.37 (t, J = 2.0 Hz, 1H, H_e), 6.02 (s, 2H, H_b + H_c), 5.32 (pt, J = 7.8 Hz, 1H, H_a), 5.08–4.99 (dd, J = 12.9, 7.8, 2H, C^1H_2), 4.89 (br s, 4H, CH_2Ph), 3.70 (s, 3H, OMe^4), 3.66 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (125.77 MHz, $CDCl_3$) δ, ppm: 160.62, 159.80, 159.00 (C^7, C^9, C^{11}, C^{14}, C^{16}), 142.95–108.38 (C^6, C^{12}, C, Ph), 107.19 (C^{13}, C^{17}), 100.15 (C^{15}), 91.24 (C^8, C^{10}), 78.31 (C^1), 70.06 (CH_2Ph^{18}, CH_2Ph^{19}), 55.82, 55.33 (C^3, C^4, C^5), 38.72 (C^2). HPLC: Chiralpak AD-H (80:20, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 11.2 (minor), 13.4 (major).

4.3.18. 2-(1-(3-Benzyloxy-4-methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10s



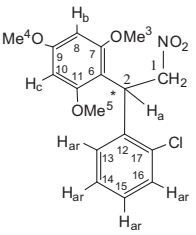
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.32–7.18 (m, 5H, Ph^{18}), 6.80 (m, 2H, H_e + H_f), 6.70 (br d, 1H, H_d), 6.02 (s, 2H, H_b + H_c), 5.27 (pt, J = 7.8 Hz, 1H, H_a), 5.05–4.92 (m, 4H, C^1H_2 + CH_2Ph), 3.76, 3.71 (s, 6H, OMe^4 + OMe^{19}), 3.64 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 160.50, 158.86 (C^7, C^9, C^{11}, C^{14}, C^{15}), 148.48–108.86 (C^6, C^{12}, C^{13}, C^{16}, C^{17}, and C, Ph), 91.27 (C^8, C^{10}), 78.64 (C^1), 71.12 (CH_2Ph^{14}), 56.00, 55.75, 55.30 (C^3, C^4, C^5, C^{19}), 38.26 (C^2). HPLC: Chiralpak AD-H (90:10, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 21.8 (minor), 36.1 (major).

4.3.19. 2-(1-(2-Fluorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10t



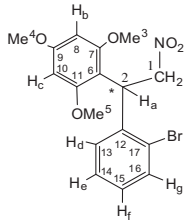
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.28–6.93 (m, 4H, H_{ar}), 6.16 (s, 2H, H_b + H_c), 5.78 (pt, J = 8.0 Hz, 1H, H_a), 5.16 (d, J = 7.8 Hz, 2H, C^1H_2), 3.82 (s, 3H, OMe^4), 3.81 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.52, (C^9), 158.97 (C^7, C^{11}), 137.47, 136.15 (C^{17}, C^6), 129.02, 127.50 (C^{13}, C^{14}, C^{15}, C^{16}), 108.80 (C^{12}), 91,19 (C^8, C^{10}), 78.52 (C^1), 55.80, 55.30 (C^3, C^4, C^5), 38.32 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 18.9 (minor), 20.0 (major).

4.3.20. 2-(1-(2-Chlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10u



^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.32, 7.14 (m, 4H, H_{ar}), 6.12 (s, 2H, H_b + H_c), 5.80 (pt, J = 7.0 Hz, 1H, H_a), 5.19, 4.99 (dd, J = 20.1, 7.0 Hz, 2H, C^1H_2), 3.79 (s, 3H, OMe^4); 3.76 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.84, (C^9), 159.51 (C^7, C^{11}), 137.25, 133.99 (C^{17}, C^6), 129.83, 129.72, 128.07, 126.62 (C^{13}, C^{14}, C^{15}, C^{16}), 106.70 (C^{12}), 91,19 (C^8, C^{10}), 76.44 (C^1), 55.77, 55.30 (C^3, C^4, C^5), 36.85 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 19.1 (minor), 20.3 (major).

