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A novel access to alicyclic phosphine oxides via ring closing metathesis

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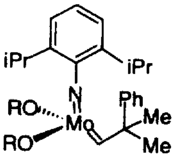
Abstract

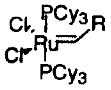
A series of cyclic phosphine oxides **5a–e** was prepared in a one-step procedure by RCM of dienes **4a–e**. The methodology was extended to the preparation of the bis-phosphine oxide **5f**. © 1999 Published by Elsevier Science Ltd. All rights reserved.

Keywords: phosphine oxide; ring closing metathesis.

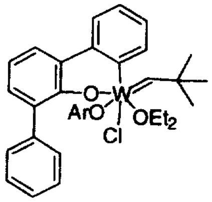
The versatility and synthetic applicability of the ring closing metathesis (RCM) reaction in the construction of functionalised carbocycles and heterocycles has recently been demonstrated.[1] The emergence of the well-defined transition metal catalysts **1**[2] and **2a**,**b**[3] has greatly expanded the scope and utility of this reaction.



1 R= $CMe(CF_3)_2$



2a R=Ph
2b R=$CHCPh_2$



3 Ar= 2,6-diphenyl-C_6H_3

To date, the literature contains only a few examples of RCM reactions of phosphorus containing compounds.[4] We are interested in the possibility of using the RCM reaction for the preparation of alicyclic phosphines. Indeed, cyclic phosphines and bis-phosphines are highly valuable synthetic compounds mainly as ligands for transition-metal catalysis.[5] Basset et al. reported that the metathesis of diallyl phenyl phosphine was feasible using 5% of aryloxide tungsten neopentylidene catalyst **3**[6] to give the cyclised product with a conversion of 95% (Scheme 1).[4d] In a preliminary experiment, we have found that, on

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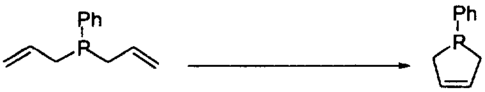
the contrary, the well explored RCM Ru-catalyst **2a** was ineffective for the ring closure of diallyl phenyl phosphine.



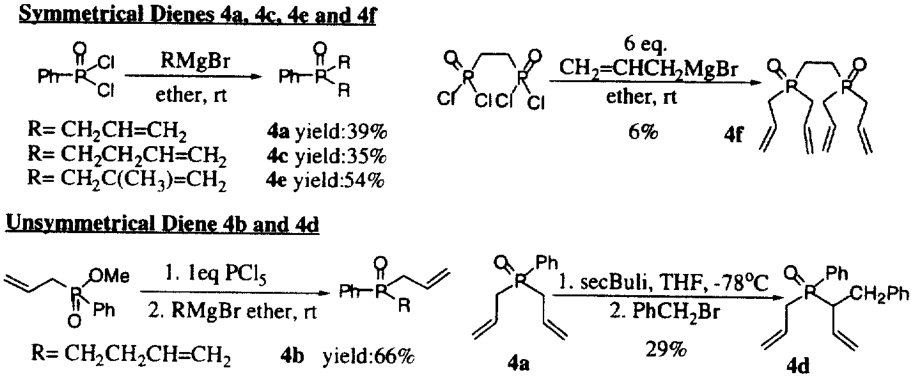
condition: 5%mol **3**, PhCl, 80°C, 50h conversion: 95% [4d]

condition: 4%mol **2a**, CH_2Cl_2, reflux, 48h conversion: 0% (recovered starting material)

Scheme 1.

However, when the same Ru-catalyst **2a** was used on phosphine oxides, the RCM was successful and five-, six-, and seven-membered alicyclic products were synthesised in good yields. These products can be subsequently reduced to the corresponding phosphines with retention of stereochemistry using well-established methods.[7]

A series of dienes **4a–f** were prepared using the following routes. The symmetrical dienes **4a**, **4c** and **4e** (Scheme 2) were synthesised by the addition of the corresponding Grignard reagents to phenylphosphonic dichloride at room temperature according to a procedure described in the literature.[8] Diene **4f** was prepared from ethanediyl-bis-phosphinic acid tetrachloride[9] using the same procedure. Even though the yield for this reaction was disappointingly low (6%), a sufficient amount of chemically pure material was isolated to test the feasibility of the RCM. The unsymmetrical diene **4b** was prepared from methyl allylphenylphosphinate.[10] The ester was first transformed into the corresponding phosphinic chloride using PCl_5. The addition of the Grignard reagent on the crude phosphinic chloride afforded the desired product in satisfactory yield. Finally, the unsymmetrical diene **4d** was prepared by the deprotonation of diallylphenylphosphine oxide **4a** at −78°C using *sec*BuLi followed by alkylation with benzyl bromide.

