Novel ruthenium–pyridinedicarboxylate complexes of terpyridine and chiral bis(oxazolinyl)pyridine: a new catalytic system for alkene epoxidation with [bis(acetoxy)iodo]benzene as an oxygen donor

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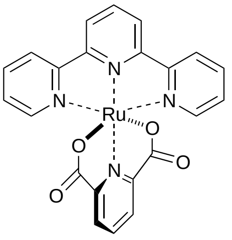
Ruthenium–pyridine-2,6-dicarboxylate (pydic) complexes 1–3 of terpyridine and chiral bis(oxazolinyl)pyridines (pybox-*ip* and pybox-*ph*), which can be synthesized from [Ru(*p*-cymene)Cl$_2$]$_2$ and the corresponding ligands, exhibit catalytic activity for epoxidation of *trans*-stilbene in combination with [bis(acetoxy)iodo]benzene: asymmetric induction with 2 was observed in 74% ee for *trans*-stilbene.

Ruthenium complexes with nitrogen-based ligands have been intensively investigated in order to develop catalysts for organic oxidation processes and to simulate the mechanism of bioorganic oxidation. This is because ruthenium complexes act as oxidation catalysts, often *via* ruthenium-oxo species, oxidizing alcohols or alkanes and epoxidizing alkenes.[1,2] We are especially interested in Balavoine's alkene epoxidation using RuCl$_3$–bipyridine–NaIO$_4$, in which addition of bipyridine can efficiently minimize cleavage of the alkene, even in the presence of NaIO$_4$.[3] In connection of our studies of transition-metal catalysis with terdentate bis(oxazolinyl)pyridine (Pybox) ligands,[4] we have been studying an applicaton of Ru–bisoxazoline catalysts for catalytic epoxidation of alkenes accompanied by asymmetric induction.[5] In this respect, Waegell reported an asymmetric alkene epoxidation with Ru–oxazoline catalysts with low asymmetric induction,[6] and Che described an asymmetric and stoichiometric oxygen transfer from a chiral ruthenium complex to styrene; 56% ee for 4-chlorostyrene.[7] As a new catalyst design, we adopted the introduction of dual closed meridional stereotopes around an active metal and consequently chose pyridine-2,6-dicarboxylate (pydic) as the counterpart. Here we disclose a synthesis of Ru(pydic)(terpy) (terpy = 2,2′:6′,2″-terpyridine) **1** as a non-chiral catalyst and Ru(pydic)(pybox-R) **2** (R = Pr^i) and **3** (R = Ph) as chiral catalysts, and their catalytic activity for alkene epoxidation is also demonstrated.



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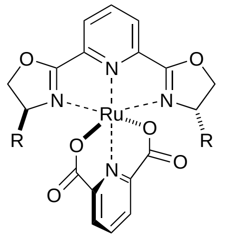
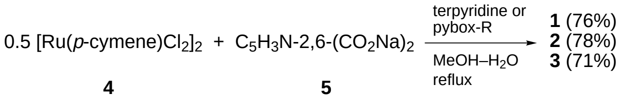


2 R = Pr^i
3 R = Ph

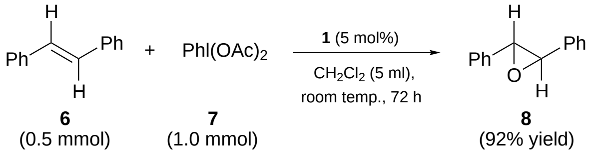
A mixture of [Ru(*p*-cymene)Cl$_2$]$_2$ **4**, disodium pyridine-2,6-dicarboxylate **5**, and 2,2′:6′,2″-terpyridine was treated in MeOH–H$_2$O at reflux for 1 h under argon atmosphere. After cooling the reaction mixture, Ru(pydic)(terpy) **1** was obtained in 78% yield as a dark violet precipitate by filtration (Scheme 1).† Complex **1**, which is stable in air, is slightly soluble in MeOH (*ca.* 10 mg in 25 ml), but almost insoluble in CH$_2$Cl$_2$ and CHCl$_3$ (*ca.* < 10 mg in 200 ml). Chiral complexes **2** and **3** were also prepared by the same procedure as shown in Scheme 1.‡



$$\underset{\mathbf{4}}{0.5\ [\text{Ru}(p\text{-cymene})\text{Cl}_2]_2} + \underset{\mathbf{5}}{\text{C}_5\text{H}_3\text{N-2,6-(CO}_2\text{Na)}_2} \xrightarrow[\text{MeOH–H}_2\text{O, reflux}]{\text{terpyridine or pybox-R}} \mathbf{1}\ (76\%),\ \mathbf{2}\ (78\%),\ \mathbf{3}\ (71\%)$$