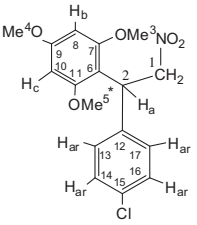
4.3.21. 2-(1-(2-Bromophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10v



^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.55 (d, J = 8.2 Hz, 1H, H_g), 7.34 (d, J = 7.7 Hz, 1H, H_d), 7.21 (pt, J = 7.2 Hz, 1H, H_f), 7.08 (pt, J = 7.7 Hz, 1H, H_e), 6.15 (s, 2H, H_b + H_c), 5.77 (pt, J = 8.2 Hz, 1H,

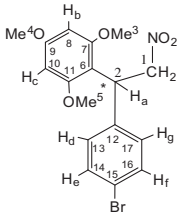
H_a), 5.25, 4.95 (dd, J = 12.8, 8.2, 2H, C^1H_2), 3.81 (s, 3H, OMe^4), 3.79 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 160.85 (C^9), 159.56 (C^7, C^{11}), 139.01, 124.52 (C^{17}, C^6), 133.10, 130.10, 128.38, 127.36 (C^{13}, C^{14}, C^{15}, C^{16}), 106.97 (C^{12}), 91.29 (C^8, C^{10}), 76.49 (C^1), 55.77, 55.30 (C^3, C^4, C^5), 39.61 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 18.6 (minor), 19.2 (major).

4.3.22. 2-(1-(4-Chlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10w



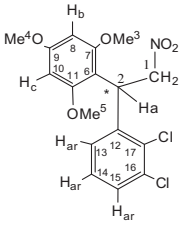
^1H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.29–7.22 (m, 4H, H_{ar}), 6.14 (s, 2H, H_b + H_c), 5.47 (pt, J = 8.1 Hz, 1H, H_a), 5.26, 5.06 (dd, J = 12.8, 8.1 Hz, 2H, C^1H_2), 3.82 (s, 6H, OMe^3 + OMe^5), 3.81 (s, 3H, OMe^4). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.77 (C^9), 158.83 (C^7, C^{11}), 139.11 (C^{15}), 132.33 (C^6), 129.01, 128.42 (C^{13}, C^{14}, C^{16}, C^{17}), 108.18 (C^{12}), 91.13 (C^8, C^{10}), 78.08 (C^1), 55.80, 55.35 (C^3, C^4, C^5), 37.98 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 34.6 (minor), 40.2 min (major).

4.3.23. 2-(1-(4-Bromophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10x



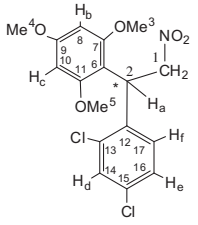
^1H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.37 (d, J = 8.4 Hz, 2H, H_e + H_f), 7.19 (d, J = 8.4 Hz, 2H, H_d + H_g), 6.12 (s, 2H, H_b + H_c), 5.45 (pt, J = 7.4 Hz, 1H, H_a), 5.24, 5.04 (dd, J = 19.8, 7.4 Hz, 2H, C^1H_2), 3.80 (s, 9H, OMe). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 160.83 (C^9), 158.86 (C^7, C^{11}), 139.69 (C^{15}), 131.36 (C^{14}, C^{16}), 129.37 (C^{13}, C^{17}), 120.43 (C^6), 108.22 (C^{12}), 91.24 (C^8, C^{10}), 78.00 (C^1), 55.80, 55.33, (C^3, C^4, C^5), 38.06 (C^2). HPLC: Chiralpak AD-H (90:10, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 14.6 (minor), 16.6 (major).

4.3.24. 2-(1-(2,3-Dichlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10y



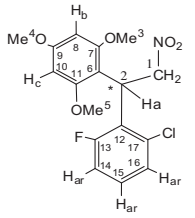
^1H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.60–6.64 (m, 3H, H_{ar}), 6.14 (s, 2H, H_b + H_c), 5.78 (pt, J = 6.9 Hz, 1H, H_a), 5.22, 4.95 (dd, J = 12.7, 6.9, 2H, C^1H_2), 3.75 (s, 3H), 3.81, 3.69 (s, 9H, OMe^3 + OMe^4 + OMe^5). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 26.7, 28.9.

