Tetrahedron Letters, Vol.31, No.21, pp 3003-3006, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

HETEROGENEOUS CATALYTIC ASYMMETRIC DIHYDROXYLATION: USE OF A POLYMER-BOUND ALKALOID

B. Moon Kim and K. Barry Sharpless*

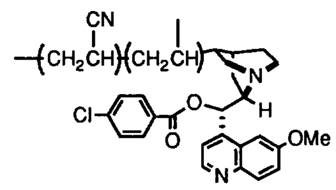
Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

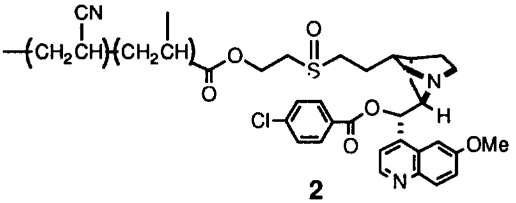
Summary: By employing polymer-bound alkaloid derivatives, heterogeneous catalytic asymmetric dihydroxylation has been achieved with good to excellent enantioselectivities in the dihydroxylation of *trans*-stilbene. It has also been shown that the OsO_4–polymer complex can be used for iterative processes.

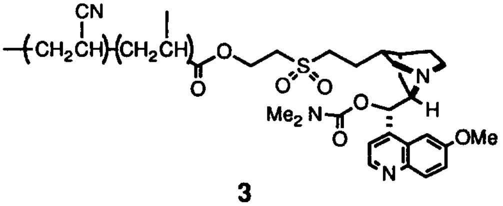
Recently we reported a practical catalytic asymmetric dihydroxylation (ADH) of olefins using a catalytic amount of osmium tetroxide in the presence of cinchona alkaloid derivatives.[1] Industrial scale syntheses of optically active vicinal diols are now possible with this catalytic system. As part of our continuing effort to further improve convenience and economy of this new process, we investigated the possibility of recycling the alkaloid–OsO_4 complex; we now wish to report an efficient heterogeneous asymmetric dihydroxylation utilizing polymer-bound cinchona alkaloid derivatives.[2]

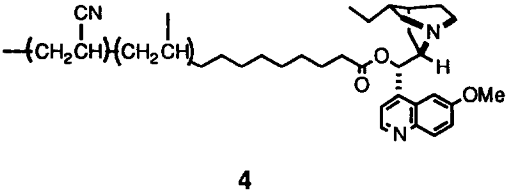
Reports of polymer-bound cinchona alkaloids in connection with asymmetric heterogeneous catalysis are common, and many routes exist for the preparation of various polymer-bound cinchona alkaloids.[3-13] We initiated our study of heterogeneous asymmetric dihydroxylation with copolymer **1** obtained by the straightforward copolymerization of 9-(*p*-chlorobenzoyl)quinidine with acrylonitrile.[9] The asymmetric dihydroxylation of *trans*-stilbene using **1** proceeded very slowly (entry 1 in the Table) presumably due to steric congestion resulting from the alkaloid being too close to the polymer backbone. Accordingly, we investigated copolymers with longer spacer groups such as **2**, **3**, and **4**.

Polymers **2** and **3** were prepared by slightly modifying[14] literature procedures (Scheme 1).[13] Polymer **4** was prepared by copolymerizing 9-(10-undecenoyl)dihydroquinidine in the presence of acrylonitrile (5 eq) in 13% yield with lower level of alkaloid incorporation (4%). With these polymers in

