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Intermolecular asymmetric cyclopropanation with diazoketones catalyzed by chiral ruthenium porphyrins

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Abstract

The asymmetric addition of diazoacetophenone to styrene derivatives to give optically active cyclopropyl ketones (ee up to 86%) was carried out by using chiral ruthenium porphyrins as homogeneous catalysts.

Keywords: Diazoacetophenone; Ruthenium porphyrins; Optically active cyclopropyl ketone; Chiral porphyrins

Optically active metalloporphyrins have been reported to be efficient catalysts for carbene transfer reactions, especially with ethyl diazoacetate.[1,2] Despite high asymmetry inducing ability of chiral metalloporphyrins to cyclopropanation reactions, their application is essentially limited to diazoester addition to styrene derivatives. In the course of our study on asymmetric cyclopropanation, we also found however, that other diazo derivatives, rarely used in asymmetric cyclopropanation, such as diazophosphonates,[3] trifluorodiazoethane[4] and diazoacetonitrile[5] showed high asymmetric additions to alkenes. Thus, achievements in asymmetric catalytic metal carbene transformations are impressive, but they are however, by no means complete. Surprisingly, if many chiral complexes have proven to be selective catalysts for intramolecular cyclopropanation with diazoketones,[6] they have not been extended to intermolecular asymmetric cyclopropanation except for one example with chiral bis [camphorquinone-α-dioximato] cobalt complex (20% enantiomeric excess).[7] To extend the utility of metalloporphyrin complexes as cata- lysts, we examined herein the use of ruthenium complexes of chiral porphyrins as catalysts for intermolecular asymmetric cyclopropanation with diazo ketones.

meso-Tetraphenylporphyrin carbonyl ruthenium (TPP)-Ru(CO) catalyzed decomposition of diazo acetophenone (DAP) in the presence of styrene in dichloromethane resulted in the formation of the corresponding cyclopropane in 70% yield with a good stereoselectivity (trans/cis ratio: 95/5) (Scheme 1) and (20%) of olefin resulting in the dimerization of the carbene. To extend the scope of this cyclopropanation, the reaction of a number of styrene derivatives with DAP in the presence of (TPP)Ru(CO) at 25 °C in dichloromethane was studied. The results are summarized in Table 1. Then, cyclopropanation competition experiments were conducted with a large excess of each substrate and limiting quantities of diazo acetophenone (substrate/DAP = 10:1) (Table 2). The relative reactivities were measured by the molar ratio in gas chromatography of cyclopropyl ketones derived from styrene and from other substrates. In all these experiments, cyclopropanes are the major products, usually obtained with carbene dimers as by-products. Electron-rich styrenes (4-methoxy or 4-methyl styrene) are cyclopropanated more efficiently than styrenes bearing electron-withdrawing groups (4-Cl or 4-CF_3). In the latter two cases, a significant amount of olefins, resulting from dimerization of the carbenes, were also detected (20–28%).

The data were fit to a Hammett plot of $\log(k_X/k_H)$ versus σ with a good correlation ($r^2 = 0.955$), which allowed

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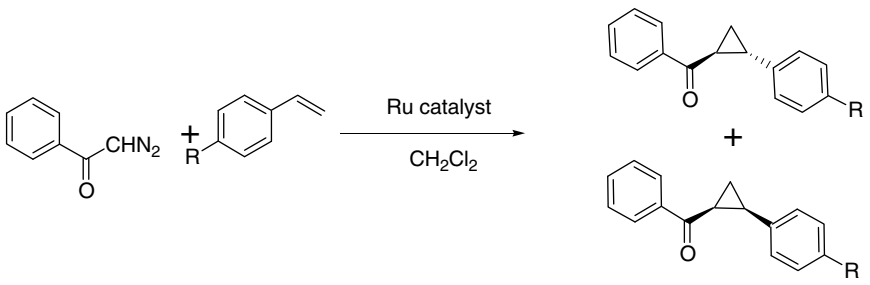

Scheme 1. Cyclopropanation of styrene with diazo acetophenone catalyzed by Ru porphyrin complex.

