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Control of Homocoupling Versus Reduction in Titanium(III)-Mediated Radical Opening of Styrene Oxides

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Abstract: We describe the use of titanocene monochloride in the implementation of an experimental procedure that enables control of the homolytic opening of styrene oxides in a chemoselectively controlled manner. This leads either to homocoupling products or to phenethyl alcohol derivatives. The process occurs via the generation of benzyl radicals, which may undergo a) recombination or b) reduction, yielding benzyl-Ti(IV) species upon subsequent addition of H_2O to the corresponding hydroxylated compounds. The main goal of this work is the study of the reactivity pattern of styrene oxides towards the formation of the mentioned products, thereby adding value to this interesting building block.

Introduction

Styrene oxide is a versatile and important building block that is widely used in organic synthesis (Figure 1). Among its significant applications, the Lewis acid-mediated ring-opening and rearrangement into phenylacetaldehyde should be highlighted.[1] The latter is a highly valuable chemical in the production of flavors and perfumes as it provides access to phenethyl alcohol. Also of interest is the Cp_2TiCl-catalyzed radical ring-opening (CRRO) of the epoxide,[2] which has been employed as an initiator in the living radical polymerization of styrene.[3] In addition, opening of the epoxide ring, predominantly through bimolecular nucleophilic substitution (SN_2) mechanisms, has been thoroughly studied in the literature. The scope of the attack is modulated by the hardness of the nucleophile.[4] Interestingly, the opening of an epoxy derivative by NaN_3 has been recently applied as key step for obtaining the alkyl moiety (side chain) of Taxol®.[5] Further, iodine[6] or Fe(III) ions[7] have been employed by means of Lewis acid catalysis for the opening of epoxides.

Styrene oxides have been reduced to obtain the corresponding anti-Markovnikov alcohols in a process catalyzed by $[Cp_2TiH]$.[8] Significantly, this year has been reported the catalyzed regioselective hydrogenation of epoxides likewise leading to anti-Markovnikov alcohols by using either Ti/Cr cooperative catalysis[9] or $Fe(BF_4)_2{\cdot}6H_2O$/tetraphos catalyst system.[10]

Preparation of 2,3-diphenyl-1,4-diols by modulated radical ring-opening reaction of styrene oxides have not been studied thoroughly up to now.[11] Structures related to the latter skeletons have been described as secondary products in intermolecular couplings of these epoxides with nitriles or vinylsulfones[12] or in catalyzed hydrogen-atom transfer reactions (CHAT).[13] The 2,3-diphenyl-1,4-diols are of great importance because of its use both as chiral auxiliaries[14] and as precursors in the synthesis of chroman,[15] 5-furanone,[16] or dibenzopentalene derivatives (Figure 1).[17]

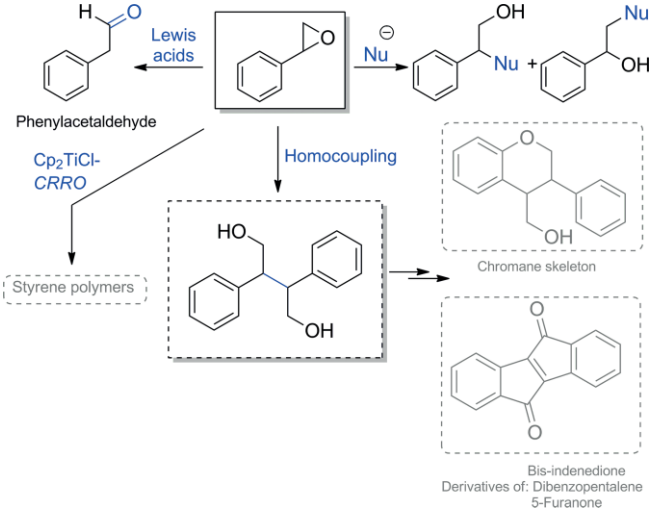

Figure 1. Use of styrene oxide as building block in organic synthesis. (CRRO = catalyzed radical ring-opening).

Herein we describe a study that potentially allows expanding the versatility of styrene oxide derivatives as functional synthons in organic synthesis. This method enables chemoselective control of either the formation of phenethyl alcohol derivatives or homocoupling products. The employed reagent, Cp_2TiCl, can guide the process towards either situation just by using different reaction conditions.

