Electronic Supplementary information

Scalable synthesis of 2,5-diformylfuran in single-phase continuous flow and segmented flow

Min Jeong Kang[a‡], Yea Seul Jang[a‡] and Chan Pil Park*[a]

[a]Graduate School of Analytical Science and Technology (GRAST), Chungnam National University, Daejeon 34134, South Korea. *E-mail: chan@cnu.ac.kr.

Contents

S1. Literature comparison of 2,5-diformylfuran synthesis in batch and flow

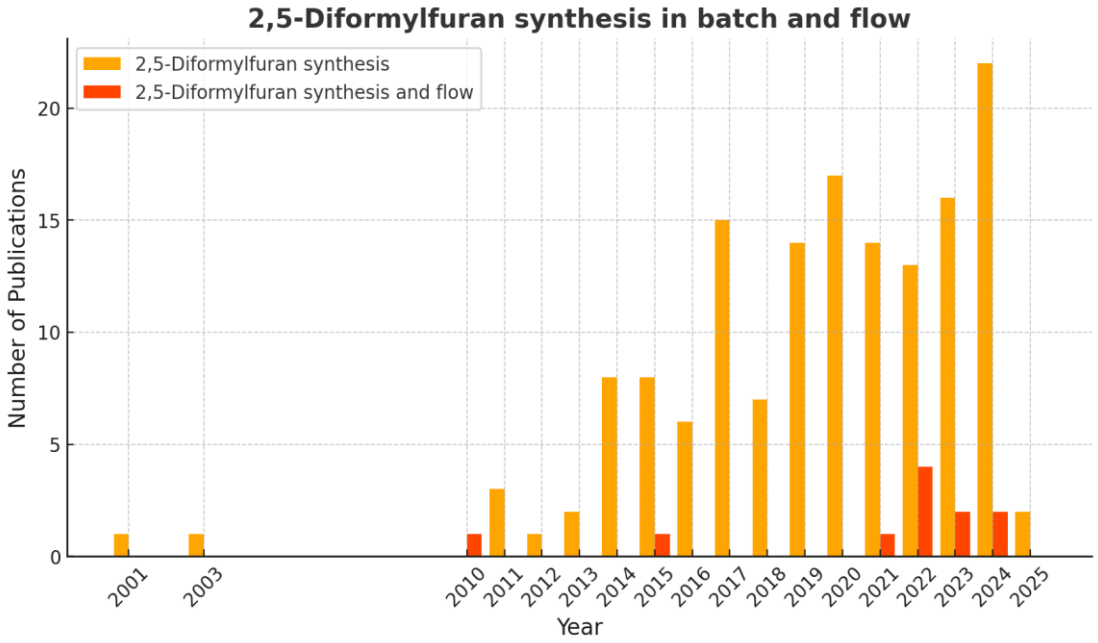


Figure S1. Number of publications on 2,5-diformylfuran synthesis in batch and flow (orange: total publications including both batch and flow systems; red: those specifically utilizing flow chemistry). Plotted data were retrieved from the Web of Science advanced search (Organic Synthesis category) using the queries "2,5-Diformylfuran synthesis" and "2,5-Diformylfuran synthesis AND flow" on March 14, 2025.

S2. Plausible mechanism for the conversion of HMF to DFF[1, 2]

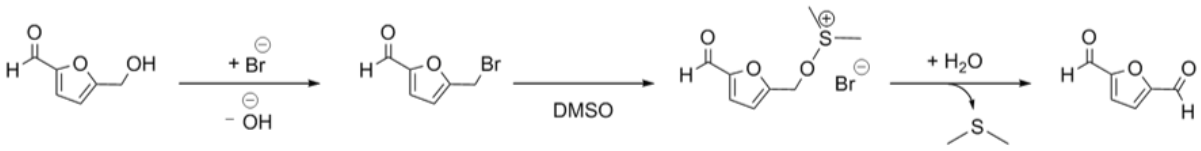


Figure S2. Plausible mechanism for the conversion of HMF to DFF via Kornblum-like oxidation. The reaction proceeds through bromination of HMF, sulfonium intermediate formation with DMSO, and elimination of DMS.

S3. Experimental procedures

A) General information

All reagents were purchased from Sigma-Aldrich, TCI, Thermo Scientific, SY innovation, and/or Daejung. All reagents were used without any further purification. Perfluoropolyether fluorinated fluids (F-oil, Galden®HT170 and HT270) were purchased from Syensqo. PTFE tubing (OD: 2.1 mm, ID: 1.5 mm, length: 4 m or 8 m or 0.385 m, and OD: 3.2 mm, ID: 2.4 mm, length: 8 m, OD: 1.6 mm, ID: 1.0 mm, length: 0.2 m) was purchased from Bohlender made in Germany. PFA tubing (OD: 3.17 mm, ID: 1.77 mm and OD: 6.35 mm, ID: 3.96 mm) was purchased from Sungkwang Silitech made in Korea. PTFE heat-shrinkable tubing (Min. shrunk OD: 0.7 mm, 1.0 mm) was purchased from Bohlender made in Germany. T-junction (IDEX. USA., PEEK cross for 1/8" OD tubing, Thru-hole 1.25 mm), back pressure regulator (BPR) assembly 100 psi, flangeless male nut was purchased from IDEX in the USA. T-junction (SUS316 for 1/8" OD tubing, Thru-hole 2.28 mm; SUS316 for 1/4" OD tubing, Thru-hole 4.82 mm), union elbow (SUS316 for 1/4" OD tubing), reducing union (SUS316, 1/4" to 1/8" tubing) were purchased from S-LOK made in Korea. Tygon® R-3603 was purchased from Saint-Gobain made in France. Among the syringe pumps, Legato 210 was purchased from KD Scientific made in the USA and Fusion 200 was purchased from Chemyx made in the USA. KP-22 was used as a dual pump purchased from FLOM made in the Japan. The autoclave reactor was purchased from SciLab Korea Co., Ltd. The electric furnace was purchased from HANTECH Co., Ltd. The separation of the mixture by liquid column chromatography was performed by using the Teledyne ISCO CombiFlash RF + UV LC instrument and the 12 g flash column from Redisep RF. The Nuclear Magnetic Resonance (NMR) spectrum was recorded on a Bruker AVANCE Neo 400. Proton chemical shifts are reported in ppm (δ) relative to TMS with the solvent employed as the internal standard ($CDCl_3$ δ = 7.20 ppm, D_2O δ = 4.70 ppm, DMSO-d_6 δ = 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiple), coupling constants (Hz). Carbon chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard ($CDCl_3$ δ = 77.0 ppm). Fluorine chemical shifts are reported in ppm (δ) relative to $CFCl_3$ (δ = 0.0 ppm) as the external standard.

B) General procedure of one-step single-flow process for DFF synthesis

5-Hydroxymethylfurfural (HMF, 1.0 M, 1 equiv.) and halide salt (0-0.3 M, 0-0.3 equiv.) were dissolved together in dimethyl sulfoxide (DMSO), and acid (H_2SO_4, 0-0.3 M, 0-0.3 equiv.) was dissolved in DMSO separately. These solutions were injected in a 1:1 ratio, with each stream at a flow rate of 0.236 mL/min (or 0.118 mL/min, 0.354 mL/min, 0.707 mL/min) using separate syringe pumps, and mixed at the initial T-junction to establish a homogeneous phase. The reaction phase was then injected into a tubular reactor (PTFE tubing (OD: 2.1 mm, ID: 1.5 mm, length: 8 m, volume: 14.14 mL) immersed in an oil bath maintained at 145 ℃. After a 30 min (or 10 min, 20min, 60 min) reaction, the resultant solution passed through a 100 psi BPR. The resultant solution with added water to facilitate phase separation, was extracted with ethyl acetate (EA, 3 × 5 mL); insoluble impurities were removed via filtration using celite. The resultant solution was purified by column chromatography (hexane/ethyl acetate).