Table 1
Cyclopropanation of styrene with diazo acetophenone by *meso*-tetraphenylporphyrin carbonyl ruthenium complex: (TPP)Ru(CO) (0.5 ml CH_2Cl_2, 0.5 mmol alkene, 0.1 mmol DAP in 0.5 ml of CH_2Cl_2, reaction time 24 h, rt)

Entry	Catalyst	*p*-R-Styrene	Yield (GC %)	Ratio (trans/cis)	Dimer (%)
1	(TPP)Ru(CO)	H	70	95:5	20
2	(TPP)Ru(CO)	Me	70	98:2	9
3	(TPP)Ru(CO)	OMe	75	99:1	0.5
4	(TPP)Ru(CO)	Cl	40	96:4	20
5	(TPP)Ru(CO)	CF_3	60	96:4	28

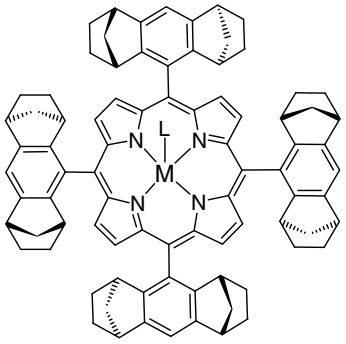

Fig. 1. Chiral metalloporphyrin catalysts (M–L: RuCO **1**, M–L: RuCH(COPh) **2**).

Table 2
Competition studies of the cyclopropanation of various substituted styrenes (substrates A) and styrene (substrate B) with DAP catalyzed by (TPP)Ru(CO) in 0.5 ml CH_2Cl_2 (catalyst: 1 mg, styrenes: 0.5 mmol; DAP 0.05 mmol; 24 h; rt)

Substrate A	Ratio of products derived from A/B
4-Methoxystyrene	2.95
4-Methylstyrene	1.65
4-Chlorostyrene	0.78
4-Trifluoromethylstyrene	0.53

Table 3
Asymmetric cyclopropanation of styrene with diazoacetophenone by chiral complex (P*)Ru(CO) **1** (see Fig. 1)

Entry[a]	*p*-R-Styrene	Yield (GC %)	Ratio (trans/cis)	ee[b] (% trans HPLC)	Dimer (%)
1	H	57	95:5	83	10
2	Me	83	98:2	83	13.8
3	OMe	80	99:1	84	1
4	CF_3	46	95:5	86	30
5	Cl	45	95:5	84	15

[a] Catalyst: Carbonyl-{5,10,15,20-tetrakis[1*S*,4*R*,5*R*,8*S*-1,2,3,4,5,6,7,8-octahydro-1,4:5,8-dimethanoanthracene-9-yl]porphyrinato}ruthenium (II), experimental conditions as in Table 1.
[b] Determined by chiral GC (CP-Chiracel OC).

us to calculate a ρ value of -1.08 ± 0.16. A similar negative value was observed for cyclopropanation reaction with ethyl diazoacetate catalyzed by (TPP)Ru(CO) ($\rho = -1.29 \pm 0.08$).[1] This value is also similar to that reported for the cyclopropanation of substituted styrenes and ethyldiazoacetate by Kodadeck and Woo et al.[8] ($\rho = -0.68$) using iron porphyrin and by Perez and Brookhart et al.[9] ($\rho = -0.85$) using copper pyrazoylborate complexes. The small negative value of ρ suggests only a moderate positive charge build-up at the carbene atom in the transition state according to an electrophilic metal-carbene complex intermediate (vide infra).

The asymmetric version was also tested using Halterman porphyrin[10] as chiral ligand (Fig. 1). To evaluate the reactivity of the diazoacetophenone, its ruthenium-catalyzed decomposition was examined in the presence of styrene in dichloromethane at room temperature by using **1** as the catalyst (Table 1). The diazo derivatives were added slowly to the reaction mixture over 30 min and the reaction was stopped after 24 h. The cyclopropane was formed in 57% yield, with 95/5 trans/cis ratio and 83% enantioselectivity for the trans isomer (entry 1). We also investigated the cyclopropanation of *para*-substituted styrenes (Table 3). As shown in Table 3, *para*-substitution (*p*-Y-styrene, Y = MeO, Br and H) does not have a significant effect upon the enantioselectivity of styrene cyclopropanation (83–86%) but better yields (80–83%) were obtained with electron-rich styrenes (4-methoxy or 4-methyl styrene).

In rutheniumporphyrin catalyzed cyclopropanation, the corresponding carbene complexes which take octahedral coordination in the presence of axial ligand (solvent) are considered as the active intermediates. As an example, we reported the first X-ray structure of a ruthenium porphyrin carbene complex with a methanol as an axial ligand trans to the Ru–carbon bond.[1] Since ketocarbenes are found to be easily inserted in metal–nitrogen bond of iron porphyrin,[11,12] preparation of the ruthenium ketocarbene

complex was undertaken. Thus, the reaction of the chiral carbonyl ruthenium complex **1** with excess of diazoacetophenone in dichloromethane results in the displacement of the CO ligand and generation of the brown carbene complex **2** (Fig. 1). The carbene complex was not stable enough to be purified by chromatography on silica gel but can be characterized by HMQC NMR at low temperature (193 K). Analysis of the NMR spectrum shows a low-field cross-peak between the carbene carbon at 234.7 ppm and the carbene proton at 13.26 ppm. The ^{1}H chemical shift is in the range of those previously reported for such Ru=CHR porphyrin complexes.[13]