Results and Discussion

The starting point of this work was from our previous experience with the use of Cp_2TiCl in epoxide opening[18] in selective

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cyclization and homocoupling protocols,[19] or in the reduction of activated halogenated derivatives[20] in the presence of Brönsted acids. Based on this precedence, we anticipated that the use of excessive quantities of Ti(III) (2.0 equivalents) would give rise to the trapping of the generated radical (**I** in Figure 2) and yield an alkyl-Ti(IV) intermediate (**II** in Figure 2). The formation of **II** directs the reaction mechanism towards the selective formation of phenethyl alcohol (**2**), which suppresses the homocoupling path (Figure 2).

An initial experiment was carried out with 1.0 mmol of commercially available styrene oxide (**1a**) and 2.2 mmol of Ti(III) (see Experimental Section) at 0 °C. Under these conditions and after 10 min of stirring, phenethyl alcohol (**2a**, 23 % yield) and styrene (**3a**, 5 % yield) (Table 1, entry 1) were obtained. The use of similar experimental conditions, but modifying the molar ratio of Ti(III), led to significantly higher amounts of the undesired by-product **3a** (Table 1, entries 2 and 3). This suggested that a large molar excess of Ti(III) could favor an elimination mechanism and, consequently, the formation of styrene (**3a**) together with Ti_2O (Figure 2, grey-colored pathway). To facilitate an efficient pathway towards the formation of the alcohol **2a**, both the effect of decreasing the reaction temperature as well as the influence of substrate concentration [C] were evaluated (Table 1, entries 4–9).

Further, the initially employed experimental procedure was modified; instead of carrying out aqueous workup, water was

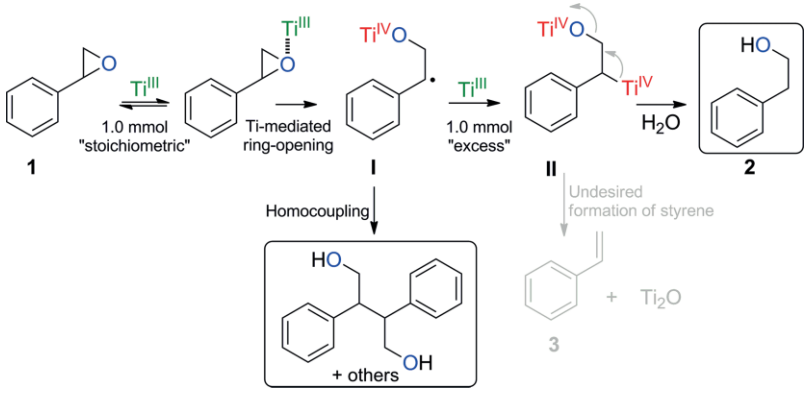
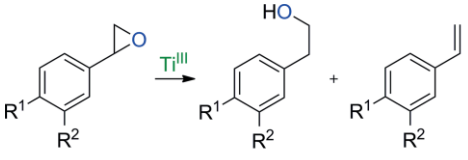


Figure 2. Proposed reaction mechanism for the Ti(III)-mediated ring opening of styrene oxides **1**, represented by **1a** (see text below). A stoichiometric amount of Ti(III) generates the radical **I** by means of Ti(III)-mediated epoxide ring-opening. A second mole of Ti(III) leads to the alkyl-Ti(IV) intermediate **II**, which, on hydrolysis, yields the phenethyl alcohol **2**.

Table 1. Reaction of styrene derivatives (**1a**–**1c**) with Cp_2TiCl; representative experiments.

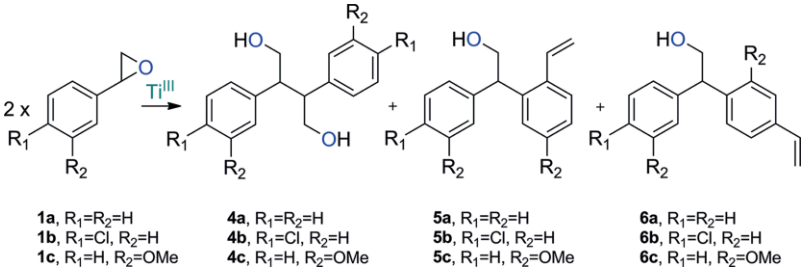


1a, R^1=R^2=H **2a**, R^1=R^2=H **3a**, R^1=R^2=H
1b, R^1=Cl, R^2=H **2b**, R^1=Cl, R^2=H **3b**, R^1=Cl, R^2=H
1c, R^1=H, R^2=OMe **2c**, R^1=H, R^2=OMe **3c**, R^1=H, R^2=OMe