C) Procedure for the separation of DMS

1) Preparation of custom-designed gas-liquid phase separator[3]

For gas-liquid separation, the separator was manufactured using the density difference between the phases. The separator was made of PFA tubing (OD: 6.35mm, ID: 3.96 mm), and the connecting tubes were made of PFA tubing (OD: 3.17 mm, ID: 1.77 mm). A thin inner tube (PTFE tubing, OD: 1.6 mm, ID: 1.0 mm) was placed inside each separator to enable rapid phase separation and product extraction. To fix the inner tube (PTFE tubing, OD: 1.6 mm, ID: 1.0 mm) to the connecting tube (PFA tubing, OD: 3.17 mm, ID: 1.77 mm), a PTFE heat-shrinkable tube (Min. shrunk OD: 1.6 mm) was wrapped around the connection area and fixed through heat-shrinking. To connect tubes, T-junction (SUS316 for 1/4" OD tubing, Thru-hole 4.82 mm), union elbow (SUS316 for 1/4" OD tubing) were used. To ensure more reliable gas–liquid phase separation, the phase separator and the connecting lines can be thermally controlled using simple insulating material (cotton) and aluminum foil or a heating jacket. A transparent Tygon®R-3603 tubing can be mounted on the outer surface of the PFA tubing to allow visual observation of the separation process while maintaining the internal temperature. Alternatively, the phase separator can simply be placed in a water bath maintained at the desired temperature (Figure S3).

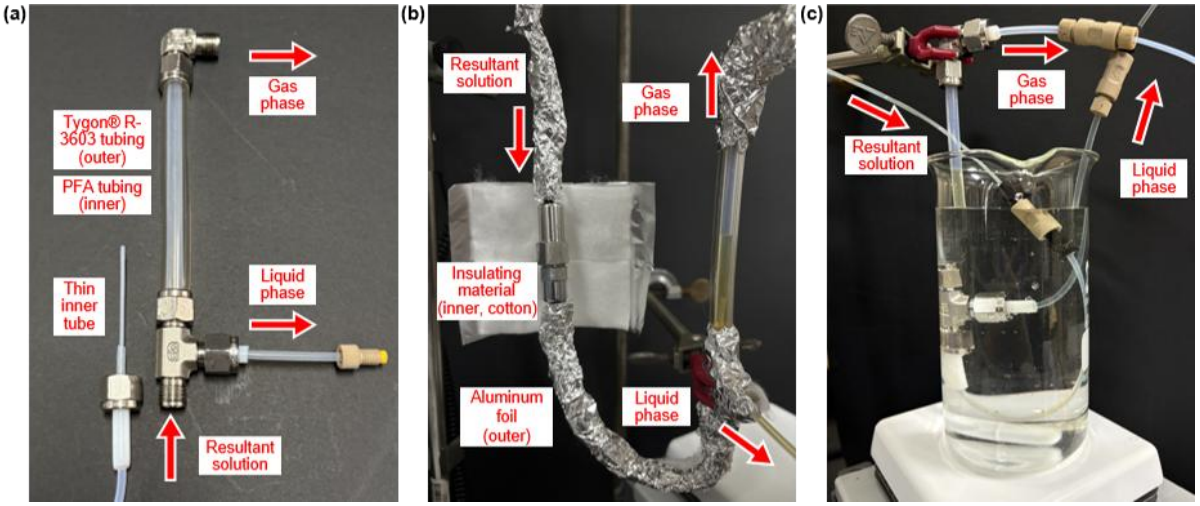


Figure S3. Composition and operation of the custom-designed gas–liquid phase separator. (a) Photograph of a custom-designed gas-liquid separator configuration. (b) Operational setup of the phase separator wrapped with cotton (insulating material) and aluminum foil to maintain temperature. (c) Operational setup of the phase separator placed in a water bath to maintain temperature.

2) Evaluation of separation efficiency of custom-designed gas-liquid phase separator[3]

To evaluate the separation performance of the phase separator, the device was operated at 50 °C and solutions collected from each outlet were dissolved in DMSO-d_6 and analyzed by ^{1}H NMR spectroscopy (^{1}H NMR DMS (in DMSO-d_6) δ = 2.05 ppm, DMSO δ = 2.55 ppm). The experiment was conducted under the same single-flow conditions (using NaBr, H_2SO_4) as described in Section S3.B, with the phase separator installed after the BPR. As a result, no residual DMS was detected in the organic phase, indicating that all DMS was released through the gas phase outlet (Figure S4). Based on these results, the DMS separation efficiency of the phase separator operated at 50 °C was determined to be 100%, confirming its high effectiveness for DMS removal in continuous processes.

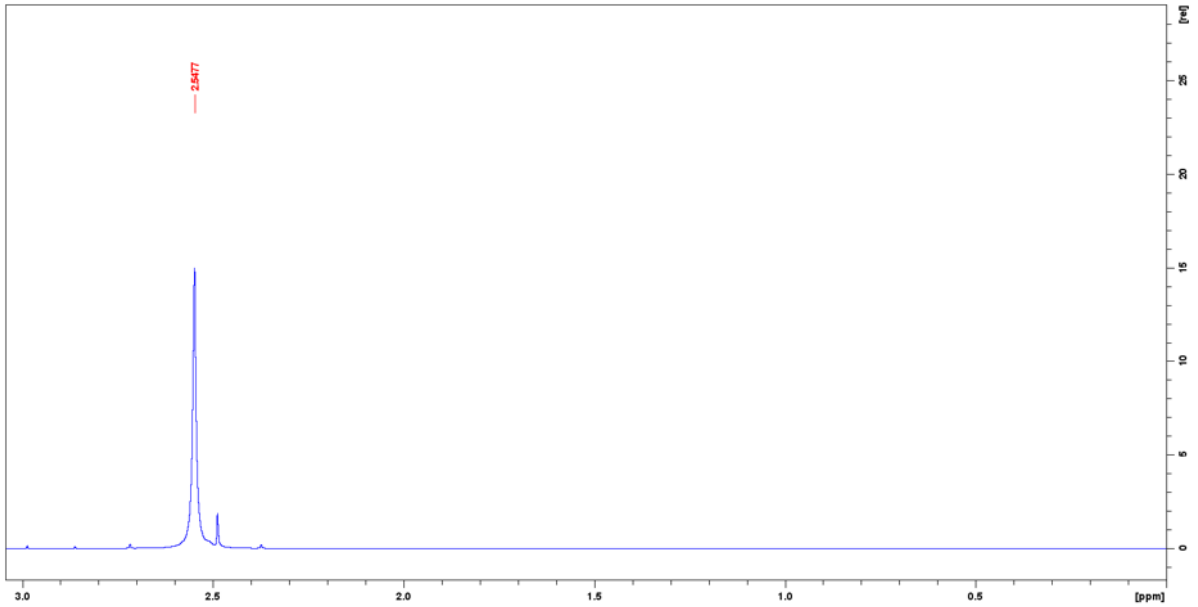


Figure S4. ^{1}H NMR spectrum (in DMSO-d_6) of the reagent solution (organic phase) after separation of DMS through a custom-designed gas–liquid phase separator.