4.3.25. 2-(1-(2,4-Dichlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10z



^1H NMR (500.13 MHz, $CDCl_3$) δ, ppm: 7.37 (d, J = 2.2 Hz, 1H, H_d), 7.30 (d, J = 8.6 Hz, 1H, H_f), 7.15 (dd, J = 8.6, 2.2 Hz, 1H, H_e), 6.14 (s, 2H, H_b + H_c), 5.77 (pt, J = 8.6 Hz, 1H, H_a), 5.14, 5.01 (dd, J = 12.7, 8.6 Hz, 2H, C^1H_2), 3.82 (s, 3H, OMe^4), 3.79 (s, 6H, OMe^3 + OMe^5). ^{13}C NMR (125.77 MHz, $CDCl_3$) δ, ppm: 161.01 (C^9), 159.37 (C^7, C^{11}), 136.02, 134.67 (C^{13}, C^{15}), 133.07 (C^6), 130.65 (C^{17}), 129.43 (C^{14}), 126.86 (C^{16}), 106.17 (C^{12}), 91.15 (C^8, C^{10}), 76.27 (C^1), 55.74, 55.32, (C^3, C^4, C^5), 36.36 (C^2). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 24.3, 26.7.

4.3.26. 2-(1-(2-Chloro-6-fluorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene 10ac

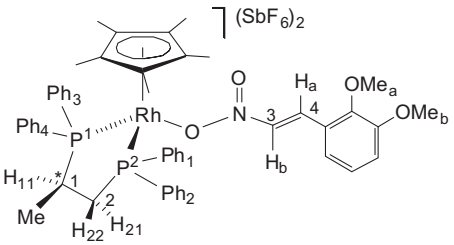


^1H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.41–6.48 (m, 3H, H_{ar}), 6.05 (s, 2H, H_b + H_c), 5.61 (pt, J = 8.0 Hz, 1H, H_a), 5.15, 4.88 (m, 2H, C^1H_2), 3.75 (s, 3H, OMe^4), 3.68 (s, 6H, OMe^3 + OMe^5). HPLC: Chiralpak AD-H (95:5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 18.4 (major), 20.5 (minor).

4.4. Preparation of the complexes (S_M,R_C)-[(Cp*M{(*R*)-prophos}(9m)](SbF$_6$)$_2$ [M = Rh 11, Ir 12]

At −25 °C, under argon, to a solution of 0.12 mmol of the corresponding complex (S_M,R_C)-[Cp*M(*R*-prophos)(H_2O)](SbF$_6$)$_2$ [M = Rh **1** 136.8 mg, Ir **2** 149.6 mg] in CH_2Cl_2 (20 mL), 75.3 mg (0.36 mmol) of **9m** and 100 mg of 4 Å MS were added. The resulting red suspension was stirred for 1 h and then filtered through a cannula. The filtrate was vacuum-concentrated to approximately 3 mL. The addition of 20 mL of *n*-hexane afforded an orange-red solid that was filtered off, washed with *n*-hexane (5 × 20 mL) and vacuum-dried. Yield: 81.3 % **11**, 78.8 % **12**.

