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

Daniel Carmona*, María Pilar Lamata, Antonio Sánchez, Fernando Viguri, Luis A. Oro

Departamento de Química Inorgánica, Instituto Universitario de Catálisis Homogénea, Instituto de Ciencia de Materiales de Aragón, Universidad de Zaragoza-Consejo Superior de Investigaciones Científicas, 50009 Zaragoza, Spain

ABSTRACT

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

*Corresponding author
E-mail address: dcarmona@unizar.es (D. Carmona)
Phone: +34 976762027; Fax: (+34) 976761187

1. Introduction

The catalytic enantioselective Friedel-Crafts (FC) 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 organocatalised [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 on asymmetric FC 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 the 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-diylbis(diphenylphosphane)).[12,13] These complexes easily lose water and the resulting unsaturated Lewis-acid cations (Figure 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.

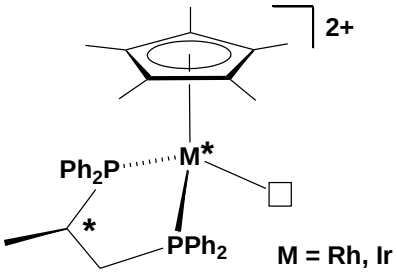


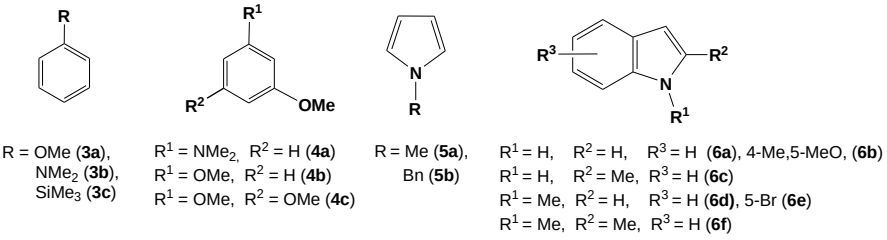
Figure 1. The chiral cations Cp*M{(*R*)-prophos)}

Taking into account these results, we envisaged the possibility of applying this metallic fragment as catalyst for the FC alkylation of aromatic and heteroaromatic substrates with activated alkenes. We report here the results obtained.

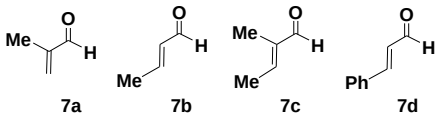
2. Results and discussion

2.1 Enals as electrophiles

We first examined the homogeneous asymmetric FC 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

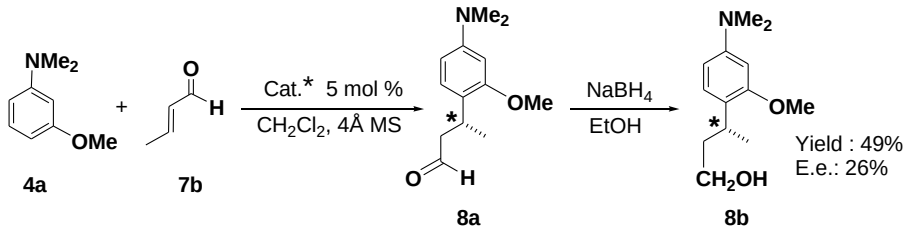


Scheme 1. Aromatics and heteroaromatics investigated



Scheme 2. Enals employed

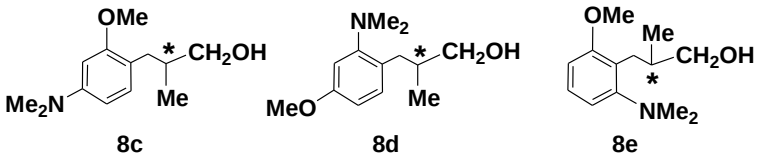
were carried out at -10ºC, in the presence of 4Å molecular sieves (MS). A 1/20/60: catalyst/aromatic/enal molar ratio was employed. According to NMR data, after 72 hours of treatment in these conditions, no reaction was observed between monosubstituted arenes **3a-c** and *trans*-crotonaldehyde nor between **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** catalyses the reaction between *m*-*N*,*N*-dimethyl anisidine (**4a**) and *trans*-crotonaldehyde (**7b**). After 72 hours of reaction, the monosubstituted FC product at the *para* position with respect to the amine was obtained in 49% isolated yield and in 26% e.e., measured on the alcohol obtained by reduction with $NaBH_4$ (Scheme 3). Analogously, complex **2** catalyses the reaction between the anisidine **4a** and methacrolein, but a mixture of three compounds was obtained. After reduction with $NaBH_4$, the major product was characterized as the alcohol **8c**. NMR data indicate that the two remaining products are



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

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

the other two possible monosubstituted FC adducts **8d** and **8e**. Quantitative conversion was achieved after 72 hours of reaction with the product distribution and enantioselectivity, measured on the alcohol derivatives, depicted in Scheme 4.

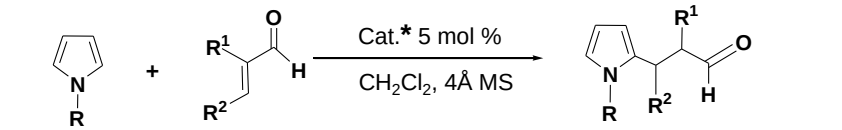


	8c	8d	8e
Yield :	67%	22%	11%
E.e.:	65%	60%	73%

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

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

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

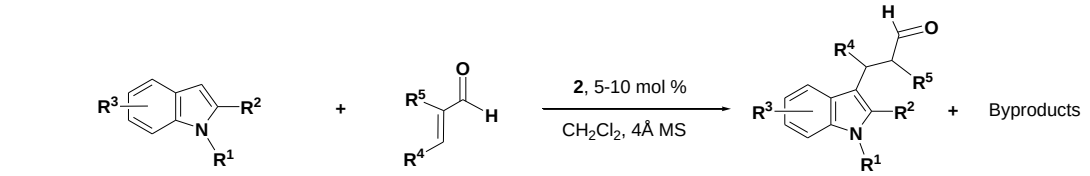


Cat.* = [Cp*M{(*R*)-profos}(H_2O)][SbF_6]$_2$ (M = Rh (**1**), Ir (**2**))

Scheme 5. Catalytic reaction between pyrroles and enals

Next, we examined the FC reaction of pyrroles and indoles with enals. At -10ºC, *N*-methyl pyrrol **5a** reacts with *trans*-crotonaldehyde **7b** giving the corresponding 2-substituted FC adduct **8f**, with 8% or 12% e.e. when the rhodium complex **1** or the iridium complex **2** were used as catalyst precursor, respectively (Scheme 5). No reaction was observed between *N*-benzyl pyrrol **5b** and the enals **7a,b** in the presence of complexes **1** or **2**.

