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One-Step Transformation of Carboxylic Acids into Aldehydes Induced by the Electrochemical Oxidation of Ph_3P

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Constant-current electrolysis (CCE) of Ph_3P and a carboxylic acid (RCO_2H, 1) in CH_2Cl_2 using a one-compartment cell equipped with two graphite plates as an anode and a cathode under a nitrogen atmosphere gave the corresponding aldehyde (2) when $Ph_3P^+H \cdot ClO_4^-$ was used as a supporting electrolyte. The partial reduction was affected by the choice of electrolysis conditions, especially temperature and current density, depending on the structure of 1. Thus, the CCE of 1 with R = Ph–, *o*-Cl-Ph–, *p*-MeO-Ph–, $Ph(CH_2)_2$–, $CH_3(CH_2)_8$–, Ph_2CH– proceeded smoothly at −30 °C in fair yields. In the case of 1 with R = cyclo-C_6H_{11}– and $(CH_3)_2CH$–, the electrolysis had to be carried out under reflux, and with R = $(CH_3)_3C$– the aldehyde was obtained only in a poor yield even under reflux. Based on the results of cyclic voltammetry of the anolyte obtained by the CCE of CH_2Cl_2 solutions of Ph_3P, $Ph_3P^+H \cdot ClO_4^-$, and 1 in a divided cell, the sequence of the partial reduction is proposed to be as follows: formation of acyloxy triphenylphosphonium ion (3) at the anode; the reaction of 3 with Ph_3P to afford the corresponding acyl triphenylphosphonium ion (4); reduction of 4 to the α-hydroxyalkyl triphenylphosphonium ion (7) at the cathode; decomposition of 7 to 2 and Ph_3P during the aqueous work-up after the CCE. The voltammetric study also suggested that the ease of the transformation of 3 to 4 is reflected in the required CCE conditions and may determine the yield of 2.

Keywords triphenylphosphine; acyl triphenylphosphonium ion; partial reduction; carboxylic acid; aldehyde; constant-current electrolysis

The preparation of aldehydes from carboxylic acids is generally performed by two methods. One is a reduction–oxidation sequence from a carboxylic acid or its ester *via* the corresponding alcohol. The other includes partial reduction of carboxylic acid derivatives such as esters, amides, and halides. Since the general methods consist of at least two steps, it would be worthwhile to develop a straightforward synthetic method of aldehydes from free carboxylic acids without over-reduction to alcohols, considering the multiple steps required for modern syntheses of complex molecules. For this purpose, the following reagents have been proposed: lithium in methylamine,[1] thexylborane,[2] bis[4-methylpiperazinyl]aluminum hydride,[3] isobutylmagnesium bromide/chlorobis[π-cyclopentadienyl]titanium,[4] *N*,*N*-dimethylchloromethyleniminium/lithium tri-*tert*-butoxyaluminum hydride,[5] and lithium 9-boratabicyclo[3.3.1]nonane/*tert*-butyl lithium.[6]

During our continuing study on the electrochemical oxidation of Ph_3P in the presence of carboxylic acids,[7] we have found that the constant-current electrolysis (CCE) of a solution of Ph_3P and $PhCO_2H$ (**1a**) using a one-compartment cell at room temperature gives $(PhCO)_2O$ as the major product when 2,6-lutidinium perchlorate (2,6-$Lut^+ \cdot ClO_4^-$) is used as a supporting electrolyte, while the use of $Ph_3P^+H \cdot ClO_4^-$ instead of 2,6-$Lut^+ \cdot ClO_4^-$ results in the formation of PhCHO (**2a**) (Chart 1). The latter process can be effectively achieved by CCE at −30 °C and this transformation has been applied to the synthesis of optically pure *N*-Cbz-L-α-amino aldehydes from the corresponding *N*-Cbz-L-α-amino acids.[8]

In this paper, we describe the generality and the mechanism of this unique one-step partial reduction of carboxylic acids into aldehydes induced by the anodic oxidation of Ph_3P.

Results and Discussion

The conversion of various carboxylic acids (**1**) into aldehydes (**2**) was carried out by CCE of a mixture of Ph_3P, $Ph_3P^+H \cdot ClO_4^-$, and **1** in CH_2Cl_2[9] using a one-compartment cell equipped with two graphite plates as an anode and a cathode under an N_2 atmosphere. The results are summarized in Table I.

