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Das Reagenz • The Reagent

Dirhodium(II) Tetrakis(Methyl Pyrrolidone-5-carboxylate) [Rh_2(5*R*-mepy)$_4$ and Rh_2(5*S*-mepy)$_4$] and Related Chiral Rhodium Catalysts

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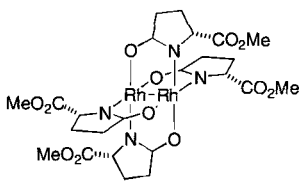
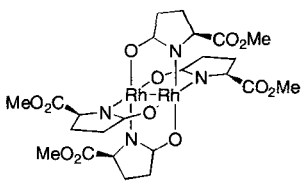
Catalytic methods for the decomposition of diazoketones and their use for a variety of carbenoid transformations (*e.g.* cyclopropanations, C-H insertions or ylide formations) are well established [1–3]. Enantioselective modifications of these reactions have been studied since 30 years; especially chiral copper or rhodium catalysts have been used for enantioselective cyclopropanations and *C–H* insertions. A breakthrough in enantioselectivity could be achieved with chiral dirhodium carboxamidates developed by Doyle and coworkers. Though several different catalysts of this type have been developed (and most of them have advantages in special reactions), dirhodium(II) tetrakis(methyl 2-pyrrolidone-5-carboxylate) [Rh_2(mepy)$_4$] seems to give the best results [4–14].

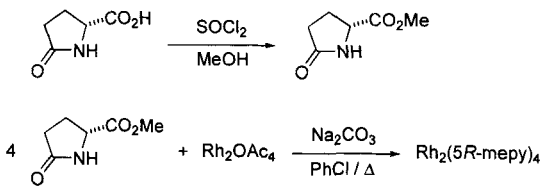


Rh_2(5*R*-mepy)$_4$



Rh_2(5*S*-mepy)$_4$

The preparation of Rh_2(mepy)$_4$ starts with pyroglutamic acid which is readily available in both enantiomeric forms. Esterification and subsequent ligand displacement from dirhodium(II) tetraacetate gives the title compound (Scheme 1). It can be purified by chromatography and recrystallization (58% yield) [15]. In addition it is commercially available (Aldrich or Acros).

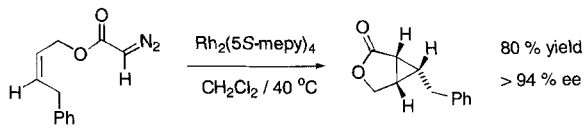


Scheme 1 Preparation of Rh_2(mepy)$_4$ [15]

One of the four possible diastereoisomers is formed exclusively, the two nitrogen donors being *cis*-arranged at each rhodium atom [16–18]. The ligands form a chiral environment around the catalytic centre and influence both the conformation of the carbene and the approaching substrate. This seems to be the major benefit in comparison with other chiral rhodium catalysts, in which the stereogenic centres are much farther from the carbene center attached to the rhodium catalyst.

Cyclopropanations and Cyclopropenations

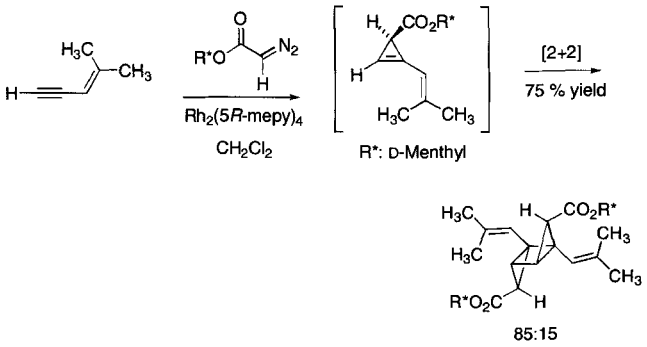
Enantioselective cyclopropanations can be efficiently performed in the presence of chiral catalysts. Whilst some copper catalysts are sometimes superior in intermolecular reactions [19–23] in comparison with Rh_2(mepy)$_4$ [24–26], the latter is generally more effective in intramolecular cyclopropanation reactions [27–32] (Scheme 2). With this catalyst the intramolecular cyclopropanation of (Z)-alkenes proceeds with a significantly higher level of enantiocontrol compared with (*E*)-alkenes [27].



Scheme 2 Intramolecular cyclopropanation [27]

The enantioselective cyclopropenation of alkynes using Rh_2(mepy)$_4$ has been published, but only a double stereodifferentiation using chiral diazoacetate esters gives satisfying enantioselectivities [25, 33, 34]. In reactions of diazoketones with eneynes, selective cyclopropenation is observed [33] (Scheme 3).

