[6] H-β zeolite (CP811E-22, protonated form, ZEOLYST Int.; Si/Al atomic ratio of 12/1) was used after it had been pelletized to 0.3–0.8 mm.

[7] a) H. Tsuneki, *Appl. Catal. A* **2001**, *221*, 209–217; b) M. Ueshima, H. Tsuneki in *Catalytic Science and Technology, Vol. 1* (Eds.: S. Yoshida, N. Takezawa, T. Ono), Kodansha-VCH, Tokyo, **1991**, pp. 357–360; c) M. Ueshima, Y. Shimasaki, Y. Hino, H. Tsuneki in *Acid-Base Catalysis* (Eds.: K. Tanabe, H. Hattori, T. Yamaguchi, T. Tanaka), Kodansha, Tokyo, **1989**, pp. 41–52; d) M. Ueshima, H. Yano, H. Hattori, *Sekiyu Gakkaishi* **1992**, *35*, 362–365; e) H. Tsuneki, Y. Shimasaki, K. Ariyoshi, Y. Morimoto, M. Ueshima, *Nippon Kagaku Kaishi* **1993**, *11*, 1209–1216.

[8] H-Mordenite (HSZ640HOA, protonated form, Tosoh Co.; Si/Al atomic ratio of 9/1) was used after it had been pelletized to 0.3–0.8 mm.

[9] Amorphous silica-alumina (N632L, Nikki Chemical Co.; SiO_2/Al_2O_3 molar ratio of 11/1, specific surface area 400 m^2g^{-1}) was used after it had been pelletized to 0.3–0.8 mm.

[10] γ-Alumina (N612N, Nikki Chemical Co.; specific surface area 200 m^2g^{-1}) was used after it had been pelletized to 0.3–0.8 mm.

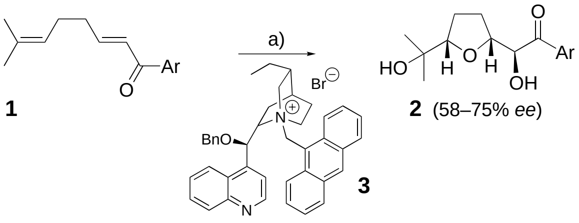
[11] After 6 h reaction time under supercritical conditions the H-mordenite catalyst was still white and very active. In contrast, reaction in the gas phase resulted in immediate blackening and deactivion of the catalyst due to coking.

[12] Effect of water: Water generated from methylation of **1** may possibly inhibit the reaction by competitive adsorption with the reactants on the catalyst surface. In fact, we found that the adsorption equilibrium constants (K) of CH_3OH and water are much larger than that of **1** by a simulation in the reaction kinetics by Langmuir–Hinshelwood mechanism, $K_{CH_3OH}/K_1 = 100$, $K_{water}/K_1 = 3000$. An increase in the portion of $scCH_3OH$ by changing the molar ratio of CH_3OH to **1** at the same amine contact time (W/F) improved the reaction conversion and the space–time yields, which suggests that desorption of the generated water from the catalyst surface could be promoted by $scCH_3OH$.

An Asymmetric Phase-Transfer Dihydroxylation Reaction**

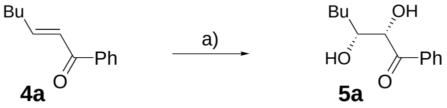
Riaz A. Bhunnoo, Yulai Hu, Dramane I. Lainé, and Richard C. D. Brown*

The asymmetric dihydroxylation of olefins using osmium tetraoxide is a powerful process that has found widespread application in organic synthesis.[1] Systems developed to date realize enantioinduction through the use of chiral ligands on the osmium center,[2] or chiral auxilliaries present in the substrate.[3,4] Here we report a conceptually different approach to asymmetric dihydroxylation using permanganate in the presence of a chiral phase-transfer reagent.[5,6]Recently, we reported the asymmetric oxidative cyclization of 1,5-dienes **1** by permanganate using a chiral phase-transfer catalyst (Scheme 1).[5] Whereas the permanganate promoted oxidative cyclization reaction of 1,5-dienes and the formation of α-ketols from olefins occur under slightly acidic conditions, permanganate oxidations conducted under basic conditions favor dihydroxylation.[7] Therefore, permanganate oxidations using chiral phase-transfer agents in alkaline media should provide a new approach to asymmetric dihydroxylation.



Scheme 1. Asymmetric oxidative cyclization of 1,5-dienes **1**. a) $KMnO_4$ (powder) (1.6 equiv), AcOH (6.5 equiv), **3** (0.1 equiv)/CH_2Cl_2, −30 °C.

Enones had been shown to undergo permanganate oxidative cyclization reactions to afford tetrahydrofuran diols **2** with good levels of enantioselectivity (Scheme 1),[5,8] and were therefore chosen as substrates for initial dihydroxylation studies (Scheme 2). Oxidation of **4a** under liquid–liquid achiral phase-transfer conditions gave racemic diol **5a** as the major isolated product in reasonable yield (entry 1, Table 1). The majority of the remaining mass balance was accounted



Scheme 2. Phase-transfer promoted dihydroxylation of enone **4a**. For conditions and yields see Table 1.