As is apparent from Table I, aromatic and aliphatic primary carboxylic acids (**1a**—**c**, **1e**, **1f**) were transformed to the corresponding aldehydes in fair yields by CCE at −30 °C, when the current density was carefully chosen depending on the nature of **1** (*cf.* runs for **1h**). The slightly lower yield of **2c** is probably due to the poor solubility of **1c** in the CH_2Cl_2 solution of Ph_3P and $Ph_3P^+H \cdot ClO_4^-$. In the case of the α, β-unsaturated acid **1d**, the corresponding aldehyde was not obtained at all. Instead, a saturated aldehyde, 3-phenylpropionaldehyde was isolated in 13% yield. The secondary aliphatic aldehyde **2g** was obtained from **1g** in a reasonable yield under the same conditions but with a low current density. The electrolyses of other secondary aliphatic acids such as **1h** and **1i** resulted in poor yields of **2** (trace and 38%, respectively), though the CCE was performed at a low current density. However, CCE at higher temperature, namely under reflux, and with higher current density was

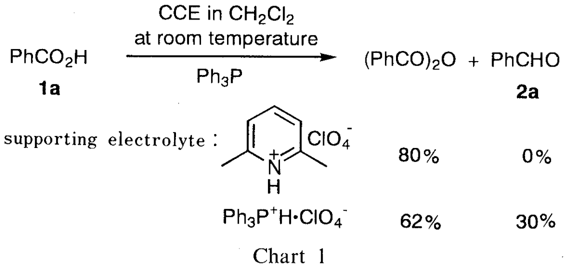

Chart 1

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TABLE I. One-Step Transformation of RCO_2H (**1**) into RCHO (**2**) by CCE in CH_2Cl_2 Using One-Compartment Cell[a)]

	R	Electrolysis temperature	Current density (mA/cm^2)	Electricity (F/mol)[b)]	Yield (%) of **2**[c)]
a	Ph–	−30 °C	2.0	3.2	76[d)]
b	*o*-Cl–Ph–	−30 °C	2.0	3.2	71[d)]
c	*p*-MeO–Ph–	−30 °C	1.0	3.0	51
d	PhCH=CH–	−30 °C	2.0	4.0	—[e)]
e	$Ph(CH_2)_2$–	−30 °C	0.4	2.2	75
f	$CH_3(CH_2)_8$–	−30 °C	2.0	2.4	70[d)]
g	Ph_2CH–	−30 °C	0.4	2.2	68
h	cyclo-C_6H_{11}–	−30 °C	0.4	2.7	Trace[f)]
		−10 °C	0.4	2.7	23[f)]
		Reflux	0.4	2.7	42[f)]
		Reflux	1.0	3.0	54[f)]
		Reflux	2.4	3.0	61[f)]
		Reflux	4.0	3.0	46[f)]
i	$(CH_3)_2CH$–	−30 °C	0.4	2.7	38[f)]
		Reflux	2.4	3.0	53[f)]
j	$(CH_3)_3C$–	−30 °C	0.4	2.7	—[f)]
		−10 °C	0.4	2.7	—[f)]
		Reflux	2.4	3.0	7[f)]

a) A mixture of Ph_3P (6 mmol), **1** (3 mmol), and $Ph_3P^+H \cdot ClO_4^-$ (4 mmol) was subjected to CCE under an N_2 atmosphere with graphite plate anode and cathode (12.5 cm^2). *b*) Against **1**. *c*) Isolated yield. *d*) Three mmol of Ph_3P was used. *e*) 3-Phenylpropionaldehyde was obtained in 13% yield. *f*) Determined by GLC.