Scheme 1

We first examined epoxidation of *trans*-stilbene **6** (0.5 mmol) with iodosobenzene (PhIO) (1.5 mmol) in CH$_2$Cl$_2$ (5 ml) in the presence of **1** (5 mol%) (Scheme 2) (Table 1, run 1) *trans*-Stilbene oxide **8** was obtained in good to excellent yield (67%) with a small amount of benzaldehyde (8%), and some **6** (5%) was recovered. After screening of several oxidants, we found that [bis(acetoxy)iodo]benzene **7** [PhI(OAc)$_2$]§ served as an efficient oxygen donor assisted by complex **1**; PhI(OAc)$_2$ has better solubility in CH$_2$Cl$_2$. When **7** (1.0 mmol) was added to a suspension of complex **1** (14 mg, 5 mol%) in a CH$_2$Cl$_2$ (5 ml) solution of **6** (0.5 mmol), complex **1** spontaneously reacted, dissolved and gave a dark brown solution. The catalytic epoxidation proceeded slowly at room temperature for 72 h to give *trans*-stilbene oxide in excellent yield (92%) (run 3). However, use of NaIO$_4$ resulted in exclusive cleavage of the alkene (run 5). Epoxidation under aerobic epoxidation with Bu^{t}CHO/O$_2$ (1 atm). (run 6) and use of Bu^{t}OOH (run 7) resulted in yields of 86 and 81%, respectively.



Scheme 2

We then examined asymmetric epoxidation of *trans*-stilbene **6** with Ru(pydic)(pybox-*ip*) **2** (5 mol%), which also exhibited catalytic activity with PhIO (3 equiv.) and PhI(OAc)$_2$ (3 equiv.)

Table 1 Catalytic epoxidation of *trans*-stilbene with Ru(pydic)(terpy) **1**[a]

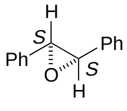
Run	Oxidant	Oxidant : *trans*-stilbene/mmol	*t*/h	Yield (%)	Recovered alkene (%)
1	PhIO	1.5 : 0.5	72	67	5
2	PhI(OAc)$_2$	0.5 : 0.5	96	49	39
3	PhI(OAc)$_2$	1.0 : 0.5	72	92	0
4	PhI(OAc)$_2$[b]	1.0 : 0.5	96	90	5
5	NaIO$_4$[c]	2.5 : 0.5	96	0	0[d]
6	O$_2$/Bu^{t}CHO[e]	2.5 : 0.5	48	86	1
7	Bu^{t}OOH	2.0 : 0.5	24	81	1

[a] Catalyst **1** (0.025 mmol, 5 mol% of *trans*-stilbene), CH$_2$Cl$_2$ (5 ml), at room temperature. The yields are based on 0.5 mmol of *trans*-stilbene. Benzaldehyde was obtained in the range 2–10%. [b] Acetone (5 ml) was used as a solvent. [c] NaIO$_4$ (3.5 mmol), H$_2$O (2.5 ml), room temp. [d] Benzaldehyde (27%) was obtained. [e] Bu^{t}CHO (2.5 mmol), O$_2$ (1 atm).

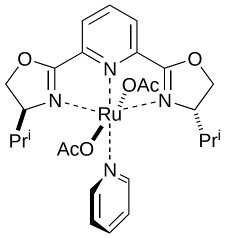
Table 2 Asymmetric catalytic epoxidation of *trans*-stilbene with Ru(pydic)(pybox-*ip*) **2**[a]

Run	Oxidant	Oxidant : *trans*-stilbene/mmol	Solvent	*T* °C	*t*/h	*trans*-Stilbene oxide		Recovered alkene (%)
						Yield (%)	Ee (%)	
1	PhIO	1.5 : 0.5	PhMe	25	96	67	24	9
2	$PhI(OAc)_2$	1.5 : 0.5	PhMe	25	96	80	63	3
3	$PhI(OAc)_2$	1.5 : 0.5	PhMe	0	96	63	74	18
4	$PhI(OAc)_2$	1.5 : 0.5	C_6H_6	25	96	43	52	22
5	$PhI(OAc)_2$	1.5 : 0.5	CH_2Cl_2	25	96	40	36	27
6	$NaIO_4$[b]	2.5 : 0.5	PhMe	5	96	trace	—	trace
7	O_2/Bu^tCHO[c]	2.5 : 0.5	PhMe	25	96	67	5	3
8	Bu^tOOH	2.0 : 0.5	CH_2Cl_2	25	72	38	16	38

[a] Catalyst **2** (0.025 mmol, 5 mol% of *trans*-stilbene), solvent (10 ml). The yields are based on 0.5 mmol of *trans*-stilbene. Benzaldehyde was obtained in the range 2–14%. The ees were determined by chiral LC (Daicel Chiralcel OD). All epoxides had (1*S*,2*S*) configuration. [b] $NaIO_4$ (3.5 mmol), H_2O (2.5 ml). [c] Bu^tCHO (2.5 mmol), O_2 (1 atm).