Then, the reaction of a series of indoles with methacrolein and *trans*-crotonaldehyde was examined, using the iridium complex **2** as catalyst precursor† (Scheme 6). The



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

indole was alkylated at the 3-position in all the attempted cases. After 24-48 hours of reaction at -10ºC, isolated yield, in the alcohol obtained by subsequent reduction of the FC product, ranged from 15 to 58%. Enantiomeric excesses from 7 to 33% e.e. were achieved. The low yield was accompanied by the formation of several byproducts we were unable to completely characterize. However, when *trans*-crotonaldehyde **7b** was used as electrophile, together with the expected alkylated indole (**8h**, **8j**, **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 byproduct in all the three cases. Figure 2 shows the ^{1}H NMR peaks encountered in the crude 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, in general, poor results obtained in the

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

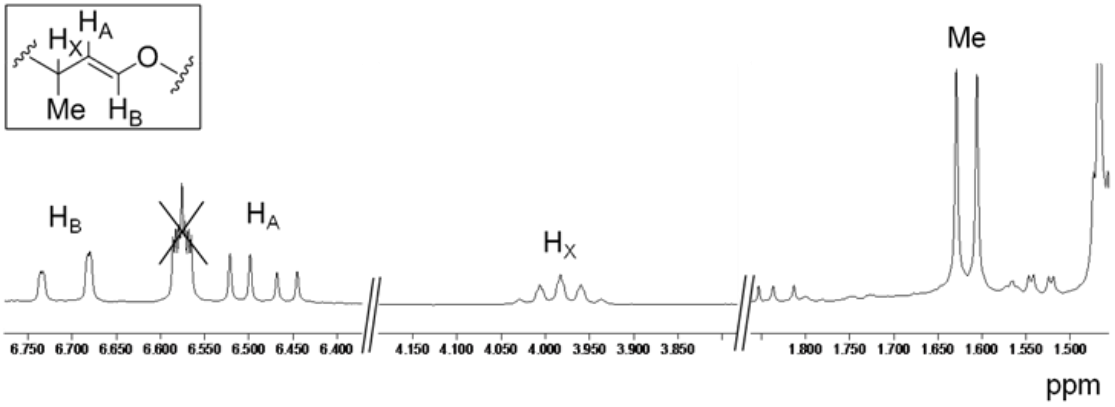


Figure 2. Selected fragments of the ^{1}H NMR spectrum of the crude of the reaction between **6a** and **7b**.

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

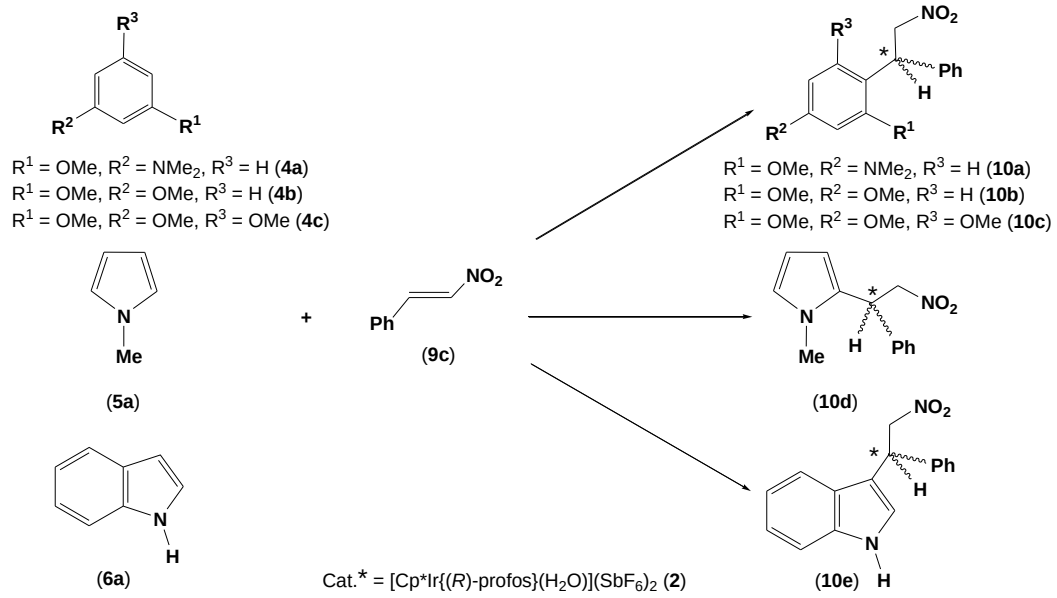
alkylation reaction of enals, prompted us to try nitrostyrenes as electrophiles. We expected that the nitro group on the one side would provide the substrate with binding capability and on the other would activate the C=C double bond without interfering in its FC reactivity.

2.2 *trans*-*β*-Nitrostyrenes as electrophiles

Examples of homogeneous catalytic enantioselective addition of aromatic and heteroaromatic C-H bonds to nitroolefins appeared only recently. In 2005, Bandini, Umani-Ronchi, 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 and coworkers 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 employed with nitrogen and/or oxygen donor ligands as chiral source. The organocatalysts tried

are based on thioureas,[38-40,45] phosphoric acids[42-44] or quinolinium amido(thio)amides.[41] Indoles 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 one example of the addition of nitroolefins to 2-methoxyfuran[27] has been recently published.

Taking into account all precedent, we decide to investigate the FC 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 chiral source.

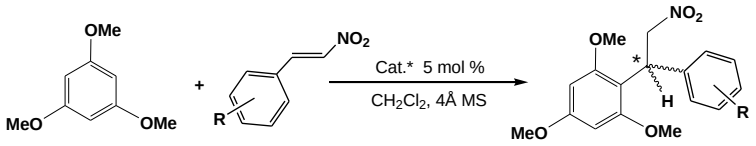


Scheme 7. Reaction of several aromatics and heteroaromatics with *trans*-β-nitrostyrene

First, we examined the reaction of *trans*-β-nitrostyrene, as alkene model, with a series of activated arenes (**3c**, **4a-c**), *N*-methyl pyrrol (**5a**) and indole (**6a**) using the iridium complex **2** as catalyst precursor (Scheme 7). Dichloromethane was used as solvent and reactions were carried out at -10ºC, in the presence of 4Å MS. A 1/20/20: catalyst/aromatic/*trans*-β-nitrostyrene molar ratio was employed. According to spectroscopic and chromatographic data, quantitative yield was obtained in all cases, but for phenyltrimethylsilane **3c** and 1,3-dimethoxybenzene **4b**. No reaction was observed for the monosubstituted arene **3c** after 72 hours of treatment and a yield of 17%, with 2% of e.e., was measured, after the same time of reaction, for **4b**. Reactions were completely regioselective. Only monosubstituted FC adducts were detected: the

arene substituted at the *para* position with respect to the 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% e.e. were achieved.