3) Conversion of DMS to DMSO[4]

a. In batch

After procedure C-1 of S3, the separated DMS gas was re-liquidified at room temperature, and the liquid DMS was first treated by H_2O_2 oxidation under batch conditions. H_2O_2 (30% w/w, 1.2 mmol) and borax catalyst (0.1 mmol) were dissolved in a round flask containing a water/methanol (2:1, v/v, 3 mL) and the gas phase outlet was connected to a flask, followed by reaction at room temperature for 1 hour. After the reaction, ^{1}H NMR analysis of the sample dissolved in D_2O confirmed that DMS was completely (100%) converted to DMSO (Figure S5). ^{1}H NMR (in D_2O) of DMS δ = 2.05 ppm and DMSO δ = 2.66 ppm

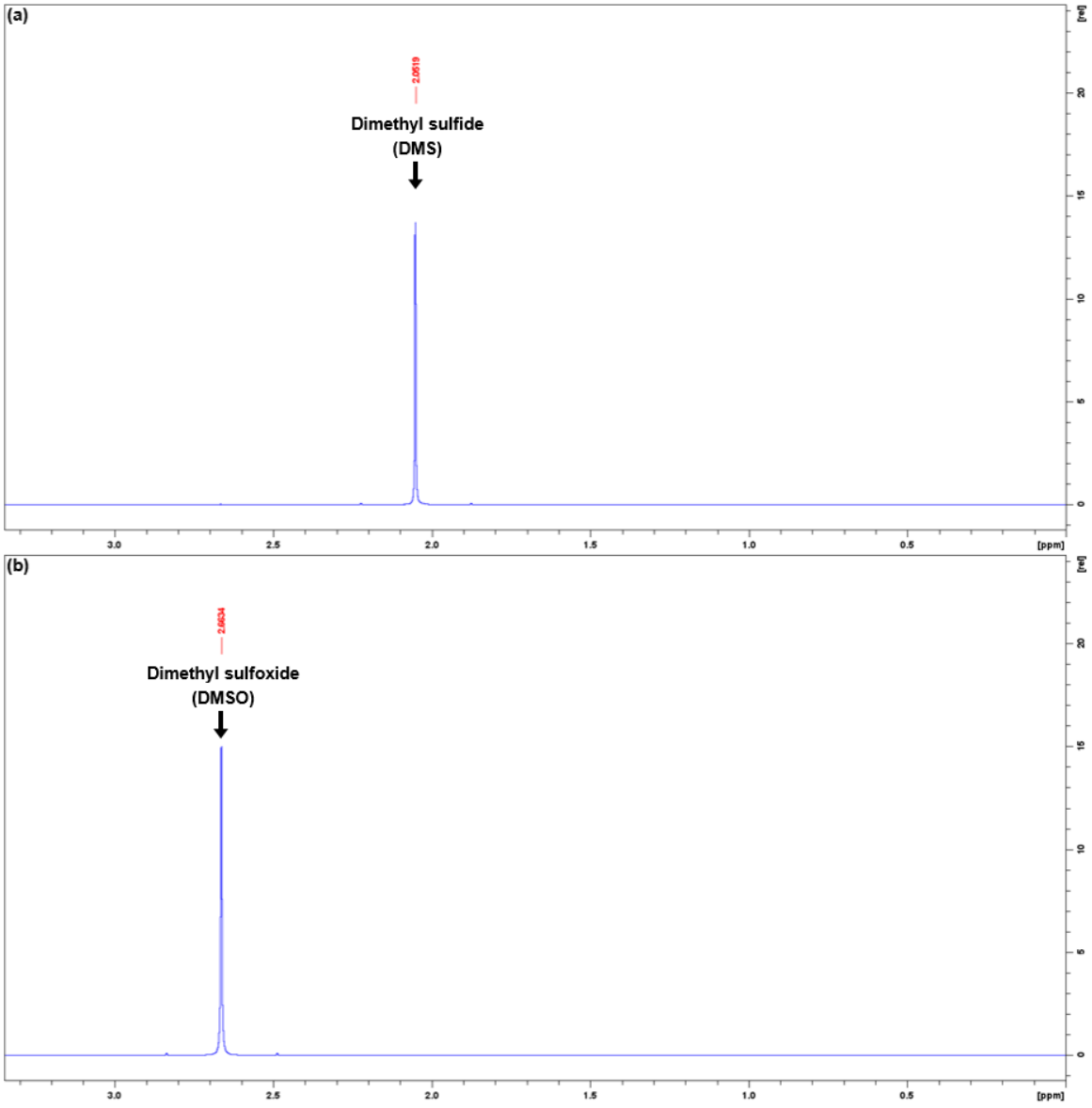


Figure S5. ^{1}H NMR spectra (in D_2O) of the reaction solution before and after oxidation of DMS (a) only DMS separated from the reactant solution. (b) after oxidation of DMS to DMSO in batch.

b. In flow

After procedure C-1 of S3, the re-liquidified DMS was subjected to H_2O_2 oxidation under continuous flow conditions. H_2O_2 (30% w/w, 1.2 mmol) and borax catalyst (0.1 mmol) were dissolved in a water/methanol mixture (2:1, v/v, 3 mL), and this solution was introduced using a syringe pump at a flow rate of 0.131 mL/min. The solution was mixed with the separated DMS at a T-junction to form a homogeneous phase, which was then introduced into a tubular reactor (PTFE tubing, OD: 2.1 mm, ID: 1.5 mm, length: 0.385 m, volume: 0.68 mL) at room temperature for 5 min (Figure S6a). After the reaction, the resulting solution was collected in a vial, dissolved in D_2O, and ^1H NMR analysis confirmed that DMS was completely (100%) converted to DMSO (Figure S 5a, 6b) ^1H NMR (in D_2O) of DMS δ = 2.05 ppm and DMSO δ = 2.66 ppm.