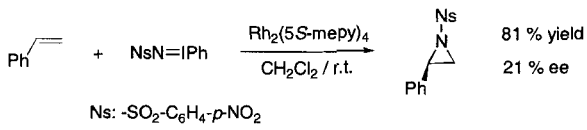
The cyclopropanation of racemic 1,3-dimethylallenes with methyl diazophenylacetate in the presence of Rh_2(mepy)$_4$ led to a mixture of methylene-cyclopropanes without any diastereoselectivity and in poor yield (35%) [35].



Scheme 3 Cyclopropenation rather than cyclopropanation of an eneyne [33]

Aziridination

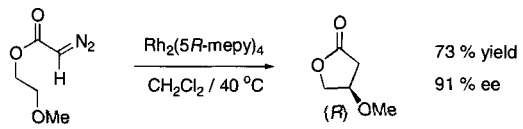
Utilization of $Rh_2(mepy)_4$ as a chiral catalyst for the enantioselective aziridination of olefins with sulfonyl imino iodinanes has been reported recently (Scheme 4) [36]. Nevertheless, though the yields are quite good, the enantioselectivity is poor (21% ee) in comparison with a binaphthyl-derived rhodium catalyst (55% ee, 74% yield) [36].



Scheme 4 Aziridination of an olefin [36]

C–H Insertion

Rhodium carbenes – generated as intermediates from diazoketones – are able to insert into almost any type of X–Y bond [1–3]. Especially insertions into C-H bonds can be performed enantioselectively. $Rh_2(mepy)_4$ has proved to be a powerful catalyst for the differentiation of enantiotopic C-H bonds (Scheme 5) [37–44].

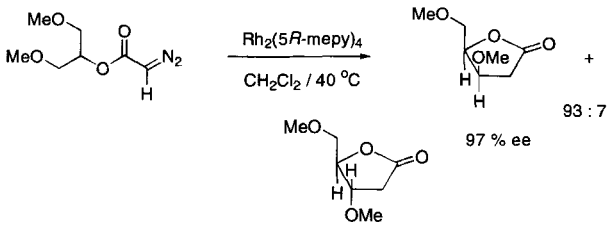


Scheme 5 Intramolecular C-H insertion [37]

This reaction has been successfully applied in the preparation of 2-desoxyxylolactones starting with 1,3-dialkoxy-2-propyl diazoacetates. Again, $Rh_2(mepy)_4$ turned out to be superior compared to other catalysts. In this reaction as little as 0.1 mol% of the catalyst was required to effect a complete reaction with yields ranging from 65–81% [45] (Scheme 6).

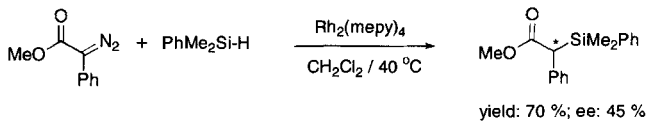
Si-H, O-H and S-H Insertion

The enantioselective intermolecular insertion of a rhodium carbene into a Si-H bond has been investigated using several chiral rhodium catalysts [46, 47]. The title compound proved



Scheme 6 Synthesis of 2-desoxyxylolactones [45]

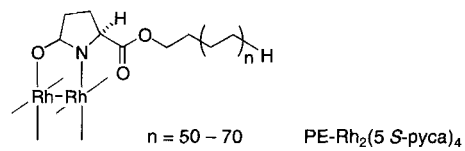
to give the best results with up to 72% ee (Scheme 7). Asymmetric insertions into the O-H bond of alcohols [48] or into the S-H bond of thiophenol [49] gave poor enantioselectivities not exceeding 12% ee.



Scheme 7 Asymmetric rhodium carbene insertion into a Si-H bond. The absolute configuration of the products was not determined in this example [46]

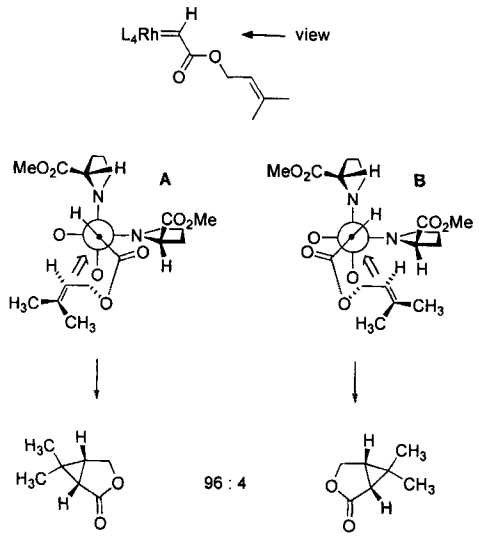
Polymer-bound Catalysts

Based on the work of Bergreiter and coworkers [50], Doyle *et al.* developed a recoverable polymer-bound rhodium catalyst [polyethylene dirhodium(II) 2-pyrrolidone-5*S*-carboxylate: PE-Rh_2(5*S*-pyca)$_4$] [51]. The enantioselectivity with this catalyst was shown to be even better than with $Rh_2(mepy)_4$. A small loss of activity during eight runs with the recovered catalyst could be compensated by adding 2.7 mol% of the ligand 5*S*-mepyH.



