

## Chiral Discrimination in Electrocatalytic Oxidation of (*R*)- and (*S*)-1-Phenylethanol Using a Chiral Nitroxyl Radical as Catalyst

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A chiral nitroxyl radical, (6*R*,7*S*,10*R*)-4-oxo-2,2,7-trimethyl-10-isopropyl-1-azaspiro[5.5]undecane-*N*-oxyl, was used as catalyst in the electrooxidation reaction of (*R*)- and (*S*)-1-phenylethanol. Cyclic voltammetric studies showed that the catalytic current for the oxidation of (*R*)-1-phenylethanol is highly enhanced as compared with a very small enhancement in the oxidation current for the (*S*)-isomer. The (*R*)-isomer can be detected selectively in a mixture of (*R*)- and (*S*)-1-phenylethanol, even in the presence of an excess amount of (*S*)-isomer.

**Key words** chiral nitroxyl radical; electrocatalytic oxidation; chiral discrimination; cyclic voltammetry

Nitroxyl radicals such as 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO) are known to be catalysts in the electrocatalytic oxidation of alcohols and amines.<sup>1,2</sup> In TEMPO-catalyzed electrooxidation reactions, the active form of TEMPO is reproduced rapidly by the electrode reaction from its reduced form, resulting in an efficient electrocatalytic system. This system has recently been employed by Ohmori *et al.* for the amperometric detection of alcohols in flow injection analysis.<sup>3</sup> On the other hand, we have reported that carbon felt electrodes coated with a polymer film containing chiral TEMPO derivatives can be used successfully for the purpose of enantioselective electrosyntheses.<sup>4-6</sup> If the chiral TEMPO derivatives can be used as catalysts in the amperometric detection system, chiral alcohols and other compounds may be determined enantioselectively. Such a sensing system would be extremely attractive in view of the fact that enzymes usually must be used as catalysts for the amperometric detection of chiral compounds. In other words, it may be possible to replace enzymes with the chiral TEMPO derivatives in the electrochemical determination of chiral alcohols. In the present communication, we report the possible use of a chiral TEMPO derivative, (6*R*,7*S*,10*R*)-4-oxo-2,2,7-trimethyl-10-isopropyl-1-azaspiro[5.5]undecane-*N*-oxyl (**1**)<sup>7</sup> (Chart 1), as a catalyst for the amperometric determination of (*R*)-1-phenylethanol in the presence of (*S*)-isomer.

To evaluate the redox properties of **1** in solution, a cyclic voltammogram (CV) of **1** was measured in an acetonitrile so-

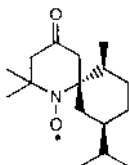


Chart 1. Structure of Chiral TEMPO Derivative **1**

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lution containing **1** (100 mM) and NaClO<sub>4</sub> (100 mM) as a supporting electrolyte. A glassy carbon disk electrode (diameter: 3 mm) and a platinum wire were used as working and auxiliary electrodes, respectively. An Ag/AgCl electrode was used as a reference electrode. All measurements were performed at room temperature (20 ± 2 °C). Figure 1 shows a typical CV of **1**, which clearly exhibits a reversible redox wave. The peak potentials of the CV for oxidation (anodic) and reduction (cathodic) waves are observed at +720 and +650 mV, respectively. Thus the peak separation of the CV was 70 mV, which is close to the theoretical value (*ca.* 59 mV) for the CV of the reversible one-electron redox system.<sup>8</sup> The CV was stable during the repeated scans of the electrode potential over +200—+1000 mV. The redox properties of an isomer of **1**, (6*R*,7*R*,10*R*)-4-oxo-2,2,7-trimethyl-10-isopropyl-1-azaspiro[5.5]undecane-*N*-oxyl (**2**), were also examined similarly. However, unfortunately **2** was found to be somewhat unstable: decomposition was suggested by the decay of the CV during repeated potential scans. These results suggest that **1** may be used as a catalyst for the electrocatalytic oxidation reactions.

The electrocatalytic behavior of **1** for the oxidation reaction of (*R*)- and (*S*)-1-phenylethanol was studied by measuring the CV of **1** in the presence of the alcohols (Fig. 2). The CVs for (*R*)- and (*S*)-1-phenylethanol were remarkably dif-

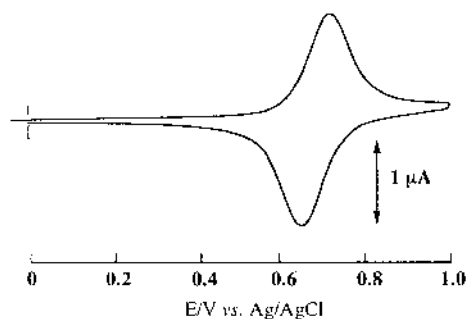


Fig. 1. Cyclic Voltammogram of **1** (0.1 M) in NaClO<sub>4</sub>/CH<sub>3</sub>CN (0.1 M). Scan rate: 25 mV s<sup>-1</sup>.

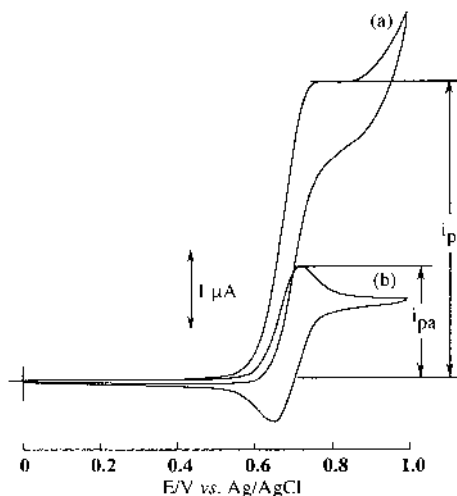


Fig. 2. Cyclic Voltammograms of **1** (0.1 mM) in NaClO<sub>4</sub>/CH<sub>3</sub>CN (0.1 M) in the Presence of (*R*)- 1.6 mM (a) and (*S*)-1-Phenylethanol 1.6 mM (b)

The sample solution contains 2,6-lutidine (3.2 mM). Scan rate: 25 mV s<sup>-1</sup>.

