Supporting Information

A Flow Microreactor Approach to Highly Efficient Diels-Alder Reaction with Electrogenerated o-Quinone

Kenta Tanaka, Hirona Yoshizawa, and Mahito Atobe*

Department of Environment and System Sciences, Yokohama National University, 79-7 Tokiwadai, Hodogaya-ku, Yokohama 240-8501, Japan.

E-mail: atobe@ynu.ac.jp

Contents:
1. General..................................................................................................................2
2. Electrochemical flow microreactor........................................................................2
3. Synthesis and characterization of authentic sample for HPLC analysis................3
4. Linear sweep voltammetry....................................................................................6
5. Reference.............................................................................................................6
6. $^1$H-NMR and $^{13}$C-NMR spectrum data..........................................................6
1. General

Constant current electrolysis were conducted using a galvanostat (HOKUTO DENKO HABF-501A). HPLC analyses were performed with a LC pump (Shimadzu LC-20AD), a UV detector (Shimadzu SPD-10A), and a column (Kanto Kagaku Mightysil RP-18 GP Aqua 250-4.6 (5 μm)). Chromatograms were recorded by a LC workstation (Shimadzu LabSolutions DB). Infrared (IR) spectra were recorded using an IRAffinity-1 (SHIMADZU). 1H NMR spectra were recorded on a Bruker DRX-500 (500 MHz) spectrometer using tetramethylsilane (TMS) as an internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants, integration. 13C NMR spectra were recorded on a Bruker DRX-500 (126 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from TMS internal standard with the solvent resonance (CDCl3: δ 77.0).

2. Electrochemical flow microreactor

The reactor was constructed from an anode plate (Graphite, Glassy carbon (GC), Platinum (Pt), 30 mm width, 30 mm length) and a cathode plate (Pt, 30 mm width, 30 mm length) (Fig. S1). A spacer (20 - 100 μm thickness double faced adhesive type) was used to leave a rectangular channel exposed, and the two electrodes were simply sandwiched together (area of the two electrodes: 10 × 30 mm²). After connecting Teflon tubing to inlets and outlet, the reactor was sealed with epoxy resin (Fig. S2).

![Fig. S1. Schematic illustration of the electrochemical flow microreactor.](image)
Fig. S2. Schematic illustration of construction procedure for the electrochemical flow microreactor.

3. Synthesis and characterization of authentic sample for HPLC analysis

(3aR*,4S*,7R*,7aS*)-6-(tert-butyl)-1-(propan-2-ylidene)-3a,4,7,7a-tetrahydro-1H-4,7-ethanoidene-8,9-dione (4)

The Diels-Alder cycloadduct 4 was synthesized according to the literature. A mixture of 4-tert-butylpyrocatechol 1 (0.47 g, 2.8 mmol) and Ag₂O (1.30 g, 5.6 mmol) in benzene (10 mL) was stirred for 10 minutes. After the reaction mixture was filtered to remove Ag₂O, 6,6-dimethylfulvene 3 (0.58 g, 4.7 mmol) was added, and was stirred at room temperature for 8 h. The reaction was concentrated and purified by column chromatography on silica gel (hexane : ethyl acetate = 20 : 1 to 3 : 1) to afford the product 4 (yellow solid, 84% yield).

¹H-NMR (500 MHz; CDCl₃): δ 6.42 (dd, J = 5.7, 1.9 Hz, 1H), 5.86 (ddd, J = 6.6, 2.2, 0.6 Hz, 1H), 5.58 (dd, J = 5.7, 2.5 Hz, 1H), 3.70 (dd, J = 3.0, 2.4 Hz, 1H), 3.61 (dd, J = 6.8, 2.7 Hz, 1H), 3.56 (d, J = 7.9 Hz, 1H), 3.31 (d, J = 7.9 Hz, 1H), 1.80 (s, 3H), 1.77 (s, 3H), 1.00 (s, 9H);

¹³C-NMR (126 MHz; CDCl₃): δ 191.5, 191.2, 151.8, 139.4, 135.6, 132.2, 125.2, 118.3, 50.5, 46.4, 40.6, 35.3, 28.3, 21.7, 21.4; IR (KBr): 2964, 1732, 1508, 1473, 1458, 1363, 1099, 812 cm⁻¹; HRMS (ESI) m/z calcd for C₁₈H₂₀O₂Na [M+Na]⁺, 293.1512; found, 293.1498
(3aR*,4S*,7R*,7aS*)-6-(tert-butyl)-1-(heptan-2-ylidene)-3a,4,7,7a-tetrahydro-1H-4,7-ethanoindene-8,9-dione (6)

A mixture of 4-tert-butylpyrocatechol 1 (0.32 g, 2.0 mmol) and Ag₂O (0.92 g, 4.0 mmol) in benzene (5 mL) was stirred for 10 minutes. After the reaction mixture was filtered to remove Ag₂O, 6,6-dipropylfulvene 5 (0.4 g, 2.5 mmol) was added and was stirred at room temperature for 8 h. The reaction was concentrated and purified by column chromatography on silica gel (hexane : ethyl acetate = 20 : 1 to 3 : 1) to afford the product 6 (yellow solid, 74% yield).

