Cycloisomerisation of 1,6-Dienes in the Presence of Cationic Palladium Catalysts

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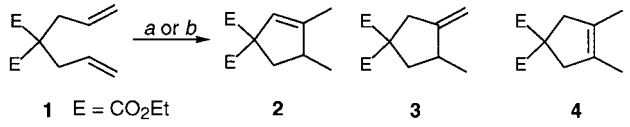
Abstract: Mono- and dicationic palladium efficiently catalyses the cycloisomerisation of bis allyl substrates with high chemo-, regio- and enantioselectivities (60% ee).

Unsaturated cycloalkanes are an integral part of many natural products and their preparation is of permanent interest in organic synthesis. One important method under the conditions of homogeneous catalysis concerns the (atom economically) interesting cycloisomerisation[1] of alkynes[2] and 1,3-dienes.[3] In this context, the cycloisomerisation of 1,6-dienes (diallylmalonates, e.g. **1**) described by Grigg and coworkers[4] has been shown to lead to unsaturated five-membered rings with late transition metals, and, more precisely, palladium acetate in chloroform containing HCl gave selectively 1,2-dimethylcyclopent-2-enes **2** whereas rhodium(I) chloride triphenylphosphine complexes catalyse the formation of 1-methyl-2-methylenecyclopentanes **3**. It seemed to us interesting to develop this reaction for several reasons. First of all, the starting material is easily available and it is possible to introduce heteroatoms (N, O, S, Si, and others) between the allyl groups, allowing an access to carbo- and heterocylic five-membered rings. On the other hand, the generation of a chiral centre is an opportunity to study enantioselective catalytic transformations, provided the system tolerates chiral ligands. Now, we are able to show that palladium complexes can catalyse both reactions efficiently with high regioselectivity and, more importantly, that the addition of nitrogen centered chelating ligands does not alter the reactivity thus permitting enantioselective palladium catalysis with chiral complexes.

It is well known that cationic palladium complexes favour the dimerisation of ethylene compounds.[5] When **1** was treated in chloroform at 60°C with cationic $[(MeCN)_3PdCl]BF_4$ generated *in situ* from bisacetonitrile palladium(II) chloride and $AgBF_4$, 4,4-biscarboxylato-1,2-dimethylcyclopent-2-ene **2** was formed in more than 79% yield, after distillation. The compound is isomerically pure, and only trace amounts of **3** or symmetrical **4** could be detected.



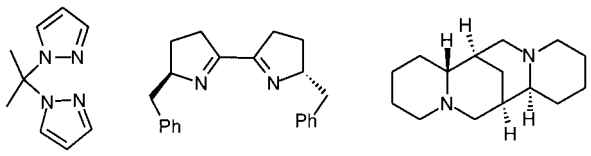
1 E = CO_2Et **2** **3** **4**

Scheme 1 *a* $(MeCN)_2PdCl_2$ (0.05 equiv.), MeCN, $AgBF_4$ (0.045 equiv.) 20°C, filtration and $CHCl_3$, 60°C, 18h, **2** 79% (distilled); *b* $(MeCN)_4Pd(BF_4)_2$ (0.05 equiv.), $CHCl_3$, 20°C, 8h, **3** (39%) (NMR).

The reaction course and the yield of **2** is not notably altered when the cationic catalyst is coordinated to polypyrazoles, e.g. the methano bis pyrazole $(CH_3)_2C(pz)_2$ **5**, prepared from $(MeCN)_2PdCl_2$ in dichloromethane.[6] Though the exact mechanism for the formation of **2** is not yet clear,[4] it is trivial that at least two hydride migrations must be involved. It has been shown that dicationic palladium species favour carbocationic rearrangements of substituted olefins[7] but, at the same time, are highly selective dimerisation catalysts of styrene when coordinated to pyridine ligands.[8] In the latter reaction no double bond migration was observed.

When the catalyst precursor $PdCl_2$-**5** was treated with 2 equivalents of silver salt, presumably a dicationic palladium complex is formed, which, in the presence of bis pyrazole ligands leads to the formation of the isomeric exomethylene cyclopentane **3** (75%) accompanied with circa 20% of **2** (60°C, 4 hours, ratio determined by ^1H NMR). A similar result is obtained with commercial $(MeCN)_4Pd(BF_4)_2$ (39% yield, 8 hours) at room temperature. The latter catalyst is less stable and decomposes slowly during the reaction. In addition the lack of heterocyclic ligands decreases the selectivity and isomeric, but non cyclised alkadienes are observed (Table 1). The formation of endocyclic cyclopentene **2** from **1** (*vide supra*) follows a different reaction pathway, than the isomerisation to exomethylene-**3** though **2** could isomerise to **3** (and *vice versa*). Thus, when heating **2** with $[Pd^{2+}]$ (7 hours, $CHCl_3$) no modification of **2** is observable in the NMR spectra. The situation is more complicated with the kinetic product **3** which does not form exclusively. Treatment of **3** (product mixture from entry 5) with $[PdCl^{2+}]$ (50°C, 22 hours, $CHCl_3$) effectively leads to isomerisation (**2** 45%, **3** 53%). This kind of experiment was the sole case where the symmetrical cyclopentene **4** could be detected.[9]

