Tetrahedron Letters,Vol.27,No.29,pp 3391-3394,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

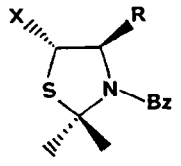
ASYMMETRIC INDUCTION TO SULFUR ATOM: STEREOCONTROLLED S-OXIDATION OF THIAZOLIDINES

Wataru Ando*, and Liren Huang
Department of Chemistry, The University of Tsukuba
Sakura, Ibaraki 305, Japan

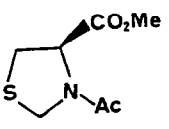
Summary: Oxidation of (2R,4R)-2,4-disubstituted thiazolidines with m-CPBA affords the trans sulfoxide exclusively. Oxidation of (2R,4R)-4-hydroxymethyl thiazolidines with $Ti(O^iPr)_4$/TBHP, however, favors to give the cis sulfoxide.

The steric course of oxidation at thiazolidine derivatives deserves attention for implication of biological processes and for the importance in synthesis of natural products. Baldwin[1] and Iwakawa[2] reported that oxidation of 3-benzoyl-2,2-dimethyl-4(R)-substituted thiazolidine 1 and 2 using benzoyl peroxide affords the trans 5-benzenecarboxyl thiazolidine 3 and 4 stereospecifically. Nachtergaele[3] showed that oxidation of 3-acetyl-4-carbomethoxyl thiazolidine 7 with H_2O_2 or $NaIO_4$ results in the two possible sulfoxides(cis and trans) in a ratio of 60:40, and Ando[4] described that photooxidation of 2 gives trans 5-hydroxy thiazolidine 5 stereospecifically, but affords corresponding sulfoxides as by-products nonselectively. Chlorination of 5 with thionyl chloride affords the trans thiazolidine 6 as the only product.[5]

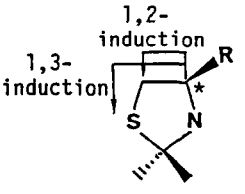
From these outcomes, we can draw the conclusion that 1,2-asymmetric induction occured easily in the system 8 while 1,3-asymmetric induction on sul-



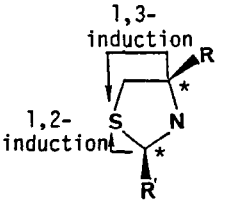
thiazolidine



7



8



9

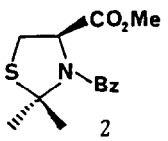
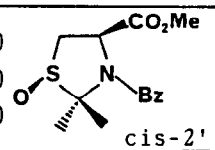
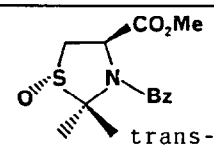
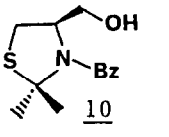
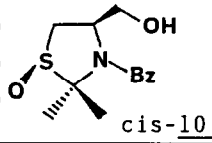
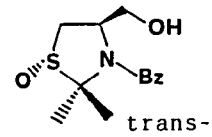
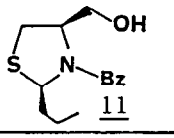
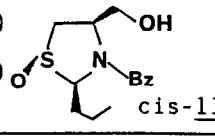
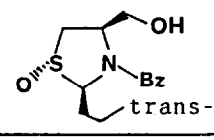
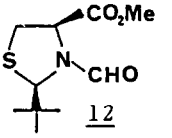
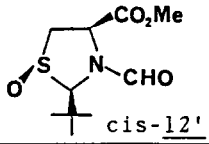
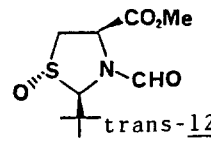
Thaizolidines: 1: R=-CNHC(^{i}Pr)CO_2Me; X=-H. 2: R=-CO_2Me; X=-H
3: R=-CNHC(^{i}Pr)CO_2Me; X=-OCOPh. 4: R=-CO_2Me; X=-OCOPh.
5: R=-CO_2Me; X=-OH. 6: R=-CO_2Me; X=-Cl.

fur atom is not so easily filfulled in a usual way. Now, we wish to report the stereocontrolled oxidations of thiazolidines with m-CPBA and $Ti(O^iPr)_4$/TBHP by 1,3- and 1,2-induction in system 8 and 9.

