Pergamon

Tetrahedron Letters 41 (2000) 2415–2418

TETRAHEDRON
LETTERS

Dichlorotin oxide-catalyzed new direct functionalization of olefins: synthesis of *trans* β-azidohydrins and 1,2-diols

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Received 27 December 1999; revised 20 January 2000; accepted 21 January 2000

Abstract

We have succeeded in developing direct syntheses of *trans* β-azidohydrins and *trans* 1,2-diol derivatives from olefins catalyzed by dichlorotin oxide. The regioselectivity of these reactions with tri-substituted olefins is high (10:1 in the synthesis of 1,2-diol derivatives) to excellent (>99:1 in the synthesis of azidohydrins). It has been found that these reactions do not proceed via epoxides. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: dichlorotin oxide; *trans* β-substituted alcohol; olefin.

Syntheses of *trans* β-substituted alcohols from olefins usually require two steps, epoxidation of an olefin and the following opening of the epoxide. Although this two-step method is well-established, only one inefficient example is known, where *trans* 1,2-diol derivatives are formed directly from olefins.[1] Therefore, the development of a direct *trans* β-substituted alcohol synthesis from olefins is very important. We recently reported on the $SnCl_4$-catalyzed direct *trans* chlorohydrin synthesis from olefins using bis(trimethylsilyl) peroxide (BTSP) and trimethylsilyl chloride (TMSCl) (Scheme 1).[2] The active catalytic species of this reaction is dichlorotin oxide $(Cl_2SnO)_n$ which is generated from $SnCl_4$ by BTSP. From mechanistic studies, we proposed a catalytic cycle that involves the insertion of a C=C double bond to dichlorotin oxide, nucleophilic attack of BTSP on Sn and regeneration of $(Cl_2SnO)_n$ by S_N2 attack of TMSCl. Accordingly, it was expected that it would be possible to apply this catalytic cycle to other *trans* β-substituted alcohol syntheses by using the corresponding trimethylsilyl reagents ($(CH_3)_3SiX$ in Scheme 1). Herein, we report the direct syntheses of *trans* azidohydrins and *trans* 1,2-diol derivatives from olefins catalyzed by dichlorotin oxide.

First, we tried the direct *trans* β-azidohydrin synthesis from cyclohexene (1.0 mmol) using $SnCl_4$ (10 mol%), BTSP (2 mol equiv.) and trimethylsilyl azide ($TMSN_3$) (2 mol equiv.). As expected, when performing the reaction at ambient temperature for 7 h the reaction gave *trans*-2-azido-1-cyclohexanol (**1**) (yield 43%), together with the undesired *trans*-2-chloro-1-cyclohexanol (yield 17%).[3] This undesired formation of the chlorohydrin could be reduced, using pre-generated dichlorotin oxide[4] (20 mol%)

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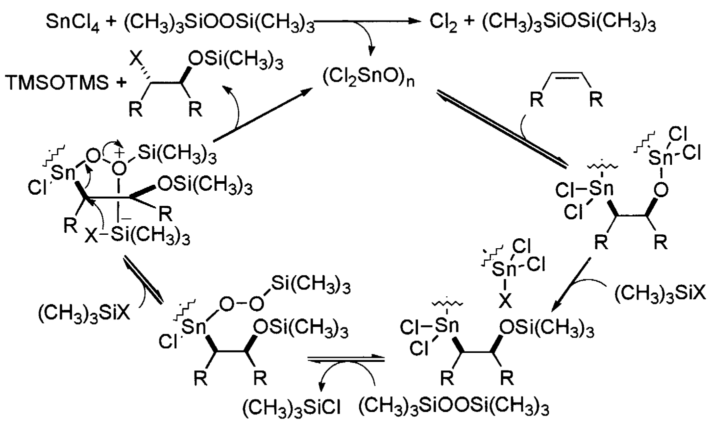
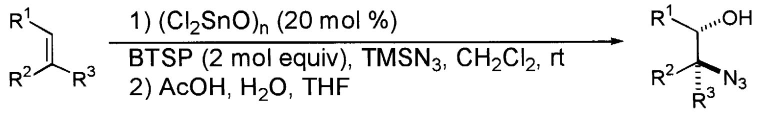
PII: S0040-4039(00)00176-3

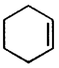
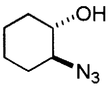
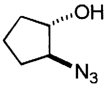
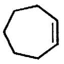
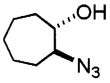
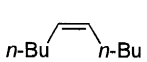
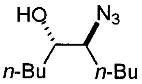
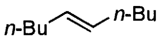
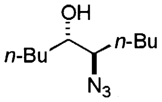
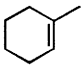
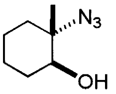


Scheme 1. Proposed mechanism

instead of $SnCl_4$, to give the azidohydrin **1** in 52% yield and the chlorohydrin in 10% yield (Table 1, entry 1).[5] Other substrates (cyclic and acyclic olefins) also gave the corresponding *trans* β-azidohydrins in acceptable yields (Table 1).[6] Furthermore, 1-methyl-1-cyclohexene (Table 1, entry 6) gave **6** with almost complete regioselectivity.[7] To the best of our knowledge, this is the first example of a direct *trans* β-azidohydrin synthesis starting with olefins.