Apart from its atom economical[1] aspect this reaction is remarkable for different reasons. First of all, the ring closure is highly chemo- and regioselective and the position of the double bond depends on the charge on the Pd-catalyst. Secondly, symmetrical compounds are absent and products form with creation of a stereogenic center. For this reason it is important that selectivity and yields are improved with heterocyclic amine-coordinated palladium. These three conditions are favorable prerequisites for the elaboration of catalytic enantioselective transformations.[10]

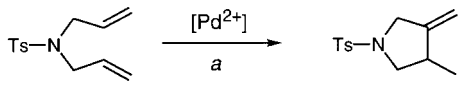


5 **6** (-)-sparteine

Scheme 2

Both cycloisomerisation reactions of **1** occur with mono- and dications of a Pd complex coordinated to **5**. In the case of monocationic Pd the transformation seems slightly more efficient. Dicationic Pd is less stable and yields are lower. Variable amounts of cyclopentene **2** are also formed as a side product, and sometimes, non-cyclised, isomerised dienes. The sterically more demanding ligand **6** reduces the reactivity and raises reaction times even at 50°C. The control of the different isomerisation processes will certainly require more profound studies of the reaction conditions, nonetheless we were pleased to observe appreciable chiral inductions with bis-oxazoline and (-)-sparteine palladium(II). Thus, under 'dicationic' conditions a mixture of scalemic **2** (23 to 37%ee) and **3** (60 %ee) form after 7 hours at 50°C. The enantioselectivies in the formation of **2** are variable and differ notably according to the catalysts. Thus, the $PdCl^+$ system is rather unselective (7% ee, sparteine) whereas the Pd^{2+} catalysis generates better, but still modest inductions of 23-37%ee (entries 3, 6 and 7).

High-induction asymmetric catalysis with cationic palladium complexes has only emerged quite recently and is documented, for example, by a catalytic aldol reaction (level of enantioselectivity: 76%ee),[11] asymmetric 1,3-dipolar cycloaddition of nitrones to olefins (91%ee)[12] or the enantioselective rearrangement of allylic imidates to allylic amides (60-67%ee)[13] Brown and coworkers[14] have shown that the enantioselective phenylation of cycloalkenes[15] is the result of a double isomerisation of cationic Pd intermediates. To our knowledge enantioselective cycloisomerisations of dienes are not known; these reactions open the way into the class of chiral cyclopentenes and represent a method for the access to sandalwood-like odorant alcohols.[16] Our findings compare to 1,6-enyne cycloisomerisation reactions with *trans* diphosphane Pd complexes (ee <76%)[17] and Trost's results with new macrocyclic palladium complexes (ee <76%).[18] Heteroatoms are compatible with the cationic systems since preliminary results with bisallyl amine **7** demonstrate the extention to heterocyclic systems and the formation of exomethylene azacyclopentane **8**.



7 **8**

Scheme 3 *a*. $(MeCN)_2PdCl_2$ (0.05 equiv.), acetone, $AgBF_4$ (0.11 equiv.) 20°C, filtration and $CHCl_3$, 50°C, 4h, **8** (45%, isolated)

Table 1 Cycloisomerisation of 1,6-diene **1** catalysed by mono- and dicationic palladium in chloroform (counter ion: BF_4^-).[a]

Entry	catalyst[b]	T/ °C	t/h	**2** (%) [%ee]	**3** (%) [%ee]	n.i.[c]
1	$[PdCl]^+$	60	18	79[d]	-	
2	$[PdCl]^+$-**5**	45	21	92[d]	-	
3	$[PdCl]^+$-**sparteine**	50	47	49[d] [5][e]	-	
4	$Pd(MeCN)_4(BF_4)_2$[f]	25	8	traces	39[g]	60
5	$[Pd]^{2+}$-**5**	60	4	22[e]	75	traces
6	$[Pd]^{2+}$-**6**	50	7	8[e] [23][e]	38[60][e]	54
7	$[Pd]^{2+}$-**sparteine**	50	7	24[37][e]	27 [60][e]	49
8	$[Pd]^{2+}$-dppe	60	23	traces	17[g]	80

[a] Reactions were carried out with 1 mmol of **1** in 5 mL of chloroform and the preformed Pd(II) catalyst; [b] $[PdCl]^+$: $(MeCN)_2PdCl_2$ (0.05 mol%) $AgBF_4$ (0.05 Mol%); $[Pd]^{2+}$: $(MeCN)_2PdCl_2$ (0.05 mol%) $AgBF_4$ (0.1 Mol%), dppe: 1,2-bis(diphenylphosphino)ethane; the catalyst is prepared *in situ* from the Pd complex and the silver salt, acetone CH_2Cl_2, or acetonitrile, 20', room temperature, AgCl is filtered. [c] Starting material and isomerised, non-cyclised dienes. [d] Distilled (Kugelrohr). [e] Determined by HPLC with Chiralcel OJ, hexane-*iso*-propanol (99.9/0.1), 0.5 mL/min. [f] Commercial product . [g] ^1H NMR.

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(9) A crude $[Pd^{2+}]$ reaction mixture of **3** (38%) and non-cyclised dienes (62%) showed the following composition after 3 months: **2** (10%), **3** (-), **4** (30%), non-cyclised dienes (60%).

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