Entry	Substrate	Cp_2TiCl [mmol]	C[a] [M]	T [° C]	T [min]	Product Yield[b] [%]		Total Yield [%]
						2[c]	3[c]	
1[d]	**1a**	2.2	0.35	0	10	23	5	28
2[d]	**1a**	3.0	0.35	0	10	20	11	31
3[d]	**1a**	5.0	0.35	0	15	12	17	29
4	**1a**	2.2	0.35	0	10	55	5	60
5	**1a**	2.2	0.35	–20	10	51	1	52
6	**1a**	2.2	0.35	–78	60	17	3	20
7	**1a**	2.2	0.07	0	10	70	6	76
8	**1a**	2.2	0.035	0	15	77	–	77
9	**1a**	2.2	0.035	–20	20	81	–	81
10	**1b**	2.2	0.07	–20	20	61	6	67
11	**1b**	2.2	0.035	–20	30	58	4	62
12	**1c**	2.2	0.07	–20	25	35	7	42
13	**1c**	2.2	0.035	–20	45	31	–	31

[a] Molar concentration of the substrate in the reaction mixture. [b] Products of a, b, or c types, for each case, according to the starting material used. [c] Yields correspond to isolated product after purification by column chromatography. [d] Test performed with aqueous treatment during the work-up of the reaction. All other experiments were conducted in a one-pot procedure by adding H_2O directly to the reaction mixture.

Table 2. Reaction of styrene derivatives (**1a**–**c**) with Cp_2TiCl; experiments towards selective homocoupling.



1a, R_1=R_2=H
1b, R_1=Cl, R_2=H
1c, R_1=H, R_2=OMe

4a, R_1=R_2=H
4b, R_1=Cl, R_2=H
4c, R_1=H, R_2=OMe

5a, R_1=R_2=H
5b, R_1=Cl, R_2=H
5c, R_1=H, R_2=OMe

6a, R_1=R_2=H
6b, R_1=Cl, R_2=H
6c, R_1=H, R_2=OMe

Entry	Substrate	Cp_2TiCl [mmol]	C[a] [M]	T [° C]	t [min]	Product Yield[b] [%] **4**[c] (α,α')	**5**[c] (α,o)	**6**[c] (α,p)	Total Homo-coupling Yield [%]
1	**1a**	1.8	0.35	25	5	27	20	20	67
2	**1a**	1.8	0.35	0	10	25	22	22	69
3	**1a**	1.8	0.35	–78	12	21	22	22	65
4[d]	**1a**	0.7	0.35	0	15	28	11	11	50
5[d]	**1a**	0.2	0.35	0	45	15	1	1	17
6	**1a**	1.0	0.35	0	10	64	8	8	80
7	**1a**	1.0	0.35	–15	10	54	14	14	82
8	**1a**	1.0	0.35	–78	15	33	24	24	81
9[d]	**1a**	0.7	0.35	–78	30	29	16	8	53
10[d]	**1a**	0.7	0.07	–78	20	28	26	22	76
11[d]	**1a**	0.7	0.035	–78	30	36	36	12	84
12	**1a**	1.0	0.035	–78	15	24	36	9	69
13	**1a**	1.0	0.07	–78	45	32	5	5	42
14	**1b**	1.0	0.35	0	2	55	–	–	55
15	**1b**	1.0	0.35	–78	5	60	–	–	60
16[d]	**1b**	0.7	0.35	–78	20	45	–	–	45
17[d]	**1b**	0.2	0.35	–78	120	19	–	–	19
18	**1b**	1.0	0.07	–78	20	56	–	–	56
19	**1b**	1.0	0.035	–78	900	14	–	–	14
20	**1c**	1.0	0.35	–78	10	65	14[e]	–	79
21[d]	**1c**	0.7	0.35	–78	45	52	7[e]	–	59
22	**1c**	1.0	0.035	–78	600	18	–	–	18

