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Cyclopropanation of alkenes with diisopropyl diazomethylphosphonate catalysed by ruthenium porphyrin complexes

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Abstract

Stereoselectivities, regioselectivities and yields for cyclopropanation reactions of diisopropyl diazomethylphosphonate (DAMP) with styrene derivatives, catalysed by ruthenium porphyrins, are reported and compared with those observed for cyclopropanation reactions catalysed by other metalloporphyrins. Linear correlations are observed when the rates for competitive cyclopropanation and ratio of the stereoisomers obtained are plotted against Hammet constants of various ring-substituted groups on styrene. Isomeric distribution for the cyclopropanation of 1,3-pentadiene with diisopropyl diazomethylphosphonate is reported. Competition studies between cyclopropanation and diazo insertion into heteroatom-hydrogen bonds and also between cyclopropanation and sigmatropic reaction are reported. A first example of asymmetric cyclopropanation with a chiral catalyst is also described.

Keywords: Catalysis; Cyclopropanation; Porphyrins; Ruthenium; Diazomethylphosphonate

1. Introduction

Metal-catalysed cyclopropanation of olefins by diazo derivatives are frequently used in organic reactions [1,2]. This reaction is widely employed in synthesis and several copper [3], rhodium [4], and more recently ruthenium [5–9] and iron [10,11] complexes have been described to be efficient in the formation of cyclopropanes. Although diazoalkanes and diazoacetates are commonly used as reactive agents, only few reactions with diazomethylphosphonate (DAMP) have been previously reported with copper catalysts [12–16] and with rhodium complexes [17–19]. However, these cyclopropane derivatives can be used as insecticides [14] or as antagonists of *N*-methyl aspartate receptor [17]. Intramolecular reactions [20,21], N–H insertions [22,23] and O–H insertions [24] have been also described using rhodium catalysts.

Cyclopropylphosphonates are also very convenient intermediates for the synthesis of diphenylmethylenecyclopropane derivatives [16] by the Wadsworth–Emmons reaction [15]. Although few routes to intermediate cyclopropylphosphonates have been described in the literature but with low chemical

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yields, they mainly involved multiple step sequences and low chemical yields [13,25,26]. Thus, reductive phosphonation for the synthesis of diethyl cyclopropane-phosphonate has been also reported [25]. The one step method of Seyferth et al. [13] involved the decomposition of diisopropyl diazomethylphosphonate to the corresponding carbenes in the presence of metallic copper and subsequent trapping of the resulting carbene with an appropriate alkene, but competitive dimerisation of the carbene intermediate producing 1,2-bis(dialkylphosphono) ethene was a major side reaction and so the yield was low. We now wish to report herein the details of the reaction of diazomethylphosphonate with simple olefins catalysed by different ruthenium porphyrins.

Since α-phosphoryl sulphides have recently found large application in organic synthesis [27,28], a direct access to the intermediate sulphonium ylide lies in the reaction between a carbene and a sulphide [29]. With allyl sulphides, the cyclopropanation of the double bond was not observed in these reactions [28]. To extend the synthetic potential of ruthenium porphyrin catalysts [30], we therefore also investigated the reaction of DAMP with alkyl allyl sulphides and allyl thiols, since a competition between cyclopropanation, S–H insertion and the rearrangement of ylide generated from reactions of phosphonate diazo compounds with allylic sulphides may occur.

2. Experimental

2.1. General procedures

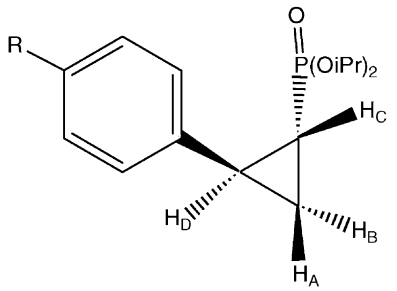
NMR spectra were recorded in $CDCl_3$ on a Bruker 200 DPX and chemical shifts are referenced to internal tetra methylsilane (TMS). GC–MS analyses were performed on a CE GC8000 coupled with a Finnigan Mat AutomassII.

2.2. Materials

Styrene derivatives were purchased from Fluka and Lancaster and used as received. Diisopropyl diazomethylphosphonate was prepared as previously reported [28]. The ruthenium porphyrins: Ru(TPP)(CO) [31], Ru(TPFPP)(CO) [32] and Ru(MPIXDME)(CO) [33] were synthesised by literature methods. The preparation of the homochiral ruthenium porphyrin was adapted from known procedure [34] (TPP, meso-tetraphenylporphyrin dianion; TPFPP, meso-tetra-pentafluorophenylporphyrin dianion; MPIXDME, mesoporphyrin dimethyl ester).

2.3. General procedure for cyclopropanation of styrene derivatives by DAMP

In a typical experiment, the styrene derivatives (2.5 mmol) and the ruthenium porphyrin complex catalyst Ru(TPP)(CO), Ru(TPFPP)(CO) or Ru(MPIXDME)(CO) complex (0.005 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. Diisopropyl diazomethylphosphonate (100 μl, 0.5 mmol) was added slowly (15 μl h^{-1}) at 40 °C. After the reaction was complete (48–72 h), during which time the reaction was monitored by GC–MS, the products were recovered by vacuum distillation. Products were purified by silica gel chromatography (pentane/CH_2Cl_2). The product was identified as *trans* product by ^1H NMR studies and comparison to literature data [16,35].



