Pergamon

Tetrahedron Letters, Vol. 38, No. 1, pp. 101-104, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(96)02226-5

Asymmetric Epoxidation of Nearly Symmetrical cis-Alkenes. Sharpless Epoxidation of (1,2-Dialkyl)vinylsilanols

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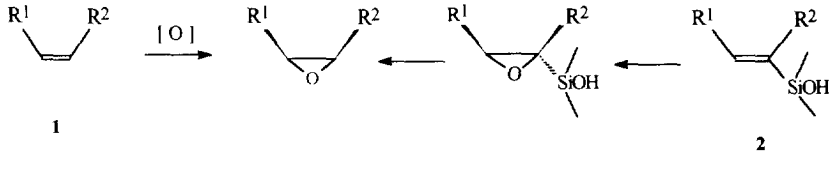
Abstract: (1,2-Dialkyl)vinylalkoxysilanes **3** were hydrolyzed in the presence of catalysts (CuCl/LiCl or $NiBr_2$) to give the corresponding silanols **2** in high yield. Sharpless epoxidation of **2** followed by protodesilylation gave optically active epoxides **7**. The overall approach can be considered as asymmetric epoxidation of nearly symmetrical simple cis-alkenes and has been applied to the synthesis of (+)-disparlure.

Following the pathbreaking success of the Sharpless epoxidation,[1] much recent research have been directed towards the asymmetric epoxidation (and dihydroxylation) of simple alkenes where the allylic hydroxy function is absent. Highly enantioselective epoxidation of simple olefins using chiral salen-based complexes has been reported.[2] In cases involving 1,2-disubstituted alkenes (1), chiral discrimination rests on the difference in properties, steric or electronic, between the two substituents R^1 and R^2 (Scheme 1). For cis 1,2-disubstituted alkenes where the two substituents are nearly equivalent, enantioselectivity is not expected to be high.[3]



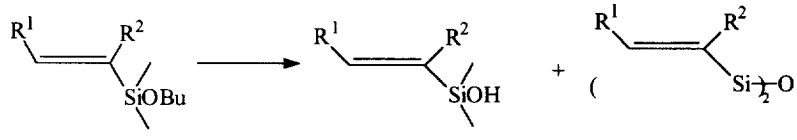
1 2

Scheme 1

We have reported[4] that the silanol function in vinylsilanols (**2**) can play the role of allylic hydroxy group in the Sharpless epoxidation reaction. Furthermore, since the silanol function can be protodesilylated with ease by fluoride ion with retention of stereochemistry,[5] the overall transformation can be considered as an asymmetric epoxidation of simple alkenes (Scheme 1). The approach has been successfully applied to the enantioselective synthesis of terminal epoxides through the reactions of (2-alkyl)vinylsilanols and (2,2-dialkyl)vinylsilanols with the Sharpless reagents. We now report that (E)-(1,2-dialkyl)vinylsilanols can be similarly epoxidised under the Sharpless conditions to give the corresponding epoxides in good chemical and optical yields. Protodesilylation produces the chiral epoxides. The process can be applied to prepare chiral cis 1,2-disubstituted

epoxides where the two substituents are nearly equivalent, as demonstrated by the synthesis of (+)-disparlure, the sex pheromone produced by the female gypsy moth, *Porthetriadispar L.*[6]

(E)-(1,2-dialkyl)vinyldimethylbutoxysilanes (**3**) were prepared through the regioselective addition of organocopper reagents to ethynylbutoxydimethylsilane (**4**) followed by alkylation with alkyl halides.[7] The hydrolysis of **3** to the corresponding silanols **2** proved to be difficult because the relatively strong acidic or basic conditions required for hydrolysis also led to the conversion of **2** to the disiloxanes **5**. In order to circumvent this problem, we found that some metal salts (CuBr/LiCl or $NiBr_2$) can catalyze the hydrolysis of alkoxysilanes. The results are summarized in Table 1.



