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A convenient procedure for the synthesis of racemic *syn*-1,2-diarylethane-1,2-diols by osmate catalyzed dihydroxylation of *trans*-stilbenes facilitated by Tröger base

Sakilam Satishkumar & Mariappan Periasamy*

School of Chemistry, University of Hyderabad, Central University P.O., Hyderabad 500 046, India

E-mail: mpsc@uohyd.ernet.in

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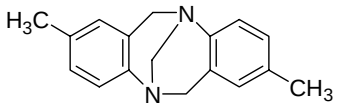
Racemic (*dl*) mixture of *syn*-1,2-diarylethane-1,2-diols are prepared from the corresponding substituted *trans*-stilbenes using osmate catalyzed dihydroxylation facilitated by racemic Tröger base under ambient conditions.

Keywords: Tröger base, *syn*-1,2-diols, *trans*-stilbenes, racemic dihydroxylation, potasium osmate (VI) dihydrate

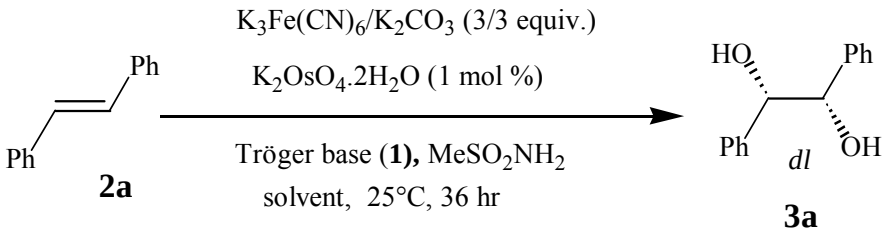
Generally, racemic mixtures can be more easily obtained than the corresponding chiral compounds. An interesting exception is the Sharpless osmium catalyzed asymmetric dihydroxylation reaction of alkenes facilitated by cinchona alkaloid ligands[1-3]. This reaction produces the chiral *syn*-1,2-diols in high yields with excellent enantioselectivities[3]. Unfortunately, the corresponding racemic cinchona alkaloid bases are not commercially available and hence it is very difficult to access racemic *syn*-1,2-diols using the Sharpless reaction and there are only a few methods reported[4]. The most widely used method for this purpose is the Upjohn procedure involving the volatile OsO_4 as catalytic oxidant and hazardous N-methylmorpholine-N-oxide (NMO) as the stoichiometric oxidant[4a]. The other available methods involve circuitous and tedious steps. For example, the meso and racemic isomeric mixture of 1,2-diarylethane-1,2-diols can be accessed by the $NaBH_4$ reduction of the corresponding substituted benzoin derivatives, which need to be prepared in turn from the corresponding aldehydes by benzoin condensation[5]. The racemic (*dl)* and meso mixture obtained in this way can be converted to racemic mixture by a base catalyzed reaction under vacuum following a somewhat tedious and sensitive procedure[5]. Herein, is reported a convenient procedure for the osmate catalyzed racemic dihydroxylation of olefins in the presence of racemic Tröger base **1**.



Tröger base **1**

Results and Discussion

In the course of efforts toward understanding the mechanism of the Sharpless asymmetric dihydroxylation reaction[6], there was a need for racemic *syn*-1,2-diols. Previously, Warren *et al.*[4f] reported $OsCl_3$ catalyzed dihydroxylation facilitated by the expensive quinuclidine base for the *syn*-1,2-diol synthesis. In continuation of the studies on the synthesis and application of chiral Tröger base **1** (Ref 7), the use of this easily accessible ligand has been examined for the osmium catalyzed dihydroxylation to produce *syn*-1,2-diols. Accordingly, the dihydroxylation of *trans*-stilbene **2a** was carried out using solid $K_2OsO_4.2H_2O$ as catalytic oxidant, $K_3Fe(CN)_6$ as stochiometric oxidant and the chiral Tröger base as accelerating ligand in the presence of K_2CO_3 and methanesulfonamide in $^tBuOH/H_2O$ solvent system. Indeed, the dihydroxylation of *trans*-stilbene **2a** was facilitated by Tröger base and the corresponding *syn*-1,2-diol **3a** was obtained in good yields but with poor enantioselectivity (6% *ee*) under these conditions. It was thought that the use of racemic Tröger base would give an easy access to racemic diols and hence