[a] Molar concentration of the substrate in the reaction mixture. [b] Products of a, b, or c types, for each case, according to the starting material used. [c] Yields correspond to isolated product after purification by column chromatography. [d] For the substoichiometric protocol for homocoupling reaction, see Experimental Section. [e] Determined from impure chromatography fractions, which could not be purified further in our hands. Therefore, these yields are considered rough estimates, and no definite spectroscopic characterization is provided for compound **5c**.

added directly to the mixture once **1a** had reacted with the previously generated Ti(III). This provides the H atom that is necessary for the formation of the OH group via in situ protonation of -OTi(IV) (Figure 2, last step). On the one hand, the yields of **2a** were found to improve in the experiments that were performed at 0 and –20 °C (Table 1, entries 4–5). However, at a significantly lower temperature (–78 °C) no such effect was seen (Table 1, entry 6). On the other hand, by varying the molar substrate concentration (Table 1, entries 7–9), it was found that the best experimental conditions for the formation of **2a** were those corresponding to entry 9, leading to an 81 % yield of **2a** without the observation of by-product **3a**. Moreover, the use of other styrene oxide derivatives, such as **1b** and **1c**, led to the formation of the corresponding alcohols **2b** and **2c** in moderate to good yields (Table 2, entries 10–13). It is noteworthy that significant amounts of homocoupling products (see below) were not observed for the employed experimental conditions of an excess amount of Ti(III).

Encouraged by successful chemoselectivity control, via addressing the fate of intermediate **II**, we attempted to direct the process towards the formation of homocoupling products (see Figure 2). Being aware of the role of excess Ti(III) in the transformation of the benzyl radical **I** into **II**, the Ti(III) molar ratio was lowered with respect to those listed in Table 1. Thus, 1.0 mmol of **1a** was treated with 1.8 mmol of Ti(III) at room temperature. This first test evidenced a predominant formation of the homocoupling products (**4a**–**6a**, 67 % yield) along with smaller amounts of phenethyl alcohol **2a** and styrene **3a**, in 23 % yield and 3 % yield, respectively (Table 2, entry 1). Noteworthily, the homocoupling resulted in a mixture of **4a** (being a 1:1 mixture of diastereomers), **5a**, and **6a** in a 3:2:2 ratio (Table 2, entry 1). It was observed that a tenfold increase of the concentration helped to shift the selectivity in favor of **4** (see Table 1, entry 9, and Table 2, entry 1).

This observation and the distribution of the reaction products is rationalized in the mechanistic proposal depicted in Figure 3. The coordination of the epoxide oxygen atom in **1** with Cp_2TiCl initiates the ring-opening towards the benzyl radical **I,** which is stabilized by the delocalization of the radical center (see resonance structures $\mathbf{I}_\alpha$, $\mathbf{I}_o$, and $\mathbf{I}_p$). Thus, the homocoupling products **4**–**6** derive from three different combinations that imply these resonance structures: $\mathbf{I}_\alpha + \mathbf{I}_\alpha$ (α, α' coupling yields **4**),

I_α + I_o (α, *ortho* coupling yields **5** via intermediate **III**), and I_α + I_p (α, para coupling yields **6** via intermediate **IV**). Products that derive from direct coupling of only I_o and/or I_p were not detected. The formation of the vinylic double bond in products **5** and **6** is caused by the elimination of a hydroxy-titanium species, facilitating the re-aromatization of the system (Figure 3, I_α + I_o and I_α + I_p couplings). Additionally, as shown in Figure 2, intermediate **I** can be trapped by a second mole of Ti(III), yielding the intermediate **II**. This enables the formation of compounds **2** and **3**, as described above. However, when using less than 2 mol equivalents of the Ti(III) reagent, this path is not effective.

