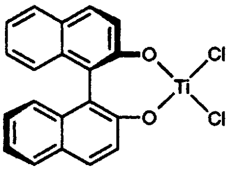
Binaphthol-derived Titanium μ-Oxo Complex: a New Type of Asymmetric Catalyst for Carbonyl-ene Reaction with Glyoxylate

Masahiro Terada and Koichi Mikami*

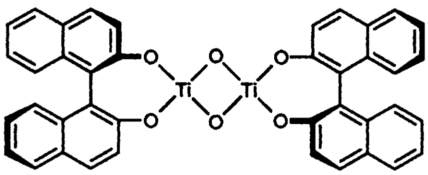
Department of Chemical Technology, Tokyo Institute of Technology, Meguro-ku, Tokyo 152, Japan

The binaphthol (binol)-derived chiral titanium μ-oxo complex **O** is obtained accidentally upon toluene azeotropy from a solution of binol and $(Pr^iO)_2TiCl_2$ after filtration of ms 4 Å and shown to be an efficient asymmetric catalyst for the glyoxylate-ene reaction with α-methylstyrene to give 98.7% entaniomeric excess and 88% yield even by the use of 0.2 mol% of the complex **O**.

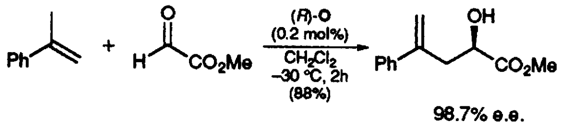
Development of an asymmetric catalyst for carbon–carbon bond formation, in particular, is the most challenging and formidable endeavor in organic synthesis.[1] We have recently developed an enantioselective catalysis of carbonyl-ene reaction with glyoxylate catalysed by the binaphthol-derived chiral titanium dihalide complexes **X**, which provide an efficient access to the asymmetric synthesis of α-hydroxyesters of biological and synthetic importance.[2] We now report a binaphthol-derived chiral titanium μ-oxo complex **O**, which is obtained accidentally and found to be an efficient asymmetric catalyst for the glyoxylate-ene reaction.



(*R*)-X



(*R*)-O



(1)

Table 1 Molecular mass of binol-derived titanium complexes **O**

O	Conc. $g\,l^{-1}$	Molecular mass
(*R*)-**O**[a]	12.00	786
	6.00	752
	3.00	748
	1.50	682
(±)-**O**[b]	11.64	811
	5.82	795
	2.91	793
	1.46	815

[a] Prepared from (*R*)-binol and $(Pr^iO)_2TiCl_2$. [b] Prepared from (±)-binol and $(Pr^iO)_2TiCl_2$.

The chiral titanium dihalide catalysts **X** have been prepared *in situ* from optically pure binaphthol (binol) and diisopropoxytitanium dihalide [$(Pr^iO)_2TiX_2$: X = Br or Cl] in the presence of molecular sieves (ms 4 Å).[2] We have thus examined the isolation of **X** through azeotropic removal of propan-2-ol (toluene, 110 °C) from a toluene solution of binol and $(Pr^iO)_2TiCl_2$ after filtration of ms 4 Å employed for the alkoxy–ligand exchange, but surprisingly obtained the binol-derived chiral titanium μ-oxo complex **O**. Complex **O** is shown to be an efficient asymmetric catalyst for glyoxylate-ene reaction with α-methylstyrene even by the use of 0.2 mol% of complex **O** to give 98.7% enantiomeric excess (e.e.) of the ene product in 88% chemical yield [eqn. (1)]. Methylenecyclohexane also provides the glyoxylate-ene product with >99% e.e. in 68% isolated yield using 1 mol% of complex **O**. Surprisingly indeed, the IR spectra of **O** show clearly the strong absorption at 770 and 791 cm^{-1} of μ-oxotitanium bonds (Ti–O–Ti) rather than Ti=O bands.[3] Consequently, the elemental analyses of **O** indicates essentially no content of chlorine atom [found: 1.2%, calcd. for the dichloride complex (**X**: X = Cl): 17.6%]. These results suggest that the thermolysis of titanium dichloride with propan-2-ol would result in the formation of a titanium μ-oxo complex.[4]

The μ-oxo, namely dimeric nature of our binol-derived complex **O** is further proven by the vapour pressure osmometric molecular mass (M_r) measurement in dichloromethane at 30 °C (Table 1).[5] Interestingly, the M_r of homochiral complex (*R*)(*R*)-**O** (Fig. 1,† A) prepared from enantiomerically pure binol was concentration dependent, ranging from 682 [calc. 696.4 for $(C_{20}H_{12}O_2TiO)_2$] in 1.5 $g\,l^{-1}$ solution to 786 in 12 $g\,l^{-1}$ solution. By contrast, the M_r of the heterochiral

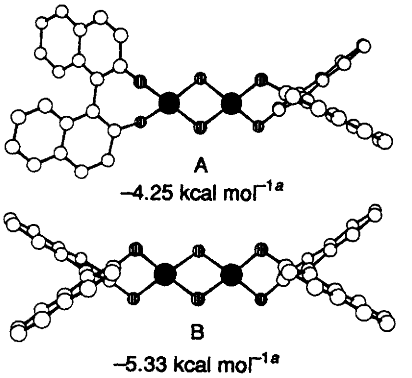


Fig. 1 3D Representation of (*R*)(*R*)-**O** A and (*R*)(*S*)-**O** B; 1 cal = 4.184 J. [a] Final steric energy.