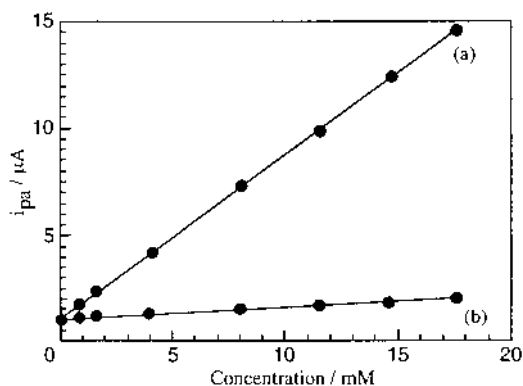


Fig. 3. An Anodic Peak Current in Cyclic Voltammograms of **1** as a Function of the Concentration of (*R*)- (a) and (*S*)-1-Phenylethanol (b)

Scan rate: 25 mV s<sup>-1</sup>.

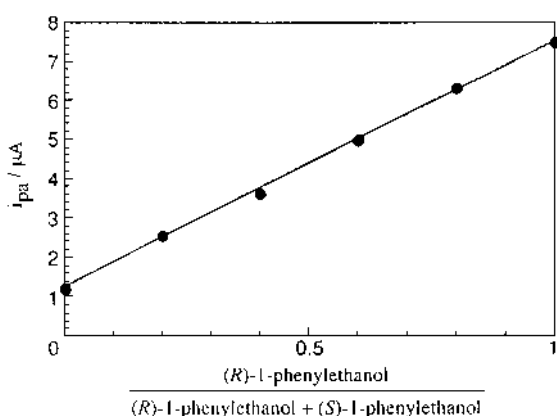


Fig. 4. An Anodic Peak Current in Cyclic Voltammograms of **1** as a Function of the Mole Ratio of (*R*)-1-Phenylethanol in a Mixture of (*R*)- and (*S*)-1-Phenylethanol

The total concentration of (*R*)- and (*S*)-1-phenylethanol is 8.1 mM. Scan rate: 25 mV s<sup>-1</sup>.

ferent from each other. The anodic peak current ( $i_{pa}$ ) of **1** was highly enhanced in the presence of (*R*)-1-phenylethanol and its cathodic peak disappeared, while the enhancement in  $i_{pa}$  was small in the presence of (*S*)-isomer. The CV behavior of **1** should be explained based on the electrocatalytic oxidation mechanism.<sup>1-3)</sup> In this mechanism, the active form of **1** oxidizes (*R*)-1-phenylethanol and is converted into the reduced form of **1**, which in turn is oxidized electrochemically into the original active form of **1**. In other words, the active **1** can be recycled electrocatalytically, in which one electron is transferred from one alcohol molecule to the electrode by the mediation of **1**. In any event, **1** can discriminate the chirality of (*R*)- and (*S*)-1-phenylethanol in electrocatalytic oxidation.

For the use of **1** in amperometric determination of alcohols, the peak current of the CV depends on the concentration of the alcohols. For this reason, we checked the dependence of the peak current on the concentration of (*R*)- and (*S*)-1-phenylethanol. The CV was measured in an acetonitrile solution containing **1** (0.1 mM) and NaClO<sub>4</sub> (20 mM) in the

presence of the alcohols. 2,6-Lutidine was also added to the sample solution because a deprotonating agent is required for the TEMPO-mediated oxidation reaction.<sup>1-3)</sup> The peak current of the CV was plotted as a function of the concentration of (*R*)- and (*S*)-1-phenylethanol (Fig. 3). The peak current of the CV increased linearly with the increasing concentration of (*R*)-1-phenylethanol in the sample solution, while in the presence of (*S*)-isomer the current increased very slightly. These data suggest that one can determine the concentration of (*R*)-isomer of the alcohol by measuring the anodic peak current of the CV of **1**. Judging from the low response to the (*S*)-isomer, the (*R*)-isomer may be determined selectively even in the presence of (*S*)-isomer in the sample solution.

The effects of (*S*)-isomer on the peak current of the CV of **1** were estimated using sample solutions containing both (*R*)- and (*S*)-1-phenylethanol. The CV of **1** was measured in the presence of different ratios of (*R*)- and (*S*)-isomers of the alcohol (Fig. 4). The peak current depended linearly on the ratio of (*R*)-isomer in a mixture of (*R*)- and (*S*)-isomers, even in the presence of an excess amount of (*S*)-isomer. This suggests that the present system may be also applicable to the determination of optical purity of racemic mixtures of 1-phenylethanol.

Thus, we have demonstrated that the chiral TEMPO derivative **1** discriminates the chirality of (*R*)- and (*S*)-1-phenylethanol in the electrocatalytic oxidation reaction. For example, the enhanced current for the oxidation of (*R*)-isomer 8 mM is *ca.* 14 times higher than that for the same concentration of (*S*)-isomer. The **1**-catalyzed oxidation reaction can be used for the amperometric determination of (*R*)-isomer of the alcohol even in the presence of an excess amount of (*S*)-isomer. The present system may be applicable to the electrochemical detector in chromatography, as suggested previously by Ohmori *et al.*<sup>3)</sup> Furthermore, if **1** is immobilized on the surface of metal or carbon electrodes, the modified electrodes will be a novel class of electrochemical sensors which discriminate the chirality of the substrates without using enzymes.

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