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Ruthenium catalyzed asymmetric dihydroxylation with sultams as chiral auxiliaries

Albert W. M. Lee,* W. H. Chan, W. H. Yuen, P. F. Xia and W. Y. Wong

Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Kowloon, Hong Kong, People's Republic of China

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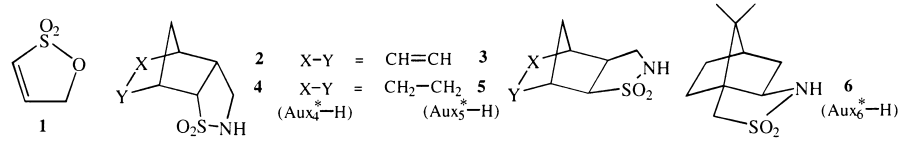
Abstract

Ruthenium catalyzed asymmetric dihydroxylations of α,β-unsaturated carbonyl compounds with sultams **4**, **5** and **6** as chiral auxiliaries are reported. © 1999 Elsevier Science Ltd. All rights reserved.

Stereoselective OsO_4 mediated dihydroxylation of alkene moieties has always attracted considerable interest from synthetic chemists because of its role in the construction of valuable diol building blocks for the syntheses of polyoxygenated compounds and natural products. Both stoichiometric and catalytic OsO_4 based asymmetric dihydroxylation are well known in the literature including the extremely well received Sharpless asymmetric dihydroxlation.[1,2] A few reports on using chiral auxiliaries such as the Oppolzer's camphorsultam in OsO_4 asymmetric dihydroxylation have also appeared in the literature.[3]

Despite its popularity and reliability as an oxidizing reagent, osmium tetraoxide is highly toxic and relatively expensive. Recently, Shing et al. demonstrated a procedure for the highly efficient dihydroxylation of olefins catalyzed by ruthenium tetraoxide.[4] Because of its low toxicity, affordable price, and accelerated rate of reaction, the use of ruthenium tetraoxide has certain advantages over osmium tetraoxide in dihydroxylation reactions. However, no asymmetric version of the ruthenium catalyzed reaction has yet been reported. Recently, we reported a practical synthesis of α,β-unsaturated γ-sultone **1** and its application as a dienophile in Diels–Alder reactions.[5] We also demonstrated that homochiral sultams such as compounds **2** and **3** can be derived from the Diels–Alder cycloadducts of sultone **1**. These synthetic sultams can serve as chiral auxiliaries in several asymmetric processes such as Diels–Alder reactions and alkylations.[6] In this report, we discuss our results using Oppolzer's and our synthetic sultams as chiral auxiliaries in ruthenium catalyzed asymmetric dihydroxylations.



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* Corresponding author. Tel: (852) 2339 7064; fax: (852) 2339 7348; e-mail: alee@hkbu.edu.hk

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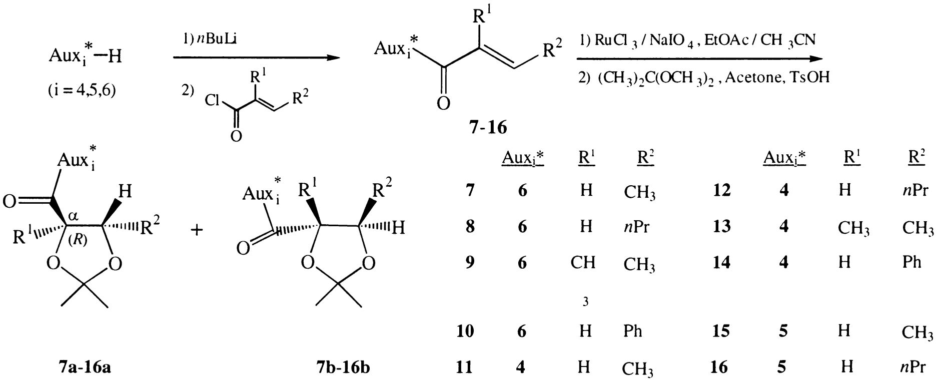
Our original homochiral sultams **2** and **3** derived from the *exo*- and *endo*-Diels–Alder cycloadducts of **1** with cyclopentadiene contain olefinic moieties and therefore are not suitable for dihydroxylation reactions. They were modified to the saturated series **4** and **5** through hydrogenation. All the *N*-enoyl sultams **7**–**16** were then prepared in quantitative yields from the corresponding chiral sultam auxiliaries (**4**, **5**, **6**) and acyl chlorides using *n*-butyl lithium as the base. Dihydroxylation of the *N*-enoyl sultams (**7**–**16**) were carried out in 1:1 CH_3CN:EtOAc for 2 to 5 hours after the Shing's protocol (0.07 mol equiv. $RuCl_3$, 1.5 equiv. $NaIO_4$). The resulting diols were converted in situ to the corresponding dimethyl acetals (**7a**–**16a** and **7b**–**16b**) in good overall yields (Scheme 1).