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



4c 9 10

Entry	R	t (h)	Yield (%)	E.e. (%)	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% e.e.) of **10m** can be obtained by crystallization from CH_2Cl_2/*n*-hexane

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

As the best result was obtained for 1,3,5-trimethoxybenzene (**4c**) (quantitative yield after 6 hours of reaction, 40% e.e.) and this substrate has not been investigated previously in this type of FC 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 catalyst precursor, under the conditions above reported 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 4Å MS before the addition of the arene. In these conditions, [Cp*M{(*R*)-prophos}(nitroolefin)]$^{2+}$ were the sole metallic complexes present in solution (see below).

In general, high yield are obtained after a few hours of reaction at -10ºC. E.e.'s up to 73% were achieved. Both, electron donating and electron withdrawing groups generate less active systems (compare, for example, 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) present a catalytic rate comparable to that of the unsubstituted nitroolefin. In this line, the lowest rates correspond to nitroolefins with two substituents on the aromatic ring. Probably, this trend is originated by the increase in the steric hindrance of the alkylation reagent.

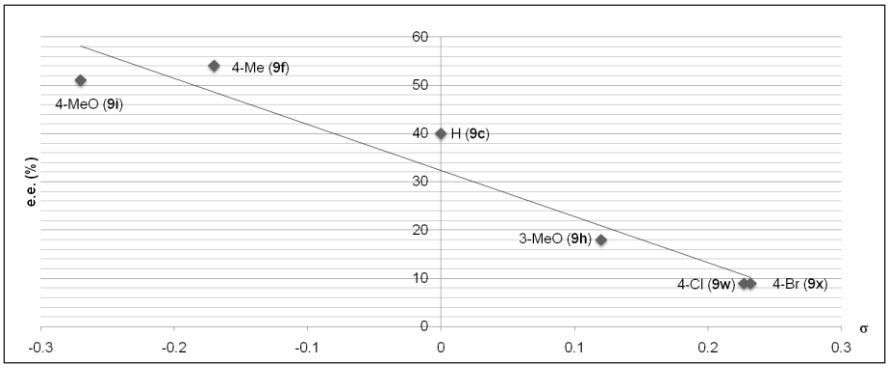


Figure 3. Plot of the e.e. obtained in the reaction of the nitroolefins **9c**, **9f**, **9h**, **9i**, **9w**, and **9x**, versus the Hammet parameter σ

Electronic factors strongly affect the enantioselectivity of the system. Thus, while electron donating substituents located at 2 or 4 positions of the aromatic ring improve

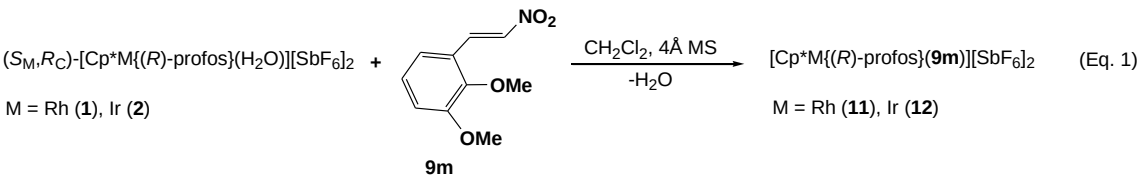
[§] The low yield does not allow the complete NMR characterization of adducts **10ab** and **10ad**.

e.e. (compare entry 1 with entries 3 and 5 or 6 and 8), it diminishes when substituents of this type are placed at position 3 (compare entry 1 with entries 4 or 7). However, two donor substituents situated at positions 2 and 4 do not produce further improvement on the e.e. (compare entries 3 and 5 with entry 10). Conversely, lower e.e.'s are obtained with electron withdrawing substituents. The 2,6-disubstituted nitroolefin **9ac**, that gives a 47 % e.e. (entry 24), is the only exception to this trend. In this context, Bandini, Umani-Ronchi, et al. found a good degree of correlation between the enantiomeric excess of the products and the Hammet parameter[46] associated to the nitroalkene substituent, for the FC reaction between indoles and nitroalkenes, catalysed by aluminium-salen complexes.[21] Reflecting the influence of the electronic factors on the e.e. outcome, we have found a similar trend by plotting the e.e.'s obtained versus the reported Hammet parameter σ values for a series of nitroalkenes (Figure 3).

2.3 Isolation and characterization of the catalyst/electrophile intermediate

In spite of the fact that several metal-based catalytic systems have been applied to the FC reaction between aromatic or heteroaromatic substrates and nitroalkenes,[21,23-37] as far as we know, no experimental data about the metallic intermediates involved in the catalytic reaction have been reported up to date. In some cases, the stereochemical outcome of the catalytic reactions has been explained by assuming that activation of the nitroalkene occurs through its 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 get an insight into the catalytic mechanism we studied the reaction between the catalyst precursors (S_M,R_C)-[Cp*M{(*R*)-prophos}(H_2O)][SbF_6]$_2$ (M = Rh (**1**), Ir (**2**)) and the nitroalkene **9m**, as a model. When 3 equivalents 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*)-prophos}(**9m**)]$^{2+}$ are instantaneously and quantitatively formed. From the solution solids of formula [Cp*M{(*R*)-prophos}(**9m**)][SbF_6]$_2$ (M = Rh (**11**), Ir (1**2**)) can be isolated in around 80% yield (Equation 1).



Complexes **11** and **12** were characterized by microanalysis and by IR, ^{1}H, ^{13}C, and ^{31}P NMR spectroscopies (see Experimental). The reaction is completely diastereoselective; from -50ºC to RT only one set of sharp signals in observed in the NMR spectra of the three nuclei investigated. Assignment of the NMR peaks has been fulfilled by a combination of mono- and bi-dimensional, homo- and hetero-nuclear experiments. The ^{1}H NMR spectrum reveals 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 centered at 7.31 (H_b, see Fig. 4) and 7.47 (H_a) ppm, with a coupling constant of 13.9 Hz, are 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.

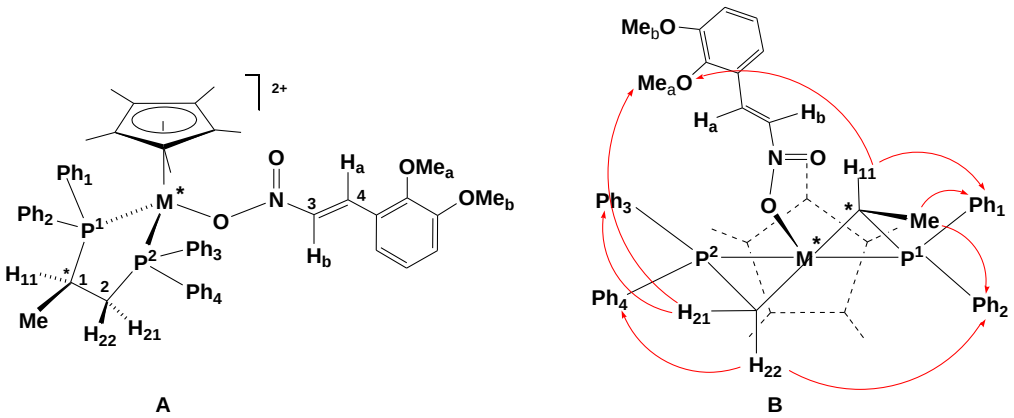


Figure 4. A: Cation of the complexes **11** (M = Rh) and **12** (M = Ir) showing the NMR labeling scheme. **B**: NOE pattern measured for these cations

The ^{31}P NMR spectrum of the rhodium complex **11** consists of two double doublets centered 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) and that of the iridium compound **12** comprises two doublets centered 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 metal for both complexes. Thus, the reaction depicted in Eq. 1 takes place with retention of the configuration at metal. 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.

