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Direct and Stereoselective Preparation of Optically Active 1,3-Dioxolanes from the Corresponding Chiral Styrene Oxides

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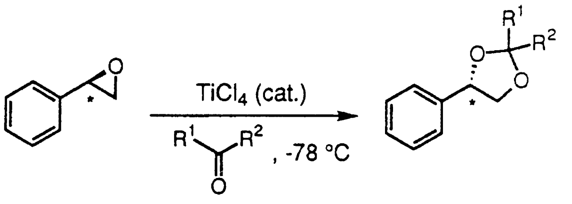
(Received May 13, 1994)

Synopsis. In the presence of a catalytic amount of titanium(IV) chloride, optically active styrene oxide and its analogs are directly converted into the corresponding acetals such as acetonides or cyclopentylidene acetals keeping up high to complete optical purity on the treatment with ketones.

Optically active epoxides are one of the most useful building blocks in synthetic chemistry; for example, they would readily react with various nucleophiles to form 1,2-bifunctionalized derivatives such as 1,2-diols or 1,2-amino alcohols with regio- and stereoselectivities. These reactions have been frequently employed in key steps for the stereoselective synthesis of a wide variety of natural products.1) Since the resulting 1,2-diols are generally protected as 1,3-dioxolanes for isolation or easy handling,2) the development of direct and stereoselective conversion of optically active epoxides into the corresponding acetonides is desired in order to achieve stereoselective synthesis of polyfunctionalized oxygen-containing compounds. Although the direct formation of acetonides from epoxides and ketones was developed by using Lewis acids,3) few studies have been done concerning stereochemistry4) until Sharpless asymmetric epoxidation of allyl alcohols was developed.5) Stereoselective conversion of epoxides into the corresponding acetonides have been well studied in the cases of the optically active epoxides of allyl alcohols,6) and also the intramolecular acetalization was successfully applied to the stereoselective synthesis of *exo*-brevicomin derivatives.7) Though several acid catalysts have been examined for the promotion of the acetalization of styrene oxide,8) few examples have been reported on the stereoselective conversion of various styrene oxide derivatives because effective methods for their asymmetric synthesis were limited.9) Recently practical enantioselective procedures have been developed for the epoxidation of unfunctionalized olefins into the optically active epoxides; for example, biological oxidation of terminal olefins,10) optically active manganese(III)-catalyzed epoxidation of unfunctionalized olefins with sodium hypochlorite,11) iodosylbenzene12) or hydrogen peroxide13) as a terminal oxidant. Furthermore, an enantioselective aerobic epoxidation was achieved in the presence of an aldehyde and a catalytic amount of manganese(III) complex.14)

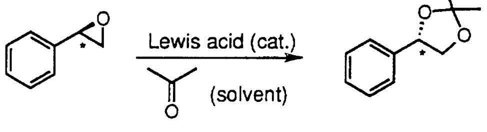
Here, we would like to report the direct and stereoselective conversion of optically active styrene oxide derivatives into the corresponding acetals by using a catalytic amount of titanium(IV) chloride (Scheme 1).

In the first place, various Lewis acids were examined in the acetonization reaction of optically active styrene oxide with acetone. By using tris(pentafluorophenyl)borane or zirconium(IV) tetrachloride, the corresponding optically active acetonide was obtained with inversion of configuration while the selectivities at 0 °C were not in satisfactory level (Table 1, Entries 1 and 2). When diehtyl ether–boron trifluoride (1/1), aluminum trichloride and tin(IV) chloride were respectively employed as catalysts at −40 °C, the selectivities were increased up to 77—93%, but the reac-



Scheme 1.

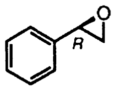
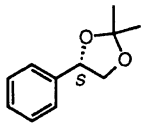
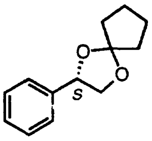
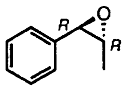
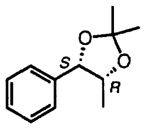
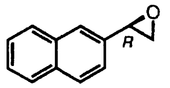
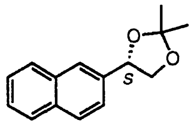
Table 1. Acetalization of Optically Active Epoxide



Entry[a)]	Lewis acid	Temperature/°C	Selectivity[b)]
1	$B(C_6F_5)_3$	0	63
2	$ZrCl_4$		63
3	$BF_3\cdot OEt_2$	−40	77
4	$AlCl_3$		86
5	$SnCl_4$		93
6	$TiCl_4$	−78	94
7	SbF_5		80
8	$TiCl_2(OTf)_2$		84
9	$SbF_5\cdot TiCl_4$		86

a) Reaction conditions (*R*)-styrene oxide (99.5% ee, Aldrich, Inc.) 0.50 mmol, dry acetone 5.0 ml, catalyst 0.05—0.15 mmol, under argon atmosphere, 6—8 h. b) Selectivity=100×(% ee of acetal)/(% ee of epoxide), and optical purity of acetal was determined by GC analysis (Chiraldex B-PH, ASTEC Co.).