Mechanistic Considerations

Several attempts have been made to explain the good enantioselectivities achieved in reactions catalyzed by $Rh_2(mepy)_4$ [12, 18, 31, 43]. Though the intermediacy of a rhodium carbene complex is not yet proven [52], it is assumed that a species similar to the conformers **A** or **B** is involved (Scheme 8). Due to the greater bulk in the quadrants where the nitrogen ligands are located, the carbene should favourable arrange as conformer **A** or **B**. Although conformer **A** seems to be more hindered (steric interaction of the ester function with the pyrrolidone ring and the hydrogen atom at this position), the attack of the double bond is more likely in conformer **A** [12]. Similar mechanistic investigations for C–H insertions have been made [1].



Scheme 8 A possible explanation for the stereochemical outcome of cyclopropanations with Rh_2(5*S*-mepy)$_4$ [12] (The Fischer-projections depicts a view along the carbenoid carbon–rhodium double bond)

Other Rhodium Carboxamidate Catalysts

Several similar rhodium carboxamidate catalysts have been prepared (table) and used in reactions of diazoketones.

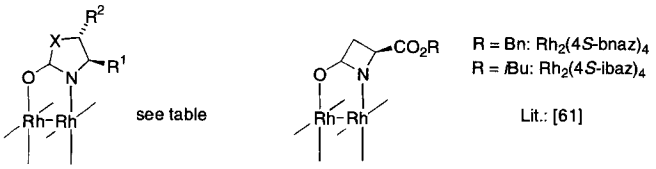
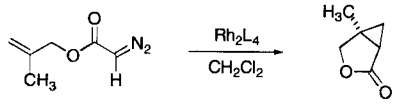


Table Rhodium Carboxamidate Catalysts

Catalyst	R^1	R^2	X	Lit.
Rh_2(5*S*-mepy)$_4$	CO_2Me	H	CH_2	
Rh_2(5*S*-nepy)$_4$	CO_2*i*Bu	H	CH_2	[37, 53]
Rh_2(5*S*-dmap)$_4$	$CONMe_2$	H	CH_2	[54]
Rh_2(5*S*-meox)$_4$	CO_2Me	H	O	[31, 32, 39, 43–45, 53, 55, 56]
Rh_2(5*S*-bnox)$_4$	Bn	H	O	[18, 24, 39, 57]
Rh_2(5*S*-ipox)$_4$	*i*Pr	H	O	[24]
Rh_2(5*S*-phox)$_4$	Ph	H	O	[26, 57]
Rh_2(4*S*-macim)$_4$	CO_2Me	H	NCOMe	[41, 42, 53, 58, 59]
Rh_2(4*S*-mppim)$_4$	CO_2Me	H	$NCOCH_2Bn$	[44, 58, 59]
Rh_2(4*S*-mpaim)$_4$	CO_2Me	H	NCOBn	[53]
Rh_2(4*S*-mboim)$_4$	CO_2Me	H	NCOPh	[59, 60]
Rh_2(4*S*-tboim)$_4$	CO_2Me	H	NCO–C_6H_4-*p*-*t*Bu	[60]
Rh_2(4*S*-mchim)$_4$	CO_2Me	H	NCO*cy*He	[58, 59]
Rh_2(5*S*-treox)$_4$	CO_2Me	CH_3	O	[56]

Some of these catalysts are useful alternatives to Rh_2 (mepy)$_4$. Rh_2(meox)$_4$ and Rh_2(threox)$_4$ – catalysts available from serine and threonine, respectively – provide higher enantiocontrol in C–H insertions of sterically demanding diazoketones [56]. The imidazolidinone derived catalysts Rh_2(mppim)$_4$, Rh_2(mpaim)$_4$, Rh_2(tboim)$_4$ and Rh_2(mchim)$_4$ sometimes lead to significantly better results than Rh_2(mepy)$_4$ (Scheme 9) [53, 59, 60]. Rh_2(macim)$_4$ was reported to be an especially versatile catalyst for C–H insertions [41]. In intermolecular cyclopropanations the *cis*/*trans* ratio can be inverted in favour of the *cis*-substituted cyclopropanes, when Rh_2(phox)$_4$ instead of Rh_2(mepy)$_4$ is used as catalyst [57].



Rh_2L_4	yield (%)	ee (%)
Rh_2(5*S*-mepy)$_4$	72	7
Rh_2(5*S*-meox)$_4$	84	1
Rh_2(5*S*-mppim)$_4$	72	89
Rh_2(5*S*-mchim)$_4$	75	83

Scheme 9 Intramolecular cyclopropanation with different rhodium carboxamidate catalysts [59]. Explanation of the ligand abbreviations see table

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