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

After 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 Figure 4). Each double doublet in this zone is related to one Rh{(*R*)-prophos} containing complex. Trace **A** corresponds to complex **11**, formed in situ by addition of 2 equivalents 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 Equation 1. At -50ºC, two double doublets (labelled as complexes **I** and **II**, trace **B**) emerge when one equivalent of the arene **4c** is 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**) and the formation of FC adduct was not detected by ^{1}H NMR spectroscopy. Heating up to -25ºC produces the decreasing of the concentration of **II** and the slowly formation of FC adduct (trace **D**). Finally, at -10ºC, the FC alkylation is quickly completed remaining very low concentrations of **I** and **II** (trace **E**).

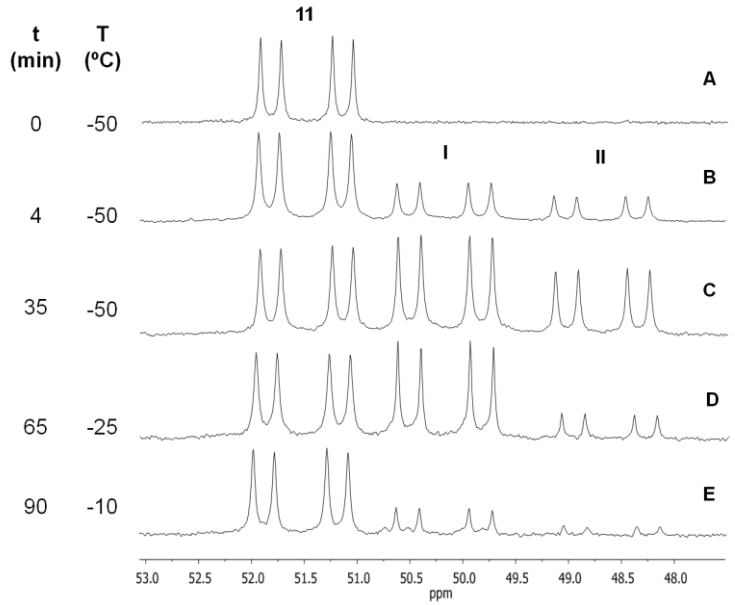
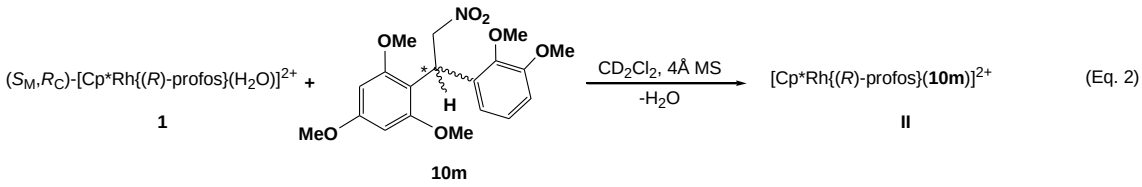


Figure 5. Fragment of the ^{31}P NMR spectra for the reaction between the rhodium complex **11** and 1,3,5,-trimethoxybenzene (see text)

To obtain more information about the nature of the species **I** and **II**, in an independent experiment, we added 1 equivalent of enantiopure FC 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 (Equation 2). At -50ºC, a new compound was formed that was characterized as **II** by comparison of its ^{1}H and ^{31}P NMR spectra with those recorded in the preceding experiment.



Similarly, it was also monitored the reaction between the aqua complex **1** and a sample of **10m** of 70% e.e. As expected, two new complexes appeared. The major one was complex **II** and the minor, complex **III**, presented a P^2 double doublet centered 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 FC adduct **10m** is coordinated to the [Cp*Rh{(*R*)-prophos} moiety and the structure of the intermediate **I** remains unclear. We 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.

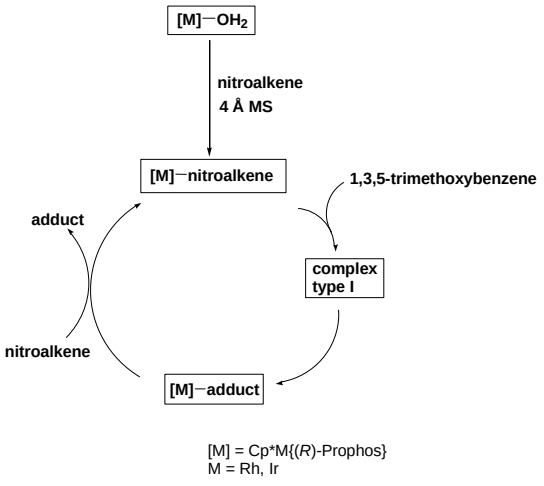


Figure 6. Proposed catalytic cycle

2.5 Proposed catalytic cycle

Taking together all the above observations we propose de catalytic cycle depicted 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, that is the true catalyst. These complexes react with free 1,3,5-trimethoxybenzene rendering catalyst-adduct complexes probably via intermediates of the type **I**, that we have not been able to characterize. Adduct is dissociated by a new molecule of nitroalkene with concomitant regeneration of the metal-nitroalkene complex that re-stars 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 FC product are observed in most of the investigated cases. In particular, quantitative y 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

General: All solvents were treated in a PS-400-6 Innovative Technologies Solvent Purification System (SPS) and degassed prior to use. All preparations have been 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).

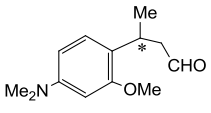
The complexes (S_M,R_C)–[Cp*M{(*R*)–Prophos}(H_2O)](SbF_6)$_2$ (M = Rh (**1**), Ir (**2**)) were prepared using literature procedures[13] with the following slightly modifications: To a suspension of [(Cp*MCl)$_2$(μ-Cl)$_2$] (0.400 mmol) in acetone (20 mL) 549.9 mg (1.6 mmol) of $AgSbF_6$ were added. 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 -25ºC (Rh) or -50ºC (Ir). Under argon, at the corresponding temperature, 330.4 mg (0.800 mmol) of (*R*)-prophos were added and the solution stirred for 30 min. Addition of *n*-hexane (20 mL) and subsequent stirring gives 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 -25ºC (Rh) or -50ºC (Ir) from CH_2Cl_2/*n*-hexane, 1/5, v/v. Yield: 92.3% (Rh), 88.7% (Ir).