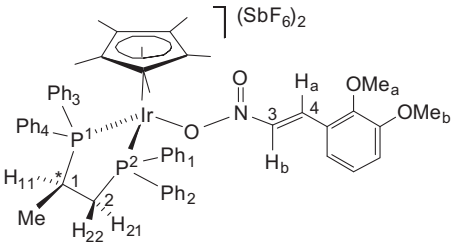
4.4.1. (S_{Rh},R_C)-[Cp*Rh{(*R*)-prophos}(9m)](SbF$_6$)$_2$ 11



^1H NMR (400.16 MHz, CD_2Cl_2, −25 °C) δ, ppm: 7.85–6.95 (23H, Ph), 7.47 (d, J = 13.9 Hz, 1H, H_a), 7.31 (d, J = 13.9 Hz, 1H, H_b), 3.89 (s, 3H,

OMe_b), 3.87 (s, 3H, OMe_a), 3.59 (dm, J(P,H) = 52.7 Hz, 1H, H_{21}), 3.19 (m, 1H, H_{11}), 2.70 (t, J = 16.1 Hz 1H, H_{22}), 1.44 (pt, J = 3.3 Hz, 15H, C_5Me_5), 1.31 (dd, J(P,H) = 13.5, 7.0 Hz, 3H, Me). ^{13}C NMR (100.61 MHz, CD_2Cl_2, −25 °C) δ, ppm: 152.85–118.98 (Ph), 142.56 (C^4), 134.98 (C^3), 107.29 (br s, C_5Me_5), 61.67 (OMe_b), 56.00 (OMe_a), 33.5 (dd, J(P,C) = 35.1, 13.9 Hz, C^2), 31.22 (dd, J(P,C) = 31.5, 9.5 Hz, C^1), 15.86 (dd, J(P,C) = 17.6, 5.1 Hz, Me), 10.08 (C_5Me_5). ^{31}P NMR (161.96 MHz, CD_2Cl_2, −25 °C) δ, ppm: 75.99 (dd, J(Rh,P^1) = 130.8 Hz, J(P^2,P^1) = 38.3 Hz, P^1), 51.52 ppm (dd, J(Rh,P^2) = 133.1 Hz, P^2). IR (KBr, cm^{-1}): ν(SbF_6): 658 s. Elemental Anal. Calcd for $C_{47}H_{53}F_{12}RhO_4NP_2Sb_2$: C, 42.4; H, 4.0. Found: C, 42.3; H, 4.0.

4.4.2. (S_{Ir},R_C)-[Cp*Ir{(*R*)-prophos}(9m)](SbF_6)$_2$ 12



^{1}H NMR (400.16 MHz, CD_2Cl_2, −25 °C) δ, ppm: 7.60 (br d, 1H, H_a), 7.59–7.26 (m, 23H, Ph), 7.35 (br d, 1H, H_b), 3.91 (s, 6H, OMe_a + OMe_b), 3.57 (dm, J(P,H) = 48.1 Hz, 1H, H_{21}), 3.14 (m, 1H, H_{11}), 2.64 (m, 1H, H_{22}), 1.53 (br s, 15H, C_5Me_5), 1.35 (dd, J(P,H) = 16.1, 9.5 Hz, 3H, Me). ^{13}C NMR (100.61 MHz, CD_2Cl_2, −25 °C) δ, ppm: 143.93 (C^3), 134.28–119.83 (Ph, C^4), 101.40 (C_5Me_5), 61.69, 56.00 (OMe_a, OMe_b), 33.90, 31.67 (m, C^1, C^2), 14.76 (dd, J(P,C) = 16.3, 3.8 Hz, 3H, Me), 9.67 ppm (C_5Me_5). ^{31}P NMR (161.96 MHz, CD_2Cl_2, −25 °C) δ, ppm: 49.04 (d, J(P^2,P^1) = 10.7 Hz, P^1), 27.71 ppm (d, P^2). IR (KBr, cm^{-1}): ν(SbF_6): 658 s. Elemental Anal. Calcd for $C_{47}H_{53}F_{12}IrO_4NP_2Sb_2$: C, 39.7; H, 3.7. Found: C, 39.6; H, 3.7.