2.3.1. Diisopropyl [2-(phenyl)cyclopropyl]-phosphonate (R = H)

^1H NMR (DEPT 135, proton decoupling, NOE difference): 7.13–7.39 (m, 5H, aryl), 4.76 (m, 2H, C*H*$(CH_3)_2$), 1.38–1.25 (m, 12H, (CH_3)$_2$CH); cyclopropyl system: 2.46 (H_D, m, $^3J_{HH}$ = 5.6 Hz (*trans* with H_C and H_A), $^3J_{HH}$ = 8.6 Hz (*cis* with H_B), $^3J_{HP}$ = 16 Hz), 1.48 (H_B, m, $^3J_{HH}$ = 8.6 Hz (*cis*/H_D), $^3J_{HP}$ = 19 Hz), 1.19 (H_A, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_D), $^3J_{HP}$ = 12 Hz), 1.17 (H_C, m, $^3J_{HH}$ = 5.6 Hz). ^{31}P NMR: 27.07 ppm. MS: m/z^+, 282, 239, 197, 180, 115, 43.

2.3.2. Diisopropyl [2-(4-methoxyphenyl)-cyclopropyl]-phosphonate (R = OMe)

^{1}H NMR (DEPT 135, proton decoupling, NOE difference): 7.09 (d, 2H, AB system, aryl) and 6.85 (d, 2H, AB system, aryl), 4.75 (m, 2H, C*H*$(CH_3)_2$), 3.82 (s, 3H, OC*H*$_3$), 1.42–1.25 (m, 12H (C*H*$_3)_2$CH); cyclopropyl system: 2.48 (H_D, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_C and H_A), $^3J_{HH}$ = 8.8 Hz (*cis* with H_B), $^3J_{HP}$ = 15.9 Hz), 1.49 (H_B, m, $^3J_{HH}$ = 8.8 Hz (*cis*/H_D), $^3J_{HP}$ = 19 Hz), 1.15 (H_A, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_D), $^3J_{HP}$ = 12 Hz), 1.06 (H_C, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_B and H_D)). MS: *m*/*z*$^+$, 312, 228, 212, 148, 43.

2.3.3. Diisopropyl [2-(4-methylphenyl)cyclopropyl]-phosphonate (R = Me)

^{1}H NMR (DEPT 135, proton decoupling, NOE difference): 7.18 (d, 2H, aryl) and 7.05 (d, 2H, aryl), 4.76 (m, 2H, C*H*$(CH_3)_2$), 2.37 (s, 3H, C*H*$_3$), 1.42–1.25 (m, 12H (C*H*$_3)_2$CH); cyclopropyl system: 2.51 (H_D, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_C and H_A), $^3J_{HH}$ = 8.8 Hz (*cis* with H_B), $^3J_{HP}$ = 15.9 Hz), 1.47 (H_B, m, $^3J_{HH}$ = 8.8 Hz (*cis* with H_D), $^3J_{HP}$ = 19 Hz), 1.23 (H_A, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_D), $^3J_{HP}$ = 12 Hz), 1.14 (H_C, m, $^3J_{HH}$ = 5.6 Hz (*trans* with H_B and H_D)). MS: *m*/*z*$^+$, 296, 254, 237, 212, 195, 148, 43.

2.3.4. Diisopropyl [2-(4-chlorophenyl)cyclopropyl]-phosphonate (R = Cl)

^{1}H NMR (DEPT 135, proton decoupling, NOE difference): 7.31 (d, 2H, aryl) and 7.11 (d, 2H, aryl), 4.78 (m, 2H, C*H*$(CH_3)_2$), 1.44–1.35 (m, 12H $(CH_3)_2$CH(C*H*$_3)_2$CH); cyclopropyl system: 2.51 (H_D, m, $^3J_{HH}$ = 5.6 Hz (*trans* with H_C and H_A), $^3J_{HH}$ = 8.8 Hz (*cis* with H_B), $^3J_{HP}$ = 15.9 Hz), 1.57 (H_B, m, $^3J_{HH}$ = 8.8 Hz (*cis* with H_D), $^3J_{HP}$ = 19 Hz), 1.27 (H_A, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_D), $^3J_{HP}$ = 12 Hz), 1.21 (H_C, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_B and H_D)). MS: *m*/*z*$^+$, 316, 275, 259, 232, 216, 151, 115, 89, 43.

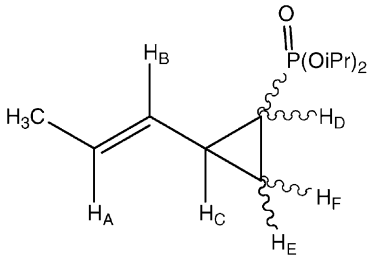
2.3.5. Diisopropyl [2-(4-trifluoromethylphenyl)-cyclopropyl]-phosphonate (R = CF$_3$)

^{1}H NMR (DEPT 135, proton decoupling, NOE difference): 7.26 (d, 2H, aryl) and 7.10 (d, 2H, aryl), 4.75 (m, 2H, C*H*$(CH_3)_2$), 1.40–1.25 (m, 12H (C*H*$_3)_2$CH); cyclopropyl system: 2.52 (H_D, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_C and H_A), $^3J_{HH}$ = 8.8 Hz (*cis*/H_B), $^3J_{HP}$ = 15.9 Hz), 1.56 (H_B, m, $^3J_{HH}$ = 8.8 Hz (*cis* with H_D), $^3J_{HP}$ = 19 Hz), 1.21 (H_A, m, $^3J_{HH}$ = 5.6 Hz (*trans* with H_D), $^3J_{HP}$ = 12 Hz), 1.17 (H_C, m, $^3J_{HH}$ = 5.6 Hz (*trans*/H_B and H_D)). MS: *m*/*z*$^+$, 331, 293, 266, 247, 231, 185, 123, 96, 43.

2.4. Cyclopropanation of trans-1-3-pentadiene by DAMP

trans-1,3-Pentadiene (2.5 mmol) and Ru(TPP)(CO) or Ru(TPFPP)(CO) complex (0.005 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. DAMP (100 μl, 0.5 mmol) was added slowly (15 μl h^{-1}) at 40 °C. After the reaction was complete (3 days), during which time the reaction was monitored by GC–MS, the product was recovered by vacuum distillation. The product was identified by different NMR studies.