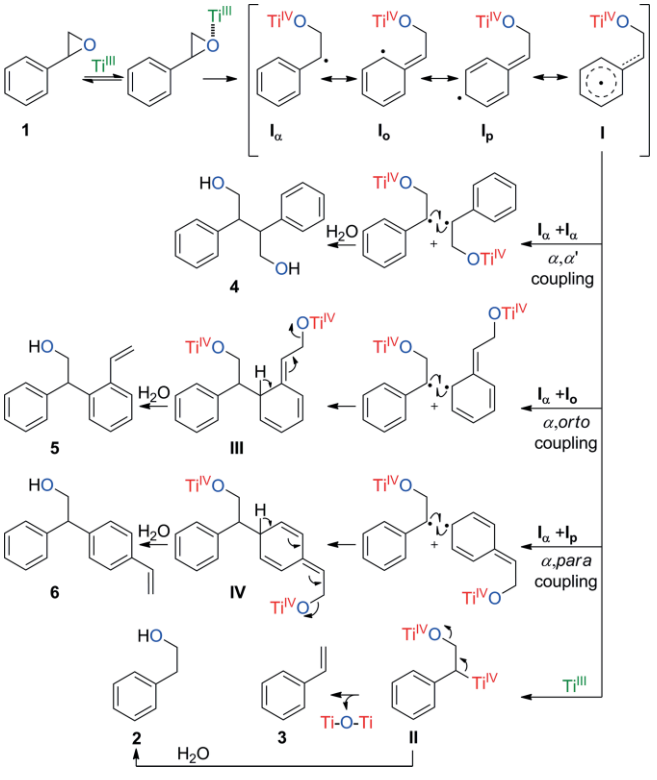


Figure 3. Proposed mechanism for Ti(III)-mediated homocoupling of styrene oxide derivatives. The substrate is symbolized as **1,** being represented by structure **1a**.

The obtained results encouraged us to optimize the formation of homocoupling products (Table 2). Thus, the initial reaction conditions for substrate **1a** were repeated, but temperatures were decreased to 0 and –78 °C (Table 2, entries 2–3). However, the yield of the homocoupling product did not improve significantly; only a slight change in the relative distribution of products **4a**–**6a** was noted. Then, in accordance with the mechanistic proposal, a further decrease of the Ti(III): substrate molar ratio was tested. This should disfavor the formation of **II**, shifting the competition between the reaction paths of **I** towards the homocoupling products. Thus, the reactions were performed with 0.7 or 0.2 mmol of Cp_2TiCl at room temperature. However, the substoichiometric amounts of reagent led to significantly lower yields of **4a**–**6a** (50 % and 17 % yields, respectively; Table 2, entries 4–5). Hence, the use of 1.0 mmol of Ti(III) was considered as ideal, being consistent with the theoretical 1:1 Ti(III)/substrate reaction stoichiometry. Conducting the experiment for this ratio and at 0 °C led to the observation of 80 % yield of the homocoupling products and a strong preference for product **4a** (64 % yield; see Table 2, entry 6). Lowering the temperature to –15 or –78 °C and keeping the Ti(III):**1a** ratio had no effect on the total yield of the homocoupling products, but it changed the ratio of **4a**–**6a** and disfavored the formation of **4a**; Table 2, entries 7–8.

Additional tests were carried out to gain further insights into the control of the formation of homocoupling products and the involved regioselectivity (i.e., formation of **4a**, **5a** or **6a**). A series of experiments were designed to optimize the substrate concentration in relation to the amount of Ti(III). For all conditions, significant yields of α,*ortho* (**5a**) and α,*para* (**6a**) coupling products were obtained (Table 2, entries 9–13). This allowed us to conclude that the best conditions for the selective formation of **4a** are those used in entry 6 of Table 2. Regarding optimization of the other homocoupling products, it can be affirmed that a decrease of the substrate concentration and operation at –78 °C led to **5a** as the major product (Table 2, entries 11–12). 4-Chloro-styrene oxide (**1b**) was tested with the idea to evaluate the impact of the electronic effect of the aryl substituent. We speculated that increasing the electronic density of the aromatic ring could exert a direct influence, favoring the formation of the benzyl radicals I_o and I_p; Figure 3. This would significantly increase the yield of **5b** and **6b** homocoupling products. A first test (Table 2, entry 14) under standard conditions led to a moderate yield of 55 % for **4b** in very short reaction time. The products **5b** and **6b** were not observed. The yield of **4b** (1:1 mixture of diastereomers) was slightly increased by carrying out the reaction at –78 °C (Table 2, entry 15). Other modifications of the experimental conditions, such as the substrate concentration, the amount of reagent, or the reaction time, did not yield the formation of **5b** or **6b** (Table 2, entries 16–19). Hence, substrate **1b** yields selectively **4b** as the only coupling product. Finally, the behavior of the substrate epoxide **1c** was studied. The location of the methoxy group in the meta position should stimulate the opening of the epoxide ring and the formation of benzyl radical **I**. Accordingly, the corresponding homocoupling product **4c** (1:1 mixture of diastereomers) was obtained, but no product **6c** was seen. It must be also mentioned that no diastereoselectivity was found for **4a**–**c** derivatives in under any of the conditions tested throughout the study.