The optically active thiazolidines 2, 10, 11, and 12 are prepared by acylating 2-substituted 4(R)-carbomethoxyl thiazolidines obtained from the commercial methyl ester hydrochloride of L-cysteine and aldehyde. The cis isomer 12[6] was isolated by crystallization in about 62% from the diastereomers. 4(R)-Hydroxymethyl thiazolidines 10 and 11 were prepared by reducing the corresponding 4(R)-carbomethoxyl thiazolidines[7] with large excess of $NaBH_4$.[2]

The oxidation using m-CPBA is exemplified in the case of 12. To a solution of 12(1.0mmol) in CH_2Cl_2(5ml) was added m-CPBA(1.2mmol) and the solution was stirred at 0°C for 3 hours and then washed with NaOH solution. After work-up, trans-12' was obtained in 60%.[8] Oxidation of 10 and 11 was operated as followings. To a solution of 10 or 11(1mmol) and $Ti(O^iPr)_4$(0.3ml, 1mmol) in CH_2Cl_2 was added an anhydrous TBHP solution(1.5mmol) in 1,2-dichloroethane[9] and than stirred at room temperature for one or two days. After reaction, water(0.5ml) and alumina were added. The cis-10'[10] was obtained after filteration and evaporation. The cis- and trans-11' were isolated by column

Table. The sulfoxides obtained by oxidation of thiazolidines

Run	Thiazolidine	Oxidation conditions	Sulfoxide yield(%)	Ratio of Sulfoxides cis(%)	trans(%)
1)	 2	a)	86[e]	 cis-2' 57	 trans-2' 43
2)		b)	95[e]	29	71
3)		c)	50[f]	58	42
4)	 10	a)	84[e]	 cis-10' 42	 trans-10' 58
5)		b)	100[e]	30	70
6)		c)	48[f]	100	0
7)	 11	a)	70[f]	 cis-11' 0	 trans-11' 100
8)		c)	50[f]	75	25
9)	 12	a)	60[6]	 cis-12' 0	 trans-12' 100
10)		b)	56[f]	0	100
12)		d)	46[f]	0	100

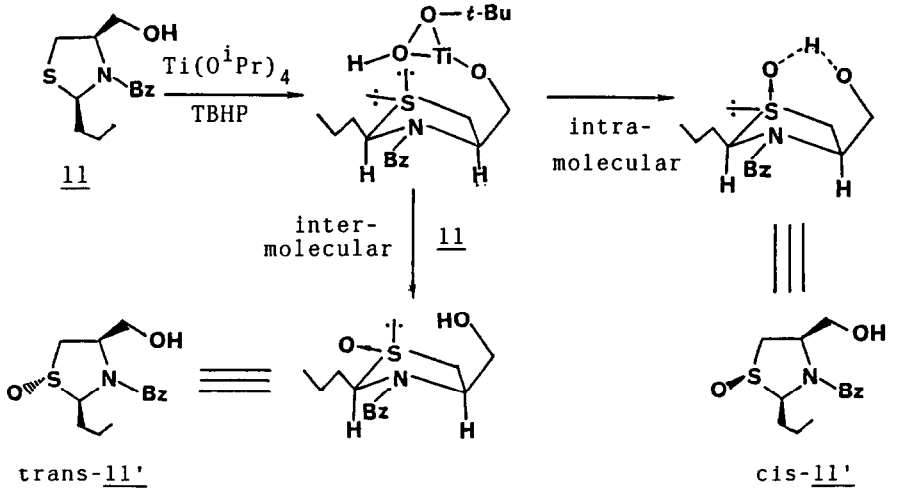
a) m-CPBA/CH_2Cl_2, r.t.; b) $NaIO_4/H_2O$-MeOH, r.t.; c) $Ti(O^iPr)_4$/TBHP, r.t.; d) TPP/hν/O_2/MeOH, Me_2S, -40°C;[4] e) Chromatography yield; f) Isolated yield. Because of the solubility of the sulfoxides, the yield is low.

chromatography(solvent: AcEt:EtOH=19:1; Rf_{cis}=0.35;Rf_{trans}=0.20). The results are summarized in the Table.

From the Table, we find that 12, with t-butyl group at C-2, could be oxidized to trans-12' regardless of oxidizing reagents used(Run 9, 10, 11). 2, with dimethyl at C-2, however, results in two possible sulfoxides with little selectivity(Run 1,2). This implies that the asymmetric center at C-4 of 12 is not effective on S-position and the stereospecificity is attributed to asymmetric center cited at C-2. In contrast to above results, oxidaiton of 10 whose C-4 is substituted by hydroxymethyl group instead of carbomethoxy group in 2, is performed stereospecifically with $Ti(O^iPr)_4$/TBHP(Run 6). It is obvious that oxidation of 10 proceeds via a step of coordination of hydroxy group with Ti(IV) just as Sharpless oxidation does,[11] not being due to the steric effect raised from the 4-substituted group in which the trans sulfoxide should be resulted. Oxidation of 11 with m-CPBA affords trans-11', but with $Ti(O^iPr)_4$/TBHP, cis- and trans-11' were obtained in a ratio of 3:1.[12]