The main product of cycloaddition with *trans*-1-3-pentadiene was characterised by ^{1}H and ^{13}C NMR and proton decoupling experiments (DEPT 135, proton decoupling, NOE difference):



^{1}H NMR in $CDCl_3$: 5.61 (dq, 1H, H_A); 4.99 (ddq, 1H, H_B); 4.73 (m, 2H, C*H*(Me)$_2$); 1.89 (m, 1H, H_C); 1.64 (3H, CH_3); 1.39–1.25 (m, 12H (C*H*$_3)_2$CH); 1.18 (m, 1H, cyclopropane: H_E); 0.80 (m, 2H, cyclopropane: H_D and H_F). ^{13}C NMR in $CDCl_3$/TMS: 131.35 (*C*H_B); 125.95 (*C*H_A); 70.35 (2*C*H, C*H*$(CH_3)_2$); 24.25 (4Me); 19.78 (*C*H_C); 17.70 (*C*H_3); 13.35 (*C*H_D); 11.15 (*C*$H_E H_F$). MS: *m*/*z*$^+$, 246, 204, 187, 162, 123, 80, 43.

2.5. Coupling reaction of DAMP using ruthenium porphyrin complexes as catalysts

DAMP (100 μl, 0.5 mmol) and Ru(TPP)(CO) or Ru(TPFPP)(CO) complex (0.5 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. The reaction mixture was stirred at 40 °C.

After the reaction was complete (3 days), during which time the reaction was monitored by GC–MS, the product was recovered by vacuum distillation. The products were identified by NMR studies and by comparison to literature data [36].

2.6. Competition studies of cyclopropanation of various substituted styrene (substrate A) and styrene (substrate B) with DAMP using ruthenium porphyrin complex Ru(TPP)(CO) or Ru(TPFPP)(CO) as catalyst

The various substituted styrene (substrate A) (2.5 mmol), and styrene (substrate B) (2.5 mmol), and the Ru(TPP)(CO) or Ru(TPFPP)(CO) complex (0.005 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. DAMP (100 μl, 0.5 mmol) was added slowly (15 μl h^{-1}) at 40 °C. After 48 h, during which time the reaction was monitored by GC–MS, the product was recovered by vacuum distillation. Products were purified by silica gel chromatography (pentane/CH_2Cl_2). The product ratio were identified by ^1H NMR studies and GC–MS.

2.7. Competition studies of cyclopropanation of 4-methoxystyrene (substrate A) and 4-fluoromethylstyrene (substrate B) with DAMP using ruthenium porphyrin complex Ru(TPP)(CO) or Ru(TPFPP)(CO) as catalyst

4-Methoxystyrene compound (2.5 mmol), trifluoromethylstyrene (2.5 mmol), and ruthenium porphyrin complex (1/100 to DAMP, 0.005 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. DAMP (100 μl, 0.5 mmol) was added slowly (15 μl h^{-1}) at 40 °C. After 48 h, during which time the reaction was monitored by GC–MS; the ratio products were identified by ^1H NMR studies and GC–MS.

2.8. Competition studies of the cyclopropanation of styrene versus [2,3] sigmatropic reaction of allyl methyl sulphide with DAMP catalysed by Ru(TPP)(CO)

The allyl sulphide compound (2.5 mmol), the styrene (2.5 mmol), and the Ru(TPP)(CO) (0.005 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. Diisopropyl diazomethylphosphonate (100 μl, 0.5 mmol) was added slowly (15 μl h^{-1}) at 40 °C. After 48 h, during which time the reaction was monitored by GC–MS, the product was recovered by vacuum distillation. The product was identified by the comparison to literature data [28] and the product ratio were identified by NMR studies and GC–MS.

2.9. Competition studies of the cyclopropanation of styrene versus S–H insertion reaction for 2-propene-1-thiol with DAMP catalysed by Ru(TPP)(CO)

2-Propene-1-thiol (2.5 mmol), styrene (2.5 mmol), and Ru(TPP)(CO) (1/100 to DAMP, 0.005 mmol) were dissolved in 200 μl of dry chloroform in a schlenk flask under argon. Diisopropyl diazomethylphosphonate (100 μl, 0.5 mmol) was added slowly (15 μl h^{-1}) at 40 °C. After 48 h, during which time the reaction was monitored by GC–MS, the product was recovered by vacuum distillation. The product was identified by comparison to literature data [28] and the product ratio were identified by NMR studies and GC–MS.

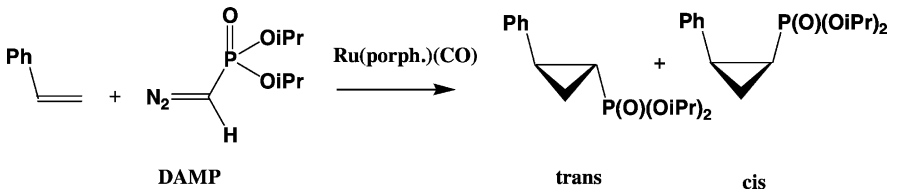
2.10. Cyclopropanation of styrene by DAMP using asymmetric ruthenium porphyrin complex as catalyst

The asymmetric catalytic reaction was performed as reported above with the non-chiral porphyrin except the temperature was increased to 60 °C. Enantiomeric excess (ee) for cyclopropyl esters was determined by GC, utilising a CP-Chirasil-Dex CB capillary column. The absolute configuration of this new optically active phosphonate ester is not known.