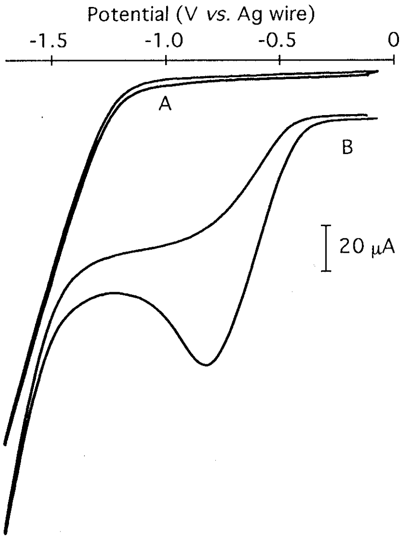

Fig. 1. Cyclic Voltammograms of a Solution of Ph_3P, $Ph_3P^+H \cdot ClO_4^-$, and **1a** in CH_2Cl_2 (A) before and (B) after CCE

At a glassy carbon disk electrode; voltage sweep rate, 100 mV/s; at −30 °C; for details, see the text.

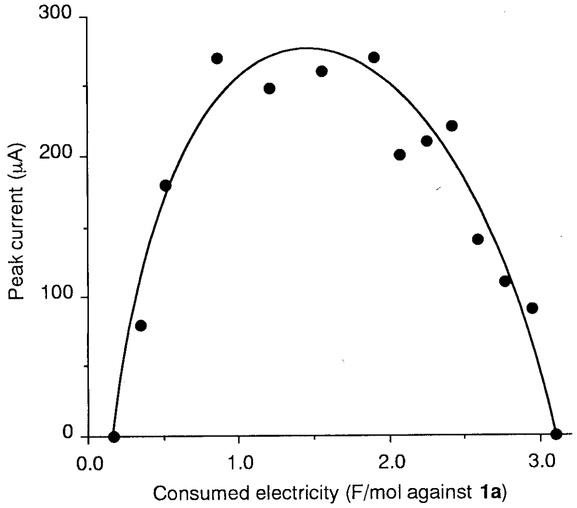

Fig. 2. Change in the Peak Current of the Voltammetric Reduction Wave Obtained during the Preparative CCE of a Solution of Ph_3P, $Ph_3P^+H \cdot ClO_4^-$, and **1a** in CH_2Cl_2

At a glassy carbon plate electrode; voltage sweep rate, 100 mV/s; at −30 °C; for details, see the text.

found to be effective for the transformation. A tertiary aliphatic acid **1j** was more refractory than **1h** and **1i** and CCE even under these conditions gave little **2j**.

As previously reported,[8)] **2a** was not obtained by the CCE of **1a** using a two-compartment cell under essentially the same conditions, and the cathodic process turned out to be crucial for the present transformation. In order to clarify the reaction course at the cathode during the electrolysis, a mixture of Ph_3P, $Ph_3P^+H \cdot ClO_4^-$, and **1a** in CH_2Cl_2 was subjected to anodic oxidation by CCE in a divided cell at −30 °C and cyclic voltammetry (CV) was performed on the anolyte. Before the electrolysis, no voltammetric peak was observed in the potential range of 0—−1.7 V *vs.* Ag wire as shown in Fig. 1A. However, after passing 0.35 F/mol of electricity with respect to **1a** a cathodic wave appeared at −0.8 V (Fig. 1B).

The cathodic peak was also recognized on CV of the electrolyte from the CCE of the same mixture in the undivided cell employed preparatively. Measurements of CV performed at suitable intervals during the CCE (Fig. 2) suggested that the cathodic peak is ascribed to an intermediate in the course of the transformation of **1a** to **2a**. Thus, the peak current increased as the electrolysis proceeded, reached a maximum at about 1.0 F/mol of consumed electricity, and then decreased eventually to disappear at about 3 F/mol. This observation is in line with the fact that the preparative CCE required 3.2 F/mol of electricity to totally consume **1a** and give **2a** in a fair yield.

The existence of a cathodically active intermediate of the same type was also confirmed voltammetrically in the cases of **1b**—**g** during CCE performed as described above in a divided cell at −30 °C. These results were at first considered to indicate that an acyloxy triphenylphosphonium ion (**3**), which was formed by anodic oxidation of Ph_3P in the presence of **1**,[7)] must be the intermediate cathodically reduced to afford **2** and Ph_3PO (Chart 2). However, this hypothesis failed and had to be revised as discussed below.

