

Investigation of Controlled Parameters to Electrocatalytic Semihydrogenation using Proton-Exchange Membrane Reactor and Utilization of Bayesian Optimization

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1. General Remarks.

Abbreviations. ampere (A), degrees Celsius (°C), coulomb (C), centimeter(s) (cm), direct-current (DC), gas chromatography (GC), hertz (Hz), coupling constant (*J*), liter(s) (L), mol L⁻¹ of molar concentration (M), milligram(s) (mg), megahertz (MHz), minute(s) (min), milliliter(s) (mL), mole(s) (mol), nuclear magnetic resonance (NMR), proton-exchange membrane (PEM), phenyl (Ph), parts per million (ppm), polytetrafluoro-ethylene or Teflon (PTFE), alkyl group (R), room temperature (25 ± 3 °C, rt), second(s) (s), tetramethylsilane (TMS), chemical shift in ppm downfield from TMS (δ), micrometer(s) (μ m).

General. ¹H NMR spectra were recorded by Varian MERCURY plus-400 (¹H 400 MHz). Chemical shifts are recorded using a TMS (0.0 ppm) signal as an internal standard. GC analysis was performed on a SHIMADZU GC-2014 gas chromatograph equipped with a flame ionization detector using a fused silica capillary column (column, CBP1; 0.22 mm x 25 m). GC yields were calculated by GC analyses with *n*-tetradecane as an internal standard using calibration lines derived from commercial or isolated compounds with the internal standards. Mass spectra were obtained on Thermo Fisher Scientific EXACTIVE plus (ESI) and JEOL JMS-700 (EI).

Flow Electrochemical Synthesis. DC power source (P4K8-3-LDe, MATSUSADA Precision Inc.) was used for an electrolysis. The syringe pumps (Harvard Model PHD 2000 or PHD ULTRA) equipped with gastight syringes (purchased from SGE) were used for introduction of the reaction solutions into the PEM reactor via PTFE tubes. The assembly of the gold-plated stainless type PEM reactor is according to the previously reported procedure.¹ The newly designed PEM reactor consisting of a titanium metal was manufactured by DFC Co., Ltd. The PEM (Nafion® NR212) was purchased from Chemours Japan Co., Ltd. and cut for the reactions (1 × 4 cm² active area). For the reaction in the new PEM reactor, the metal on carbon (30.4 wt% in ketjenblack EC300J, crystallite diameter: 4.3 nm, specific surface area or metal: 70 m²/g/Pd) was manufactured by ISHIFUKU Metal Industry Co., Ltd., and was dispersed onto a carbon-based gas diffusion layer (Pd 0.5 mg/cm², diffusion layer: SIGRACET GDL39BB, SGL Carbon SE) by Chemix Inc. to make the electrode catalyst. The electrode catalyst (4.0 cm × 1.0 cm, thickness: 0.25 cm) was placed in a PTFE spacer manufactured by DFC Co., Ltd. The PEM reactor is depicted in Figure S1, and the reaction setup is shown in Figure S2.

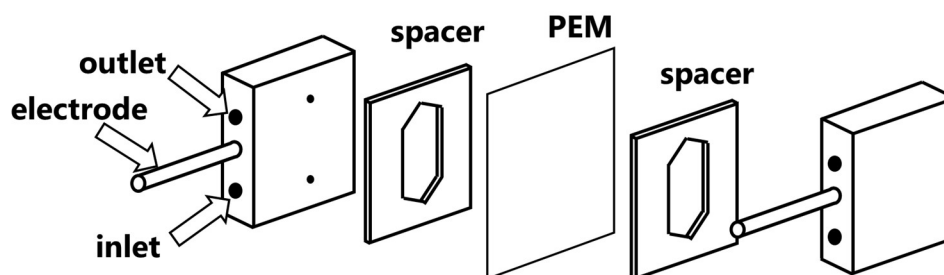


Figure S1. Schematic for new PEM reactor.