3. Results

3.1. Cyclopropanation of styrene derivatives

Ruthenium porphyrin complexes are active catalysts for the cyclopropanation of styrene derivatives by diisopropyl diazomethylphosphonate with



Scheme 1. Catalytic cyclopropanation of styrene.

good diastereoselectivity. The Ru(II) porphyrin complex, in catalytic amounts, reacts with (DAMP) in the presence of excess of styrene to give quantitatively the corresponding cyclopropyl phosphonate, with a large excess of the *trans* isomer (Scheme 1). As shown in Table 1, the decomposition of diisopropyl diazomethylphosphonate, catalysed by meso-tetraphenylporphyrin carbonyl ruthenium Ru(TPP)(CO) (Fig. 1), in the presence of styrene, resulted in the formation of the corresponding cyclopropane in more than 90% yield. Proton NMR and

Table 1
Cyclopropanation of styrene derivatives by diisopropyl diazomethylphosphonate (DAMP) using ruthenium porphyrin complex Ru(TPP)(CO) as catalyst

Ru(TPP)(CO)	*cis* (%)[a]	*trans* (%)[a]	Yield (%)	Dimer (%)[b]
4-Methoxystyrene	2	94	96	4
Styrene	6	84	90	10
4-Chlorostyrene	7	91	98	2
4-Trifluoromethylstyrene	20	73	93	7

[a] Determined by GC–MS and NMR.
[b] Tetraisopropylethene-1,2-diyl-bis(phosphonate).

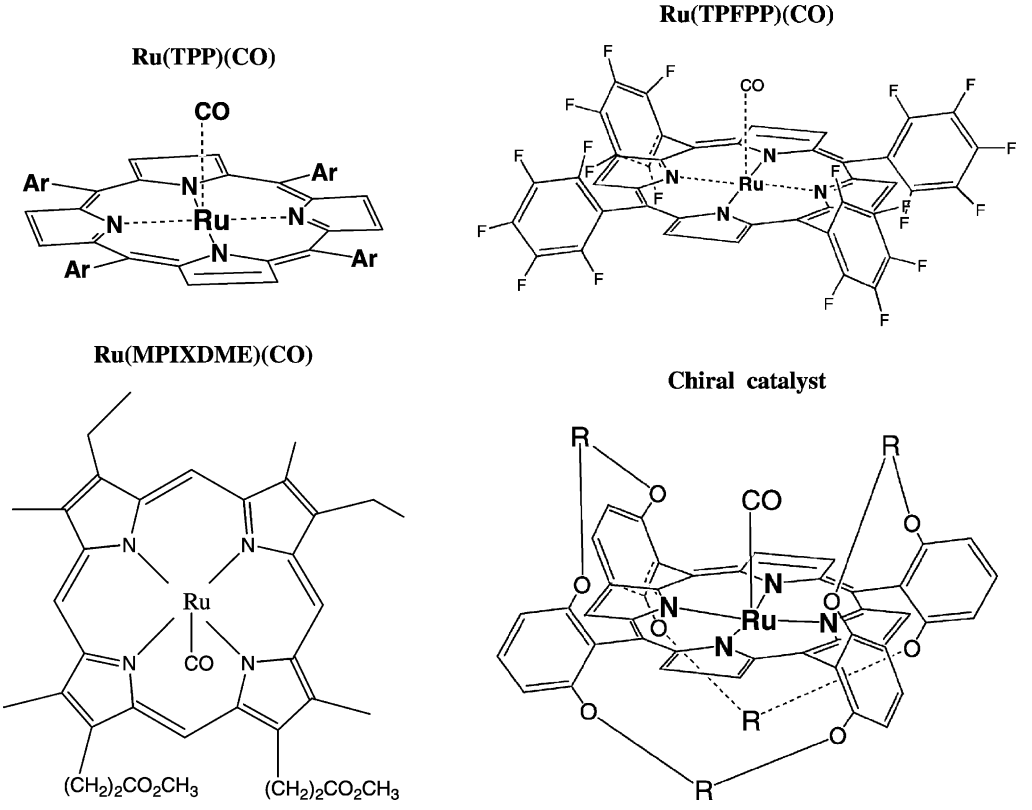


Fig. 1. Catalysts used in this study.

Table 2
Cyclopropanation of styrene derivatives by DAMP using ruthenium porphyrin complex Ru(TPFPP)(CO) as catalyst

Ru(TPFPP)(CO)	*cis* (%)[a]	*trans* (%)[a]	Yield (%)	Dimer (%)[b]
4-Methoxystyrene	<1	95	95	5
Styrene	<1	94	95	5
4-Chlorostyrene	4	92	96	3
4-Trifluoromethylstyrene	8	86	94	6

[a] Determined by GC–MS and NMR.
[b] Tetraisopropylethene-1,2-diyl-bis(phosphonate).

Table 3
Cyclopropanation of the substituted styrene derivative α-methylstyrene by DAMP using ruthenium porphyrin complexes as catalysts

α-Methyl styrene	*cis* (%)[a]	*trans* (%)[a]	Yield (%)	Dimer(%)[b]
Ru(TPP)(CO)	5	75	80	20
Ru(TPFPP)(CO)	41	49	90	10

[a] Determined by GC–MS and NMR.
[b] Tetraisopropylethene-1,2-diyl-bis(phosphonate).

GC analysis of the crude reaction mixture indicated a *trans*/*cis* stereoselectivity of 12/1. The catalyst is also sensible to the electronic and steric nature of the olefin since terminal alkenes are better substrates. For example, only traces of the cyclopropane products are detected when the reaction is carried out with cyclohexene.