On CV of the anolyte from the CCE using **1i**, a secondary aliphatic acid, in a divided cell under the conditions employed for **1a**—**g** (see above), two cathodic peaks appeared at −0.95 and −1.35 V (Fig. 3A) in contrast to a single peak observed by using the secondary acid **1g** (*cf.* Fig. 1B). When the anolyte was allowed to stand for 5 h under stirring at −30 °C without passing electricity, the cathodic peak at −1.35 V disappeared and that at −0.95 V was enhanced (Fig. 3B). Similar voltammograms were obtained with another secondary carboxylic acid **1h**.

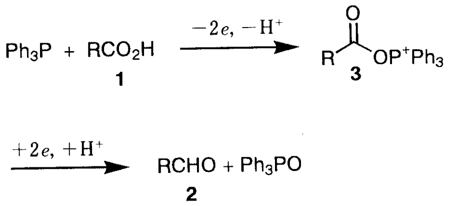

Chart 2

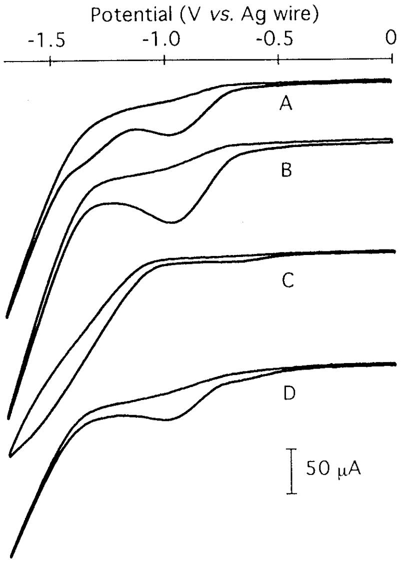

Fig. 3. Cyclic Voltammograms of a CH_2Cl_2 Solution of Ph_3P and $Ph_3P^+H \cdot ClO_4^-$ Containing **1i** (A) after CCE, (B) after Stirring the Electrolyte for 5 h, and That Containing **1j** (C) after CCE, (D) after Warming the Electrolyte Once to Room Temperature

At a glassy carbon disk electrode; voltage sweep rate, 100 mV/s; at −30 °C; for details, see the text.

In the case of the tertiary acid **1j**, again only one cathodic peak was observed around −1.5 V (Fig. 3C), which did not change on keeping the anolyte for a prolonged period at −30 °C but gave place to a new wave at −1.0 V on warming the anolyte to room temperature (Fig. 3D). These findings together with the results shown in Table I and Fig. 2 suggest that at least two kinds of cathodically active intermediates are generated successively in the transformation of **1** to **2**, and that the direct species reduced at the cathode to give **2** is the one exhibiting the voltammetric peak at the less negative potential. Thus, a revised process as depicted in Chart 3 is proposed for the present electrochemical transformation.

The single cathodic peak observed on CV of the electrolyzed solution using **1a**—**g** (*cf.* Fig. 1), the peak that appeared at the less negative potential in the CCE of **1h** and **1i** (*cf.* Fig. 3A), and the peak in the case of **1j** observed after warming the anolyte (Fig. 3D) can be assigned to the reduction of the acyl phosphonium ion **4**. The cathodic peak at the more negative potential for **1h** and **1i** (Fig. 3A) and the peak for **1j** shown in Fig. 3C can then be attributed to the acyloxy phosphonium ion **3**. It is not electrochemically unreasonable to assume that the phosphonium ion **4** is more easily reduced than the phosphonium ion **3**.(10) The reaction of an acyloxy phosphonium ion **3** generated at the anode with Ph_3P to give the corresponding acyl phosphonium ion **4** is supported by the facts that the phosphonium ions **3** are more effective than acyl halides as acylating agents,(7) and that acyl halides react with phosphites and tributylphosphine to give acyl phosphonates(11) and acyl tributylphosphonium ions,(12) respectively.