Table 1
Synthesis of *trans* azidohydrins

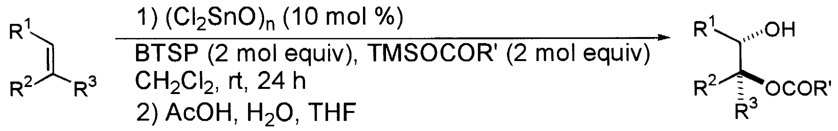


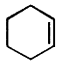
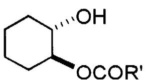
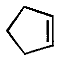
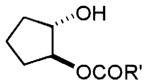
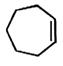
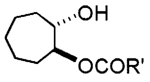
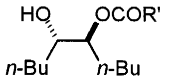
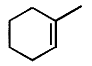
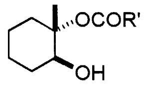
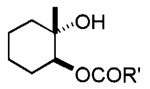
entry	olefin	azidohydrin[a]	TMSN3 (mol equiv)	time (h)	yield[b] (%)	chlorohydrin[c] (%)
1		 **1**	2	24	52	10
2		 **2**	2	24	47	9
3		 **3**	3	48	52	6
4		 **4**	2	24	54	6
5		 **5**	2	24	58	8
6		 **6**	2	24	34	11

a) Relative configurations of all products were unequivocally determined.[8] b) Isolated yield. c) Calculated from the ratio of azidohydrins and chlorohydrins according to ^{1}H-NMR data.

Next, we extended the reaction for the synthesis of *trans* 1,2-diol derivatives. We were pleased to find that, by using trimethylsilyl acetate (TMSOAc) instead of $TMSN_3$, cyclic and acyclic olefins were also successfully converted to the corresponding *trans* β-acetoxy alcohols (Table 2, entries 1, 3, 5 and 6).[6] Furthermore, in order to improve the yield, other trimethylsilyl carboxylates were investigated.[9] As a result, we found that trimethylsilyl methoxyacetate, which can coordinate to Sn because of the α-oxygen atom, improved the yield in the case of cyclohexene and cyclopentene (Table 2, entries 2 and 4).[10] Also in this case, high regioselectivity (10:1) was obtained for 1-methyl-1-cyclohexene to give **13** as the major product (Table 2, entry 7).

Table 2
Synthesis of *trans* 1,2-diol derivatives

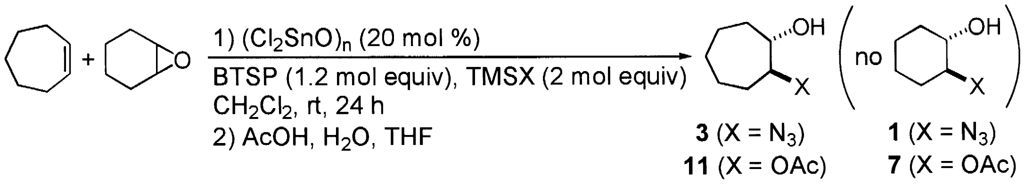


entry	olefin	product[a]		R'	yield (%)[b]	chlorohydrin (%)[c]
1			**7**	CH_3	52	10
2			**8**	CH_2OCH_3	65	12
3			**9**	CH_3	47	9
4[d]			**10**	CH_2OCH_3	55	12
5[e]			**11**	CH_3	52	6
6			**12**	CH_3	54	6
7			**13**	CH_2OCH_3	50	19
			**14**		5	

a) Relative configurations of all products were unequivocally determined.[8] b) Isolated yield. c) Calculated from the ratio of acetoxy alcohols and chlorohydrins according to ^{1}H-NMR data. d) The reaction time was 6 h. e) $(Cl_2SnO)_n$ (20 mol %), TMSOAc (3 mol eq.), 48 h.

Interestingly, it was found from the following experiment, that epoxides were not the intermediate in these azidohydrin and acetoxy alcohol syntheses (Scheme 2). Thus, the reaction of a mixture of cycloheptene and cyclohexene oxide using $(Cl_2SnO)_n$ (20 mol%), BTSP (1.2 mol equiv.) and $TMSN_3$ (2 mol equiv.) gave only **3**, and **1** was not detected in the reaction mixture. The same reaction using TMSOAc (2 mol equiv.) instead of $TMSN_3$ gave only **11**. In agreement with this result, the epoxide derived from cycloheptene was not detected in the reaction mixtures by TLC and ^{1}H NMR analyses. Therefore, we postulate the reaction mechanism as shown in Scheme 1.[11]

In summary, we have developed a one-step procedure for the synthesis of azidohydrins and acetoxy alcohols from olefins by the catalysis of $(Cl_2SnO)_n$. The development of a catalytic asymmetric version of these reactions is currently under investigation.