The relation between the diastereoselectivity of the reaction and the electronic effect of the *para*-substituent of styrene was also studied. Reactions of styrene derivatives with diisopropyl diazomethylphosphonate in the presence of Ru(TPP)(CO) at 40 °C during 48 h were studied (Tables 1–3). In all these experiments, cyclopropanes are the major products, usually obtained with the dimer tetraisopropylethene-1,2-diyl-bis(phosphonate) as by product [36]. The catalytic cyclopropanations of alkenes were run in chloroform, at 40 °C under argon atmosphere, with a substrate/DAMP/catalyst ratio of 300/60/1. The diastereoselectivity (Table 1) is reminiscent of that observed with ruthenium catalysts and ethyl diazoacetate (EDA) [33] but differs from the *cis* selectivity observed with rhodium porphyrins [37,38].

The plot of the log(*trans*/*cis*) against Hammet constant is displayed in Fig. 2 for both catalysts: Ru(TPP)(CO) and Ru(TPFPP)(CO). The data were fit to a Hammet plot with a good correlation: $r^2 = 0.946$ for Ru(TPP)(CO) catalyst and $r^2 = 0.972$ for Ru(TPFPP)(CO). This allowed us to calculate a ρ-value of -1.29 ± 0.01 for TPP complex and -1.92 ± 0.01 for TPFPP complex. The *trans*/*cis* ratio is strongly affected by the electronic effect of the alkenes substituents: the reaction with an electron donating group in the *para* position of the styrene (methoxy group) is almost 10 times more selective than the reaction with 4-trifuoromethylstyrene.

The cyclopropane formation exhibits also a shape substrate preference that may be useful for selective cyclopropanation of polyolefins. Thus, styrene

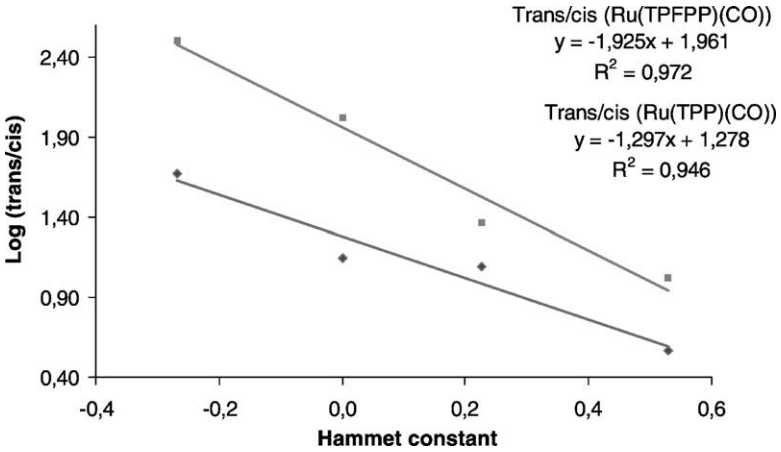


Fig. 2. The *trans*/*cis* ratio against Hammet parameters for cyclopropanation of styrene derivatives with DAMP.

Table 4
Diastereoselectivity in the cyclopropanation of 4-substituted styrene derivatives and styrene with DAMP, catalysed by Ru(MPIXDME)(CO)

Substrate	*trans*/*cis* ratio[a]	Yield(%)[a]
4-Methoxystyrene	51/49	37
Styrene	67/33	18
4-Chlorostyrene	75/25	56

[a] Determined by GC–MS and NMR.

is cyclopropanated with high efficiency whereas α-methyl styrene is less reactive (yield 80%) due to an encumbered double bound (Table 3). Surprisingly, α-methyl styrene shows a dramatic loss of selectivity (*trans*/*cis* ratio: 49/41) but not in reactivity (yield 90%) when the electro-deficient TPFPP core is used.

The relation between the diastereoselectivity of the reaction and the electronic effect of the *para*-substituent of styrenes was also studied with a different ruthenium complex. The catalyst used was mesoporphyrin methyl ester carbonyl ruthenium complex (MPIXDME)Ru(CO) [39]. By using this catalyst, we should avoid steric interactions between the meso-substituents of the porphyrin ring and the olefin. The *trans*/*cis* ratio is largely affected by the electronic effect of the alkenes substituents: the reaction with alkenes bearing electron withdrawing groups like 4-chlorostyrene (*trans*/*cis* ratio: 75/25) is almost three times more selective than the reaction with the electron rich 4 methoxy-styrene (*trans*/*cis* ratio: 51/49). However, changing the porphyrin ring results in a notable decreasing yield for the cyclopropanation reaction. Data are summarised in Table 4.

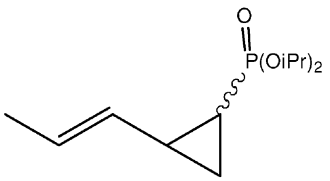
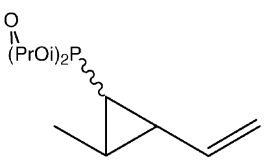
3.2. Cyclopropanation of diene

To complete these data, we also studied the cyclopropanation of *trans*-1,3-pentadiene. Isomeric distribution is reported in Table 5. These results emphasise the pronounced electronic and shape preference of the catalyst. In particular, one can see that the cyclopropanation not preferentially occurred at the electron rich double bound (15%) when electron-deficient complex, Ru(TPFPP)(CO), is used. In this case, the terminal linear olefin was cyclopropanated with a high yield (85%). On the other hand, when the less reactive Ru(TPP)(CO) complex is used as catalyst, the cyclopropanation of the electron rich double bound is enhanced (44%), despite of the steric effect. In these reactions, the precise *trans*/*cis* ratio was not determined due to complex mixture but the main isomer was the *trans* isomer.