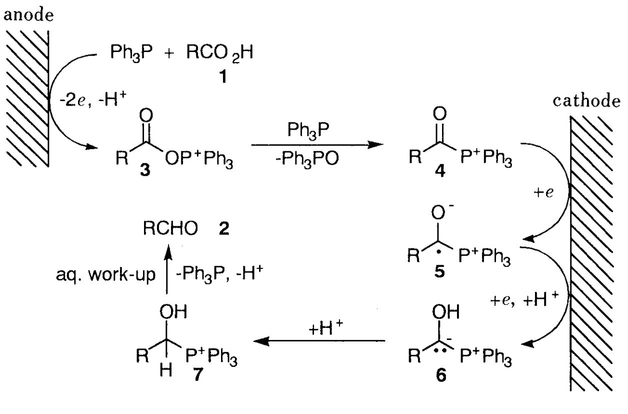

Chart 3

According to the above assignments of the cyclic voltammetric peaks, the order of reactivity of **3** toward Ph_3P to afford **4** will be **3** derived from aromatic carboxylic acids > aliphatic primary acids > aliphatic secondary acids ≫ aliphatic tertiary acids. This order, and hence the proposed mechanism, explains why different CCE conditions such as temperature and current density depending upon the structure of carboxylic acids are required for successful formation of aldehydes (see Table I). Namely, the phosphonium ions **3a**—**c** and **3e**—**g** were rapidly converted to **4** during the CCE at −30 °C and gave the corresponding aldehydes in fair yields,(13) while **3h** and **3i** may be sterically hindered, requiring a higher reaction temperature for smooth reaction with Ph_3P. In the case of **3j**, the steric hindrance at the α-carbon may be too large to allow transformation to **4j** in the time scale of the CCE even under reflux. Furthermore, the bulky *tert*-butyl group in **1j** seems to interfere with the formation of **3j** itself, because the voltammetric peak height due to **3j** (Fig. 3C) is smaller than that observed in the other cases (*cf.* Fig. 1B and Fig. 3A).

It should be mentioned here that the final product **2** is formed during the aqueous work-up (see Experimental) after the CCE; that is, the acyl phosphonium ions **4** are reduced at the cathode (the voltammetric peak potentials are summarized in Table II) to give α-hydroxyalkyl triphenylphosphonium ion (**7**), which would remain intact during the CCE. This assumption is consistent with the reports that the phosphonium ions **7** formed by the addition of Ph_3P to aldehydes in the presence of a proton source are stable under anhydrous conditions,(14) and that α-hydroxyalkyl phosphonates, analogues of **7**, generated by the $NaBH_4$ reduction of acyl phosphonates decompose readily in aqueous solution of pH 6—7 giving the corresponding aldehydes.(15) The stable formation of **7** in the electrolysis solution also explains the conversion of L-α-amino acids to L-α-amino aldehydes with no or little racemization,(8) since chiral α-amino aldehydes in their

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TABLE II. Cathodic Peak Potential of Acyl Triphenylphosphonium Ions (**4**) Observed on Cyclic Voltammetry of the Electrolyte Obtained by CCE of a CH_2Cl_2 Solution Containing Ph_3P, $Ph_3P^+H \cdot ClO_4^-$, and **1**[a)]

	R in **4**	Cathodic peak potential (V *vs.* Ag wire)
a	Ph–	−0.65
b	*o*-Cl–Ph–	−0.46
c	*p*-MeO–Ph–	−0.77
d	PhCH=CH–	−0.77
e	$Ph(CH_2)_2$–	−0.82
f	$CH_3(CH_2)_8$–	−0.93
g	Ph_2CH–	−0.74
h	cyclo-C_6H_{11}–	−0.90
i	$(CH_3)_2CH$–	−0.95
j	$(CH_3)_3C$–	−1.08

a) For details, see the text and Experimental section.

free states are expected to racemize immediately under the acidic conditions utilized in the CCE.

According to the proposed mechanism, it seems feasible that the phosphonium ion **6** formed by two-electron reduction of **4** could be used as an acyl anion equivalent. Another interesting possibility is that a neutral radical (**5**) generated by one-electron reduction of **4** might be employed as an acyl radical equivalent. In order to examine these possibilities, further work is under way.

In summary, the present method is useful for the one-step preparation of aldehydes from free carboxylic acids except for tertiary acids, and the steric bulkiness at the α-carbon in **1** dictates the efficiency of the electrochemical transformation.