Conclusions

In summary, we have developed a synthetic method to achieve control over the chemoselectivity of the homolytic Ti(III)-mediated ring opening of styrene oxides, yielding either 2,3-diphenyl-1,4-diol derivatives or phenethyl alcohol derivatives. The proposed mechanism involves the generation of benzyl radicals that evolve into homocoupling products or phenethyl alcohol derivatives in moderate to good chemical yields. The key factor is the variation of the amount of Ti(III) reagent, alongside the fine-tuning of substrate concentration and reaction temperature. The presence or absence of excess Ti(III) modulates the fate of the benzyl radicals that are either directly involved in

homocoupling or in the formation of an alkyl-Ti(IV) intermediate, being competitive pathways. The herein obtained results on the reactivity of styrene oxides broaden their scope as precursors for the synthesis of added-value building blocks.

Experimental Section

Instrumentation, reagents and solvents: All air- and water-sensitive reactions were performed in flasks that were flame-dried under a positive flow of argon and conducted under an atmosphere of argon. Tetrahydrofuran (THF) was freshly distilled prior to use from sodium/benzophenone and exhaustively deoxygenated for 30 min under argon for each of the Cp_2TiCl_2/Mn reactions. The reagents were purchased at the highest commercial quality and used without further purification unless stated otherwise. Silica gel SDS 60 (35–70 μm) was used for flash column chromatography. The reactions were monitored by thin-layer chromatography (TLC), carried out with 0.25 mm E. Merck silica gel plates (60F-254), using UV light for visualization and a solution of phosphomolybdic acid in ethanol as developing agent. NMR studies were performed with a Bruker ARX 400 (^{1}H 400 MHz/^{13}C 100 MHz) spectrometer. Accurate mass determinations were carried out with an AutoSpec-Q mass spectrometer arranged in an EBE geometry (Micromass Instrument, Manchester, UK) and equipped with a FAB source. The instrument was operated at 8.0 K V of accelerating voltage, and Cs^+ was used as the primary ion. The low-resolution mass spectra were obtained with a quadrupolar mass spectrometer Platform II (Micromass Instruments, Manchester, UK).

General Procedure for the Reduction Reaction: Standard protocol: A mixture of Cp_2TiCl_2 (2.2 mmol) and Mn dust (8.0 mmol) in thoroughly deoxygenated THF (27 mL) was stirred under an Ar atmosphere at room temperature until the red solution turned green. The corresponding styrene oxide (1.0 mmol) in deoxygenated THF (1.6 mL) was then added at –20 °C. On completion of the reaction (TLC monitoring), THF was removed, and the reaction was quenched with 1 N HCl, extracted with *t*BuOMe, washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude was purified by column chromatography on silica gel to afford the corresponding products. The NMR spectroscopic data are identical to those for commercially available compounds.

General Procedures for the Homocoupling Reaction: Representative procedures: A mixture of Cp_2TiCl_2 (1.0 mmol) and Mn dust (8.0 mmol) in thoroughly deoxygenated THF (2 mL) was stirred under an Ar atmosphere at room temperature until the red solution turned green. The corresponding styrene oxide (1.0 mmol) in deoxygenated THF (0.9 mL) was then added at –15 °C. On completion of the reaction (TLC monitoring), THF was removed, and the reaction was quenched with 1 N HCl, extracted with *t*BuOMe, washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude was purified by column chromatography on silica gel to afford the corresponding products. For substoichiometric reactions, a mixture of Cp_2TiCl_2 (0.7 mmol) and Mn dust (8.0 mmol) in thoroughly deoxygenated THF (27 mL) was stirred at room temperature until the red solution turned green. Then, a solution of the corresponding styrene oxide (1.0 mmol), 2,4,6-collidine (7.0 mmol), and TMSCl (4.0 mmol) in deoxygenated THF (1.6 mL) was added at –78 °C. The latter two served to regenerate Cp_2TiCl_2 and thereby closed the catalytic cycle [2g]. The reaction mixture was stirred for 30 min, quenched with 1 N HCl, extracted with *t*BuOMe, washed with brine, dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting crude was taken up in THF (5 mL) and stirred at room temperature. Then, TBAF 1.0 M in THF (1.1 mmol) was added, and the solution was stirred for 1 h and concentrated at reduced pressure. The resulting crude was purified by column chromatography on silica gel to afford the corresponding products.