3 **2** **5**

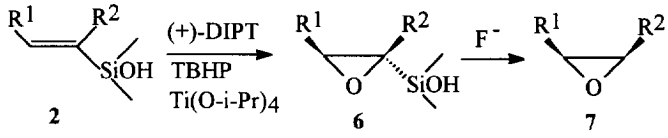
Table 1. Hydrolysis of alkoxysilanes 3 catalyzed by metal salts

	Silane R^1	R^2	Metal salt	Reac. Cond.	Yield of 5,%
3a	n-C_4H_9	CH_2OMe	CuBr/LiCl	A	57
3b	n-C_8H_{17}	Me	CuBr/LiCl	A	24
3b			CuBr/LiCl	B	63
3c	n-C_8H_{17}	CH_2=$CHCH_2$	CuBr/LiCl	A	48
3d	n-C_8H_{17}	$CH_2(CH)_2CH_3$	CuBr/LiCl	B	20
3a			$NiBr_2$	C	79
3b			$NiBr_2$	C	83
3c			$NiBr_2$	C	81
3d			$NiBr_2$	C	86
3e	n-$C_{10}H_{21}$	$Me_2CH(CH_2)_4$	$NiBr_2$	C	81

A:THF/H_2O(20:1), room temp.; B:Acetone/H_2O(30:1), room temp; C:THF/H_2O(40:1), 50°

In these catalytic systems, the reaction media were found to be nearly neutral. Even so, substantial amount of **5** was still obtained using CuBr/LiCl as the catalyst even though the rate of hydrolysis of **3** was fast. With $NiBr_2$ as the catalyst, the hydrolysis of **3** to **2** required a higher reaction temperature, but the yield of the silanols **2** was high with only a small amount of the disiloxanes.[8]

Epoxidation of the silanols **2** under Sharpless condition with t-butyl hydroperoxide (TBHP), $Ti(O\text{-}i\text{-}Pr)_4$ and (+)-diisopropyl tartrate (DIPT) in CH_2Cl_2 at -20° for 13 hr gave compounds **6**. Treatment of **6** with Et_4NF in MeCN gave the epoxides 7 in overall yield of 62-70% (Table 2).[9] The enantiomeric excess (ee) of the epoxides 7 was determined by ^1H nmr using chiral chemical shift reagent [(+)-Eu(hfc)$_3$]. The use of (+)-DET instead of (+)-DIPT did not improve the enantioselectivity of the reaction.