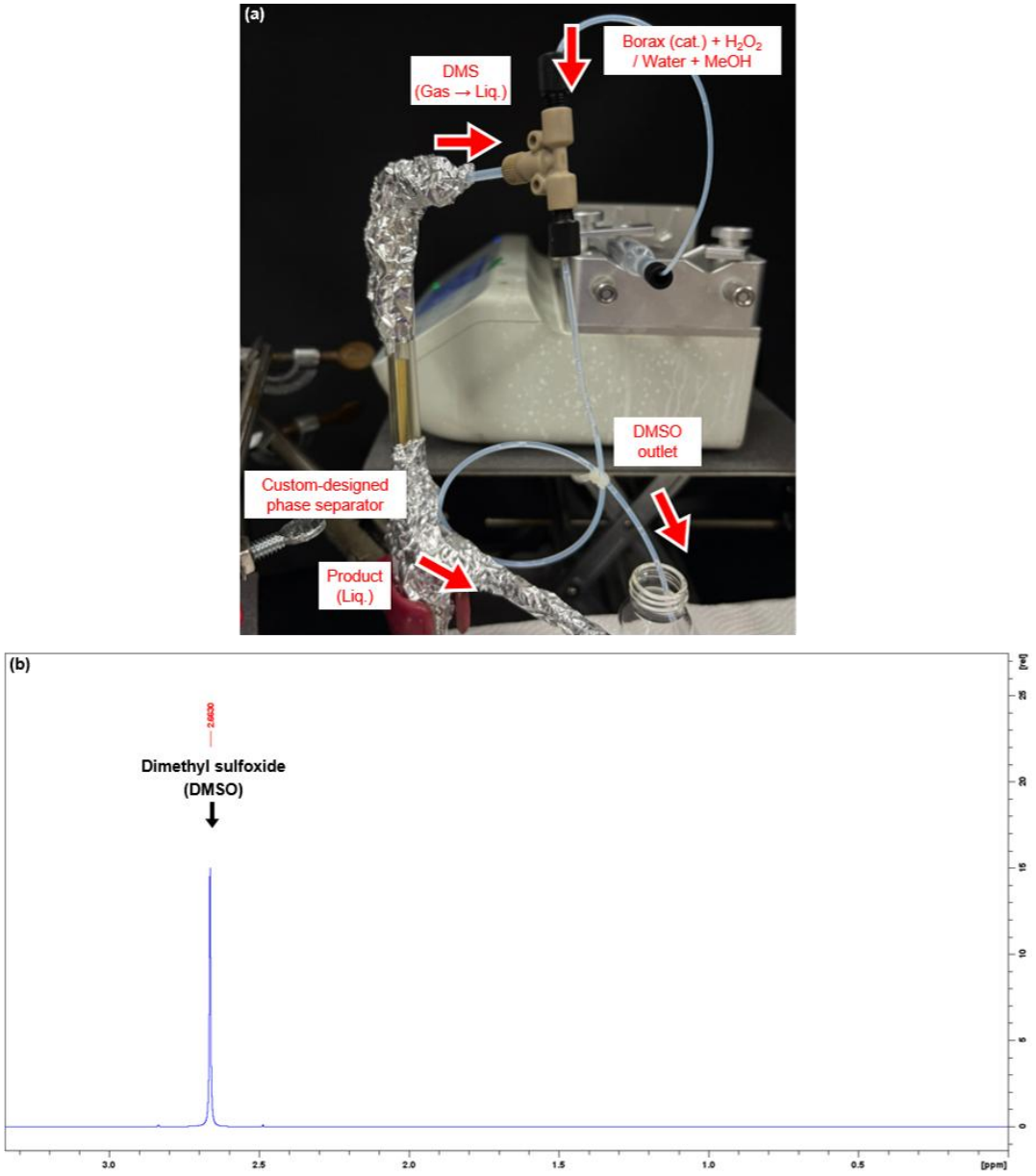


Figure S6. (a) Photograph of the continuous-flow configuration for DMS oxidation. (b) ^1H NMR spectrum (in D_2O) after the oxidation of DMS to DMSO in flow reactor.

D) General procedure of two-step single-flow process for DFF synthesis

5-Hydroxymethylfurfural (HMF, 1 mmol) and sodium bromide (NaBr, 0.15 mmol) were dissolved together in dimethyl sulfoxide (DMSO, 1 mL), while sulfuric acid (H_2SO_4, 0.15-0.2 mmol) was dissolved in DMSO (1 mL) separately. These solutions were injected in a 1:1 ratio, with each stream at a flow rate of 0.177 mL/min using separate syringe pumps, and mixed at the initial T-junction to establish a homogeneous phase. The reaction phase was then injected into a PTFE tubular reactor (OD: 2.1 mm, ID: 1.5 mm, length: 4 m, volume: 7.07 mL) immersed in an oil bath maintained at 145 ℃. After a 20 min reaction, the resultant solution exiting the back-pressure regulator (BPR) was separated into gaseous and liquid phases using a custom-designed phase separator maintained above 50 ℃. As described above (Section S3.C.3), DMS, re-liquefied from a gaseous state, was reacted with H_2O_2 and borax catalyst dissolved in water/methanol (2:1, v/v) at room temperature.[4] The liquid phase obtained from the first reaction was injected using one syringe pump, while H_2SO_4 (0.05-0.15 mmol) dissolved in DMSO(1 mL) was injected using another syringe pump. These solutions were injected in a 1:1 ratio, with each stream at a flow rate of 0.354 mL/min (or 0.177 mL/min) using separate syringe pumps, and mixed at the T-junction to establish a homogeneous phase. The reaction phase was then injected into a tubular reactor (PTFE tubing (OD: 2.1 mm, ID: 1.5 mm, length: 4 m, volume: 7.07 mL) immersed in an oil bath maintained at 145 ℃. After a 10 min (or 20 min) reaction, the resultant solution exiting the back-pressure regulator (BPR) was separated into gaseous and liquid phases using a custom-designed phase separator maintained above 50 ℃. The separated DMS was again converted to DMSO. The resultant solution with added water to facilitate phase separation, was extracted with ethyl acetate (EA, 3 × 5 mL); insoluble impurities were removed via filtration using celite. The resultant solution was purified by column chromatography (hexane/ethyl acetate).

E) General procedure of a segmented flow process for DFF synthesis

1) General procedure of a segmented flow process for DFF synthesis

5-Hydroxymethylfurfural (HMF, 1.0-2.0 M, 1 equiv.) and sodium bromide (NaBr, 0.15-0.3 M, 0.15 equiv.) were dissolved together in dimethyl sulfoxide (DMSO), while sulfuric acid (H_2SO_4, 0.2-0.6 M, 0.2-0.3 equiv.) was dissolved in DMSO separately. These solutions were injected in a 1:1 ratio, with each stream at a flow rate of 0.118 mL/min (or 0.142 mL/min, 0.236 mL/min; 0.3 mL/min in the scale-up experiment) using separate syringe pumps, and mixed at the initial T-junction to establish a homogeneous phase. Subsequently, this homogeneous phase (Flow rate: 0.236 mL/min or 0.284 mL/min, 0.472mL/min; 0.6 mL/min in the scale-up experiment) met the F-oil (continuous phase, Flow rate: 0.236 mL/min or 0.284 mL/min, 0.472mL/min; 0.6 mL/min in the scale-up experiment) at the second T-junction in a 1:1 ratio, generating a segmented flow. The segmented flow was then injected into a tubular reactor (PTFE tubing, OD: 2.1 mm, ID: 1.5 mm, length: 8 m, volume: 14.14 mL; OD: 3.2 mm, ID: 2.4 mm, length: 8 m, volume: 36.2 mL in the scale-up experiment) immersed in an oil bath maintained at 145 °C. After a 30 min (or 15 min, 25 min) reaction, the resultant solution exiting the back-pressure regulator (BPR) was separated into gaseous and liquid phases using a custom-designed phase separator maintained above 50 °C. As described above, DMS, re-liquefied from a gaseous state, was reacted with H_2O_2 and borax catalyst dissolved in water/methanol (2:1, v/v) at room temperature (Figure S7).[4] The F-oil and organic phases were subsequently separated, and the organic phase with added water to facilitate phase separation, was extracted with ethyl acetate (EA, 3 × 5 mL); insoluble impurities were removed via filtration using celite. The resulting solution was purified by column chromatography (hexane/ethyl acetate).