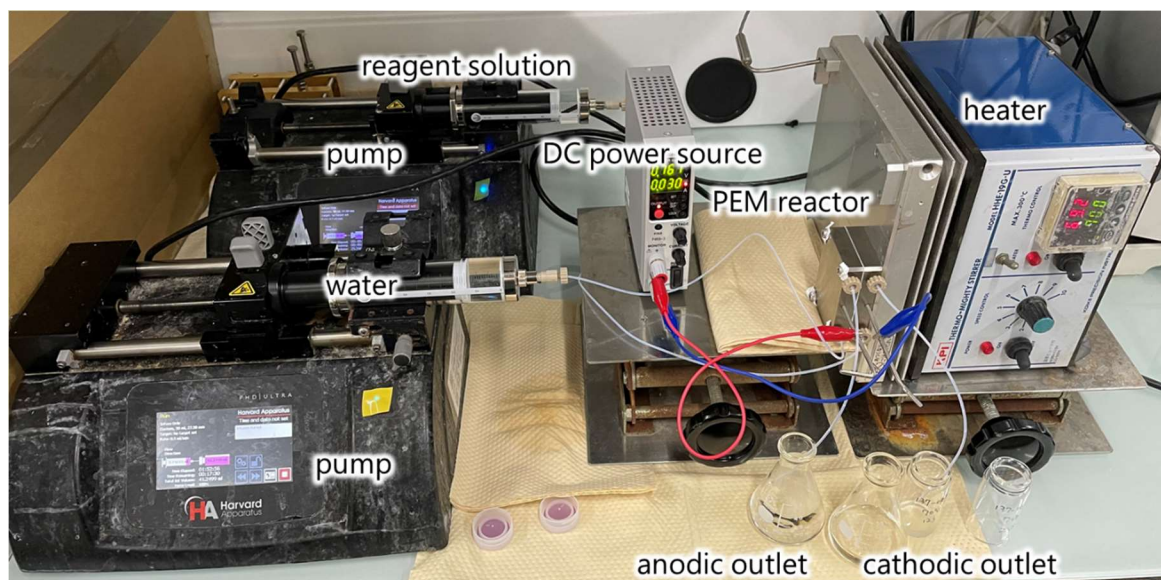


Figure S2. Picture for the Semihydrogenation Reaction under Controlled Temperature.

Materials. Chemicals were purchased from FUJIFILM Wako Pure Chemical Corporation, or Tokyo Chemical Industry Co., Ltd., and were used without further purification unless otherwise noted.

Calculation for Current Efficiency, Selectivity, and Integrated Index. After a collection of the reaction solution, an aliquot of a solution of internal standard (typically *n*-tridecane) was added, and the resulting-solution was analyzed by GC using a prepared calibration line. After determining the concentration of the products in the resultant mixture, the current efficiency and the selectivity were calculated. The selectivity was calculated according to the following equation.

$$\text{selectivity} = \frac{\text{concentration of the desired product (M)}}{\text{concentration of the desired product (M)} + \text{concentration of the byproduct (M)}}$$

As for the current efficiency, since the active volume of the electrolysis is 0.1 mL (4 cm × 1 cm × 0.25 mm), the total electron applied for the active space can be calculated according to the following equation,

$$\text{applied electron (mol)} = \frac{\text{applied current (A)} \times \text{residence time (sec)}}{\text{Faraday constant (C/mol)}}$$

where Faraday constant is 96485. In this reaction, one alkene is obtained from two electrons, whereas one alkane is obtained from four electrons. Since the resulting concentration of the products can be dealt as the 0.1 mL of aliquot, the current efficiency can be calculated according to the following equation.

$$\text{current efficiency} = \frac{0.1 \text{ (mL)} \times (2 \times \text{concentration of alkene (M)} + 4 \times \text{concentration of alkane (M)})}{\text{applied electron (mmol)}}$$

The integrated index is calculated as follows.

$$\text{integrated index} = \text{current efficiency} \times \text{selectivity}$$

2. Semihydrogenation using PEM Reactor Consists of Gold-Plated Stainless Steel.

2.1 Investigation for Electrodes

The experiment was carried out under an ambient temperature, or rt. To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (1.0 M in methylcyclohexane) was introduced (0.25 mL/min). Whereas, to an anodic flow-chamber water was introduced (0.25 mL/min). The DC power source was connected to both the anode and cathode, supplying a constant current (20, 30, and 40 mA). After a steady state was reached (typically, a collection of 2 mL), the cathodic solution was collected (typically, 3

mL). The results are summarized in Table S1.

Table S1. Semihydrogenation of diphenylacetylene in the PEM reactor varying the electrode.

anode	cathode	current (mA)	total current efficiency (%)	product ratio of <i>cis</i> -stilbene (%)
Pt	Pt	20	94	65
		30	98	63
		40	93	60
Pt	Pd	20	93	89
		30	94	81
		40	96	73
Pd	Pd	20	98	93
		30	>99	92
		40	>99	91

2.2 Investigation for Residence Time

The experiment was carried under an ambient temperature, or rt. To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (1.0 M in methylcyclohexane) was introduced (F mL/min). Whereas, to an anodic flow-chamber water was introduced with the same flow rate. The DC power source was connected to both the anode and cathode, supplying a constant current (30 mA). After a steady state was reached (typically, a collection of 2 mL), the cathodic solution was collected (typically, 3 mL). The results are summarized in Table S2.