Scheme I — Racemic dihydroxylation of *trans*-stilbene **2a** facilitated by Tröger base **1**

Table I — Optimization of dihydroxylation of *trans*-stilbene **2a** using racemic Tröger base **1** as ligand at ambient conditions[a]

Entry	Solvent[b]	Amount of ligand **1** (mole %)	Yield of diol **3a** (%)[c]
1	^{t}BuOH/H_2O	10	58
2	^{t}BuOH/H_2O/Toluene	10	72
3	^{t}BuOH/H_2O/Toluene	5	66
4	^{t}BuOH/H_2O/Toluene	5	83
5	^{t}BuOH/H_2O/Toluene	10	92
6	^{t}BuOH/H_2O/Toluene	20	93

[a]All the reactions were carried out using *trans*-stilbene (2 mmole), K_2CO_3 (6 mmole), $K_3Fe(CN)_6$ (6 mmole), $K_2OsO_4.2H_2O$ (1 mole %) and methanesulfonamide (2 mmole). [b]In entry 1, ^{t}BuOH (20 mL)/H_2O (20 mL), in entries 2, 3 ^{t}BuOH (20 mL)/H_2O (20 mL)/ toluene (20 mL) and in entries 4, 5, 6 ^{t}BuOH (10 mL)/H_2O (10 mL)/ toluene (10 mL) used as solvents. The reaction-mixture was stirred at 25°C for 36 hr. [c]Yields reported here are for isolated products.

the conditions were optimized for this transformation (**Scheme I** and **Table I**).

The reaction was also carried out using different solvent systems with different ligand molar ratios for optimization of the reaction conditions. The results are summarized in **Table I**. The acceleration effect of Tröger base is summarized in **Table II**.

The reaction was carried out with various other stilbenes and the results are summarized in **Table III**. The substituted stilbenes were prepared from the corresponding aldehydes by using McMurry coupling in very good yields[8]. The reaction was also carried out with 2-phenylpropene **2h** and styrene **2i** and the corresponding diols were obtained in very good yields **(Scheme II** and **Table III)**.

Tröger base[9] is one of the most fascinating molecules in organic chemistry. This molecule contains chiral nitrogen centers and exists in two enantiomeric forms. Due to its rigid and concave shape, it has attracted an intense research in the last several decades[10]. Most of the reports on Tröger base deals with the synthesis of its analogs and their applications in molecular replication studies[11], molecular recognition phenomenon[12], and inclusion compounds[13]. Chiral Tröger base was also used in a few reactions like hydrosilylation of alkynes[14a], asymmetric hydrogenation reaction[14b] and asymmetric aziridination of chalcones[14c]. Chiral *syn*-1,2-diarylethane-1,2-diols are very useful ligands in asymmetric oxidation of prochiral sulfides to optically active sulfoxides[15a], asymmetric synthesis of allenic esters[15b] and also in the reduction of prochiral ketones using trimethoxysilane[15c]. Since racemic *syn*-1,2-diarylethane-1,2-diols can be readily resolved using (*S*)-proline following a procedure reported from this laboratory[5b], the method described here for accessing these racemic diols by the Tröger base facilitated osmium catalyzed dihydroxylation reaction has good synthetic potential.