Experimental

Infrared (IR) spectra were taken on a JASCO A-202 spectrometer. ^1H-NMR spectra were obtained at 200 and 270 MHz on Varian VXR-200 and JEOL EX-270 spectrometers, respectively, in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. Gas-liquid chromatography (GLC) was performed on a JEOL JGC-20K gas chromatograph with a PEG 20M glass column (2 m × 3 mm). For column chromatography, SiO_2 (Wakogel C-200) was used. CCE was carried out with a Hokuto Denko HA301, HA104, or HA105 potentiostat/galvanostat. CV was performed with the combination of a Hokuto Denko HR101B potentiostat, a Fuso HECS 321B potential sweep unit, and a Rikadenki RW-21 X-Y recorder. Voltammograms were obtained with a three-electrode system consisting of a glassy carbon (GC) disk (3 mm i.d.) or plate (10 × 50 mm) working electrode, a graphite plate counter electrode having been utilized as the anode for CCE (see below), and an Ag wire as the reference electrode. The fabrication of the GC electrode has been described previously.[16)]

Materials $Ph_3P^+H \cdot ClO_4^-$ was obtained by the addition of 70% $HClO_4$ to a solution of Ph_3P in CH_3CN, and the resulting precipitate was filtered off, recrystallized from CH_3CN, and dried *in vacuo*. All other chemicals were of reagent grade, and were used without further purification. CH_2Cl_2 was distilled from P_2O_5 and stored over molecular sieves 4A.

General Procedure for the Preparation of 2 from 1 A CH_2Cl_2 solution (30 ml) of Ph_3P (6 mmol), $Ph_3P^+H \cdot ClO_4^-$ (4 mmol), and **1** (3 mmol) in an undivided cell equipped with two graphite plates as an anode and a cathode (12.5 cm^2 each) was deoxygenated by bubbling N_2 for 20 min, then CCE was carried out under the conditions shown in Table I. The amount of **1** remaining in the electrolyte was followed by TLC. After **1** had been totally consumed, the electrolyte was washed with H_2O (50 ml), and the aqueous layer was extracted with CH_2Cl_2 (30 ml × 2). The combined organic layer was dried over Na_2SO_4, and evaporated *in vacuo*. In the case of **1a**—**g**, the residue was subjected to column chromatography (SiO_2; hexane–ethyl acetate) to afford **2a**—**g**, which gave satisfactory ^1H-NMR and IR spectra. The aldehydes from CCE of the other **1** were analyzed by GLC, and the peaks coincided well with those of authentic samples.

General Procedure for CV of the Anolyte During CCE in a Divided Cell An H-type cell separated by a glass frit into two compartments (capacity, *ca.* 30 ml) was used. One compartment of the cell was equipped with a graphite plate (*ca.* 12.5 cm^2) as an anode for CCE together with a GC disk electrode and an Ag wire as the working and the reference electrodes, respectively, for CV measurements, and in the other compartment a platinum plate was installed as the cathode for CCE. A solution of Ph_3P (6 mmol), **1** (3 mmol), and $Ph_3P^+H \cdot ClO_4^-$ (2 mmol) in CH_2Cl_2 (20 ml) and a solution of $Ph_3P^+H \cdot ClO_4^-$ (4 mmol) in CH_2Cl_2 (20 ml) were placed in the anode and the cathode compartments, respectively. The solution in the anode compartment was deoxygenated by bubbling N_2 for 20 min, then CCE was performed at a current density of 0.4 mA/cm^2 (total electrolysis current, 5 mA). During the CCE, the working electrode for CV hung over the solution and dipped into the solution for CV measurement after a predetermined amount of electricity had been passed.

General Procedure for CV on the Electrolysis Solution During CCE in an Undivided Cell The preparative CCE described above was carried out in the same undivided cell except that a GC disk electrode and an Ag wire as the working electrode and the reference electrode, respectively, were additionally fitted for CV measurements. At suitable intervals the CCE was interrupted and voltammograms were obtained by essentially the same procedure as for the anolyte in a divided cell.

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10) For example, benzophenone is reduced at a less negative potential than phenyl benzoate: on CV of each of the compounds (5 mM) in CH_3CN containing 0.1 M Et_4NCl at a GC electrode (potential sweep rate, 100 mV/s), the ketone and the ester exhibited a cathodic peak at −1.37 and −1.80 V *vs.* saturated calomel electrode (SCE), respectively.
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