Table 1. Phase-transfer (PT) promoted dihydroxylation of enone **4a** (see Scheme 2).[a]

Entry	Method[b]	PT [equiv]	Time [min]	Yield of **5a** [%][c] [BRSM [%]]	*ee*[d] [%]
1	A	Adogen 464 (1.0)	45	55	N/A
2	A	**3** (1.0)	45	41 [45]	47
3	B	**3** (1.0)	30	41 [96]	63
4	B	**3** (1.0)	60	51 [87]	62
5	B	**3** (1.0)	180	27 [40]	62
6	B	**3** (0.2)	420	33 [64]	63
7[e]	B	**3** (3.0)	60	30 [42]	61

[a] Reactions were conducted on a 0.37 mmol scale. [b] Method A: $KMnO_4$ (s) (0.37 mmol), CH_2Cl_2 (16 mL), pH 9 buffer (8 mL), 0 °C. Method B: $KMnO_4$ (s) (1.5 equiv), CH_2Cl_2, −60 °C. [c] Yields represent analytically pure isolated material. BRSM indicates the isolated yield based on recoved enone. [d] Enantiomeric excess was determined by HPLC using a CHIRALCEL OD-H column, hexane/*i*PrOH (80:20) eluent. R_t = 5.28 min (major), R_t = 6.24 min (minor). [e] Reaction carried out with three equivalents of $KMnO_4$.

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for by benzoic acid, resulting from oxidative cleavage of **4a**. The same reaction using the chiral phase-transfer reagent **3** gave optically enriched diol **5a** with an encouraging level of enantioselectivity (47% *ee*) (entry 2, Table 1). Further improvement of the enantioselectivity (61–63% *ee*) was seen with the same substrate at lower temperature in solid-liquid phase-transfer reactions (entries 4–6, Table 1). The results show a relatively fast and clean dihydroxylation of the substrate after 30 and 60 min (yields based on recovered enone 96% and 87%, entries 3 and 4, Table 1). Prolonged reaction times led to lower yields, as did excess $KMnO_4$ and phase-transfer reagent (entries 5 and 7). It was observed that the cinchonidine-derived phase-transfer agent **3** was destroyed under the oxidation conditions, explaining its lack of catalytic activity. This finding is in contrast to the results obtained for the oxidative cyclization reaction where as little as 1–5 mol% of the quaternary ammonium salt has been employed.[5]

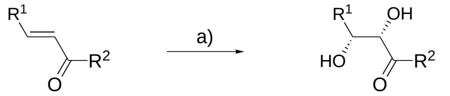
A variety of other alkenes were subjected to the dihydroxylation conditions (Table 2; Scheme 3), with all the *para*-substituted arylenones **4b–h** affording diols with *ee* values superior (up to 80% *ee*) to the simple phenyl derivative **4a**. The absolute stereochemistry of the major enantiomer was determined from the X-ray crystal structure of the bromo derivative **5b**, crystallized to enantiomeric purity from hexane.[9]

Preliminary efforts to extend the methodology to other types of olefins were less rewarding; a simple terminal olefin, 4-phenyl-1-butene, gave the corresponding diol without detectable *ee* and stilbene and chalcone gave over oxidation products. However, dihydroxylation of styrene did show a modest level of enantioselectivity, providing the (*S*)-diol with 17% *ee*.[10] The diminished enantioselectivity for dihydroxlation of other olefin classes was not unexpected on the basis of the mechanistic rationale previously presented, where a strong interaction with the chiral quaternary ammonium salt is required in the transition state.[5,6f]

Table 2. Asymmetric phase-transfer promoted dihydroxylation of enones **4b–h** (see Scheme 3).[a]

Entry	R^1	R^2	Time [min]	Yield [%][b] [BRSM [%]]	*ee*[d] [%]
1	*n*Bu	(*p*-Br)C_6H_4	60	52 [59]	77
2	*n*Bu	(*p*-Cl)C_6H_4	60	32 [64]	77
3[c]	*n*Bu	(*p*-F)C_6H_4	180	25	67
4	*n*Bu	(*p*-OMe)C_6H_4	90	34 [61]	80
5	*n*Bu	(*p*-Me)C_6H_4	60	40 [93]	75
6	Et	Ph	60	19 [37]	65
7[e]	*i*Pr	Ph	60	28 [59]	67

[a] Reactions were conducted on a 0.26–0.37 mmol scale using one equivalent of **3** and 1.5 equivalents of $KMnO_4$ at −60 °C except for entry 3. [b] Yields represent analytically pure isolated material. BRSM is the yield calculated based on recovered starting material. [c] Reaction mixture warmed to −25 °C. [d] Enantiomeric excess was determined by HPLC using CHIRALCEL OD-H or OB-H columns, hexane/*i*PrOH eluent. [e] Enatiomeric excesses of compounds **4c** and **4d** were determined by conversion to the corresponding cyclic carbonates, which were resolved on a CHIRALCEL OD-H column (hexane/*i*PrOH, 90:10).[11]



4b-h **5b-h**

4b/5b R^1=*n*Bu, R^2=*p*-BrC_6H_4-; **4c/5c** R^1=*n*Bu, R^2=*p*-ClC_6H_4-;
4d/5d R^1=*n*Bu, R^2=*p*-FC_6H_4-; **4e/5e** R^1=*n*Bu, R^2=*p*-$MeOC_6H_4$-;
4f/5f R^1=*n*Bu, R^2=*p*-MeC_6H_4-; **4g/5g** R^1=Et, R^2=Ph;
4h/5h R^1=*i*Pr, R^2=Ph.

Scheme 3. Asymmetric phase-transfer promoted dihydroxylation of enones **4b–h**. a) $KMnO_4$ (powder) (1.2–1.5 equiv), **3** (1.0 equiv)/CH_2Cl_2, −60 °C.

In conclusion, a new approach to asymmetric dihydroxylation of enones has been demonstrated. The initial enantioselectivities obtained are good, although relatively large quantities of the chiral quaternary ammonium salt are required. Efforts to apply other, more oxidatively robust phase-transfer agents and other metal–oxo species in the dihydroxylation reaction are currently underway in our laboratory.

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