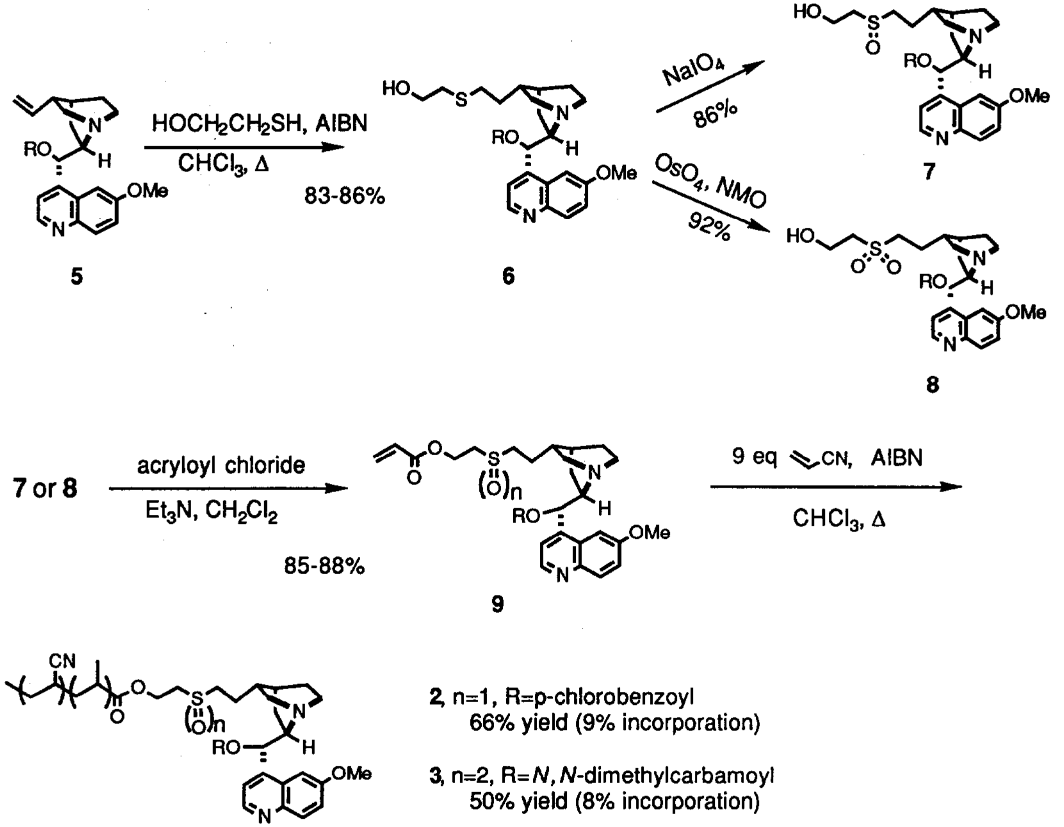

1


2


3


4

Scheme 1



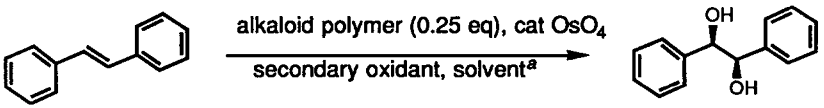
2, n=1, R=p-chlorobenzoyl
66% yield (9% incorporation)

3, n=2, R=*N,N*-dimethylcarbamoyl
50% yield (8% incorporation)

hand, we investigated the ADH of *trans*-stilbene. The results are summarized in the Table. With all the polymers examined except 1, good to excellent asymmetric induction and reasonable reaction rates were observed. Reaction with polymer 2 exhibited the highest degree of asymmetric induction (entry 2). As is exemplified in entries 6 and 8, the use of $K_3Fe(CN)_6$ as a secondary oxidant noticeably improved the yield and enantioselectivity of the reaction.[15] It is particularly noteworthy that the activity of the OsO_4–polymer complex is preserved after the reaction thus allowing repetitive use of the complex with only moderate loss of reactivity and enantioselectivity (entry 4). Studies on the scope of this reaction with various olefins as well as the screening of different types of polymers (including cross-linked polymers) are currently in progress.

In closing we note that this approach seems to be more effective at localizing the osmium in the polymer than was thought possible. Either the binding constant of the alkaloid for the OsO_4 is greater in the polymer than in free solution (where K~15–30) and/or the general environment of the polymer is also attractive for OsO_4. Some osmium seems to be lost (cf. entries 3 and 4) but one may be able to contain it by using a flow system through polymer cartridges in which the flow is periodically reversed or the cartridges are moved from one end to the other. In any case, the prospect of containing for continuous use both the osmium and the alkaloid, the two expensive components, makes this approach highly attractive.

Table. Heterogeneous Catalytic ADH of *trans*-Stilbene Using Various Polymeric Alkaloids[16]



Entry	Polymers	OsO_4	Secondary Oxidant	Reaction Temp	Reaction Time	Yield (%)	ee (%)
1	**1**	1 mol%	NMO	rt	7 d	68	–
2	**2**	1 mol%	NMO	10 °C	2–3 d	81-87	85-93[b]
3	**2**	1 mol%	NMO	rt	24 h	81	82
4	**2**	–[c]	NMO	rt	36 h	75	78
5	**3**	1 mol%	NMO	0 °C	48 h	85	80
6	**3**	1.25 mol%	$K_3Fe(CN)_6$	rt	18 h	96	87
7	**4**	1 mol%	NMO	10 °C	48 h	87	82
8	**4**	1.25 mol%	$K_3Fe(CN)_6$	rt	48 h	91	86

[a] See reference 16 for experimental details of the two general procedures. With *N*-methylmorpholine-*N*-oxide (NMO) acetone/water (10/1, v/v) was the solvent and with ferricyanide tert-butyl alcohol/water (1/1, v/v) was used as solvent. [b] Results vary slightly depending on different batches of polymer **2**.
[c] Reaction was carried out with polymer **2** which had been used in entry 3 without further addition of OsO_4.

Acknowledgments: We are grateful to the National Institutes of Health (GM 28384) for financial support.

References and Notes

1. (a) Jacobson, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (b) Jacobsen, E. N.; Markó, I.; France, M. B.; Svendsen, J. S.; Sharpless, K. B. *Ibid*, **1989**, *111*, 737. (c) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *Ibid*, **1989**, *111*, 1123. (d) Lohray, B. B.; Kalantar, T. H.; Kim, B. M.; Park, C. Y.; Shibata, T.; Wai, J. S. M.; Sharpless, K. B. *Tetrahedron Lett.* **1989**, *30*, 2041.
2. The use of achiral polymer-bound OsO_4 has been recently reported: Cainelli, G.; Contento, M.; Manescalchi, F.; Plessi, L. *Synthesis* **1989**, 45.
3. Grubhofer, N.; Schleith, L. *Naturwissenschaften* **1953**, *40*, 508.
4. (a) Yamauchi, K.; Kinoshita, M.; Imoto, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3186. (b) Yamauchi, K.; Mitsuda, Y.; Kinoshita, M. *J. Macromol. Sci., Chem.* **1976**, *A10*, 981.