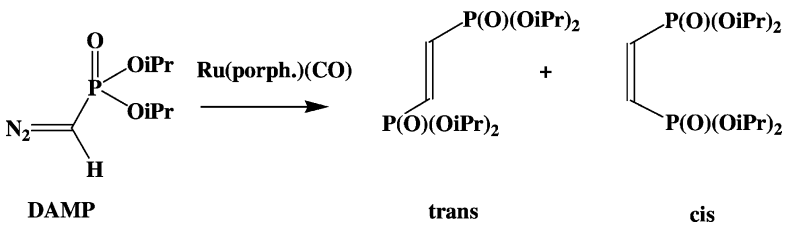
3.3. Dimerisation of DAMP

The *cis* and *trans* isomers of tetra isopropyl-ethene-1,2-diyl-bisphosphonate [36] are formed when olefins do not react efficiently (Scheme 2). These coupling products are typically obtained when the carbene transfer to the alkene is not observed. We studied this dimerisation reaction by heating the solution during 48 h at 40 °C with a catalytic amount of Ru complex in presence of DAMP. The *cis*/*trans* ratio is 2.5/1.0 when Ru(TPP)(CO) is the catalyst, and 1.2/1.0 when Ru(TPFPP)(CO) is the catalyst (Table 6). This is quite different from the large preference for diethyl maleate versus diethyl fumarate (15/1) which is observed for the dimerisation of the carbene from ethyl diazoacetate, using the same catalytic system [40].

Table 5
Isomeric distribution (%) for the cyclopropanation of *trans*-1,3-pentadiene with DAMP catalysed by ruthenium porphyrin complexes

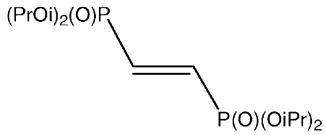
Substrate trans-1,3-pentadiene			Yield[a] (%)
Ru(TPP)(CO)	50	44	94
Ru(TPFPP)(CO)	85	15	98

[a] Determined by GC and NMR.



Scheme 2. Dimerisation of DAMP.

Table 6
Coupling reaction of the carbene phosphonate using ruthenium porphyrin complexes as catalysts[a]

Catalyst		
Ru(TPP)(CO)	2.5	1.0
Ru(TPFPP)(CO)	1.2	1.0

[a] Determined by GC–MS and NMR.

3.4. Competition study of cyclopropanation of different styrene derivatives

Reactions of a number of styrene derivatives with DAMP in the presence of the ruthenium complexes Ru(TPP)(CO) (Table 7) and Ru(TPFPP)(CO) (Table 8) at 40 °C in chloroform were also studied. These competition experiments were conducted with a large excess of each substrate and limiting quantities of DAMP (substrate/DAMP = 5/1) (Tables 7 and 8). In all these experiments, cyclopropanes are the major products, usually obtained with tetraisopropylethene-1,2-diyl-bis(phosphonate) as a byproduct.

As expected, electron rich styrenes (4-methoxystyrene and 4-methylstyrene) are cyclopropanated more efficiently than alkenes bearing electron-withdrawing groups (4-chlorostyrene and 4-trifluoromethylstyrene). As an example, competition study of the cyclopropanation of 4-methoxystyrene and styrene gave a product ratio of 5 in favour of the cyclopropanation of the activated styrene.

The data were fit to a Hammet plot (Fig. 3), with a good correlation: $r^2 = 0.916$ for Ru(TPP)(CO) and $r^2 = 0.944$ for Ru(TPFPP)(CO). This allowed us to calculate a ρ-value of -1.01 ± 0.01 for TPP complex and -1.49 ± 0.01 for TPFPP complex. Similar preferences for electron rich alkenes were observed in the corresponding cyclopropanation

Table 7
Competition studies of cyclopropanation of various substituted styrenes (substrate A) and styrene (substrate B) with DAMP using ruthenium porphyrin complex Ru(TPP)(CO) as catalyst

Ru(TPP)(CO)	Ratio of products derived from A/B[a]
4-Methoxystyrene	84/16
4-Methylstyrene	69/31
4-Chlorostyrene	53/47
4-Trifluoromethylstyrene	51/49

[a] Determined by GC–MS and NMR.

Table 8
Competition studies of cyclopropanation of various substituted styrenes (substrate A) and styrene (substrate B) with DAMP using ruthenium porphyrin complex Ru(TPFPP)(CO) as catalyst

Ru(TPFPP)(CO)	Ratio of products derived from A/B[a]
4-Methoxystyrene	90/10
4-Methylstyrene	79/21
4-Chlorostyrene	47/53
4-Trifluoromethylstyrene	35/65

[a] Determined by GC–MS and NMR.

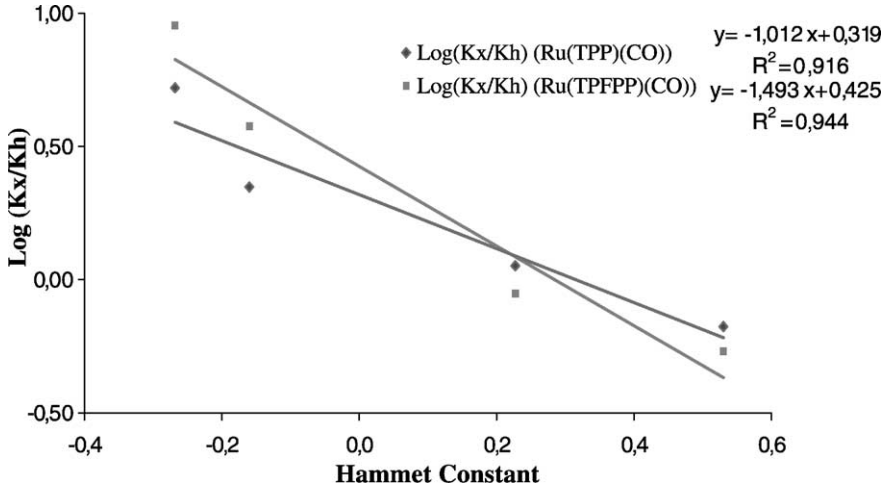


Fig. 3. Hammet plot for the competitive cyclopropanation of styrene derivatives with DAMP.