Table 2. Preparation of Optically Active Acetals

Entry[a)]	Epoxide (Optical purity)	Acetal (Optical purity)	Selectivity[b)]	Yield/%[c)]
1	 (99.5% ee)[d,e)]	 (93.5% ee)[f)]	**94**	64
2[g)]		 (95.1% ee)[f)]	**96**	72
3	 (98.5% ee)[e,h)]	 (98.5% ee)[f)]	**>99**	72[i)]
4	 (95.8% ee)[j,k)]	 (95.5% ee)[k)]	**>99**	75

a) Reaction conditions; optically active epoxide 0.50 mmol, dry acetone 5.0 ml, $TiCl_4$ 0.15 mmol in CH_2Cl_2, −78 °C, 6 h, under argon atmosphere. b) Selectivity = 100×(% ee of acetal)/(% ee of epoxide). c) Isolated yield. d) Nacalai Tesque, Inc. e) Determined by HPLC analysis (Chiralpak AD, Daicel, Ltd.). f) Determined by GC analysis (Chiraldex B-PH, ASTEC Co.). g) Cyclopentanone (3 ml) in CH_2Cl_2 (2 ml). h) Aldrich, Inc. i) Diastereomer ratio; (1*S*,2*R*)-*cis* : (1*S*,2*S*)-*trans* = 93 : 7. j) Preparation is described in Ref. 17. k) Determined by HPLC analysis (Chiralcel OB, Daicel, Ltd.).

tions proceeded too slowly to obtain the acetonides in reasonable yields (Entries 3—5). By employing rather strong Lewis acids such as titanium(IV) chloride, antimony(V) fluoride, dichlorobis(trifluoromethanesulfonato)titanium(IV),[15)] or complex of titanium(IV) chloride and antimony(V) fluoride (1 : 1), every optically active styrene oxide was completely consumed at −78 °C as shown in Entries 6—9, and titanium(IV) chloride was found to be the most efficient catalyst to achieve high selectivity among them (Entry 6).

The titanium-catalyzed acetonization was successfully applied to various optically active styrene oxide analogs. As shown in Table 2, (*R*)-styrene oxide (optical purity; 99.5% ee) was converted into the corresponding optically active acetonide, (*S*)-2,2-dimethyl-4-phenyl-1,3-dioxolane, in 64% yield and 93.5% ee. It should be pointed out that the absolute configuration was completely inverted. When the reaction was carried out in a mixed solvent of cyclopentanone and dichloromethane, the corresponding optically active (*S*)-cyclopentylidene acetal (95.1% ee) was obtained with 96% selectivity.[16)] Also (1*R*,2*R*)-1-phenylpropylene oxide (98.5% ee) was converted into the corresponding (1*S*,2*R*)-acetonide (98.5% ee) with complete inversion of the absolute configuration (Entry 3), and (*R*)-2-(2-naphthyl)oxirane (98.5% ee) afforded the corresponding optically active (*S*)-acetal (95.5% ee, Entry 4), respectively.

Thus, the present procedure provides a useful method for the direct stereoselective preparation of optically active acetonides from the corresponding chiral styrene oxide derivatives.

Experimental

Materials: (*R*)-1,2-Epoxydecane, (*R*)-benzyl glycidyl ether, (*S*)-styrene oxide, and (1*R*,2*R*)-1-phenylpropylene oxide were purchased from Japan Energy Co., Ltd., Daiso Co., Ltd., Nacalai Tesque Co., and Aldrich Inc., respectively. (*R*)-2-(2-naphthyl)oxirane was prepared by the reported method.[17)] Acetone, cyclopentanone, and dichloromethane were purified by distillation.