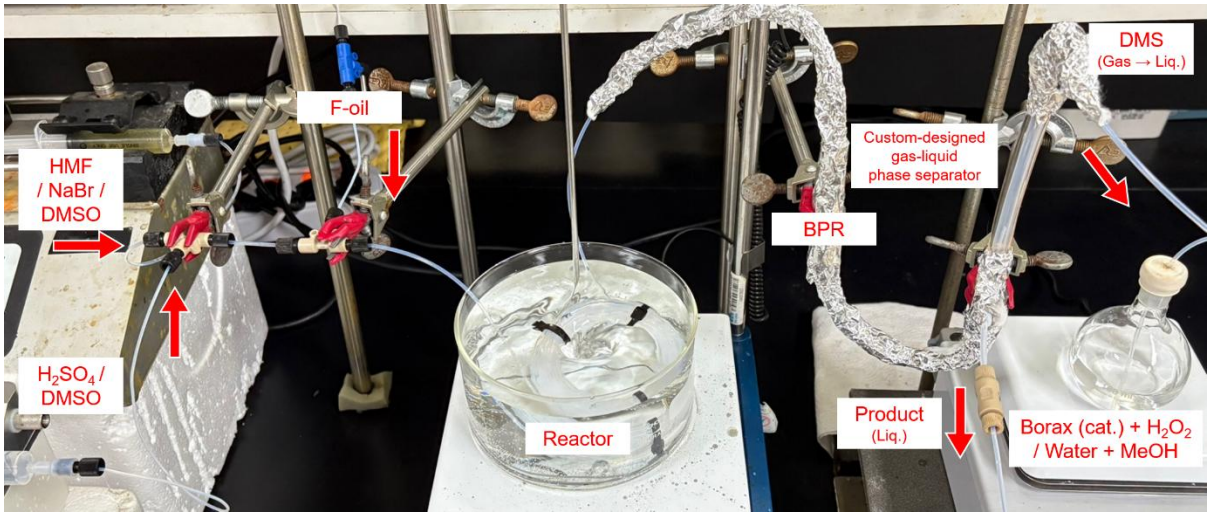


Figure S7. Overall composition of slug-flow process for DFF synthesis.

2) Contamination test of used F-oil

The F-oil and organic phases collected from the liquid phase outlet of a custom-made phase separator were subsequently separated. The separated organic phase was dissolved in $CDCl_3$ and analyzed by ^{19}F NMR spectroscopy. No fluorine-containing peaks were observed in the ^{19}F NMR spectrum, confirming that degradation products originating from F-oil did not contaminate the reaction medium (Figure S8a). Additionally, ^{1}H NMR analysis of the recovered F-oil, dissolved in $CDCl_3$ without any washing, confirmed the absence of DMS contamination (Figure S8b). ^{1}H NMR (in $CDCl_3$) of DMS δ = 2.04 ppm.

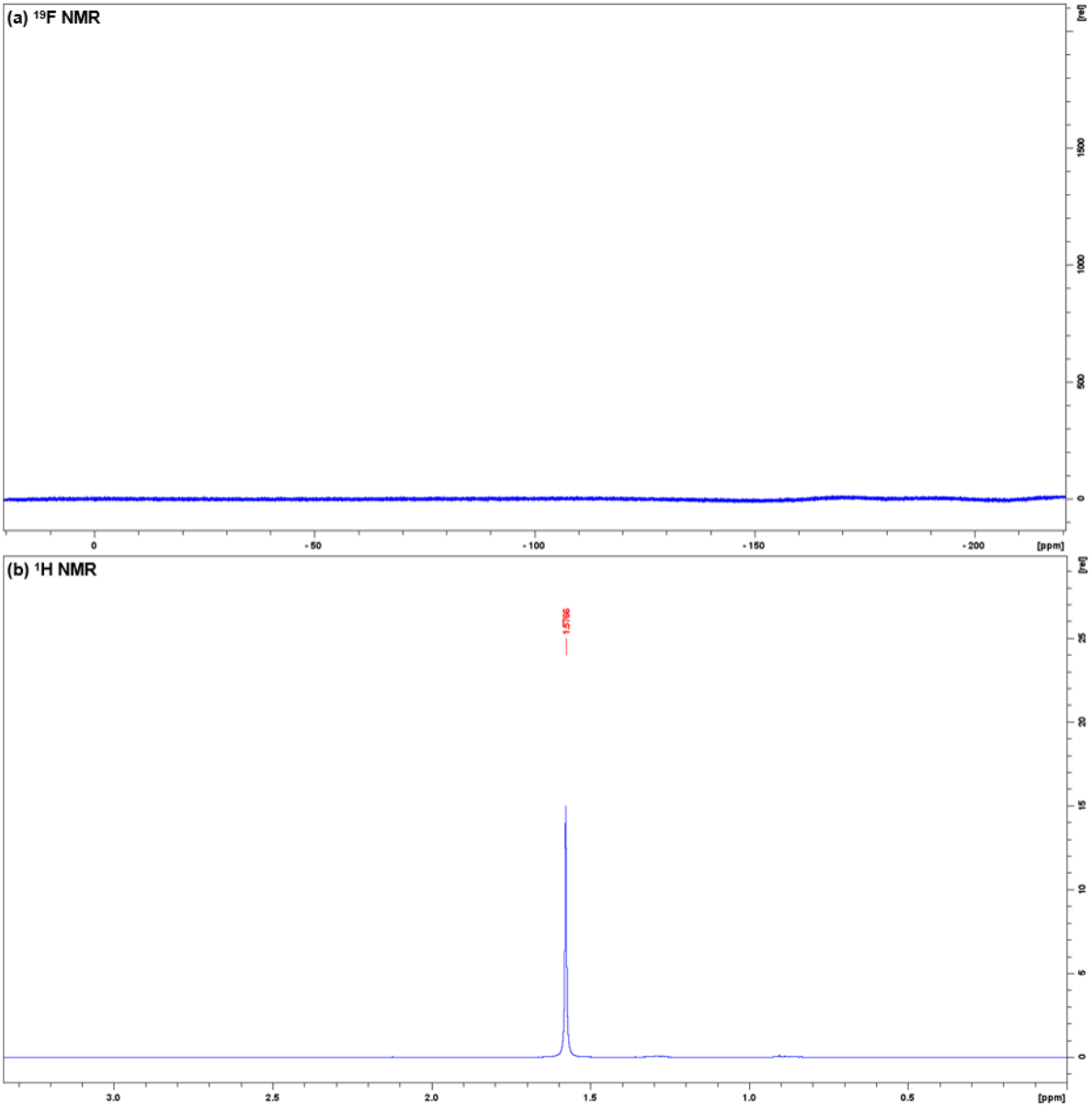


Figure S8. (a) ^{19}F NMR spectrum (in $CDCl_3$) of the separated organic phase. (b) ^{1}H NMR spectrum (in $CDCl_3$) of the recovered F-oil Only the residual HDO peak (1.58 ppm) from the NMR solvent is observed**.**

3) Comparison of single-flow and segmented-flow operation in tubular reactor

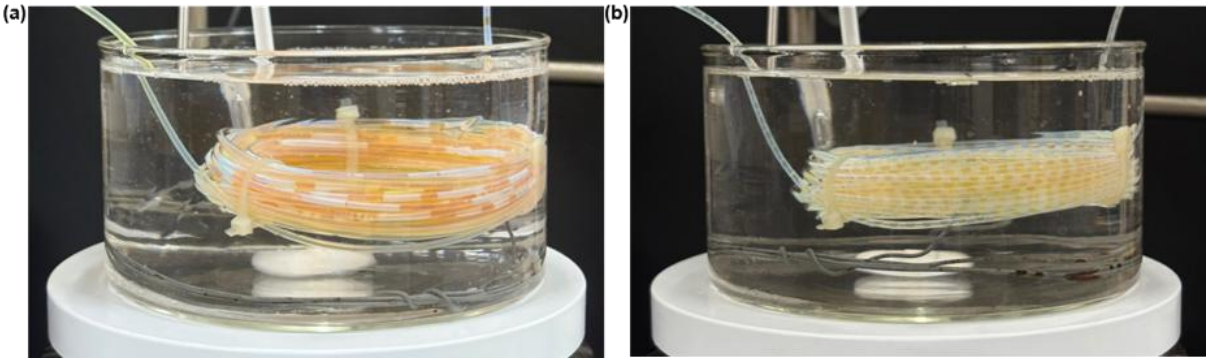


Figure S9. Photograph of the tubular reactor in an oil bath: (a) irregular bubble formation in single-flow process; (b) stable operation under segmented-flow process.