Table 9
Competition studies of cyclopropanation of 4-methoxystyrene (substrate A) and 4-fluoromethylstyrene (substrate B) with DAMP using ruthenium porphyrin complexes as catalyst

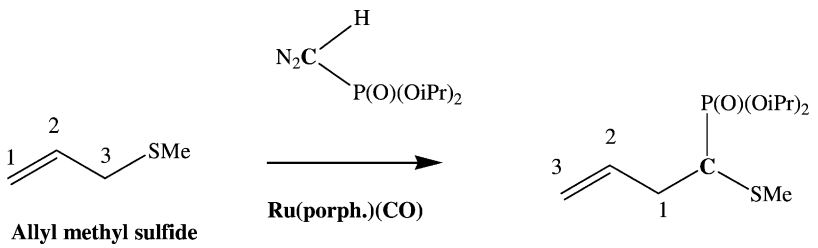
Catalyst	Ratio of products derived from A/B[a]
Ru(TPP)(CO)	74/26
Ru(TPFPP)(CO)	75/25

[a] Determined by GC–MS and NMR.

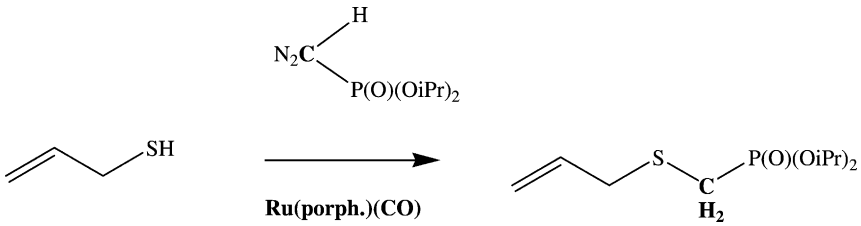
reactions obtained with EDA [33]. As an example, competition studies of cyclopropanation of 4-methoxystyrene and 4-fluoromethylstyrene with DAMP using ruthenium porphyrin complexes Ru(TPP)(CO) or Ru(TPFPP)(CO) as catalyst are also reported in Table 9. The data indicate that the cycloaddition occurred (75% in both cases) at the electron rich double bond and confirm the previous results obtained with different substituted styrenes.

3.5. Competition between cyclopropanation, sigmatropic reaction and insertion into S–H bond

We have already investigated the reaction of DAMP with alkyl allyl sulphides and allyl thiols [41]. To complete these results, we studied the competition of the cyclopropanation of styrene (substrate B) versus [2,3] sigmatropic reaction (Scheme 3) of allyl methyl sulphide (substrate A). A competition between cyclopropanation of styrene and S–H insertion (Scheme 4) with 2-propene-1-thiol (substrate A) was also performed. In both cases, we used DAMP and Ru(TPP)(CO) as catalyst. These results are summarised in Table 10. The data show that the major reaction with alkyl allyl sulphide is the [2,3] sigmatropic rearrangement of the intermediate sulphonium ylide to give C–S insertion as the final compound (98%) versus the cyclopropanation. The S–H insertion is



Scheme 3. Catalytic sigmatropic reaction.



Scheme 4. Catalytic S–H insertion.

Table 10
Competition studies of the cyclopropanation of styrene (substrate B) vs. [2,3] sigmatropic reaction of allyl methyl sulphide (substrate A) or S–H insertion reaction for 2-propene-1-thiol (substrate A) with diazomethylphosphonate catalysed by Ru(TPP)(CO)[a]

Substrate A	Ratio of products derived from A/B
Allyl methyl sulphide	98/2
2-Propene-1-thiol	81/19

[a] Determined by GC–MS and NMR.

largely observed with thiol to give α-thiophosphonic ester (81%) versus the cyclopropanation.

3.6. Asymmetric synthesis

The reaction of styrene with diisopropyl diazomethylphosphonate in the presence of an enantiomerically pure ruthenium(CO) porphyrin bearing chiral threitol units bound to both sides of the porphyrin, previously prepared by Gross and co-workers [34], gave the corresponding cyclopropyl phosphonate esters with a diastereoisomeric excess of 97% in favour of the (+) anti-isomer and an enantiomeric excess (ee) of 33% (total yield 92%). To our knowledge, this is the first asymmetric catalytic synthesis of such phosphonate esters (data are reported in Table 11).

Table 11
Cyclopropanation of styrene by DAMP using asymmetric ruthenium porphyrin complex as catalyst

Substrate	Catalyst	*cis* (%)[a]	*trans* (%)[a]	Yield (%)	ee(%)[b]
Styrene	Chiral	3	97	92	33

[a] Determined by GC–MS and ^{1}H NMR.
[b] Determined by chiral GC.

4. Discussion

We have recently shown that the carbene diisopropyl diazomethylphosphonate can react with a porphyrin ruthenium complex to form a new porphyrin ruthenium carbene complex, which was isolated and characterised [30]. We presume that the active intermediate in the ruthenium porphyrin catalysed reactions is probably this ruthenium carbene species formed by reaction of ruthenium(II) with DAMP. This suggestion is in agreement with our precedent studies showing that a ruthenium complex can be an intermediate of the cyclopropanation reaction, the limiting step being the attack of the double bond on the electrophilic carbene [33,42]. Similar conclusions were also proposed by Che et al. [8] with other ruthenium complexes and by Woo and co-workers using osmium(II) porphyrins as catalysts [43]. To get more information on the stereochemistry of these catalysed reactions, a wide range of para-substituted styrene derivatives were first tested, the results being reported in Tables 1–5.