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

At -10ºC, 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 about 100 mg of 4Å MS were added. The mixture was stirred for 15 minutes 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 (4mL) 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

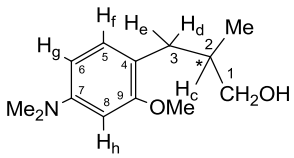
solution was vacuum-evaporated to dryness and purified by column chromatography (SiO_2; AcEt/*n*-hexane, 40/60). Evaporation of the solvent gives pale oils that were analysed and characterized by NMR and HPLC techniques.

4.1.1. 3-(4-(Dimethylamino)-2-methoxyphenyl)butanal (8a)



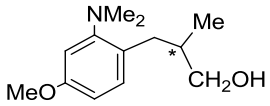
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[20] Yield: 49%. E.e.: 26% (*S*).

4.1.2. 3-(4-(Dimethylamino)-2-methoxyphenyl)-2-methylpropan-1-ol (8c)



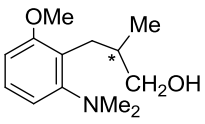
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 6.98 (pt, 1H, H_f), 6.34 (bd, 1H, H_g), 6.33 (s, 1H, H_h), 3.86 (s, 3H, OMe), 3.40, 3.45 (m, 2H, C*H*$_2$OH), 2.96 (s, 6H, NMe_2), 2.61, 2.50 (dd, *J* = 21.2, 7.3 Hz, 2H, H_d + H_e), 1.92 (m, 1H, H_c), 0.97 (d, *J* = 7.3 Hz, 3H, Me). ^{13}C RMN (75.48 MHz, $CDCl_3$) 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%. E.e.: 65%.

4.1.3. 3-(2-(Dimethylamino)-4-methoxyphenyl-2-methylpropan-1-ol (8d)



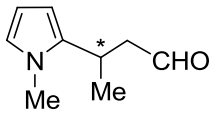
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 3.88 (s, 3H, OMe), 2.98 (s, 6H, NMe_2), 0.99 (bd, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 55.60 (OMe), 40.81 (NMe_2), 20.43 ppm (Me). HPLC: Chiralpak AS-H (97/3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 15.25 (minor), 16.31 (major). Yield: 22%. E.e.: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

4.1.4. 3-(2-(Dimethylamino)-5-methoxyphenyl-2-methylpropan-1-ol (8e)



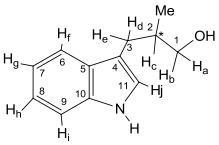
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 3.85 (s, 3H, OMe), 2.95 (s, 6H, NMe_2), 1.03 (d, *J* = 6.6 Hz, 3H, Me). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 55.56 (OMe), 40.85 (NMe_2), 19.66 (Me). HPLC: Chiralpak AS-H (97/3, *n*-hexane/ethanol, 1.0 mL/min); t_R, min: 19.57 (minor), 20.63 (major). Yield: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

4.1.5. 3-(1-Methyl-1H-pyrrol-2-yl)butanal (8f)



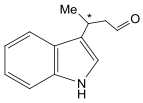
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[47] (Cat.* **1**: Yield: 82%, E.e.: 8% (*S*). Cat.* **2**: Yield: 50%, E.e.: 12% (*S*).

4.1.6. Characterization of the alcohol derived from 8g



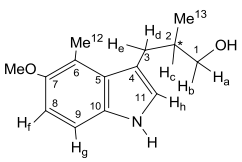
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.96 (bs, 1H, NH), 7.55 (d, J = 7.8 Hz, 1H, H_f), 7.29 (d, J = 8.1 Hz, 1H, H_i), 7.12 (pt, 1H, H_h), 7.04 (pt, 1H, H_g), 6.93 (d, J = 2.3 Hz, 1H, H_j), 3.52, 3.45 (dd, J = 10.5, 5.9 Hz, 2H, H_a + H_b), 2.80, 2.56 (dd, J = 14.4, 6.6 Hz, 2H, H_d + H_e), 2.01 (oc, 1H, J = 6.8 Hz, H_c), 1.29 (bs, 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%. E.e.: 22%.

4.1.7. 3-(1H-Indole-3-yl)butanal (8h)



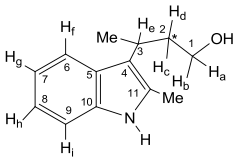
This compound was characterized by comparison of its spectroscopic data with those reported in the literature.[48] Yield: 15%. E.e.: 7%.

4.1.8. Characterization of the alcohol derived from 8i



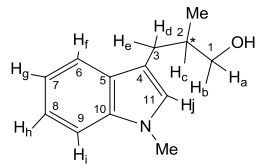
^{1}H, NMR (300.13 MHz, $CDCl_3$) δ, ppm: 8.00 (bs, 1H, NH), 7.15, 6.92 (d, J = 8.6 Hz, 1H, H_f + H_g), 6.93 (s, 1H, H_h), 3.87 (s, 3H, OMe), 3.66, 3.55 (dd, J = 10.6, 5.4 Hz, 2H, H_a + H_b), 3.00, 2.70 (dd, J = 14.7, 6.6 Hz, 2H, H_d + H_e), 2.61 (s, 3H, Me^{12}), 2.05 (ps, 1H, J = 6.7 Hz, H_c), 1.30 (bs, 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%. E.e.: 26%.

4.1.9. Characterization of the alcohol derived from 8j



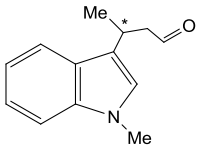
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.91 (bs, 1H, NH), 7.62 (d, J = 7.9 Hz, 1H, H_f), 7.30 (d, J = 7.9 Hz, 1H, H_i), 7.09 (pt, 1H, H_h), 7.03 (pt, 1H, H_g), 3.53 (m, 2H, H_a + H_b), 3.17 (m, 2H, H_c + H_d), 2.41 (s, 3H, C^{11}Me), 2.06 (m, 1H, J = 6.8 Hz, H_c), 1.45 (d, J = 7.1 Hz, 3H, C^3Me). ^{13}C 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%. E.e.: 5%.

4.1.10. Characterization of the alcohol derived from 8k



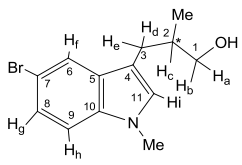
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.60 (d, J = 7.9 Hz, 1H, H_f), 7.28 (d, J = 8.2 Hz, 1H, H_i), 7.22 (pt, 1H, H_h), 7.12 (pt, 1H, H_g), 6.84 (s, 1H, H_j), 3.74 (s, 1H, NMe), 3.58, 3.50 (dd, J = 10.5, 5.9 Hz, 2H, H_a + H_b), 2.84, 2.60 (dd, J = 14.4, 6.5 Hz, 2H, H_d + H_e), 2.05 (ps, 1H, J = 6.8 Hz, H_c), 1.61 (bs, 1H, OH), 0.97 (d, J = 6.5 Hz, 3H, Me). ^{13}C-RMN (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%. E.e.: 28%.