4.5. NMR measurements for the 11/4c system

At −25 °C, under argon, to a solution of 36.4 mg (0.03 mmol) of (S_{Rh},R_C)-[Cp*Rh{(*R*)-prophos}(H_2O)](SbF_6)$_2$ **1**, in CD_2Cl_2 (1.0 mL), 12.6 mg (0.06 mmol) of **9m** and 20 mg of 4 Å MS were added. The suspension was stirred for 1 h and placed into a 5-mm NMR tube. At −50 °C, ^{1}H and ^{31}P NMR spectra showed the complete formation of complex **11**. Then, 5.0 mg (0.03 mmol) of 1,3,5-trimethoxybenzene were added and the system was monitored by ^{1}H and ^{31}P NMR spectroscopies from −50 to −10 °C.

4.6. NMR measurements for the 1/10m system

In a 5-mm NMR tube, 36.4 mg (0.03 mmol) of (S_{Rh},R_C)-[Cp*Rh{(*R*)-prophos}(H_2O)](SbF_6)$_2$ **1** were dissolved in CD_2Cl_2 (0.5 mL). At −50 °C, 11.3 mg (0.03 mmol) of **10m** and 20 mg of 4 Å MS were added. The reaction was monitored by ^{1}H and ^{31}P NMR spectroscopy.

Acknowledgements

We thank the Ministerio de Educación y Ciencia (Grant CTQ 2009-10303/BQU) and Gobierno de Aragón (Grupo Consolidado: Catalizadores Organometálicos Enantioselectivos) for financial support. C.B. thanks the IUCH for a grant.