7-16

7a-16a

7b-16b

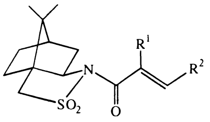
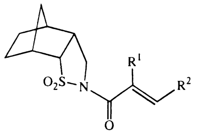
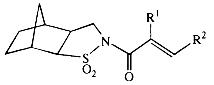
	Aux$_i$*	R^1	R^2		Aux$_i$*	R^1	R^2
7	**6**	H	CH$_3$	**12**	**4**	H	nPr
8	**6**	H	nPr	**13**	**4**	CH$_3$	CH$_3$
9	**6**	CH$_3$	CH$_3$	**14**	**4**	H	Ph
10	**6**	H	Ph	**15**	**5**	H	CH$_3$
11	**4**	H	CH$_3$	**16**	**5**	H	nPr

Scheme 1.

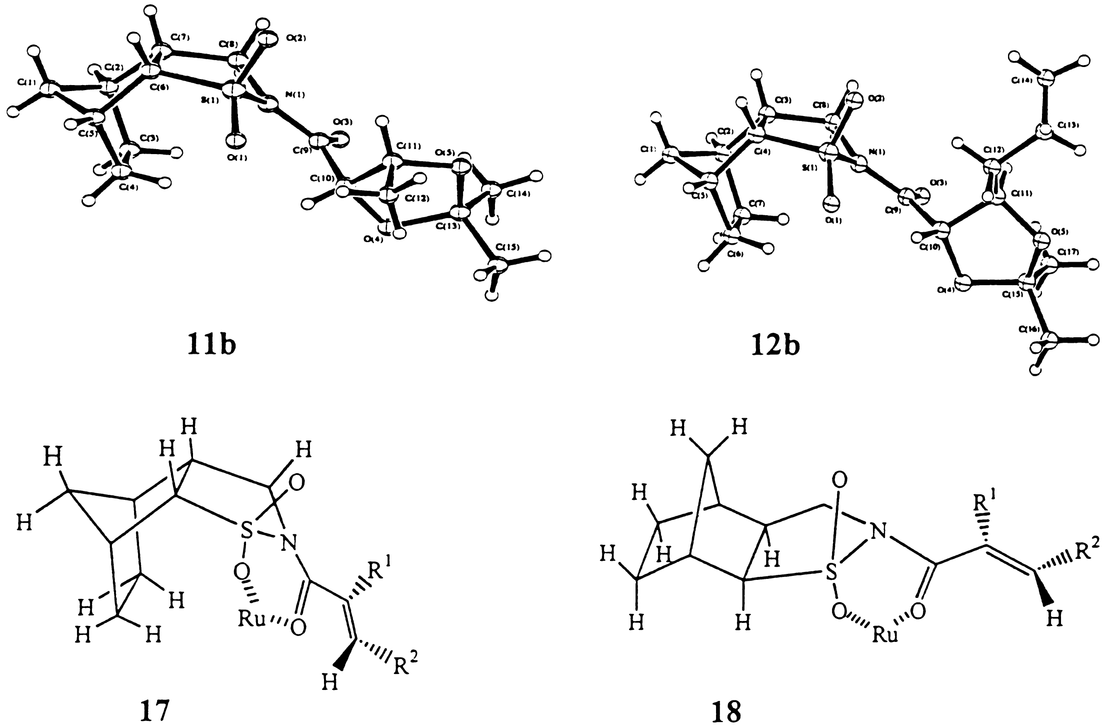
Our results on ruthenium catalyzed dihydroxylation, as depicted in Table 1, indicated that the π-facial diastereoselectivity is highly dependent on the kind of auxiliary used. For the Oppolzer's camphorsultam **6**, good selectivities up to 9:1 were observed (entries 1–4). The sense of diastereoselectivity in these cases is the same as in the OsO_4 catalyzed reaction[3] with **7a**–**16a** as the major products with *R* configuration at C(α).