Chromatography: Column chromatography was conducted under silica gel (Daiso gel IR-60). HPLC analyses were performed on a Shimadzu LC-6A using Chiralcel OB column (Daicel Ltd., Co) and the peak areas were calculated on a Shimadzu chromatopack CR-4A (254 nm detection). GC-analyses for determination of optical yields were performed on a Shimadzu GC-15A or GC-14A using a glass capillary column (Chiraldex B-PH, 0.32 mm i.d., 30 m, 0.125 μm film, ASTEC Co.), and the peak areas were obtained with a Shimadzu chromatopack CR-5A.

General Procedure: To a stirred mixture of (*R*)-styrene oxide (60 mg, 0.50 mmol) in acetone (5.0 ml), a solution of titanium(IV) chloride (0.15 mmol) in dichloromethane was added drop by drop at −78 °C, and stirring was continued for 6 h under an argon atmosphere. The reaction mixture was quenched with aqueous sodium hydrogencarbonate and methanol at −78 °C, and was extracted with dichloromethane. After removal of solvents in vacuo, the corresponding (*S*)-acetonide was obtained by column chromatography in 67% yield (60 mg) and the optical purity was determined by GC analysis on Chiraldex B-PH (93.5% ee).

(*S*)-2,2-Dimethyl-4-phenyl-1,3-dioxolane (Entry 1 in Table 2): Optical purity was determined by GC analysis (oven temperature 85 °C, retention time 30.7 min (*R*), 33.2 min (*S*)).

(*S*)-2-Cyclopentylidene-4-phenyl-1,3-dioxolane (Entry 2 in Table 2): Optical purity was determined by GC analysis (oven temperature 110 °C, retention time 100.0 min (*R*), 103.5 min (*S*)).

(4*S*,5*R*)-2,2,5-Trimethyl-4-phenyl-1,3-dioxolane (Entry 3 in Table 2): Optical purity was determined by GC analysis (oven temperature 60 °C, retention time 91.2 min (4*S*,5*R*), 94.8 min (4*R*,5*S*)).

(*S*)-2,2-Dimethyl-4-(2-naphthyl)-1,3-dioxolane (Entry 4 in Table 2): Optical purity was determined by HPLC analysis (2-propanol 0.5% in hexane, flow rate 1.0 ml min^{-1}, retention time 22.1 min (*S*), 32.9 min (*R*)).

(*S*)-2,2-Dimethyl-4-octyl-1,3-dioxolane (Scheme 2 in Ref. 18): Optical purity was determined by GC analysis (oven temperature 70 °C, retention time 67.9 min (*R*), 71.1 min (*S*)).

(*S*)-2,2-Dimethyl-4-(benzyloxymethyl)-1,3-dioxolane (Scheme 2 in Ref. 18): Optical purity was determined by HPLC analysis (2-propanol 2.0% in hexane, flow rate 1.0 ml min $^{-1}$, retention time 13.7 min (*R*), 16.1 min (*S*)).

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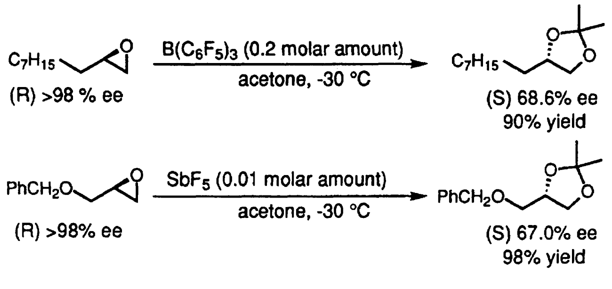
16) When the reaction was carried out in the mixture of dry cyclohexanone and dry dichloromethane at −78 °C, the corresponding (*S*)-cyclohexylidene acetal (82.7% ee) was obtained from (*R*)-styrene oxide (99.5% ee) in 67 % yield.

17) R. A. Johnson and K. B. Sharpless, "Catalytic Asymmetric Dihydroxylation," in "Catalytic Asymmetric Synthesis," ed by I. Ojima, VCH Inc., New York (1993), Chap. 4.4, p. 227. References are cited therein.

18) (*R*)-1,2-Epoxydecane was converted into (*S*)-2,2-dimethyl-4-octyl-1,3-dioxolane (68.6% ee) in 90% yield when tris(pentafluorophenyl)borane was used as a catalyst in acetone solvent at −30 °C, and (*S*)-2,2-dimethyl-4-(benzyloxymethyl)-1,3-dioxolane (67.0% ee) was obtained from (*R*)-benzyl glycidyl ether only when using antimony(V) fluoride as catalyst (Scheme 2).



Scheme 2.