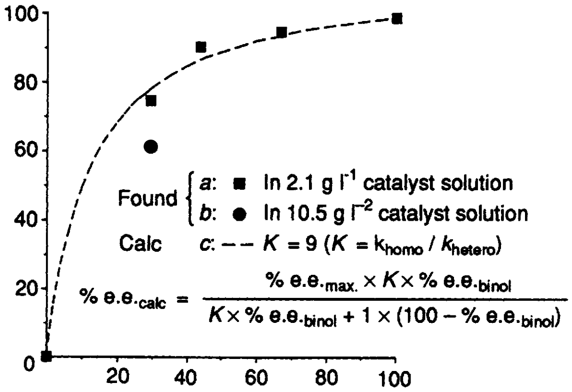


Fig. 2 Positive nonlinear effect in the glyoxylate-ene reaction with α-methylstyrene

complex (*R*)(*S*)-**O** prepared from racemic binol was not concentration dependent, indicating the stability of the *meso* complex **B**. The concentration dependence of the M_r of homochiral (*R*)(*R*)-**O** implies that the homochiral complex is relatively unstable as shown by the higher steric energy calculated for A and hence dissociates to the monomeric form to some extent in dilute solutions. Thus, we have found a positive nonlinear effect[6] (asymmetric amplification) between e.e. values of binol employed and the glyoxylate-ene product, particularly in dilute solutions [Fig. 2(*a*)].[7] Furthermore, the observed relationship of e.e.s of the ene products to those of binol fits well with the nonlinear curve *c*, calculated on the basis of a 9 times rate (catalytic activity) difference ($K = k_{homo}/k_{hetero} = 9$) between the homo- and hetero-chiral μ-oxo complexes **O**.

Received, 16th November 1993; Com. 3/06852H

Footnote

† The 3D structures of A and B were geometrically optimized with the Molecular Mechanics version 2 run on a Tectronix CaChe molecular modelling workstation.

References

1 R. Noyori and M. Kitamura, in *Modern Synthetic Methods*, ed. R. Schefford, Springer-Verlag, Berlin, 1989, vol. 5, p. 115; B. Bosnich, *Asymmetric Catalysis*, Martinus Nijihoff, Dordrecht, 1986; H. B. Kagan, in *Comprehensive Organometallic Chemistry*, ed. G. Wilkinson, Pergamon, Oxford, 1982, vol. 8, p. 463; Y. Hayashi and K. Narasaka, *J. Synth. Org. Chem., Jpn.*, 1990, **48**, 280; K. Narasaka, *Synthesis*, 1991, 1; K. Mikami, M. Terada, S. Narisawa and T. Nakai, *Synlett*, 1992, 255.

2 K. Mikami, M. Terada and T. Nakai, *J. Am. Chem. Soc.* 1989, **111**, 1940; 1990, **112**, 3949.

3 K. Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, Wiley, New York, 3rd edn., 1978, D. C. Bradley, R. C. Mehrotra and D. P. Gaur, *Metal Alkoxides*, Academic Press, London, 1978.

4 Isopropoxytitanium trichloride has been reported to decompose on heating to titanium oxydichloride: G. A. Rasuwajew, L. M. Bobinowa and U. S. Etlis, *Tetrahedron*, 1959, **6**, 154; Reviews on organotitanium complexes: R. Feld and P. L. Cowe, *The Organic Chemistry of Titanium*, Butterworths, London, 1965; D. Seebach, B. Weidmann and L. Widler, in *Modern Synthetic Methods*, ed. R. Schefford, Springer-Verlag, Berlin, 1989, vol. 3; M. T. Reetz, *Organotitanium Reagents in Organic Synthesis*, Springer-Verlag, Berlin, 1986.

5 A monomeric binol-derived titanium oxide (Ti=O) has been reported as an efficient asymmetric catalyst for the Mukaiyama aldol reaction, which is prepared from binol and $(Pr^iO)_2Ti{=}O$ obtained on hydrolysis of $(Pr^iO)_4Ti$ with water (B. C. Bradley, R. Caze, and W. Wardlaw, *J. Chem. Soc.*, 1955, 721): T. Mukaiyama, A. Inubushi, S. Suda, R. Hara and S. Kobayashi, *Chem. Lett.*, 1990, 1015.

6 For the positive nonlinear effect in the glyoxylate-ene reaction catalysed by the binol-derived titanium dihalide complexes **X**, see: K. Mikami and M. Terada, *Tetrahedron*, 1992, **48**, 5671.

7 For an excellent review on asymmetric amplification phenomena: R. Noyori and M. Kitamura, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 49.