5. (a) Pinazzi, C.; Menil, A.; Pleurdeau, A. C. R. *Acad. Sci., Ser. C* **1973**, *277*, 89. (b) Pinazzi, C.; Menil, A.; Rabadeux, J. C.; Pleurdeau, A. *J. Polym. Sci., Polum. Symp.* **1975**, *No. 52*, 1.
6. Hermann, K.; Wynberg, H. *Helv. Chim. Acta* **1977**, *60*, 2208.
7. (a) Yamashita, T.; Yasueda, H.; Nakamura, N. *Chem. Lett.* **1974**, 585. (b) Yamashita, T.; Yasueda, H.; Miyauchi, Y.; Nakamura, N. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1532. (c) Yamashita, T.; Yasueda, H.; Nakatani, N.; Nakamura, N. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1183.
8. Mitsuaki, N. *J. Polym. Sci., Polym. Chem. Ed.* **1977**, *15*, 353.
9. (a) Kobayashi, N.; Iwai, K. *J. Am. Chem. Soc.* **1978**, *90*, 7071. (b) Idem *J. Polym. Sci., Polym. Chem. Ed.* **1980**, *18*, 223. (c) Idem, *Ibid*, 923. (d) Idem, *Macromolecules* **1980**, *13*, 31. (e) Idem, *J. Polym. Sci., Polym. Lett. Ed.* **1980**, *18*, 417. (f) Idem, *Tetrahedron Lett.* **1980**, *21*, 2167. (g) Idem, *Polym. J.* **1981**, *13*, 263. (h) Idem, *J. Polym. Sci., Polym. Lett. Ed.* **1982**, *20*, 85.
10. (a) Hodge, P.; Khoshdel, E.; Waterhouse, J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2205. (b) Idem, *Ibid*, **1985**, 2327.
11. Boyer, B.; Lamaty, G.; Roque, J.-P.; Solofo, J. *Nouv. J. Chim.* **1986**, *10*, 559.
12. (a) Salvadori, P.; Rosini, C.; Pini, D.; Bertucci, C.; Altemura, P.; Uccelo-Barretta, G.; Raffaelli, A. *Tetrahedron*, **1987**, *43*, 4969. (b) Salvadori, P.; Rosini, C.; Pini, D.; Bertucci, C.; Uccelo-Barretta, G. *Chirality* **1989**, *1*, 161.
13. Inagaki, M.; Hiratake, J.; Yamamoto, Y.; Oda, J. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4121.
14 The sulfide linkage was oxidized to sulfoxide or sulfone to avoid the consumption of secondary oxidant or catalyst.
15. (a) *Tetrahedron Lett.* preceding paper in this issue. (b) Minato, M.; Yamamoto, K.; Tsuji, J. *J. Org. Chem.* **1990**, *55*, 766.
16. (a) When NMO was used as the secondary oxidant: To a magnetically stirred suspension of the alkaloid polymer (0.25 eq based on alkaloid incorporated), NMO (1.5 eq), and tetraethylammonium acetate tetrahydrate (1.0 eq) in acetone–water (10/1, v/v) was added a solution of OsO_4 (0.01 eq) in either toluene or acetonitrile. After stirring for 10 min, *trans*-stilbene (1.0 eq) was added and the reaction mixture was stirred for the given time and monitored by silica gel TLC (hexane-EtOAc 2/1, v/v). The concentration of olefin in the reaction mixture was 0.3–0.4 M. After the reaction was complete, the mixture was diluted with acetone and centrifuged to separate the polymer from the reaction mixture. The supernatant was then worked up as described in reference 1. (b) When $K_3Fe(CN)_6$ was used as the secondary oxidant: To a well-stirred mixture of the alkaloid polymer (0.05 mmol, based on alkaloid incorporated), potassium ferricyanide (0.198 g, 0.6 mmol) and potassium carbonate (0.83 g, 0.6 mmol) in tert-butanol (1.5 mL) and water (1.5 mL), was added OsO_4 solution (0.0025 mmol) in acetonitrile. After stirring for 10 min, *trans*-stilbene (36 mg, 0.2 mmol) was added and the mixture was stirred for the given time and monitored by silica gel TLC. When the reaction was complete, water (3.0 mL) was added and the mixture was filtered. The filtrate was extracted with dichloromethane (5 mL x 2) and the organic layer was stirred for 1 h with excess sodium metabisulfite and sodium sulfate. This suspension was filtered and the filtrate was concentrated to provide crude diol, which was purified on a silica gel column.

(Received in USA 12 March 1990)