References

1. Jørgensen, K. A. *Synthesis* **2003**, 1117–1125.
2. Bandini, M.; Melloni, A.; Umani-Ronchi, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 550–556.
3. Bandini, M.; Melloni, A.; Tommasi, S.; Umani-Ronchi, A. *Synlett* **2005**, 1199–1222.
4. Bandini, M.; Eichholzer, A.; Umani-Ronchi, A. *Mini-Rev. Org. Chem.* **2007**, *4*, 115–124.
5. Poulsen, T. B.; Jørgensen, K. A. *Chem. Rev.* **2008**, *108*, 2903–2915.
6. Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608–9644.
7. Marqués-López, E.; Díez-Martínez, A.; Merino, P.; Herrera, R. P. *Curr. Org. Chem.* **2009**, *13*, 1585–1609.
8. You, S.-L.; Cai, Q.; Zeng, M. *Chem. Soc. Rev.* **2009**, *38*, 2190–2201.
9. Bartoli, G.; Bencivenni, G.; Dalpozzo, R. *Chem. Soc. Rev.* **2010**, *39*, 4449–4465.
10. Bigi, F.; Casiraghi, G.; Casnati, G.; Sartori, G.; Fava, G. G.; Belicchi, M. F. *J. Org. Chem.* **1985**, *50*, 5018–5022.
11. Erker, G.; Vanderzeijden, A. A. H. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 512–514.
12. Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Oro, L. A.; Balana, A. I.; Lahoz, F. J.; Tejero, T.; Merino, P.; Franco, S.; Montesa, I. *J. Am. Chem. Soc.* **2004**, *126*, 2716–2717.
13. Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Oro, L. A.; Lahoz, F. J.; Balana, A. I.; Tejero, T.; Merino, P. *J. Am. Chem. Soc.* **2005**, *127*, 13386–13398.
14. Carmona, D.; Cativiela, C.; García-Correas, R.; Lahoz, F. J.; Lamata, M. P.; López, J. A.; de Víu, M.; Oro, L. A.; San José, E.; Viguri, F. *Chem. Commun.* **1996**, 1247–1248.
15. Barba, C.; Carmona, D.; García, J. I.; Lamata, M. P.; Mayoral, J. A.; Salvatella, L.; Viguri, F. *J. Org. Chem.* **2006**, *71*, 9831–9840.
16. Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Barba, C.; Lahoz, F. J.; Martín, M. L.; Oro, L. A.; Salvatella, L. *Organometallics* **2007**, *26*, 6493–6496.
17. Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Fischer, T.; Lahoz, F. J.; Dobrinovitch, I. T.; Oro, L. A. *Adv. Synth. Catal.* **2007**, *349*, 1751–1758.
18. Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Lahoz, F. J.; Oro, L. A. *Chem. Eur. J.* **2007**, *13*, 9476–9756.
19. Carmona, D.; Lamata, M. P.; Viguri, F.; Rodríguez, R.; Lahoz, F. J.; Fabra, M. J.; Oro, L. A. *Tetrahedron: Asymmetry* **2009**, *20*, 1197–1205.
20. Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 7894–7895.
21. Bandini, M.; Garelli, A.; Rovinetti, M.; Tommasi, S.; Umani-Ronchi, A. *Chirality* **2005**, *17*, 522–529.
22. Zhuang, W. Z.; Hazell, R. G.; Jørgensen, K. A. *Org. Biomol. Chem.* **2005**, *3*, 2566–2571.
23. Jia, Y.-X.; Zhu, S.-F.; Yang, Y.; Zhou, Q.-L. *J. Org. Chem.* **2006**, *71*, 75–80.
24. Lu, S.-F.; Du, D.-M.; Xu, J. *Org. Lett.* **2006**, *8*, 2115–2118.
25. Sui, Y.; Liu, L.; Zhao, J.-L.; Wang, D.; Chen, Y.-J. *Tetrahedron* **2007**, *63*, 5173–5183.
26. Singh, P. K.; Bisai, A.; Singh, V. K. *Tetrahedron Lett.* **2007**, *48*, 1127–1129.
27. Liu, H.; Xu, J.; Du, D.-M. *Org. Lett.* **2007**, *9*, 4725–4728.
28. Liu, H.; Lu, S.-F.; Xu, J.; Du, D.-M. *Chem. Asian J.* **2008**, *3*, 1111–1121.
29. Yuan, Z.-L.; Lei, Z.-Y.; Shi, M. *Tetrahedron: Asymmetry* **2008**, *19*, 1339–1346.
30. Trost, B. M.; Muller, C. *J. Am. Chem. Soc.* **2008**, *130*, 2438–2439.
31. Arai, T.; Yokoyama, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4989–4992.
32. Lin, S.-z.; You, T.-p. *Tetrahedron* **2009**, *65*, 1010–1016.
33. Yokoyama, N.; Arai, T. *Chem. Commun.* **2009**, 3285–3287.
34. McKeon, S. C.; Müller-Bunz, H.; Guiry, P. J. *Eur. J. Org. Chem.* **2009**, 4833–4841.
35. Guo, F.; Lai, G.; Xiong, S.; Wang, S.; Wang, Z. *Chem. Eur. J.* **2010**, *16*, 6441–6483.
36. Liu, H.; Du, D.-M. *Adv. Synth. Catal.* **2010**, *352*, 1113–1118.
37. Kim, H. Y.; Kim, S.; Oh, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 4476–4478.
38. Herrera, R. P.; Sgarzani, V.; Bernardi, L.; Ricci, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6576–6579.
39. Fleming, E. M.; McCabe, T.; Connon, S. J. *Tetrahedron Lett.* **2006**, *47*, 7037–7042.
40. Liu, T.-Y.; Cui, H.-L.; Chai, Q.; Long, J.; Li, B.-J.; Wu, Y.; Ding, L.-S.; Chen, Y.-C. *Chem. Commun.* **2007**, 2228–2230.
41. Ganesh, M.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 16464–16465.
42. Itoh, J.; Fuchibe, K.; Akiyama, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 4016–4018.
43. Sheng, Y.-F.; Gu, Q.; Zhang, A.-J.; You, S.-L. *J. Org. Chem.* **2009**, *74*, 6899–6901.
44. Sheng, Y. F.; Li, G. Q.; Kang, Q.; Zhang, A. J.; You, S. L. *Chem. Eur. J.* **2009**, *15*, 3351–3354.
45. Sohtome, Y.; Shin, B.; Horitsugi, N.; Takagi, R.; Noguchi, K.; Nagasawa, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 7299–7303.
46. Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165–195.
47. Paras, N. A.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2001**, *123*, 4370–4371.
48. Austin, J. F.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 1172–1173.