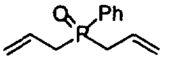
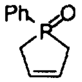
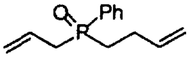
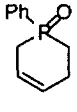
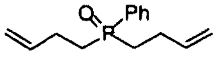
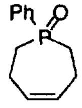
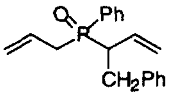
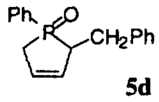
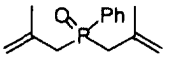
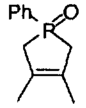
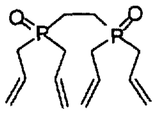
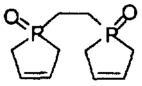
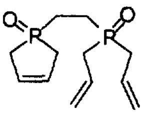


Scheme 2.

The RCM of these olefins **4a–f** in dichloromethane at reflux in the presence of 2–10% Ru-carbene **2a** at a concentration of 0.02 M gave the corresponding alicyclic phosphine oxides **5a–f** as detailed in Table 1.[11]

The five-membered ring diene precursors **4a** and **4d** readily provided the cyclised products within 24 h in good yields. The RCM of the α-substituted phosphine oxide diene **4d** afforded the cyclised product **5d** (mixture of two diastereomers, ratio 57:43) with a chemical yield that is similar to the RCM of the unsubstituted diallylphenylphosphine oxide **4a** (entries 1 and 4). However, the Ru-carbene **2a** showed no reaction with diene **4e** over 2 days supporting the hypothesis that steric effects are unfavourable for promoting ring closure (entry 5).[12] The six- and seven-membered ring systems **5b** and **5c** were synthesised in 74% and 89%, respectively, requiring prolonged reaction time for the preparation of

Table 1
Ring-closing metathesis of dienes **4a–e** and tetraene **4f** with 2–10% Ru-catalyst **2a** (0.02 M refluxing CH_2Cl_2)

Entry	Substrate	Condition	Product	Yield[a,b]
1	 **4a**	4% **2a**, 14h	 **5a**	75%
2	 **4b**	2% **2a**, 12h	 **5b**	74%
3	 **4c**	6% **2a**, 48h	 **5c**	89%
4	 **4d**	4% **2a**, 24h	 **5d**	81%
5	 **4e**	8% **2a**, 48h	 **5e**	no RCM
6	 **4f**	10% **2a**, 72h	 **5f**  **6**	36%[c] 12%[c]

a: isolated yields; b: all products have been fully characterised by ^1H, ^{13}C, ^{31}P NMR spectroscopy, mass spectrometry; c: for this reaction, 8% of the starting material was recovered.

compound **5c** only (entries 2 and 3). Tetraene **4f** was studied as a model for the preparation of alicyclic bis-phosphines. Several products were conceivable from the cyclisation of substrate **4f** resulting from a single RCM leading to either the 5-membered or 8-membered cyclic phosphine oxide or two RCM reactions yielding the desired bis-phosphine oxide **5f** or a [4,4,2] bicyclo derivative. After 3 days at reflux in dichloromethane, RCM using 10% of the catalyst **2a** (added sequentially by 2%mol portions) afforded after purification the desired bis-phosphine oxide **5f** with a chemical yield of 36% along with the starting material (8%) and product **6** (12%) resulting from a single RCM. No eight-membered ring, bicyclic product or dimer could be detected in the crude mixture for this reaction (entry 6).

In summary, the work presented in this communication has established a novel strategy based on the RCM reaction for the synthesis of alicyclic phosphine oxides. These compounds could be converted into the corresponding alicyclic phosphines by reduction.[7] Further studies to apply the RCM reaction to new chiral phosphines and bis-phosphines are presently under investigation.

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