As shown in the data (Tables 1 and 2), the porphyrin structure is important since the use of the electrodeficient meso-tetraphenylpentafluorophenylporphyrin carbonyl ruthenium Ru(TPFPP)(CO) (Fig. 1) instead of the unsubstituted TPP core results in an increase from 12 to 100 of the *trans*/*cis* ratio of cyclopropylphosphonate. Thus, steric differences in the metal complexes influence the observed stereoselectivities. In mesoporphyrin ruthenium complex, the meso positions are free, giving a low stereoselectivity since the carbene ligand encounters little steric encombrance from the alkyl groups of the porphyrin ring. Thus, the less crowded environment at the active site of Ru(MPIXDME)(carbene) leads to much lower selectivities (Table 4) compared to that

of Ru(TPFPP)(carbene). Similar results were recently observed in catalytic cyclopropanation with iron(II) porphyrin complexes [44].

Results showed that the diastereoselectivity (*trans*/*cis* ratio) is also influenced by electronic effects of the groups located on styrene derivatives. Surprisingly, as shown by data in Tables 1 and 2, and illustrated in Fig. 2, the *trans* isomer is very predominant when electron-donating group (MeO) is in the *para* position of the styrene. Thus, increasing the reactivity of the double bond results in an enhancement of the *trans*/*cis* ratio. In contrast, it must be noted that we have recently shown that the *trans*/*cis* ratio decreased with a more reactive carbene, ethyl diazoacetate, in the same conditions and with the same ruthenium catalyst [33].

The nature of the catalyst used is crucial for the observed selectivity. With iron, ruthenium or osmium porphyrins, the *trans* cyclopropyl ester is generally the major product [9]. In contrast, the *trans*/*cis* ratio could be close to unity, and a preference for the *cis* isomer is sometimes observed with rhodium porphyrin derivatives [37,45].

When the rate of the carbene transfer from the ruthenium complex to the olefin is too low, the competitive formation of the *trans* and *cis* dimers of tetraisopropylethene-1,2-diyl-bis(phosphonate) [36] is observed. This is due to the attack of DAMP on the electrophilic carbene carbon which becomes the major process, and thus the yield of the desired cyclopropyl ester is lowered.

Competition studies of cyclopropanation of various substituted styrene (substrate A) and styrene (substrate B) with DAMP using ruthenium porphyrin complex Ru(TPP)(CO) or Ru(TPFPP)(CO) as catalyst were studied. Data are reported in Tables 7 and 8 and illustrated by Fig. 3. These data show that the electronic nature of the substrate reacting with the porphyrin ruthenium carbene complex is very important. These observations are in total agreement with our previous results showing that the porphyrin ruthenium carbene complex (possibly co-ordinated by a molecule of solvent in *trans* position) is a possible intermediate in the cyclopropanation reaction [42]. The slowest step being the attack of the electrophilic carbene onto the styrene double bond. Electron donating groups in the para position increase the nucleophilic behaviour of the alkene and subsequently the cyclopropanation is favoured. In contrast, electron-withdrawing groups lowered the cyclopropanation rate. This has already been observed with a more reactive carbene precursor, ethyl diazoacetate, using ruthenium [33], iron [10] and osmium [43] porphyrins. Surprisingly, such influence was not observed for rhodium porphyrins used as catalysts [38,46], this is probably due to the higher reactivity of these metal porphyrin complexes.

Considering our previous results [33] and the actual results on reaction using the catalytic system Ru(II) porphyrins and the characterisation of a new carbene complex of DAMP [30], our current understanding of the catalytic cycle is summarised in Fig. 4. The first step of the cycle is the formation of a ruthenium

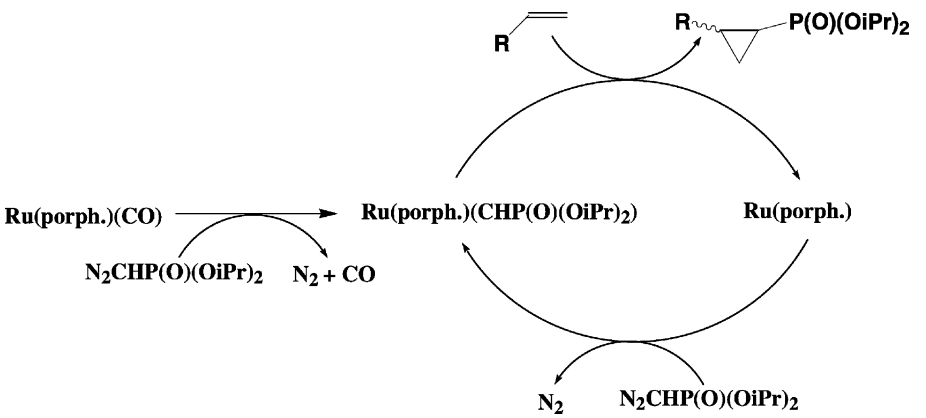


Fig. 4. Catalytic cycle for cyclopropanation reaction.

carbene complex. After the formation of the cyclopropane, a highly reactive ruthenium complex, possibly co-ordinated by a molecule of solvent is released in solution, and can react with a new molecule of diazophosphonate. This scheme is also supported by the strong shape selectivity observed with tri- and tetra-substituted alkenes.

5. Conclusions

In summary, highly efficient cyclopropanations have been observed by reaction of diisopropyl diazophosphonate with alkenes using ruthenium porphyrin catalysts. Our experiments strongly support the metallocarbene mechanism for the metal-catalysed cyclopropanation reactions. Moreover, a first catalytic enantioselective cyclopropanation of olefin with diisopropyl diazomethylphosphonate by a chiral ruthenium complex is an encouraging result which opens the way to further studies and application in asymmetric organic synthesis.

We have also demonstrated that simple ruthenium porphyrins are highly effective catalysts for carbenoid reactions with alkyl allyl sulphides and allyl thiols providing the formal C–S or S–H insertion rather than the more classical cyclopropanation. Further studies will also focus on developing enantioselective versions of these [2,3] sigmatropic rearrangements using chiral ruthenium porphyrins.

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