4) Bubble suppression effect by F-oil

To measure the solubility of DMS and evaluate the bubble suppression effect of F-oil, experiments were performed under continuous flow conditions (Total flow rate: 0.2 mL/min, 145 ℃, 100 psi BPR) using PTFE tubing (OD: 1.6 mm, ID: 1.0 mm, length: 0.2 m, volume: 0.16 mL). DMS and each solvent (DMSO, acidic DMSO containing 0.15 mmol NaBr and 0.3 mmol H_2SO_4, F-oil) were separately injected by a syringe pump and mixed at the T-junction. The solubility was determined by visually observing the maximum amount of DMS dissolved in the solvent before bubble formation. The results showed that under the tested conditions (145 °C, 100 psi), pure DMSO could dissolve up to approximately 50% DMS (Table S1, Entry 1), whereas the solubility was significantly reduced to 7% in acidic DMSO (0.15 mmol NaBr, 0.3 mmol H_2SO_4, Table S1, Entry 2). In F-oil, the solubility of DMS was found to be about 5% (Table S1, Entry 3). These results indicate that, under our experimental conditions, the introduction of F-oil in a segmented flow system partially dissolves DMS and effectively suppresses bubble formation, thereby enabling more stable process operation compared with single-flow conditions.

Table S1. Solubility test of DMS[a]

Entry	Solvent	Solubility (%)[b]
1	DMSO	50
2	Acidic DMSO (0.15 mmol NaBr, 0.3 mmol H_2SO_4)	7
3	F-oil (Galden@HT170)	5

[a] Conditions: PTFE tubing (OD: 1.6 mm, ID: 1.0 mm, length: 0.2 m, volume: 0.16 mL), total flow rate: 0.2 mL/min, 145 °C, 100 psi BPR. DMS and solvent were each injected using separate syringe pumps, and mixed at the T-junction. [b] Solubility was determined as the maximum amount of DMS dissolved before bubble formation occurred.

5) Procedure for DFF synthesis from fructose

a. HMF synthesis from fructose in batch

Fructose (0.56 M) was dissolved in a saturated aqueous potassium bromide (KBr) solution, followed by the addition of 0.1 M HCl. Acetonitrile was then added to achieve a 2:1 volume ratio with the solution. The mixture was transferred to an autoclave reactor, which was subsequently placed in an electric furnace and heated at 160 °C for 3 hours.[5] After cooling to room temperature, the reaction mixture was extracted with methyl isobutyl ketone (MIBK, 3 × 10 mL), and the organic phase was evaporated under reduced pressure. The resulting product was used directly for DFF synthesis without further purification.

b. DFF synthesis from carbohydrate-derived HMF in segmented flow

Fructose-derived HMF (1.0 M, 1 equiv.) and sodium bromide (NaBr, 0.15 M, 0.15 equiv.) were dissolved together in dimethyl sulfoxide (DMSO), while sulfuric acid (H_2SO_4, 0.3 M, 0.3 equiv.) was dissolved in DMSO separately. These solutions were injected in a 1:1 ratio, with each stream at a flow rate of 0.118 mL/min (0.3 mL/min in the scale-up experiment) using separate syringe pumps, and mixed at the initial T-junction to establish a homogeneous phase. Subsequently, this homogeneous phase (Flow rate: 0.236 mL/min; 0.6 mL/min in the scale-up experiment) met the F-oil (continuous phase, Flow rate: 0.236 mL/min; 0.6 mL/min in the scale-up experiment) at the second T-junction in a 1:1 ratio, generating a segmented flow. The segmented flow was then injected into a tubular reactor (PTFE tubing, OD: 2.1 mm, ID: 1.5 mm, length: 8 m, volume: 14.14 mL; OD: 3.2 mm, ID: 2.4 mm, length: 8 m, volume: 36.2 mL in the scale-up experiment) immersed in an oil bath maintained at 145 °C. After a 30 min reaction, the resultant solution exiting the back-pressure regulator (BPR) was separated into gaseous and liquid phases using a custom-designed phase separator maintained above 50 °C. As described above, DMS, re-liquefied from a gaseous state, was reacted with H_2O_2 and borax catalyst dissolved in water/methanol (2:1, v/v) at room temperature.[4] The F-oil and organic phases were subsequently separated, and the organic phase with added water to facilitate phase separation, was extracted with ethyl acetate (EA, 3 × 5 mL); insoluble impurities were removed via filtration using celite. The resulting solution was purified by column chromatography (hexane/ethyl acetate). product was dissolved in $CDCl_3$ and analyzed by ^{1}H and ^{13}C NMR spectroscopy.

S4. Daily output validation after long-term continuous operation (24 hr)

A) Calculated value of daily output

Throughput = Reagent concentration (mmol/mL) × flow rate of reaction medium × yield

1) Segmented flow process for DFF synthesis (ID: 1.5 mm)

Tube inner diameter: 1.5 mm
Total volume: 14.1 mL
Flow rate of reaction medium: 14.1 mL/2 × (60 min/30 min × 24 h) / 1 day
Yield: 85%
Product molecular weight: 124.09 g/mol

Daily output
= (1 mmol/2 mL) × {14.1 mL/2 × (60 min/30 min × 24 h) / 1 day} × 0.85 = 143.82 mmol/day
= 143.82 mmol/day × 124.09 mg/mmol = 17.846 g/day

2) Scaled-up process in segmented flow mode for DFF synthesis (ID: 2.4 mm)

Tube inner diameter: 2.4 mm
Total volume: 36.2 mL
Flow rate of reaction medium: 36.2 mL/2 × (60 min/30 min × 24 h) / 1 day
Yield: 76%
Product molecular weight: 124.09 g/mol

Daily output
= (1 mmol/2 mL) × {36.2 mL/2 × (60 min/30 min × 24 h) / 1 day} × 0.76 = 330.14 mmol/day
= 330.14 mmol/day × 124.09 mg/mmol = 40.97 g/day

B) Measured value of daily output

To evaluate the long-term operational stability and validate the productivity estimation under varying reactor diameters, we conducted 24-hour continuous flow experiments using PTFE tubular reactors with inner diameters of 1.5 mm and 2.4 mm. All other experimental conditions were kept identical to those described in Section S3.E.1. For each experiment, the reaction was performed continuously for 24 h, with resultant solutions collected and analyzed at 1 h intervals. The average yields over 24 h were calculated for each reactor configuration, as summarized in Table S2. Throughout each long-term operation, the yield remained stable without significant decline or abnormal fluctuation, indicating robust operational stability over the extended period (Figure S10). These results demonstrate that the productivity estimation based on reactor scale-up is reliable, as long-term continuous operation does not compromise reaction performance under the described conditions. Therefore, the previously theoretical projections (Section S4.A) in the main text are supported by experimental evidence from extended operation.