Table S2. Semihydrogenation of diphenylacetylene in the PEM reactor varying the residence time.

flow rate F (mL/min)	residence time (sec)	total current efficiency (%)	product ratio of <i>cis</i> -stilbene (%)
1.00	6	95	90
0.75	8	99	89
0.50	12	>99	89
0.25	24	>99	89
0.125	48	>99	86

2.3 Investigation for Concentration

The experiment was carried out under an ambient temperature, or rt. To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (1.0 M in methylcyclohexane) was introduced (0.25 mL/min). Whereas, to an anodic flow-chamber water was introduced with the same flow rate. The DC power source was connected to both the anode and cathode, supplying a constant current (30 mA). After a steady state was reached (typically, a collection of 2 mL), the cathodic solution was collected (typically, 3 mL). The results are summarized in Table S3.

Table S3. Semihydrogenation of diphenylacetylene in the PEM reactor varying the concentration.

concentration (M)	total current efficiency (%)	product ratio of <i>cis</i> -stilbene (%)
0.25	>99	68
0.50	>99	84
1.00	>99	89

3. Semihydrogenation using PEM Reactor Consists of Titanium.

3.1 Semihydrogenation of Diphenylacetylene Under Room Temperature.

The experiment was carried out using the new PEM reactor under an ambient temperature, or rt. To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (1.0 M in methylcyclohexane) was introduced (F mL/min). Whereas, to an anodic flow-chamber water was introduced with the same flow rate. The DC power source was connected to both the anode and cathode, supplying a constant current (30 mA). After a steady state was reached (typically, a collection of 2 mL), the cathodic solution was collected (typically, 3 mL). The results are summarized in Table S4.

Table S4. Semihydrogenation of diphenylacetylene in the new PEM reactor varying the residence time.

flow rate F (mL/min)	residence time (sec)	total current efficiency (%)	product ratio of <i>cis</i> -stilbene (%)
1.00	6	97	92
0.50	12	>99	90
0.25	24	>99	90

3.2 Semihydrogenation of Diphenylacetylene Under Controlled Temperature.

The experiment was carried out using the new PEM reactor whose cathodic part was attached to a heating plate ($T^{\circ}\text{C}$). To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (C M in methylcyclohexane) was introduced (F mL/min). Whereas, to an anodic flow-chamber water was introduced with the same flow rate. The DC power source was connected to both the anode and cathode, supplying a constant current (30 mA). After a steady state was reached (typically, a collection of 2 mL), the cathodic solution was collected (typically, 3 mL). The results are summarized in Table S5.

Table S5. Semihydrogenation of diphenylacetylene varying the concentration, temperature, and residence time.

concentration C (M)	temperature T ($^{\circ}\text{C}$)	flow rate F (mL/min)	residence time (sec)	total current efficiency (%)	product ratio of <i>cis</i> -stilbene (%)	integrated index
1	30	1.00	6	95	92	87
1	30	0.50	12	97	92	89
1	30	0.25	24	>99	92	92
1	40	1.00	6	86	95	82
1	40	0.50	12	90	94	85
1	40	0.25	24	99	93	92
1	50	1.00	6	86	95	82
1	50	0.50	12	91	95	86
1	50	0.25	24	>99	95	95
1	60	1.00	6	92	95	87
1	60	0.50	12	99	95	94
1	60	0.25	24	>99	92	92
1	70	1.00	6	94	96	90
1	70	0.50	12	>99	96	96
1	70	0.25	24	>99	96	96
1	80	1.00	6	87	95	83
1	80	0.50	12	93	95	88
1	80	0.25	24	99	96	95
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0.5	30	1.00	6	64	93	60
0.5	30	0.50	12	74	92	68
0.5	30	0.25	24	91	92	84
0.5	40	1.00	6	86	86	74
0.5	40	0.50	12	79	94	74
0.5	40	0.25	24	91	94	86
0.5	50	1.00	6	65	94	61
0.5	50	0.50	12	77	95	73
0.5	50	0.25	24	83	95	79
0.5	60	1.00	6	71	94	67
0.5	60	0.50	12	87	94	82
0.5	60	0.25	24	>99	94	94
0.5	70	1.00	6	73	96	70
0.5	70	0.50	12	89	95	85
0.5	70	0.25	24	>99	95	95
0.5	80	1.00	6	76	96	73
0.5	80	0.50	12	92	95	87
0.5	80	0.25	24	>99	95	95
<hr/>						
0.25	30	1.00	6	65	89	58
0.25	30	0.50	12	75	87	65
0.25	30	0.25	24	95	84	80
0.25	40	1.00	6	64	92	59

