Electronic Supplementary Information (ESI)

Driving an equilibrium acetalization to completion in the presence of water

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General Information:

A microchannel reactor having a channel pattern of 100 μ m width, 40 μ m depth, 20, 40, or 120 mm length, and a Y-junction (purchased from the Institute of Microchemical Technology, Co., Ltd., (Kanagawa, Japan; URL: <u>http://www.i-mt.co.jp</u>) was used, the ends of which were connected via a PTFE tubing ($\phi_{inside} = 0.2 \text{ mm}$; $\phi_{outer} = 0.4 \text{ mm}$) to a flow-controlled syringe on syringe pumps. Water was deionized with a Millipore system as a Milli-Q grade. ¹H NHR spectra were recorded with in CDCl₃ at 25 °C on a JEOL JNM-AL500 spectrometer (500 MHz). For ¹H NMR spectra, proton chemical shifts (δ) are given in ppm relative to tetramethylsilane (0.00 ppm) in CDCl₃. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), m (multiplet), and br (broad). For ¹³C NMR spectra, carbon chemical shifts were internally referenced to the deuterated solvent signal of CD Cl₃ (77.16 ppm). SEM images were obtained by using a scanning electron microscope (JEOL JSM-6700F). The flow reactions were performed in a microchannel reactor under an atmospheric air.

Experimental Section:

Preparation of a poly(4-styrenesulfonic acid)-poly(4-vinylpyridine) membrane inside a microchannel.

An aqueous solution of poly(4-styrenesulfonic acid) (60 mM: solution A) and an 2-propanol solution of poly(4-vinylpyridine) (1.0 mM: solution B) were charged oppositely into the microchannel at 25 °C for 10 min with a flow rate of 10 μ L/min. Two-phase parallel laminar flow was formed under the flowing conditions and a polymer membrane was precipitated out at the interface between the two parallel flows. (thickness of membrane = 20 μ m).

General procedure for the acetal formation using a microchannel having a polymeric acid catalyst.

A toluene solution of carbonyl compound (100 mM; solution A) and an ethylene glycol solution (solution B) were oppositely introduced the membrane-divided channel at 50-80°C with a flow rate of 0.1 μ l/min, and two parallel laminar layers flowed through the channel 19-38 seconds. The organic/ethylene glycol micro stream was collected from the outlet of the channel to give 1,3-dioxolane (64-97% conversion).

¹H and ¹³C NMR data of products

1,4-dioxaspiro[4.5]decane (3a)

¹H NMR (500 MHz, CDCl₃): δ 1.41 (brs, 2H), 1.59-1.61 (m, 8H), 3.94 (s, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 24.1, 25.3, 35.3, 64.3, 109.3. GC-TOF HRMS: calcd for C₈H₁₄O₂ [M]⁺ 142.0994, found 142.0990.

2-pentyl-1,3-dioxolane (3b)

¹H NMR (500 MHz, CDCl₃): δ 0.88-0.91 (m, 3H), 1.30-1.45 (m, 6H), 1.64-1.67 (m, 2H), 3.82-4.00 (m, 4H), 4.85 (t, *J* = 4.7 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 14.1, 22.7, 23.9, 31.9, 34.0, 65.0, 104.9. GC-TOF HRMS: calcd for C₈H₁₅O₂ [M-H]⁺ 143.1072, found 143.1042.

2-hexyl-1,3-dioxolane (3c)

¹H NMR (500 MHz, CDCl₃): δ 0.87-0.90 (m, 3H), 1.26-1.43 (m, 8H), 1.63-1.67 (m, 2H), 3.82-4.00 (m, 4H), 4.84 (t, *J* = 5.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 14.2, 22.7, 24.2, 29.4, 31.9, 34.1, 65.0, 104.9. GC-TOF HRMS: calcd for C₉H₁₇O₂ [M-H]⁺ 157.1229, found 157.1204.

2-heptyl-1,3-dioxolane (3d)

¹H NMR (500 MHz, CDCl₃): δ 0.86-0.89 (m, 3H), 1.27-1.43 (m, 10H), 1.63-1.67 (m, 2H), 3.82-4.00 (m, 4H), 4.84 (t, *J* = 5.0 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 14.2, 22.8, 24.3, 29.4, 29.7, 31.9, 34.1, 65.0, 104.9. GC-TOF HRMS: calcd for C₁₀H₁₉O₂ [M-H]⁺ 171.1385, found 171.1380.

(E)-2-(pent-3-enyl)-1,3-dioxolane (3e)

¹H NMR (500 MHz, CDCl₃): δ 0.90-0.93 (m, 3H), 1.43 (sext, J = 7.4 Hz, 2H), 2.04-2.09 (m, 2H), 3.86-4.03 (m, 4H), 5.19 (d, J = 6.3 Hz, 1H), 5.48 (dddd, J = 1.2, 1.8, 6.9, 15.5 Hz, 1H), 5.94 (dt, J = 6.9 Hz, 15.5 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 13.8, 22.0, 34.2, 65.1, 104.4, 126.4, 138.0. GC-TOF HRMS: calcd for C₈H₁₃O₂ [M-H]⁺ 141.0916, found 141.0899.