Table S2. Average yields of DFF synthesis over 24 hours

Inner diameter (mm)	Total volume (mL)	Flow rate (mL/min)		Average yield (%)
		Reaction phase	F-oil phase	
1.5	14.1	0.236	0.236	85
2.4	36.2	0.6	0.6	76

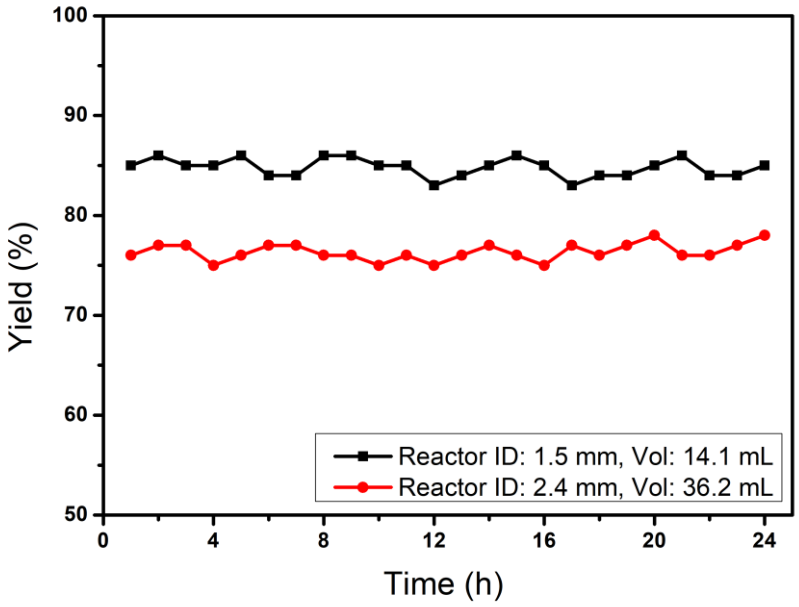


Figure S10. Hourly yield trends over 24 h continuous operation.

S5. Recovery and stability test of F-oil

To evaluate the recovery efficiency of F-oil, 24 h continuous operation was performed. During continuous operation, the recovery efficiency of F-oil was confirmed to be 96% compared to the injection volume. Furthermore, no decrease in DFF yield was observed due to the recovery and reuse of F-oil. Additionally, to evaluate potential chemical degradation of F-oil during recycling and the reaction process, ^{19}F NMR spectra were obtained for fresh F-oil, recovered F-oil after 10 cycles, and F-oil subjected to harsh conditions with each sample dissolved in $CDCl_3$ (Figure S11). For the treatment at harsh conditions, F-oil was mixed with NaBr (0.075 M) and H_2SO_4 (0.15 M) in DMSO at a ratio of 1:1 (v/v), sealed in an autoclave reactor, and heated at 250 °C for 5 h in an electric furnace. The ^{19}F NMR spectrum of fresh F-oil (Figure S11a) and that after 10 cycles of reuse (Figure S11b) remained almost identical, with no detectable changes in chemical shifts or the appearance of new resonances. This indicates that F-oil retained its structural integrity during repeated operation and recovery. For comparison, F-oil subjected to harsh conditions at 250 °C for 5 h in an autoclave reactor (Figure S11c) also showed no significant differences from the fresh sample, suggesting that no measurable decomposition or formation of fluorinated monomers occurred even under these harsh conditions. Therefore, it is confirmed that F-oil is chemically stable and reusable under the experimental conditions used in this study.

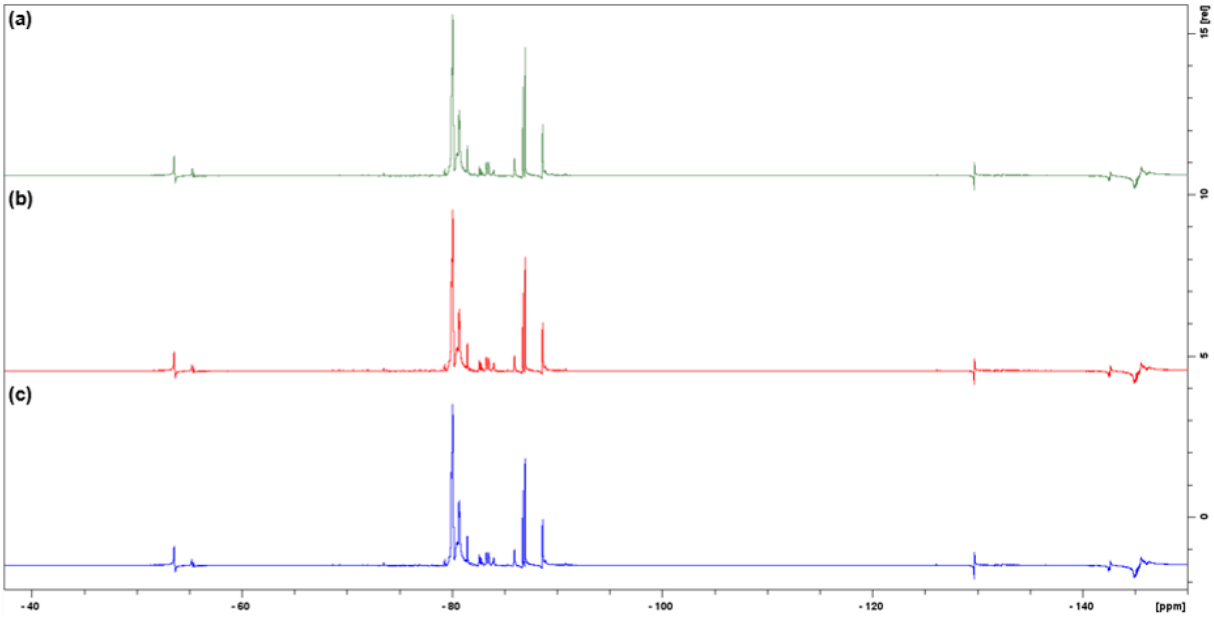


Figure S11. ^{19}F NMR (in $CDCl_3$) spectra. (a) fresh F-oil. (b) F-oil after 10 cycles of reuse. (c) F-oil subjected to harsh conditions at 250 °C for 5 h.

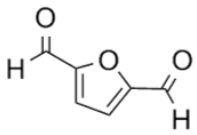
S6. Comparison of the results of this study with reported results on the flow synthesis of DFF[6, 7]

Table S3. Comparison of results for DFF synthesis from HMF in continuous flow

Entry	Type	Phase[a]	Condition	DFF yield (%)	E-factor[b]	Daily output (g/day)[c]	Ref.
1	Tubular	G-L	0.24 M HMF in acetic acid, Co/Mn/Br (1:1:3.3), O_2	23	159.7	4.14	[8]
2	Fixed-Bed	G-L-S	0.1 M HMF in H_2O, Cu/Al_2O_3, N_2	37.7	215.4[d]	0.11	[9]
3	Tube-in-tube	G-L-S	0.5 M HMF in DMSO, Fe_3O_4@SiO_2@Mn, O_2	82	17.3[d]	0.37	[10]
4	Fixed-Bed	G-L-S	0.41 M HMF in DCE, Tempo/silica, 5 mol% HNO_3, O_2	95	26[d]	6.95	[11]
5	Fixed-Bed	G-L-S	39.68 mM HMF in toluene, Ru/Al_2O_3, O_2	84	209.8[d]	0.36	[12]
6	Tubular	L-L	0.5 M HMF in DMSO, NaBr, H_2SO_4, F-oil	85	22.8	17.85	**This work**
7	Tubular	L-L	1 M HMF in DMSO, NaBr, H_2SO_4, F-oil	80	12.3	33.59	

[a] Gas (G), Liquid (L), Solid (S) phase. [b] E-factor = (Mass of total input – mass of desired product) / mass of desired product. [c] Daily output (g/day) = Flow rate of reaction phase (mL/min) x concentration (mol/mL) x yield x 1440 (min/day) x Mw of DFF (124.09 g/mol). [d] Assuming 100% recovery of the solid catalyst and excluding catalyst preparation.