^1H-NMR (500 MHz; CDCl₃): δ 6.44 (dd, J = 5.7, 1.9 Hz, 1H), 5.84 (dd, J = 6.5, 2.1, 1H), 5.60 (dd, J = 5.7, 2.5 Hz, 1H), 3.69 (m, 1H), 3.57 (dd, J = 6.8, 2.7 Hz, 1H), 3.53 (m, 1H), 3.34 (dd, J = 7.9, 2.5 Hz, 1H), 2.10 (q, J = 7.04 Hz, 4H), 1.48-1.55 (m, 1H), 1.30-1.46 (m, 3H) 1.00 (s, 9H), 0.95 (t, J = 7.41 Hz, 3H), 0.86 (t, J = 7.41 Hz, 3H); ^13C-NMR (126 MHz; CDCl₃): δ 191.2, 191.2, 151.6, 139.9, 135.5, 134.0, 132.3, 118.1, 53.8, 51.1, 46.0, 40.0, 35.0, 34.5, 33.9, 28.1, 22.1, 21.6, 14.2, 13.9; IR (KBr): 2966, 2870, 1735, 1463, 1365, 1161, 813 cm⁻¹; HRMS (ESI) m/z calcld for C₂₂H₃₁O₂ [M+H]+, 327.2309; found, 327.2319.

(3aR*,4S*,7R*,7aS*)-6-(tert-butyl)-1-cyclohexylidene-3a,4,7,7a-tetrahydro-1H-4,7-ethanoindene-8,9-dione (8)

The Diels-Alder cycloadduct 8 was synthesized according to the literature. A mixture of 4-tert-butylpyrocatechol 1 (0.83 g, 5.0 mmol) and Ag₂O (2.3 g, 10.0 mmol) in benzene (20 mL) was stirred for 10 minutes. After the reaction mixture was filtered to remove Ag₂O, 5-cyclohexylidene-1,3-cyclopentadiene 7 (1.5 g, 10.0 mmol) was added and was stirred at
room temperature for 4 h. The reaction was concentrated and purified by column chromatography on silica gel (hexane : ethyl acetate = 20 : 1 to 3 : 1) to afford the product 8 (yellow solid, 85% yield).

$^1$H-NMR (500 MHz; CDCl$_3$): $\delta$ 6.47 (dd, $J = 5.67$, 1.89 Hz, 1H), 5.86 (dd, $J = 6.78$, 2.36 Hz, 1H), 5.59 (dd, $J = 5.67$, 2.52 Hz, 1H), 3.71 (t, $J = 2.68$ Hz, 1H), 3.56 (m, 2H), 3.34 (d, $J = 8.2$ Hz, 1H), 2.25 (m, 4H), 1.56 (m, 6H), 1.01 (s, 9H); $^{13}$C-NMR (126 MHz; CDCl$_3$): $\delta$ 191.2, 191.0, 151.6, 136.2, 134.7, 133.7, 132.1, 118.0, 53.8, 51.0, 45.9, 39.7, 35.1, 32.0, 31.6, 28.2, 28.1, 28.0, 26.6; IR (KBr): 2924, 2846, 1730, 1508, 1363, 1230, 813 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for C$_{18}$H$_{22}$O$_2$Na [M+Na]$^+$, 333.1825; found, 333.1815.

(3aR*,4S*,7R*,7aS*)-6-(tert-butyl)-1-cycloheptylidene-3a,4,7,7a-tetrahydro-1H-4,7-ethanodenedione-8,9-dione (10)

The Diels-Alder cycloadduct 10 was synthesized according to the literature. A mixture of 4-tert-butylpyrocatechol 1 (0.83 g, 5.0 mmol) and Ag$_2$O (2.3 g, 10.0 mmol) in benzene (20 mL) was stirred for 10 minutes. After the reaction mixture was filtered to remove Ag$_2$O, 5-cycloheptylidene-1,3-cyclopentadiene 9 (1.6 g, 10.0 mmol) was added and was stirred at reflux for 8 h. The reaction was concentrated and purified by column chromatography on silica gel (hexane : ethyl acetate = 20 : 1 to 3 : 1) to afford the product 10 (yellow solid, 75% yield).

$^1$H-NMR (500 MHz; CDCl$_3$): $\delta$ 6.44 (dd, $J = 5.7$, 1.9, 1H), 5.85 (ddd, $J = 6.7$, 2.3, 0.8 Hz, 1H), 5.59 (dd, $J = 5.5$, 2.4 Hz, 1H), 3.71 (m, 1H), 3.61 (dd, $J = 6.8$, 2.7 Hz, 1H), 3.54 (m, 1H), 3.32 (d, $J = 8.5$ Hz, 1H), 2.28-2.44 (m, 4H), 1.43-1.81 (m, 8H), 1.00 (s, 9H); $^{13}$C-NMR (126 MHz; CDCl$_3$): $\delta$ 191.3, 191.1, 151.5, 139.0, 135.2, 135.0, 132.1, 118.0, 53.9, 50.5, 46.2, 40.3, 35.1, 32.8, 32.6, 30.0, 28.5, 28.1, 28.1, 27.8; IR (KBr): 2929, 1735, 1541, 1508, 1458, 1363, 812 cm$^{-1}$; HRMS (ESI) $m/z$ calcd for C$_{22}$H$_{29}$O$_2$ [M+H]$^+$, 325.2162; found, 325.2162
4. Linear sweep voltammetry

Linear Sweep voltammetry experiments were performed by using an undivided cell equipped with a working electrode (Graphite, GC, Pt disk electrode, 5.9 mm $\phi$), an auxiliary electrode (Pt plate, $1.0 \times 1.0$ cm$^2$), and a reference electrode (Ag wire). The ferrocene/ferrocenium couple (Fc/Fc$^+$) was also measured in the same electrochemical system, and the electrode potential was reported as values referred to the apparent standard potential of the system.

5. Reference


6. $^1$H-NMR and $^{13}$C-NMR spectrum data