Experimental Section

General procedure for dihydroxylation of *trans*-stilbenes in the presence of Tröger base 1 as ligand using toluene/^{t}BuOH/H_2O solvent system

To a mixture of potassium ferricyanide (6 mmole, 1.98 g), potassium carbonate (6 mmole, 0.84 g), ligand **1** (10 mole %, 50 mg) and potassium osmate dihydrate (1 mole %, 7 mg) was added toluene (10 mL) / ^{t}BuOH (10 mL) / H_2O (10 mL) and stirred vigorously at 25°C for 10 min and then the reaction-mixture was cooled to 0°C. To this solution was added methanesulfonamide (2 mmole, 0.19 g), substituted *trans*-stilbenes (2 mmole) at once and the mixture was stirred for 36 hr at 25°C. It was quenched with sodium sulfite (3 g). After stirring for 1.5 hr, the organic layer was separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layer was successively washed with 8 *N* hydrochloric acid, brine and then dried over anhyd. Na_2SO_4. The solvent was evaporated and the crude diol was purified by coloumn chromatography over silca gel using ethyl acetate:hexane (3:7) as eluent.

The same procedure was followed for the 2-phenylpropene **2h** and styrene **2i**.

3a: Yield: 0.39g (92%); m.p. 145-48°C (lit.[16a] 148-50°C); IR (KBr): 3499, 3400, 2893, 1452, 1197, 1043, 777, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.08-7.19 (m, 10H), 4.67 (s, 2H), 3.03 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 128.1, 127.9, 126.9, 79.1.

3b: Yield: 0.43 g (90%); m.p. 108-10°C (lit.[16b] 110°C); IR (KBr): 3490, 3400, 2892, 1450, 1197,1043, 776, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.02 (br s, 8H,), 4.65 (s, 2H), 2.82 (br s,2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.5, 137.0, 128.8, 126.8, 78.8, 21.1.

3c: Yield: 0.53 g (94%); m.p. 126-28°C (lit.[16c] 127°C); IR (KBr): 3486, 3399, 2890, 1448, 1198,1042, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, 4H, J = 8.36 Hz), 6.98 (d, 4H, J = 8.36 Hz), 4.56 (s, 2H), 3.16 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.9, 133.8, 128.4, 78.5.

3d: Yield: 0.42 g (78%); m.p. 118-19°C (lit.[16d] 118-19°C); IR (KBr): 3489, 3398, 2890, 1448, 1193, 1043, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.03 (d, 4H, J = 8.64 Hz), 6.75 (d, 4H, J = 8.64 Hz), 4.63 (s, 2H), 3.76 (s,3H), 2.80 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.2, 132.2, 128.2, 113.5, 78.8, 55.2.

3e: Yield: 0.63 g (90%); m.p. 128-30°C; IR (KBr): 3400, 3344, 2928, 1928, 1622, 1331, 1122, 1070, 839, 763, 609, 524 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, 4H, J = 8.08 Hz), 7.20 (d, 4H, J = 8.08 Hz), 4.74 (s, 2H), 3.18 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 130.3, 127.3, 125.2, 122.5, 78.3.

3f: Yield: 0.48 g (89%); IR (neat): 3419 (br), 2950, 2840, 1590, 1448, 1163, 1043, 883, 724, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13 (t, 2H, J = 8. Hz), 6.70 (m, 6H), 4.63 (s, 2H), 3.69 (s, 6H), 3.10 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 141.5, 129.1, 119.2, 113.5, 112.2, 78.8, 55.1.

3g: Yield: 0.66 g (90%); m.p. 122-24°C (lit.[16e] 118.5-19°C); IR (KBr): 3327, 3065, 2930, 2858, 1591, 1568, 1195, 1006, 844, 754, 453 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (dd, 2H, J_1 = 8. Hz and J_2 = 1.8 Hz), 7.45 (d, 2H, J = 8. Hz), 7.34 (t, 2H, J = 8. Hz), 7.13 (m, 2H), 5.32 (s, 2H), 2.83 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 132.9, 129.7, 129.2, 127.4, 122.9, 76.1.