To date, several chiral ruthenium complexes,[14] in particular, ruthenium–pybox compounds[15,16] are also excellent catalysts for homogeneous asymmetric intermolecular cyclopropanation of alkenes with diazo compounds, giving high enantioselectivity and diastereoselectivity but they suffer mainly from low catalyst turnover. Immobilization of these systems on solid supports has also received a great deal of attraction with some success in terms of recyclability.[17] However, high catalyst turnovers could be obtained with metalloporphyrins due to the relative chemical and thermal stability of the porphyrin ring and these complexes do not suffer from the problem of the low accessibility to the catalytic sites inherent to immobilized catalysts.

In summary, the asymmetric cyclopropanation using diazoacetophenone catalyzed by chiral metalloporphyrins occurs in a good stereoselective manner, offering for the first time, a general access to optically active cyclopropylketones.[18]

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References and notes

1. Simonneaux, G.; Le Maux, P. *Coord. Chem. Rev.* **2002**, *228*, 43–60.
2. Che, C. M.; Huang, J. S.; Lee, F. W.; Li, Y.; Lai, T. S.; Kwong, H. L.; Teng, P. F.; Lee, W. S.; Lo, W. C.; Peng, S. M.; Zhou, Z. Y. *J. Am. Chem. Soc.* **2001**, *123*, 4119–4129.
3. Ferrand, Y.; Le Maux, P.; Simonneaux, G. *Org. Lett.* **2004**, *6*, 3211–3214.
4. Le Maux, P.; Juillard, S.; Simonneaux, G. *Synthesis* **2006**, *10*, 1701–1704.
5. Ferrand, Y.; Le Maux, P.; Simonneaux, G. *Tetrahedron: Asymmetry* **2005**, *16*, 3829–3836.
6. Barberis, M.; Pérez-Prieto, J.; Herbst, K.; Lahuerta, P. *Organometallics* **2002**, *21*, 1667–1673.
7. Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3443–3448.
8. Wolf, J. R.; Hamaker, C. G.; Djukic, J. P.; Kodadek, T.; Woo, L. K. *J. Am. Chem. Soc.* **1995**, *117*, 9194–9199.
9. Diaz-Requejo, N. M.; Perez, P. J.; Brookhart, M.; Templeton, J. L. *Organometallics* **1997**, *16*, 4399–4404.
10. Halterman, R. L.; Jan, S. T. *J. Org. Chem.* **1991**, *56*, 5253–5254.
11. Komives, E. A.; Tew, D.; Olmstead, M. M.; Ortiz de Montellano, P. R. *Inorg. Chem.* **1988**, *27*, 3112–3117.
12. Artaud, I.; Gregoire, N.; Battioni, J. P.; Dupré, D.; Mansuy, D. *J. Am. Chem. Soc.* **1988**, *110*, 8714–8716.
13. Simonneaux, G.; Le Maux, P. Carbene complexes of metalloporphyrins and heme proteins. In Kadish, K. M., Smith, K. M., Guilard, R., Eds.; The Pophyrin Handbook; Academic Press: San Diego, 2003; 11, pp 133–159.
14. For a recent paper, see: Hoang, V. D. M.; Reddy, P. A. N.; Kim, T. J. *Tetrahedron Lett.* **2007**, *48*, 8014–8017.
15. Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S. B.; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116*, 2223–2224.
16. Nishiyama, H. *Top. Organomet. Chem.* **2004**, *11*, 81–92.
17. Cornejo, A.; Fraile, J. M.; Garcia, J. I.; Gil, M. J.; Luis, S. V.; Martinez-Merino, V.; Mayoral, J. A. *J. Org. Chem.* **2005**, *70*, 5536–5544.