4.1.11. 3-(1-Methyl-1H-indole-3-yl)butanal (8l)



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

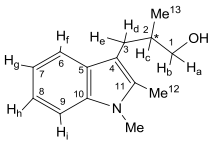
4.1.12. Characterization of the alcohol derived from 8m



^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.72 (s, 1H, H_f), 7.17 (bd, 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 (bs, 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%. E.e.: 19%.

4.1.13. Characterization of the alcohol derived from 8n

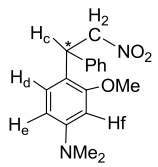


^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.42 (bd, 1H, H_f), 7.29 (bd, 1H, H_i), 7.19 (pt, 1H, H_h), 7.08 (pt, 1H, H_g), 3.69 (s, 3H, NMe), 3.61, 3.51 (m, 2H, H_a + H_b), 2.85, 2.59 (m, 2H H_d + H_e), 2.40 (s, 3H, Me^{12}), 2.05 (m, 1H, *J* = 6.8 Hz, H_c), 0.91 (d, *J* = 6.8 Hz, 3H, Me^{13}). ^{13}C 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%. E.e.: 33%.

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

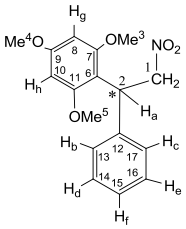
A Schlenk flask equipped with a magnetic stirrer was introduced in a thermostatic bath at -10ºC. Under argon, 0.03 mmol of (S_M,R_C)–[Cp*M{(*R*)–Prophos}(H_2O)](SbF_6)$_2$, CH_2Cl_2 (4 mL), the corresponding *trans*-*β*-nitrostyrene (0.60 mmol) and about 100 mg of 4Å MS were added. The resulting red mixture was stirred for 15 minutes 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.

4.2.1. 3-Methoxy-*N*,*N*-dimethyl-4-(2-nitro-1-phenilethyl)aniline (10a)



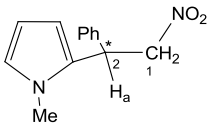
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.45-7.36 (m, 5H, Ph), 6.78 (d, *J* = 9.4 Hz, H_e), 6.14-6.13 (m, 2H, H_d + H_f), 5.06 (dd, *J* = 8.3, 6.1 Hz, H_c), 4.82-4.93 (m, 2H, CH_2), 3.73 (s, 3H, OMe), 2.84 ppm (s, 6H, NMe_2). HPLC: Chiralcel AD-H (95/5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: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

4.2.2. 2-(1-Phenyl-2-nitroethyl)-1,3,5-trimethoxybenzene (10c)



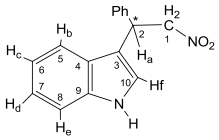
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.33 (d, J = 7.8 Hz, 2H, H_b + H_c), 7.28 (pt, J = 6.8 Hz, 2H, H_d + H_e), 7.21 (pt, J = 6.8 Hz, 1H, H_f), 6.15 (s, 2H, H_g + H_h), 5.52 (pt, J = 7.95 Hz, 1H, H_a), 5.26, 5.16 (dd, J = 12.7, 7.9 Hz, 2H, C^1H_2), 3.82 (s, 9H, OMe). ^{13}C NMR (100.61 MHz, $CDCl_3$) 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).

4.2.3. 2-(1-Phenyl-2-nitroethyl)-pyrrol (10d)



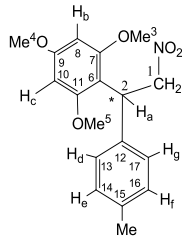
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.07-7.21 (m, 5H, Ph), 6.43 (s, 1H, H_{py}), 6.01-6.06 (m, 2H, H_{py}), 4.52-4.76 (m, 3H, CH_2 + H_a), 3.05 (s, 3H, NMe). HPLC: Chiralcel OD-H (80/20, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 22.8 (minor), 29.5 (major).

4.2.4. 3-(1-Phenyl-2-nitroethyl)-indole (10e)



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

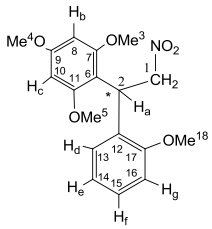
4.2.5. 2-(1-(4-Methylphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10f)



^{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).

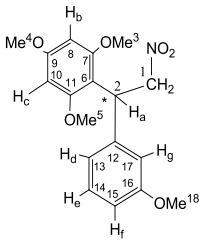
4.2.6. 2-(1-(2-Methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10g)

^{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,



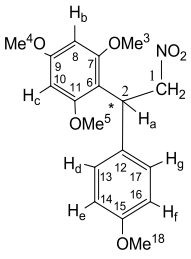
OMe). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.59 (C^9), 159.17 (C^7, C^{11}), 157.16, (C^{17}), 129.14 (C^{13}), 127.96 (C^{15}), 127.48 (C^6), 120.33 (C^{14}), 110.43 (C^{16}), 107.39 (C^{12}), 91,24 (C^8, C^{10}), 77.31 (C^1), 55.82, 55.44, 55.30 (C^3, C^4, C^5, OMe^{18}), 34.10 (C^2). HPLC: Chiralpak AD-H (98/2, *n*-hexane/2-propanol, 0.25 mL/min); t_R, min: 78.0 (minor), 80.3 (major).

4.2.7. 2-(1-(3-Methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10h)



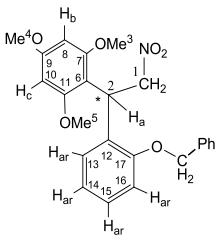
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.19 (pt, 1H, H_e), 6.92 (d, J = 8.5 Hz, 1H, H_d), 6.90 (t, J = 1.9 Hz, 1H, H_g), 6.74 (dd, J = 8.5, 1.9 Hz, 1H, H_f), 6.14 (s, 2H, H_b + H_c), 5.48 (pt, J = 7.7 Hz, 1H, H_a), 5.23, 5.13 (dd, J = 20.3, 7.7 Hz, 2H, C^1H_2), 3.79 (s, 3H, OMe^4); 3.82, 3.81, 3.78 (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).

4.2.8. 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-RMN (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).

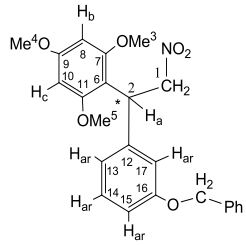
4.2.9. 2-(1-(2-Benzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10j)



^{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

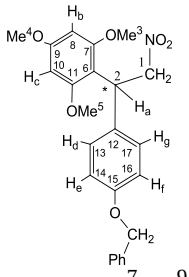
(C^7, C^9, C^{11}, C^{17}), 137.62 (C^6), 129.14-112.11 (C^{13}, C^{14}, C^{15}, C^{16}, C^{12}, and C, Ph), 91.35 (C^8, C^{10}), 76.85 (C^1), 69.77 (CH_2Ph), 55.20, 54.70 (C^3, C^4, C^5), 33.86 (C^2). HPLC: Chiralpak AD-H (95/5, *n*-hexane/2-propanol, 0.25 mL/min); t_R,min: 75.2 (minor), 77.3 (major).