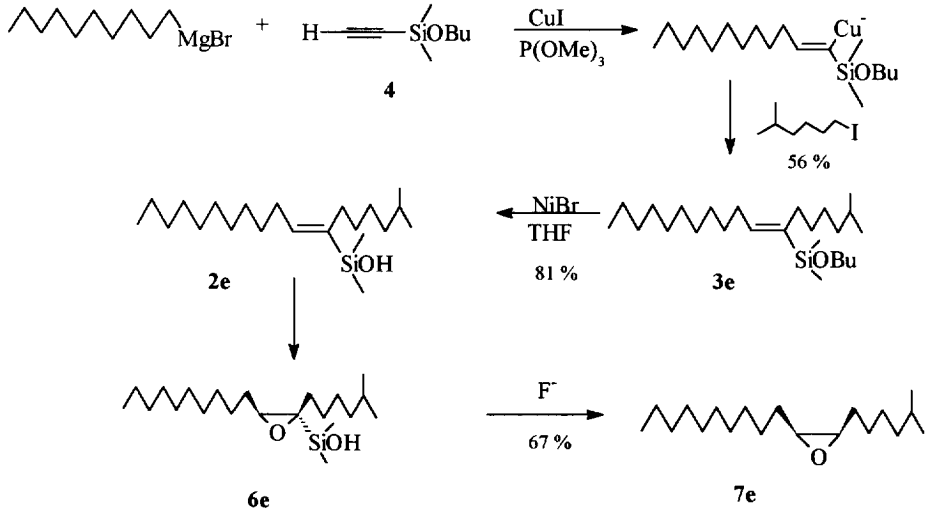


2 6 7

Table 2. Sharpless epoxidation of silanols 2

	Silanol R^1	R^2	Tartrate	Yield of 7,%	Ee of 7,%
2a	n-C_4H_9	CH_2OMe	(+)-DIPT	59	57
2b	n-C_8H_{17}	CH_3	(+)-DIPT	62	60
2b			(+)-DET	54	51
2c	n-C_8H_{17}	$CH_2CH{=}CH_2$	(+)-DIPT	63	44
2d	n-C_8H_{17}	$CH_2(CH_2)CH_3$	(+)-DIPT	70	70
2e	n-$C_{10}H_{21}$	$Me_2CH(CH_2)_4$	(+)-DIPT	67	52

The approach was applied to the enantioselective synthesis of (+)-disparlure (Scheme 2).[10] Epoxidation of **2e** under Sharpless conditions produced **6e** which on protodesilylation gave (7R, 8S)-(+)-epoxy-2-methyloctadecane [**7e**, (+)-disparlure,$[\alpha]_D$=0.45 (c=2.2, CCl_4)] in 30% overall yield based on ethynylbutoxydimethylsilane (**4**). The configuration of **7e** is in agreement with the stereochemical model proposed by Sharpless for allylic alcohols.[11] This suggests that in the Sharpless epoxidation of vinylsilanols, the silanol function assumes the role of the allylic hydroxy group.



Scheme 2

Acknowledgement We thank the National Natural Science Foundation of China and the Natural Science and Engineering Research Council of Canada for financial support of this research.

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3. For an ingenious example of highly enantioselective epoxidation of symmetrical trans 1,2-disubstitutedalkenes, see Chang, S.; Galvin, J. M.; Jacobsen, E. N., *J. Am. Chem. Soc.*, **1994**, *116*, 6937

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8. Typical procedure: A mixture of $NiBr_2$ (1g) in THF (40mL) was stirred at 50°C, forming a solution and cooled to room temperature. An amount of **3b** (3mmol) was added to the solution and stirred at 50° overnight. The mixture was cooled to room temperature and diluted with pet ether (40mL). The mixture was filtered through a short silica gel column. The filtrate was evaporated and the residue was purified by flash chromatography to give colorless liquid **2b** in 83% yield.

9. Typical procedure: To a mixture of 4A molecular sieves (1g), and $Ti(O\text{-}i\text{-}Pr)_4$ (0.89g,2.8mmol) in CH_2Cl_2 (10mL) at -20°, a solution of (+)-DIPT (0.86g, 3.6mmol) in CH_2Cl_2 (10mL) was added. The mixture was stirred for 15 min. A solution of **2b** (2mmol) in CH_2Cl_2 (10mL) was added and stirred for 15 min. Then, a solution of TBHP in isooctane (1.2mL, 5.5M) was added and stirred for 13 h at -20°. Water (20mL) and an aqueous solution of 30% NaOH (6mL) was added and stirred for 1 h. The aqueous phase was extracted with ether (3x30mL). The combined organic phase was dried over $MgSO_4$ and evaporated. To the residue a solution of Et_4NF (1g) in CH_3CN (20mL) was added and then stirred at 80° for 5 h. The mixture was diluted with water (40mL) and extracted with ether (3x30mL). The combined organic phase was dried over $MgSO_4$ and evaporated. The residue was purified with flash chromatography to give a colorless liquid **7b** in 60% yield.

10. A number of synthesis have been reported. See for example: Brevet, J.L.; Mori, K., *Synthesis*, **1992**, 1007; Keinan, E.; Sinha, S. C.; Sinha, B. A.; Wang, Z. M.; Zhang, X. L.; Sharpless, K. B., *Tetrahedron Letters*, **1992**, *33*, 6411

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(*Received in China* 5 *May* 1996; *revised* 17 *June* 1996; *accepted* 28 *September* 1996)