Scheme 2. Experiment using a mixture of olefin and epoxide

Acknowledgements

We thank CREST and RFTF for financial support.

References

1. *trans* 1,2-Diol synthesis from olefin (via dibenzoate): Wilson, C. V. In *Organic Reactions*; Adams, R., Ed.; John Wiley & Sons, Inc.: New York, 1957; Chapter 6, Vol. 9, p. 350.
2. Sakurada, I.; Yamasaki, S.; Iida, T.; Göttlich, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* in press.
3. The undesired chlorohydrin formation may be due to the in situ generation of TMSCl by the ligand exchange between $SnCl_4$ (or even $(Cl_2SnO)_n$) and TMSX (X=N_3, OCOR).
4. Preparation of dichlorotin oxide: To a solution of BTSP[12] (0.94 M in CH_2Cl_2, 64 mL, 60 mmol, 3 mol equiv.) was added $SnCl_4$ (1.0 M in CH_2Cl_2, 20 mL, 20 mmol) at 0°C under argon. After the mixture was stirred at rt for 2 h, volatiles (solvent, excess BTSP, chlorine, hexamethyldisiloxane) were evaporated in vacuo to afford dichlorotin oxide (2.4 g, 69%) as a white powder.
5. General procedure of azidohydrin synthesis: To a CH_2Cl_2 solution (0.5 mL) of dichlorotin oxide[4] (41.1 mg, 0.2 mmol) was added BTSP (neat, 0.44 mL, 2.0 mmol), cyclohexene (101 μL, 1.0 mmol) and $TMSN_3$ (265 μL, 2.0 mmol) at 0°C under argon. After 24 h at rt, the reaction was quenched with AcOH–H_2O–THF (1.5:1.0:4.0 mL). The mixture was stirred at rt for 10 min, and added dropwise to a mixture of sat. aq. $NaHCO_3$ (20 mL) and 10% aq. Na_2SO_3 (4 mL) at 0°C. Extraction with $CHCl_3$ (10 mL×3), evaporation of the solvent and purification by silica gel column chromatography (hexane–AcOEt 10:1) afforded **1** (74.0 mg, 52%).
6. The moderate isolated total yield of the products (azidohydrins or acetoxy alcohols+chlorohydrins) could be due to the formation of unknown by-products, whose structure determinations are under investigation.
7. The regioselective synthesis of **6** from 1,2-epoxy-1-methylcyclohexane is usually difficult. (a) Mereyala, H. B.; Frei, B. *Helv. Chim. Acta* **1986**, *96*, 415–418. (Et_3Al/HN_3, yield 68%; the ratio is not described). (b) Meguro, M.; Asao, N.; Yamamoto, Y. *Chem. Commun.* **1995**, 1021–1022. (cat. $Yb(O^iPr)_3/TMSN_3$, total yield 95% (26:74); the regio isomer of **6** is the major product). (c) Crotti, P.; Bussolo, V. D.; Favero, L.; Macchia, F.; Pineschi, M. *Tetrahedron Lett.* **1996**, *37*, 1675–678 [cat. $Hf(OTf)_4$/1,1,3,3-tetramethylguanidinium azide, total yield 72% (58:42)]. (d) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *J. Org. Chem.* **1999**, *64*, 6094–6096 [$NaN_3/H_2SO_4/H_2O$ (pH 4.2), yield 67% (80:20)].
8. The configuration of azidohydrins was determined by comparison with the literature data (compounds **1** and **2**: Ref. 13; compounds **7**, **9** and **11**: Ref. 2) or by preparing authentic samples from corresponding epoxides.
9. Trimethylsilyl benzoate, trimethylsilyl *o*-nitrobenzoate, trimethylsilyl chloroacetate or trimethylsilyl dichloroacetate gave unsatisfactory results.
10. Unexpectedly, cycloheptene and *cis*-5-decene gave the corresponding *trans* carbonate in 42 and 46% yields, respectively. The mechanism is not clear at present. The relative configuration was determined by a comparison with authentic samples prepared from **11** and **12** [(1) 10% aq. NaOH/MeOH; (2) $(Cl_3CO)_2CO/Et_3N/CH_2Cl_2$].
11. For a detailed discussion about the reaction mechanism, see Ref. 2.
12. Jackson, W. P. *Synlett.* **1990**, 536.
13. Zhang, Z.; Scheffold, R. *Helv. Chim. Acta* **1993**, *76*, 2602–2615.