(*S*,*S*)-**8**



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to give 67 and 80% yields of (1*S*,2*S*)-*trans* stilbene oxide (*S*,*S*)-**8** (24 and 63% ee), respectively (Table 2, runs 1 and 2). The best result for this catalytic system was obtained at 0 °C (74% ee, run 3). When performed in toluene rather than CH_2Cl_2 or C_6H_6, epoxidation using complex **2** (5 mol%) and $PhI(OAc)_2$ (3 equiv.) gave higher yields (runs 2, 4 and 5). Aerobic oxidation and oxidation with Bu^tOOH proceeded but gave relatively low yields and enantiomeric excesses (runs 7 and 8).

The Ru(pydic)(pybox-*ph*) complex **3** gave slightly lower enantioselectivities than **2**; oxidation of *trans*-stilbene under the same conditions as in run 2 of Table 2 gave the epoxide in 84% yield (58% ee).

In comparison, *trans*-$(AcO)_2$Ru(pybox-*ip*)(pyridine) **9**, prepared by reaction of [Ru(*p*-cymene)$(OAc)_2]_2$,[8] pybox-*ip* and pyridine, was examined as an oxidation catalyst with $PhI(OAc)_2$. The complex **9** (5 mol%) similarly catalysed the epoxidation of **6** under the same conditions as in run 2 of Table 2 to give racemic *trans*-stilbene oxide in 49% yield; 15% of the alkene was recovered. This finding implies that the meridional tridentate connected structure of pydic on **2** and **3** must be rigid enough during the catalysis to help pybox maintain the chiral environment, inducing the enantioselection.

Thus, we have found a new alkene epoxidation methodology utilizing ruthenium(II) complexes having the dual meridional system of pydic with terpyridine and pybox, in combination with $PhI(OAc)_2$ as the oxygen donor. Our studies are now focused on the scope and limitations of this alkene epoxidation and its mechanism.

Footnotes and References

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† Synthesis of Ru(pydic)(terpy) **1**. To a solution of [Ru(*p*-cymene)$Cl_2]_2$ **4** (150 mg, 0.24 mmol) and 2,2′:6′,2″-terpyridine (144 mg, 0.48 mmol) in MeOH (8 ml) was added a solution of disodium pyridine-2,6-dicarboxylate **5** (0.48 mmol) in MeOH–H_2O (2 : 1, 7.2 ml) under argon atomosphere. The mixture was stirred at 60 °C for 1 h. The dark violet precipitate was collected by filtration to give **1** (183 mg, 0.37 mmol) in 76% yield. Calc. for $C_{22}H_{14}N_4O_4Ru(H_2O)$: C, 49.35; H, 3.39; N, 10.46. Found: C, 49.11; H, 3.52; N, 10.65%; ν_{max}(KBr)/cm^{-1} 1650, 1620.

‡ Synthesis of Ru(pydic)(pybox-*ip*) **2**. To a solution of [Ru(*p*-cymene)$Cl_2]_2$ **4** (306 mg, 0.5 mmol) and pybox-*ip* (301 mg, 1.0 mmol) in MeOH (7 ml) was added a solution of disodium pyridine-2,6-dicarboxylate **5** (1.0 mmol) in MeOH–H_2O (2 : 1, 15 ml) under argon atmosphere. The mixture was stirred at 60 °C for 1 h. The mixture was extracted with CH_2Cl_2 (40 ml). The combined organic layers were concentrated and the residue was purified by silica gel column chromatography with CH_2Cl_2–MeOH (50 : 1) to give **2** as a dark violet solid (444 mg, 0.78 mmol) in 78% yield; mp > 240 °C (decomp.) δ_H (270 MHz, $CDCl_3$, Me_4Si) 0.48 (d, *J* 6.8, 6 H), 0.62 (d, *J* 6.8, 6 H), 1.09 (m, 2 H), 3.71 (m, 2 H), 4.61 (dd, 2 H), 4.70 (dd, 2 H), 7.64 (t, 1 H), 7.88 (d, 2 H), 8.11 (t, 1 H), 8.34 (d, 2 H). Calc. for $C_{24}H_{26}N_4O_6Ru$: C, 50.79; H, 4.62. Found: C, 50.59; H, 4.72%.

§ $PhI(OAc)_2$ was purchased from ACROS. See *Encyclopedia of Reagents for Organic Synthesis*, ed. L. A. Paquette, Wiley, New York, 1995, vol. 2, p. 1479.

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