2,3-Diphenylbutane-1,4-diol 4a.[21] **(2*R*,3*S*)-2,3-Diphenylbutane-1,4-diol:** White amorphous solid. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.22 (m, 6H), 7.18 (m, 4H), 3.48–3.36 (m, 4H), 2.96 (m, 2H) ppm*; ^{13}C NMR (100 MHz, CD_3OD): δ = 142.0 ($2C_{Ar,quat}$), 128.4 ($4C_{Ar}$), 128.1 ($4C_{Ar}$), 126.3 ($2C_{Ar}$), 64.5 ($2CH_2OH$), 50.7 (2CH) ppm. FABHRMS calcd. for $C_{16}H_{18}O_2Na$ $[M + Na]^+$ 265.1199, found 265.1189. ***(2S,3S)-2,3-Diphenylbutane-1,4-diol*: Yellow syrup. ^{1}H NMR (400 MHz, $CDCl_3$):** δ = 7.16–7.09 (m, 6H), 6.96 (d, 4H), 3.99–3.89 (ddd, 4H), 3.25 (t, 2H), 2.56 (bs, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.6 ($2C_{Ar,quat}$), 128.6 ($4C_{Ar}$), 128.1 ($4C_{Ar}$), 126.5 ($2C_{Ar}$), 65.6 ($2CH_2OH$), 51.0 (2CH) ppm. FABHRMS calcd. for $C_{16}H_{18}O_2Na$ $[M + Na]^+$ 265.1199, found 265.1193. *Signals for OH protons were not observed.

2,3-Bis(4-chlorophenyl)butane-1,4-diol (4b)*:* Diastereoisomer 1: White amorphous solid. ^{1}H NMR (400 MHz, CD_3OD): δ = 7.21 (m, 8H), 3.46–3.36 (m, 4H), 2.98 (t, 2H) ppm*; ^{13}C NMR (100 MHz, CD_3OD): δ = 140.6 ($2C_{Ar,quat}$), 132.0 ($2C_{Ar,quat}$), 130.0 ($4C_{Ar}$), 128.1 ($4C_{Ar}$), 64.0 ($2CH_2OH$), 49.8 (2CH) ppm. CIMS calcd. for $C_{16}H_{16}O_2Cl_2$ $[M]^+$ 310.0527, found 310.0514. Diastereoisomer 2: Yellow syrup. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12 (d, *J* = 8.4 Hz, 4H), 6.87 (d, *J* = 8.4 Hz, 4H), 3.89 (d, 4H), 3.18 (t, 2H), 2.46 (bs, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.1 ($2C_{Ar,quat}$), 132.4 ($2C_{Ar,quat}$), 129.8 ($4C_{Ar}$), 128.4 ($4C_{Ar}$), 65.2 ($2CH_2OH$), 50.2 (2CH) ppm. CIMS calcd. for $C_{16}H_{16}O_2Cl_2$ $[M]^+$ 310.0527, found 310.0515. *Signals for OH protons were not observed.

2-Phenyl-2-(2-vinylphenyl)ethanol (5a): Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 7.3 Hz, 1H), 7.30–7.22 (m, 8H), 7.01 (dd, *J* = 14.2, 9 Hz, 1H), 5.57 (dd, *J* = 14.5, 1 Hz, 1H), 5.28 (dd, *J* = 9, 1 Hz, 1H), 4.53 (t, *J* = 6 Hz, 1H), 4.16 (d, *J* = 6 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.3 ($C_{Ar,quat}$), 138.4 ($C_{Ar,quat}$), 138.2 ($C_{Ar,quat}$), 134.9 (CH_{olef}), 128.9 ($2C_{Ar}$), 128.7 ($2C_{Ar}$), 128.2 (C_{Ar}), 127.3 (C_{Ar}), 127.2 ($2C_{Ar}$), 126.9 (C_{Ar}), 117.0 ($CH_{2\text{-}Olef}$), 66.2 (CH_2OH), 49.4 (CH) ppm. CIMS calcd. for $C_{16}H_{16}O$ $[M + H]^+$ 224.1201, found 224.1202.