3h: Yield: 0.28 g (94%); IR (neat): 3387 (br), 3059, 2978, 1602, 1494, 1446, 1039, 954, 866, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.48-7.45 (m, 2H), 7.39-7.36(m, 2H), 7.28-7.30 (m, 1H), 3.81 (d, 1H, J = 8 Hz), 3.64 (d, 1H, J = 12 Hz), 2.56 (br s, 1H), 1.78 (br s, 1H), 1.54 (s, 3H); ^{13}C NMR (100

Table II — Acceleration of dihydroxylation of *trans*-stilbene **2a** by Tröger base[a]

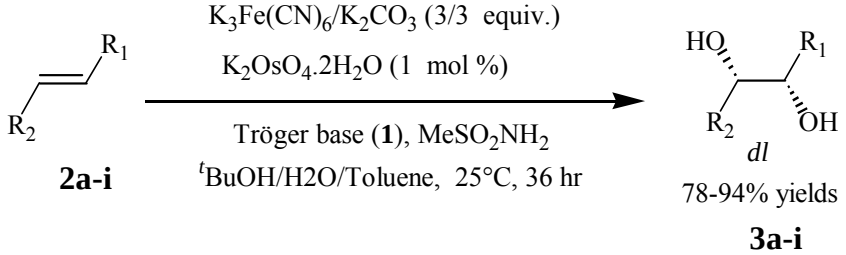
Entry	Additive	Time	Yield of diol **3a** (%)[b]
1	None	24 hr	10
2	Tröger base	24 hr	55
3	Tröger base	36 hr	66
4	Tröger base and methanesulfonamide	36 hr	92

[a]All the reactions were carried out using *trans*-stilbene (1 mmole), K_2CO_3 (3 mmole), $K_3Fe(CN)_6$ (3 mmole), $K_2OsO_4.2H_2O$ (1 mole %), Tröger base (10 mole %) in ^{t}BuOH (5 mL)/H_2O (5 mL)/ toluene (5 mL) solvent system.
[b]Yields reported here are for isolated products.

Table III — Racemic dihydroxylation of various olefins[a]

Entry	Olefin	Diol yield (%)[b]
1	**2b**, R_1, R_2 = 4-MePh	**3b**, 90
2	**2c**, R_1, R_2 = 4-ClPh	**3c**, 94
3	**2d**, R_1, R_2 = 4-MeOPh	**3d**, 78
4	**2e**, R_1, R_2 = 4-CF_3Ph	**3e**, 90
5	**2f**, R_1, R_2 = 3-MeOPh	**3f**, 89
6	**2g**, R_1, R_2 = 2-BrPh	**3g**, 90
7	**2h**, R_1 = Ph, R_2 = Me	**3h**, 94
8	**2i**, R_1 = Ph, R_2 = H	**3i**, 80

[a]All the reactions were carried out using olefin (2 mmole), K_2CO_3 (6 mmole), $K_3Fe(CN)_6$ (6 mmole), $K_2OsO_4.2H_2O$ (1 mole %), Tröger base (10 mole %), methanesulfonamide (2 mmole) and ^{t}BuOH (10 mL)/H_2O (10 mL)/ toluene (10 mL) was used as solvent. The reaction-mixture was stirred at 25°C for 36 hr.
[b]Yields reported here are for isolated products.



Scheme II — Racemic dihydroxylation of *trans*-olefins

MHz, $CDCl_3$): δ 145.0, 128.4, 127.1, 125.1, 74.9, 70.9, 26.0.

3i: Yield: 0.22 g (80%); IR (neat): 3375 (br), 3040, 2988, 1596, 1494, 1440, 1039, 958, 860, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.19-7.29 (m, 5H), 4.75 (dd, 1H, J_1 = 2.8 Hz and J_2 = 2.4 Hz), 3.72 (d, 1H, J = 12 Hz), 3.60 (m, 1H), 2.56 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 136.6, 128.4, 127.8, 126.1, 74.7, 68.0.

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