4.2.10 2-(1-(3-Benzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10k)



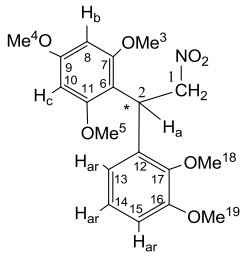
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.50-6.81 (m, 9H, H_{ar}), 6.14 (s, 2H, H_b + H_c), 5.47 (pt, *J* = 7.8 Hz, 1H, H_a), 5.23, 5.12 (dd, *J* = 12.8, 7.8 Hz, 2H, C^1H_2), 5.03 (s, 2H, CH_2Ph), 3.81 (s, 3H, OMe^4),3.79 (s, 6H, OMe^3 + OMe^5). ^{13}C-RMN (100.61 MHz, $CDCl_3$) δ, ppm: 161.94, 160.59, 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).

4.2.11. 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).

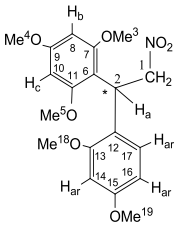
4.2.12. 2-(1-(2,3-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10m)



^{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

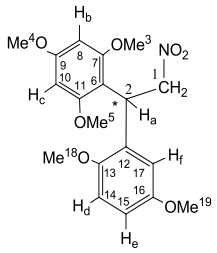
(C^{13}), 111.11 (C^{14}), 125.94 (C^{15}), 107.73 (C^{12}), 91,26 (C^{8}, C^{10}), 77.34 (C^{1}), 60.44-55.28 (C^{3}, C^{4}, C^{5}, C^{18}, C^{19}), 33.94 (C^{2}). HPLC: Chiralpak AD-H (95/5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 34.3 (minor), 35.9 (major).

4.2.13. 2-(1-(2,4-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10n)



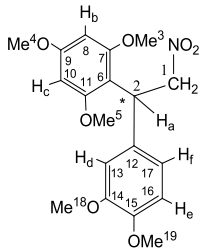
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 6.95-6.80 (m, 3H, H_{ar}), 6.14 (s, 2H, H_b + H_c), 5.30 (pt, *J* = 7.0 Hz, 1H, H_a), 4.80, 4.64 (dd, *J* = 11.8, 7.0 Hz, 2H, C^1H_2), 3.58 (s, 6H, OMe^3 + OMe^5), 3.57, 3.55, 3.52 ppm (s, 9H, OMe^4 + OMe^{18} + OMe^{19}). HPLC: Chiralpak AD-H (95/5, *n*-hexane/2-propanol,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

4.2.14. 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).

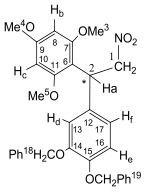
4.2.15. 2-(1-(3,4-Dimethoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10p)



^{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).

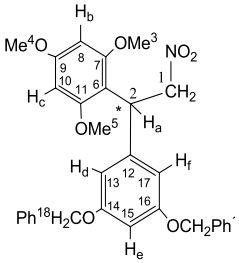
4.2.16. 2-(1-(3,4-Dibenzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10q)

^{1}H NMR (500.13 MHz, $CDCl_3$) δ, ppm: 7.44-7.28 (m, 10H, Ph^{18} + Ph^{19}), 6.94 (bd, 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



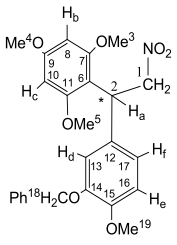
+ OMe^5). ^{13}C NMR (125.77 MHz, $CDCl_3$) δ, ppm: 160.52, 158.88, (C^7, C^9 , C^{11}, C^{14}, C^{15}), 137.46 (C^6), 148.58-108.78 (C^{13}, C^{16}, C^{17}, C^{12}, and C, Ph), 91.25 (C^8, C^{10}), 78.60 (C^1), 71.42, 71.31 (CH_2Ph^{18}, CH_2Ph^{19}), 55.77, 55.31 (C^3, C^4, C^5), 38.25 (C^2). HPLC: Chiralpak AD-H (80/20, *n*-hexane/2-propanol, 1 mL/min); t_R, min: 20.5 (minor), 34.2 (major).

4.2.17. 2-(1-(3,5-Dibenzyloxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10r)



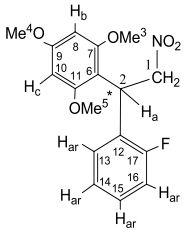
^1H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.32-7.21 (m, 10H, Ph^{18} + Ph^{19}), 6.48 (d, *J* = 2.0 Hz, 2H, H_d + H_f), 6.37 (t, *J* = 2.0 Hz, 1H, H_e), 6.02 (s, 2H, H_b + H_c), 5.32 (pt, *J* = 7.8 Hz, 1H, H_a), 5.08-4.99 (dd, *J* = 12.9, 7.8, 2H, C^1H_2), 4.89 (bs, 4H, CH_2Ph), 3.70 (s, 3H, OMe^4), 3.66 (s, 6H, OMe^3 + OMe^5). ^{13}C-RMN (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).

4.2.18 2-(1-(3-Benzyloxy-4-methoxyphenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10s)



^1H 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 (bd, 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-RMN (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).

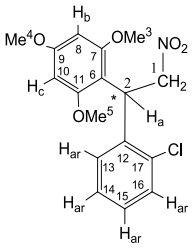
4.2.19. 2-(1-(2-Fluorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10t)



^1H 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-RMN (100.61 MHz, $CDCl_3$) δ, ppm: 160.52, (C^9), 158.97 (C^7, C^{11}), 137.47,

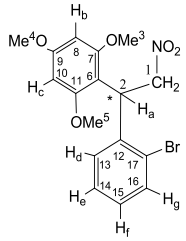
136.15 (C^{17}, C^{6}), 129.02, 127.50 (C^{13}, C^{14}, C^{15}, C^{16}), 108.80 (C^{12}), 91,19 (C^{8}, C^{10}), 78.52 (C^{1}), 55.80, 55.30 (C^{3}, C^{4}, C^{5}), 38.32 (C^{2}). HPLC: Chiralpak AD-H (95/5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 18.9 (minor), 20.0 (major).

4.2.20. 2-(1-(2-Chlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10u)



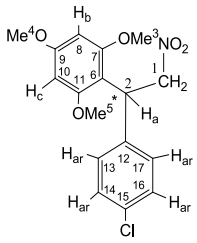
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.32, 7.14 (m, 4H, H_{ar}), 6.12 (s, 2H, H_b + H_c), 5.80 (pt, *J* = 7.0 Hz, 1H, H_a), 5.19, 4.99 (dd, *J* = 20.1, 7.0 Hz, 2H, $C^{1}H_2$), 3.79 (s, 3H, OMe^{4}); 3.76 (s, 6H, OMe^{3} + OMe^{5}). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.84, (C^{9}), 159.51 (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).