2-Phenyl-2-(4-vinylphenyl)ethanol (6a): Colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.15 (m, 9H), 6.61 (dd, *J* = 17, 11 Hz, 1H), 5.64 (d, *J* = 17 Hz, 1H), 5.14 (d, *J* = 11 Hz, 1H), 4.15–4.08 (m, 3H) ppm; ^{13}C NMR (125 MHz $CDCl_3$): δ = 141.5 ($C_{Ar,quat}$), 141.3 ($C_{Ar,quat}$), 136.6 ($C_{Ar,quat}$), 136.5 (CH_{Olef}), 129.0 ($2C_{Ar}$), 128.7 ($2C_{Ar}$), 128.5 ($2C_{Ar}$), 127.1 (C_{Ar}), 126.8 ($2C_{Ar}$), 113.9 ($CH_{2\text{-}Olef}$), 66.3 (CH_2OH), 53.6 (CH) ppm. CIMS calcd. for $C_{16}H_{16}O$ $[M]^+$ 223.1123, found 223.1121.

2,3-Bis(3-methoxyphenyl)butane-1,4-diol (4c): Diastereoisomer 1: White amorphous solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.30 (t, *J* = 7.9 Hz, 2H), 6.92 (d, *J* = 7.6 Hz, 2H), 6.88 (s, 2H), 6.83 (dd, *J* = 2.2, 8.2 Hz, 2H), 3.83 (s, 6H), 3.59 (dd, *J* = 7.9, 11.0 Hz, 2H), 3.53 (dd, *J* = 2.6, 10.9 Hz, 4H), 3.06 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 160.3 ($2C_{Ar,quat\text{-}OMe}$) 142.3 ($2C_{Ar,quat}$), 130.0 ($2C_{Ar}$), 120.6 ($2C_{Ar}$), 114.3 ($2C_{Ar}$), 112.4 ($2C_{Ar}$), 65.6 ($2CH_2OH$), 55.2 (2OMe), 50.8 (2CH) ppm. FABHRMS calcd. for $C_{18}H_{22}O_4Na$ $[M + Na]^+$ 325.1416, found 325.1426. Diastereoisomer 2: Yellow syrup. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.07 (t, *J* = 7.9 Hz, 2H), 6.64 (dd, *J* = 8.1, 2.0 Hz, 2H), 6.60 (d, *J* = 7.5 Hz, 2H), 6.52 (s, 2H), 3.96 (dd, *J* = 10.9, 4.4 Hz, 2H), 3.92 (dd, *J* = 10.8, 4.4 Hz, 2H), 3.67 (s, 6H), 3.22 (m, 2H), 1.89 (bs, 2H) ppm; ^{13}C NMR (150 MHz $CDCl_3$): δ = 159.4 ($2C_{Ar,quat\text{-}OMe}$), 142.1 ($2C_{Ar,quat}$), 129.1 ($2C_{Ar}$), 121.0 ($2C_{Ar}$), 114.5 ($2C_{Ar}$), 112.0 ($2C_{Ar}$), 65.4

($2CH_2OH$), 55.0 (2OMe), 50.8 (2CH) ppm. HRFABMS calcd. for $C_{18}H_{22}O_4$ $[M]^+$ 303.1596, found 303.1584.

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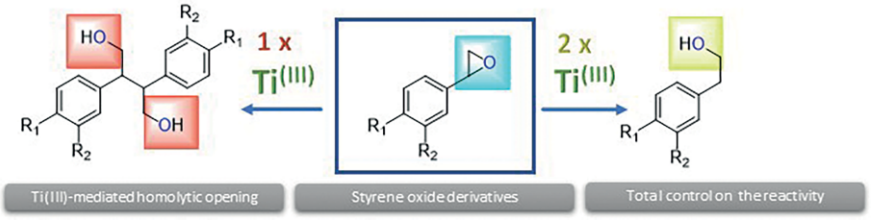

Titanocene monochloride mediates the homolytic opening of styrene oxides in a chemoselectively controlled manner, leading either to homocoupling products or to phenethyl alcohol derivatives. Remarkably this protocol encompasses the diverse reactivity pattern of styrene oxides towards the desired products, thereby adding value to this interesting building block.

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