18. All new compounds reported here gave spectral data consistent with the assigned structures. Selected data: For *trans*-1-benzoyl-2-phenylcyclopropane: $[\alpha]_D$ +390 (*c* 1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.05 (d, 2H, $J = 7.8$ Hz, Ph); 7.66–7.22 (m, 8H, COPh and Ph); 2.95 (m, 1H, C*H*(COPh)); 2.75 (m, 1H, C*H*Ph); 2.02–1.56 (m, 2H, CH_2). ^{13}C ($CDCl_3$, 75 MHz): δ 198.79 (CO); 139.10 (Ph); 136.20 (COPh); 132.91 (COPh); 128.56 (COPh); 128.56 (Ph); 128.11 (COPh); 126.60 (Ph); 126.23 (Ph); 30.01 (CH–Ph); 29.30 (CH–COPh); 19.24 (CH_2). HR-MS (*m*/*z*): calcd for $C_{16}H_{14}O$ ($M^{+\cdot}$): 222.10447. Found: 222.1037. For *trans*-1-benzoyl-2-(*p*-methoxyphenyl)cyclopropane: $[\alpha]_D$ +240 (*c* 1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.03 (d, 2H, $J = 8$ Hz, Ph); 7.64–7.46 (m, 3H, Ph); 7.18–6.87 (dd, 4H, $J = 10$ Hz, $J = 76$ Hz, *p*-OMe*Ph)*; 3.84 (s, 3H, OMe); 2.87 (m, 1H, C*H*(COPh)); 2.69 (m, 1H, C*H*(*p*-OMePh)); 2.39 (s, 3H, CH_3); 1.98–1.51 (m, 2H, CH_2). ^{13}C ($CDCl_3$, 75 MHz): δ 199.15 (CO); 158.84 (*p*-OMePh); 138.21 (Ph); 133.29 (Ph); 130.49 (*p*-OMePh); 128.97 (Ph); 128.52 (CH–COPh); 21.03 (CH_3); 19.41 (CH_2). For *trans*-1-benzoyl-2-(*p*-methylphenyl)cyclopropane: $[\alpha]_D$ +270 (*c* 1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.01 (d, 2H, $J = 8.1$ Hz, Ph); 7.65–7.45 (m, 3H, Ph); 7.20–7.09 (dd, 4H, $J = 6$ Hz, $J = 13.8$ Hz, *p*-Me*Ph*); 2.90 (m, 1H, C*H*(COPh)); 2.71 (m, 1H, C*H*(*p*-MePh)); 2.39 (s, 3H, CH_3); 1.95–1.59 (m, 2H, CH_2). ^{13}C ($CDCl_3$, 75 MHz): δ 198.68 (CO); 137.77 (*p*-MePh); 137.42 (Ph); 136.26 (*p*-MePh); 133.55 (Ph); 129.54 (Ph); 129.24 (*p*-MePh); 128.10 (Ph); 126.15 (*p*-MePh); 30.93 (CH-*p*-MePh); 29.32 (CH–COPh); 21.03 (CH_3); 19.09 (CH_2). HR-MS (*m*/*z*): calcd for $C_{17}H_{16}O$ ($M^{+\cdot}$): 236.12012. Found: 236.1216. For *trans*-1-benzoyl-2-(*p*-trifluoromethylphenyl) cyclopropane: $[\alpha]_D$ +216.8 (*c* 1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.05 (d, 2H, $J = 6.6$ Hz, Ph); 7.66–7.47 (m, 3H, Ph); 7.34–7.30 (d, 4H, $J = 7.6$ Hz, *p*-CF_3*Ph*); 2.97(m, 1H, C*H*(COPh)); 2.77 (m, 1H, C*H*(*p*-CF_3Ph)); 2.05–1.50 (m, 2H, CH_2). ^{13}C ($CDCl_3$, 75 MHz): δ 198.43 (CO); 145.15 (*p*-CF_3Ph); 137.88 (Ph); 133.60 (Ph); 129.10 (*p*-CF_3Ph); 128.99 (*p*-CF_3Ph); 128.56 (Ph); 128.40 (*p*-CF_3Ph); 126.88 (Ph); 125.92 (CF_3); 29.85 (CH–*p*-CF_3Ph); 29.63 (CH–COPh); 19.89 (CH_2). HR-MS (*m*/*z*): calcd for $C_{17}H_{13}OF_3$ ($M^{+\cdot}$): 290.09185. Found: 290.0902. For *trans*-1-benzoyl-2-(*p*-chlorophenyl)cyclopropane: $[\alpha]_D$ +298.8 (*c* 1, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.03 (d, 2H, $J = 7.2$ Hz, Ph); 7.66–7.46 (m, 3H, Ph); 7.34–7.12 (dd, 4H, $J = 8.44$ Hz, $J = 34$ Hz, *p*-Cl*Ph*); 2.91 (m, 1H, C*H*(COPh)); 2.69 (m, 1H, C*H*(*p*-ClPh)); 1.96–1.57 (m, 2H, CH_2). ^{13}C ($CDCl_3$, 75 MHz): δ 198.23 (CO); 139.01 (*p*-ClPh); 137.16 (Ph); 133.05 (Ph); 130.38 (*p*-ClPh); 128.91 (*p*-ClPh); 128.62 (Ph); 128.50 (*p*-ClPh); 127.96 (Ph); 29.24 (CH-*p*-ClPh); 29.15 (CH–COPh); 19.16 (CH_2). HR-MS (*m*/*z*): calcd for $C_{16}H_{13}O^{35}Cl$ ($M^{+\cdot}$): 256.06549. Found: 256.0664.