The diastereoselectivities with synthetic sultams **4** and **5** as chiral auxiliaries (entries 5–10) were poorer. Around 4:6 selectivities were observed for sultam **4**, and basically no selectivity was afforded by sultam **5**. Furthermore, the sense of diastereoselectivity in sultam **4** is just opposite to that of sultam

Table 1
Ruthenium catalyzed asymmetric dihydroxylation[7]

Entry			R^1	R^2	Diastereoselectivity **a** : **b**	Yield [%]
1		**7**	H	CH$_3$	87 : 13	81
2		**8**	H	nPr	90 : 10	83
3		**9**	CH$_3$	CH$_3$	84 : 16	74
4		**10**	H	Ph	83 : 17	71
5		**11**	H	CH$_3$	40 : 60	83
6		**12**	H	nPr	33 : 67	81
7		**13**	CH$_3$	CH$_3$	33 : 67	78
8		**14**	H	Ph	40 : 60	68
9		**15**	H	CH$_3$	50 : 50	81
10		**16**	H	nPr	50 : 50	77

6 with **7b**–**16b** as the major products. X-Ray crystallographic analyses of **11b** and **12b** unambiguously confirmed that the C(α) centers have the *S* configuration (Scheme 2).



Scheme 2.

The poorer and opposite diastereoselectivity observed for sultam **4** and **5** can be explained as follows. Based on the model proposed by Oppolzer[3c] featuring a *syn*-orientation of the C=O and SO_2 groups (a chelation by a Ru-atom) and *S*-*cis*-related C=O/C(α)–(β) bonds, models of the enoylsultams of chiral auxiliaries **4** and **5** are depicted in Scheme 2. As pointed out by Oppolzer, it is obvious that for the enoyl derivatives of camphorsultam **6**, the bottom face attack is more favorable as the top face is shielded by the *gem*-dimethyl groups of the [2.2.1] bicyclic ring structure. For the enoyl derivatives of the *endo*-sultam **4**, model **17** shows that it has a bent conformation: the bottom face is slightly shielded. A more favorable attack from the top face afforded opposite selectivity as compared with sultam **6**. For the *exo*-sultam **5**, model **18** shows that a rather flat conformation is adopted. The steric demand from either the top or the bottom faces are almost the same: therefore, no diastereoselectivity was observed.

In summary, this is the first report of ruthenium catalyzed asymmetric hydroxylation using sultams as chiral auxiliaries. Facial selectivities were highly dependent on the type of chiral sultams used. Financial support from the Hong Kong Research Grant Council (HKBU 136/94P) and the Faculty Research Grant are gratefully acknowledged.

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7. All new compounds were characterized by spectroscopic methods (IR, ^{1}H, ^{13}C NMR, HRMS and/or elemental analysis). Typical procedure: to a vigorously stirred solution of *N*-enoylsultam **11** (1.0 mmol) in EtOAc:CH_3CN (10 ml:10 ml) at −20°C was slowly added a solution of $RuCl_3 \cdot (H_2O)_x$ (0.1 mmol) and $NaIO_4$ (1.5 mmol) in water (2 ml). The two-phase mixture was stirred vigorously for 2 h and monitored by TLC. When the reaction was almost completed, it was gradually warmed up to −10°C for 15 min. A saturated aqueous solution of $Na_2S_2O_3$ (10 ml) was then added. The aqueous phase was separated and extracted with EtOAc (3×20 ml). The combined organic extracts were then dried (Na_2SO_4) and filtered. Concentration of the dried (Na_2SO_4) organic extracts provided a crude mixture of the diols. The crude diols was stirred in 1:1 CH_3COCH_3:$(CH_3)_2C(OCH_3)_2$ mixture (8 ml) in the presence of TsOH (1 mg) at rt for 2 h. Saturated $NaHCO_3$ solution was added followed by extraction with CH_2Cl_2. After passing through a short silica gel column, 0.274 g (83%) of **11a** and **11b** was obtained. The two diastereomers can be further purified by silica gel column chromatography eluted with 1:4 EtOAc:pet-ether. **11b**: m.p. 111–113°C; $[\alpha]_D^{23}=+54.8$ (c=0.17, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.47–1.63 (14H, m), 2.12 (1H, m), 2.51 (1H, s), 2.80 (1H, s), 2.85–2.94 (1H, m), 3.50 (1H, dd, *J*=8 and 13 Hz), 3.62 (1H, dd, *J*=4.6 and 10.8 Hz), 4.34 (1H, d, *J*=13 Hz), 4.40 (1H, t, *J*=6.21 Hz), 4.98 (1H, d, *J*=6.5 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ 18.69, 21.88, 22.32, 26.38, 27.95, 37.59, 40.78, 40.83, 41.63, 42.67, 63.72, 76.27, 79.54, 111.3 and 169; IR (KBr) ν/cm^{-1} 1694 (C=O). Anal. calcd for $C_{15}H_{23}NO_5S$: C, 54.69; H, 7.04; N, 4.25; found: C, 54.79; H, 7.12; N, 4.38.