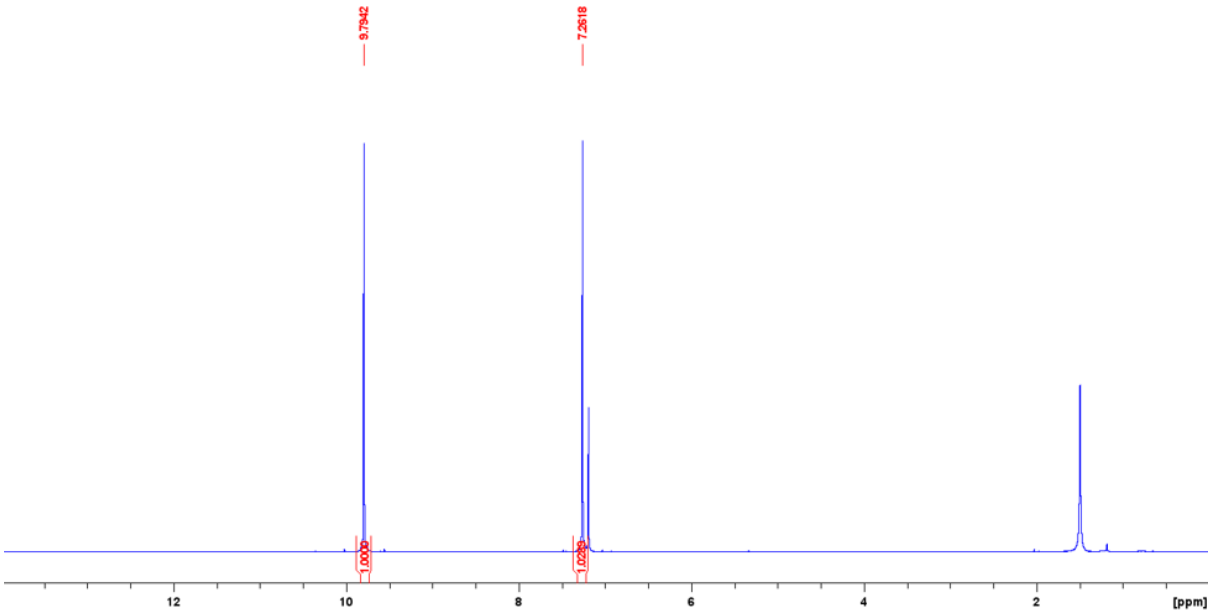
S7. ^{1}H and ^{13}C NMR Spectral data of 2,5-diformylfuran



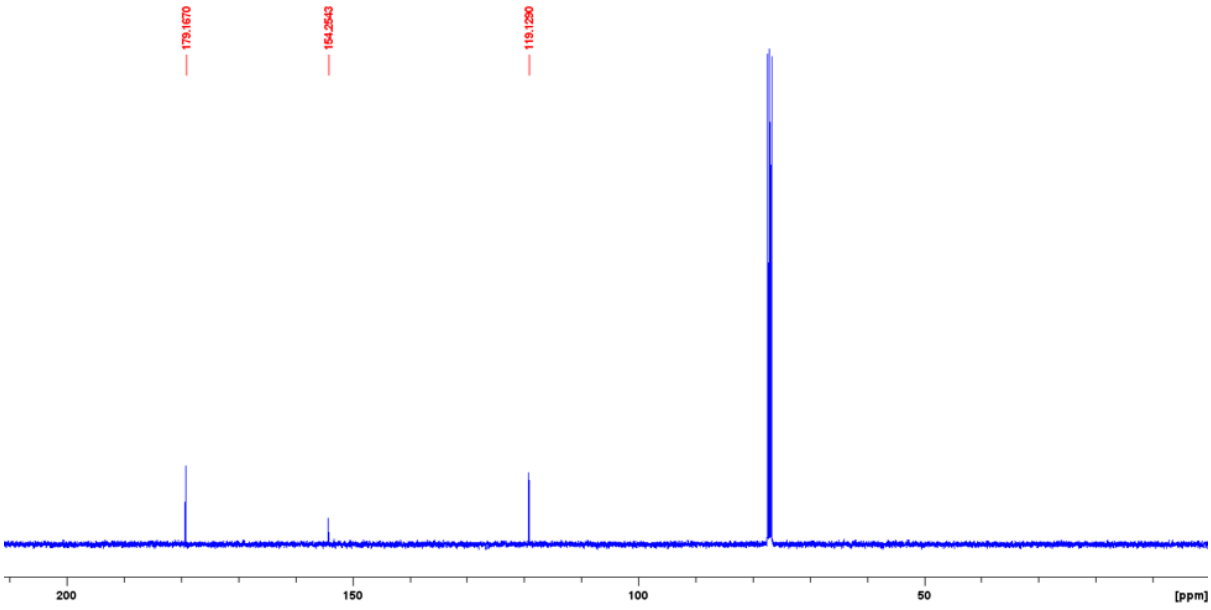
2,5-Diformylfuran

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.79 (s, 2H), 7.26 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 179.17, 154.25, 119.13 ppm

^{1}H NMR



^{13}C NMR



S8. References

1. Q. Girka, B. Estrine, N. Hoffmann, J. Le Bras, S. Marinković and J. Muzart, *React. Chem. Eng.*, 2016, **1**, 176–182.
2. D. A. Kolykhalov, A. N. Golysheva and B. Y. Karlinskii, *Catal. Commun.*, 2024, **186**, 106831.
3. Y. S. Jang, J. M. Park, J. W. Lee, C. H. Song and C. P. Park, *Chem. Eng. J.*, 2025, **509**, 161346.
4. S. Hussain, S. K. Bharadwaj, R. Pandey and M. K. Chaudhuri, *Eur. J. Org. Chem.*, 2009, **20**, 3319–3322.
5. P. Wrigstedt, J. Keskiväli and T. Repo, *RSC Adv.*, 2016, **6**, 18973–18979.
6. R. A. Sheldon, *Green Chem.*, 2023, **25**, 1704–1728.
7. C. Petrucci, G. Strappaveccia, F. Giacalone, M. Gruttadauria, F. Pizzo and L. Vaccaro, *ACS Sustain. Chem. Eng.*, 2014, **2**, 2813–2819.
8. A. Hommes, B. Disselhorst, H. M. M. Janssens, R. J. A. Stevelink, H. J. Heeres and J. Yue, *Chem. Eng. J.*, 2021, **413**, 127552.
9. B. Chen, X. Li, P. Rui, Y. Ye, T. Ye, R. Zhou, D. Li, J. H. Carter and G. J. Hutchings, *Catal. Sci. Technol.*, 2022, **12**, 3016–3027.
10. G.-Y. Jeong, A. K. Singh, S. Sharma, K. W. Gyak, R. A. Maurya and D.-P. Kim, *NPG Asia Mater.*, 2015, **7**, e173–e173.
11. C. Aellig, D. Scholz, S. Conrad and I. Hermans, *Green Chem.*, 2013, **15**, 1975–1980.
12. S. Pumrod, N. Akkarawatkhoosith, A. Kaewchada, T. Tongtummachat, K.-Y. A. Lin and A. Jaree, *RSC Adv.*, 2024, **14**, 29014–29023.