0.25	40	0.50	12	74	91	67
0.25	40	0.25	24	87	86	75
0.25	50	1.00	6	50	93	47
0.25	50	0.50	12	61	92	56
0.25	50	0.25	24	69	91	63
0.25	60	1.00	6	47	94	44
0.25	60	0.50	12	58	93	54
0.25	60	0.25	24	70	91	64
0.25	70	1.00	6	54	93	50
0.25	70	0.50	12	65	89	58
0.25	70	0.25	24	76	82	62
0.25	80	1.00	6	61	91	56
0.25	80	0.50	12	72	86	64
0.25	80	0.25	24	86	87	75

3.3 Semihydrogenation of Diphenylacetylene Under Optimized Condition.

The experiment was carried out using the new PEM reactor whose cathodic part was attached to a heating plate (70 °C). To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (1.0 M in methylcyclohexane) was introduced (0.5 mL/min, residence time is 12 sec). Whereas, to an anodic flow-chamber water was introduced with the same flow rate. The DC power source was connected to both the anode and cathode, supplying a constant current (30 mA). After a steady state was reached (4 min), the cathodic solution was collected for 100 min. The GC analysis indicated >99% current efficiency and 98% selectivity.

3.4 Semihydrogenation of Diphenylacetylene Using D₂O.

Prior to the reaction, the proton-exchange membrane was dipped in 35% DClaq to exchange the protons on the membrane to deuteriums. The experiment was carried out using the new PEM reactor whose cathodic part was attached to a heating plate (70 °C). To a cathodic flow-chamber of the PEM reactor, a solution of diphenylacetylene (1.0 M in methylcyclohexane) was introduced (0.5 mL/min, residence time is 12 sec). Whereas, to an anodic flow-chamber water was introduced with the same flow rate. The DC power source was connected to both the anode and cathode, supplying a constant current (30 mA). After a steady state was reached, the cathodic solution was collected for 20 min. The GC analysis indicated 81% current efficiency and 93% selectivity. The deuterated ratio was determined by ¹H NMR where the benzylic proton was shown as 7% relative to the commercial one.

4. Bayesian Optimization.

The script was written with Python, and GPyOpt library was used. Expected improvement (EI) was chosen as an acquisition function because it showed better performance in the literature.² Default values were used for other parameters. Statistical analysis was carried out based on a script shown in Figure S3. The function f returns the integrated index. After 1000-times virtual optimizations, the ratio of the experiment finding a condition allowing >95% of integrated index at each iteration cycle is shown in Figure S4.

```
import GPyOpt

pbounds = [{ 'name': 'conc', 'type': 'discrete', 'domain': (0.25, 0.5, 1.0)},
            { 'name': 't^R2', 'type': 'discrete', 'domain': (6, 12, 24)},
            { 'name': 'temp', 'type': 'discrete', 'domain': (30, 40, 50, 60, 70, 80)},
            ]

for n in range(1000):
    np.random.seed(n)
    myBopt = GPyOpt.methods.BayesianOptimization(f=f,
                                                domain=pbounds,
                                                acquisition_type='EI',
                                                X=initial_X,
                                                Y=initial_y,
                                                maximize=True,
                                                )
    myBopt.run_optimization(max_iter=25)
```

Figure S3. Script for statistical analyses.

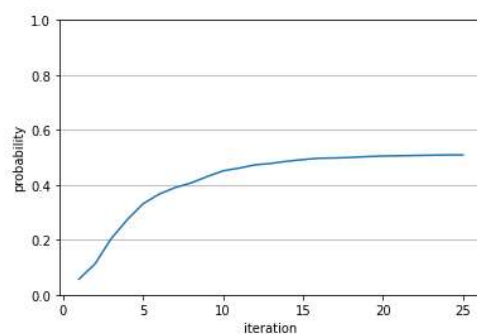


Figure S4. Results for 1000-times virtual optimization experiments.

5. References.

- [1] Fukazawa, A., Minohima, J., Tanaka, K., Hashimoto, Y., Kobori, Y., Sato, Y., *et al.* (2019). ACS Sustainable Chem. Eng. 7, 11050.
- [2] Shields, B.J., Stevens, J., Li, J., Parasram, M., Damani, F., Alvarado, J.I.M., *et al.* (2021). Nature 590, 89.