4.2.21. 2-(1-(2-Bromophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10v)



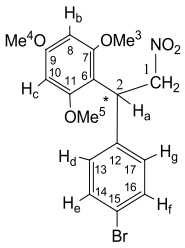
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.55 (d, *J* = 8.2 Hz, 1H, H_g), 7.34 (d, *J* = 7.7 Hz, 1H, H_d), 7.21 (pt, *J* = 7.2 Hz, 1H, H_f), 7.08 (pt, *J* = 7.7 Hz, 1H, H_e), 6.15 (s, 2H, H_b + H_c), 5.77 (pt, *J* = 8.2 Hz, 1H, H_a), 5.25, 4.95 (dd, *J* = 12.8, 8.2, 2H, $C^{1}H_2$), 3.81 (s, 3H, OMe^{4}), 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).

4.2.22. 2-(1-(4-Chlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10w)



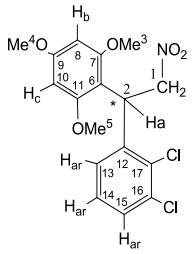
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.29-7.22 (m, 4H, H_{ar}), 6.14 (s, 2H, H_b + H_c), 5.47 (pt, *J* = 8.1 Hz, 1H, H_a), 5.26, 5.06 (dd, *J* = 12.8, 8.1 Hz, 2H, $C^{1}H_2$), 3.82 (s, 6H, OMe^{3} + OMe^{5}), 3.81 (s, 3H, OMe^{4}). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ, ppm: 160.77 (C^{9}), 158.83 (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).

4.2.23. 2-(1-(4-Bromophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10x)



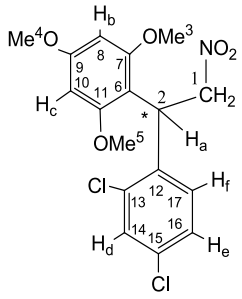
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.37 (d, *J* = 8.4 Hz, 2H, H_e + H_f), 7.19 (d, *J* = 8.4 Hz, 2H, H_d + H_g), 6.12 (s, 2H, H_b + H_c), 5.45 (pt, *J* = 7.4 Hz, 1H, H_a), 5.24, 5.04 (dd, *J* = 19.8, 7.4 Hz, 2H, C^1H_2), 3.80 (s, 9H, OMe). ^{13}C NMR (75.48 MHz, $CDCl_3$) δ, ppm: 160.83 (C^9), 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).

4.2.24. 2-(1-(2,3-Dichlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10y)



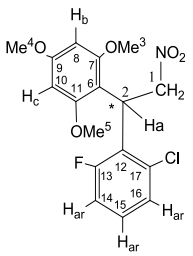
^{1}H NMR (300.13 MHz, $CDCl_3$) δ, ppm: 7.60-6.64 (m, 3H, H_{ar}), 6.14 (s, 2H, H_b + H_c), 5.78 (pt, *J* = 6.9 Hz, 1H, H_a), 5.22, 4.95 (dd, *J* = 12.7, 6.9, 2H, C^1H_2), 3.75 (s, 3H,), 3.81, 3.69 (s, 9H, OMe^3 + OMe^4 + OMe^5). HPLC: Chiralpak AD-H (95/5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: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

4.2.25 2-(1-(2,4-Dichlorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10z)



^{1}H RMN (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.

2.2.26 2-(1-(2-Chloro-6-fluorophenyl)-2-nitroethyl)-1,3,5-trimethoxybenzene (10ac)



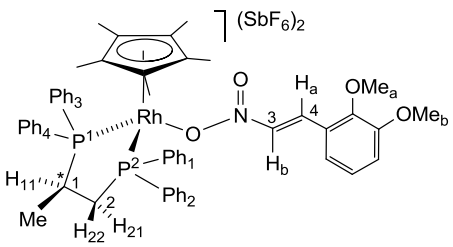
^{1}H NMR (400.16 MHz, $CDCl_3$) δ, ppm: 7.41-6.48 (m, 3H, H_{ar}), 6.05 (s, 2H, H_b + H_c), 5.61 (pt, *J* = 8.0 Hz, 1H, H_a), 5.15, 4.88 (m, 2H, C^1H_2), 3.75 (s, 3H, OMe^4), 3.68 (s, 6H, OMe^3 + OMe^5). HPLC: Chiralpak AD-

H (95/5, *n*-hexane/2-propanol, 0.5 mL/min); t_R, min: 18.4 (major), 20.5 (minor).

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

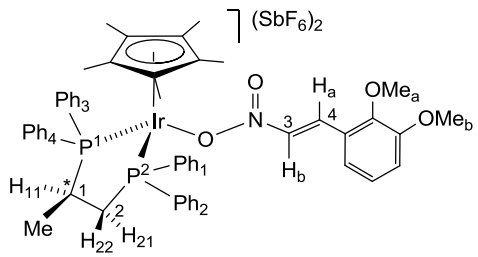
At -25ºC, under argon, to a solution of 0.12 mmol of the corresponding complex (S_M,R_C)-[Cp*M(*R*-prophos)(H$_2$O)](SbF$_6$)$_2$ [M = Rh (**1**) 136.8 mg, Ir (**2**) 149.6 mg] in CH_2Cl_2 (20 mL), 75.3 mg (0.36 mmol) of **9m** and 100 mg of 4Å MS were added. The resulting red suspension was stirred for 1 hour and then filtered through a cannula. The filtrate was vaccum-concentrated to about 3mL. The addition 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**).

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



^{1}H NMR (400.16 MHz, CD_2Cl_2, -25ºC) 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, -25ºC) δ, ppm: 152.85-118.98 (Ph), 142.56 (C^4), 134.98 (C^3), 107.29 (bs, 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, -25ºC) 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 analysis: 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.

4.3.2. (S_{Ir},R_C)-[Cp*Ir{(*R*)-prophos}(9m)](SbF$_6$)$_2$ (12)



^{1}H-RMN (400.16 MHz, CD_2Cl_2, -25ºC) δ, ppm: 7.60 (bd, 1H, H_a), 7.59-7.26 (m, 23H, Ph), 7.35 (bd, 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 (bs, 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, -25ºC) 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-RMN (161.96 MHz, CD_2Cl_2, -25ºC) 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 analysis: 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.

4.4. NMR measurements for the 11/4c system

At -25ºC, 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 4Å MS were added. The suspension was stirred for 1 hour and placed into a 5-mm NMR tube. At -50ºC, ^{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 -10ºC.

4.5. 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 -50ºC, 11.3 mg (0.03 mmol) of **10m** and 20 mg of 4Å MS were added. The reaction was monitored by ^{1}H and ^{31}P NMR spectroscopies.

Acknowledgements

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