The $Ti(O^iPr)_4$/TBHP system has been used in some efficient asymmetric oxidations. Kagan extended the Sharpless oxidaiton system to oxidizing prochiral sulfides to asymmetric sulfoxides,[13] but it is not clare whether $Ti(O^iPr)_4$ coordinates with sulfur or not. According to the literatures and our experiments, it is apparent that hydroxy group coordinates with Ti(IV) and TBHP initially to form an intermediate, which is oxidized from cis direction intramolecularly. In the case of 11, because of a n-propyl group at C-2, the steric factors apparently reduce the rate of cis sulfoxide formatiom and trans-11' is formed by competive intermolecular reaction(Scheme).

The reaction provided us with an idea that an asymmetric center can be induced further on sulfur-containing ring by the coordination of functional group on the substrate with reagent. We wonder if it is possible to extend the method to some compounds such as penicillin and cephalosporin. Active investigation is being continued.



Scheme

REFERENCES

1) J.E.Baldwin, A.Au, M.Christie, S.B.Haber, and D.Hesson, J. Am. Chem. Soc. 97, 5957(1975).

2) M.Iwakawa, B.M.Pinto, and W.A.Szarek, Can. J. Chem., 56, 326(1978).

3) W.A.Nachtergaele, and M.J.O.Anteunis, Bull. Soc. Chim. Belg., 89/n°,747(1980).

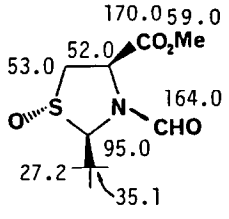
4) a) T.Takata, K.Ishibashi, and W.Ando, Tetrahedron Lett., 26, 4609(1985).
b) T.Takata, K.Hoshino, E.Takeuchi, Y.Tamura, and W.Ando, Tetrahedron Lett., 25, 4767(1984).
c) T.Takata, Y.Tamura, and W.Ando, Tetrahedron, 41, 2133(1985).

5) T.Takata, L.Huang, and W.Ando, Chem. Lett., 1705(1985).

6) 12: mp=68-70°C; $[\alpha]_D^{24}$=63.8°(c,0.0094,$CHCl_3$).
It exists in two rotamers in a ratio of 90:10 according to the orientation of formyl group relative to carbomethoxy and t-butyl group. The ^{1}H-NMR of the major rotamer ($CHCl_3$, δ): 8.45(s,1H); 4.94(m,1H); 4.76(s,1H); 3.80(s, 3H); 3.30(d,2H); 1.05(s,9H).

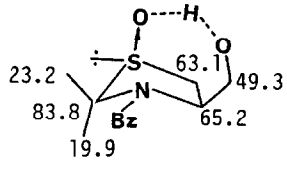
7) H.T.Nagasawa, D.J.W.Goon, and F.N.Shirota, J. Heterocyclic Chem., 18, 1047(1981).

8) Trans-12': mp=160-161°C; $[\alpha]_D^{24}$=-47.6°(c,0.010;$CHCl_3$).
It also exists in two rotamers in a ratio of 85:15. The ^{13}C-NMR of the major rotamer:



9) K.B.Sharpless and T.R.Verhoeven, Aldrichica Acta, 12, 63(1979).

10) Cis-10': mp=123-125°C. ^{13}C-NMR:

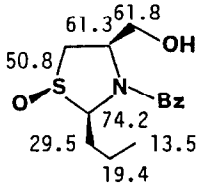


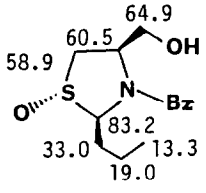
The extremely high shift of the mathane of hydroxymethyl group indicates a hydrogen bond between the O-S bond and the C-O bond.

11) I.D.Williams, S.F.Pederson, K.B.Sharpless, and S.J.Lippard, J. Am. Chem. Soc., 106, 6430(1984).

12) Cis-11': mp=147-148°C; $[\alpha]_D^{24}$=64.0°(c,0.010;$CHCl_3$). Trans-11': difficult to crystallize; $[\alpha]_D^{24}$=-77.6°(c,0.010;$CHCl_3$).

^{13}C-NMR:





13) P.Pitchen, E.Duñach, M.N.Deshmakh, and H.B.Kagan, J. Am. Chem. Soc., 106, 8188(1984).

(Received in Japan 20 May 1986)