2-phenyl-1,3-dioxolane (3f)

¹H NMR (500 MHz, CDCl₃): δ 4.01-4.16 (m, 4H), 5.82 (s, 1H), 7.35-7.40 (m, 3H), 7.46-7.49 (m, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 65.5, 103.9, 126.5, 128.5, 129.3, 138.0. GC-TOF HRMS: calcd for C₉H₁₀O₂ [M]⁺ 150.0681, found 150.0683.

2-(4-bromophenyl)-1,3-dioxolane (3g)

¹H NMR (500 MHz, CDCl₃): δ 4.00-4.14 (m, 4H), 5.77 (s, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H). ¹³C NMR (125 MHz, CDCl₃): δ 65.5, 103.2, 123.4, 128.3, 131.7, 137.2. GC-TOF HRMS: calcd for C₉H₉O₂Br [M]⁺ 227.9786, found 227.9801.

2-(furan-2-yl)-1,3-dioxalane (3h)

¹H NMR (500 MHz, CDCl₃): δ 3.97-4.97 (m, 4H), 5.92 (s, 1H), 6.35 (dd, J = 1.2, 2.0 Hz, 1H), 6.44 (d, J = 2.9 Hz, 1H), 7.42 (m, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 65.3, 97.8, 108.8, 110.2, 143.3, 151.2. GC-TOF HRMS: calcd for C₇H₈O₃ [M]⁺ 140.0473, found 140.0485.

2-(thiophen-2-yl)-1,3-dioxolane (3i)

¹H NMR (500 MHz, CDCl₃): δ 3.99-4.17 (m, 4H), 6.12 (s, 1H), 6.70 (dd, J = 1.2, 3.7 Hz, 1H), 7.17

(d, J = 2.9 Hz, 1H), 7.33 (dd, J = 1.2, 5.2 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 65.4, 100.4, 126.4, 126.5, 126.8, 141.9. GC-TOF HRMS: calcd for C₇H₈O₂S [M]⁺ 156.2032, found 156.2057.

6-methyl-1,4-dioxaspiro[4.5]decane (3j)

¹H NMR (500 MHz, CDCl₃): $\delta 0.88$ (d, J = 6.9 Hz, 3H), 1.21-1.38 (m, 3H), 1.43-1.77 (m, 6H), 3.90-3.98 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): $\delta 14.4$, 24.3, 24.9, 32.5, 35.0, 39.7, 65.0, 65.2, 110.9. GC-TOF HRMS: calcd for C₉H₁₆O₂ [M]⁺ 156.1150, found 156.1167.

1,4-dioxa-8-aza-spiro[4.5]decane-8-carboxylic acid tert-butyl ester (3k)

¹H NMR (500 MHz, CDCl₃): δ 1.46 (s, 9H), 1.65 (t, *J* = 5.6 Hz, 4H), 3.50 (t, *J* = 5.6 Hz, 4H), 3.97 (s, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 28.6, 35.0, 42.0, 64.5, 79.7, 107.3, 154.8. GC-TOF HRMS: calcd for C₁₂H₂₁O₄N[M]⁺ 243.1471, found 243.1445.

octahydro-spiro[1,3-dioxolane-2,1'(2'H)-naphthalene] (3l)

¹H NMR (500 MHz, CDCl₃): δ 0.90-1.44 (m, 8H), 1.46-1.84 (m, 8H), 3.85-3.98 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 23.2, 24.3, 26.3, 26.3, 33.5, 34.5, 35.8, 40.0, 50.4, 65.1, 65.4, 110.4. GC-TOF HRMS: calcd for C₁₂H₂₀O₂ [M]⁺ 196.1463, found 196.1439.

8a'-methyl-3',4',8',8a'-tetrahydro-2'*H*-spiro[1,3-dioxolane-2,1'-naphthalen]-6'(7'*H*)-one (3m)
¹H NMR (500 MHz, CDCl₃): δ 1.36 (s, 3H), 1.63-1.82 (m, 5H), 1.87-1.93 (m, 1H), 2,26-2.47 (m, 6H), 3.92-4.00 (m, 4H), 5.82 (d, *J* = 2.3 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ 20.7, 21.9, 27.0, 30.2, 31.6, 34.1, 45.2, 65.2, 65.5, 112.5, 125.8, 167.8, 199.4. GC-TOF HRMS: calcd for C₁₃H₁₈O₃

[M]⁺ 222.1256, found 222.1244.

1,5-dioxaspiro[5.5]undecane (3n)

¹H NMR (500 MHz, CDCl₃): δ 1.39-1.43 (m, 2H), 1.50-1.54 (m, 4H), 1.69-1.78 (m, 6H), 3.89-3.91 (m, 4H). ¹³C NMR (125 MHz, CDCl₃): δ 22.5, 25.9, 25.9, 33.2, 59.2, 98.0. GC-TOF HRMS: calcd for C₉H₁₆O₂ [M]⁺ 156.1150, found 156.1152.

Reaction Snapshots with GC

Cyclohexanone (1a: retention time: 3.2 min) and 1,4-dioxaspiro[4.5]decane (3a: retention time: 3.8 min)



GC 3. Snapshot at 90 min











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