Electronic Supplementary Information (ESI)

One-flow Upscaling Neutralization of Organophosphonate derived Pesticide/Nerve Agent Simulant to Value-Added-Chemicals in Novel Teflon Microreactor Platform

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1. Experimental Procedures

1.1 Computational Fluid Dynamics Simulation setup:

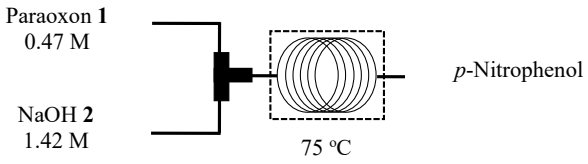
The fluid flow inside a microchannel can be described by the incompressible Navier-stokes equation together with a mass-conservation equation. Assuming steady state, the governing equation for fluid flow can be simplified to[1]

$$\rho \mathrm{v} \cdot \nabla \mathrm{v} = -\nabla \mathrm{p} + \mu \nabla^2 v + \rho g \quad \text{: Navier-Stokes equation}$$

$$\nabla \cdot \mathrm{v} = 0 \quad \text{: Mass conservation equation}$$

Where ρ [kg·m^{-3}] is the fluid density, v [m·s^{-1}] is the fluid linear velocity, p [Pa] is the pressure, μ [kg·m^{-1}·s^{-1}] is the fluid dynamic viscosity and g (= 9.8m·s^{-2}) is the gravitational acceleration. The governing equations were solved with appropriate boundary conditions (no slip boundary condition on channel walls, mass flow rate for inlets, and outflow conditions for outlets, zero normal gradients for all flow variables except pressure). The equations were discretized using finite-volume method. Commercial numerical software FLUENT 2020 R1 (ANSYS, INC.) and COMSOL Multiphysics 5.4 were used for the numerical simulation. The physical property (density and viscosity) of acetonitrile (786 kg/m^3, 0.0089 kg/m/s) and water (998.2 kg/m^3, 0.001 kg/m/s) at 25 °C as a carrier solvent were used for fluid property. The fluid property of the mixture of acetonitrile and water was estimated using a simple mixing rule based on the acetonitrile volume fraction adopted in the following paragraph. That is, the density and the viscosity of the mixture fluid are calculated in each point depending on the volume fraction of acetonitrile.

1.2 General Procedure for alkaline hydrolysis of CWA simulant under flow condition:



Scheme S1. Continuous-flow procedure for the degradation of paraoxon using single capillary

Continuous-flow reactor system was comprised of a coiled PTFE capillary and two separate feeds. **1** contained 0.473 M solution of the paraoxon (2.925 g, 11.84 mmol) dissolved in CH_3CN: H_2O (15.81 ml : 7.07 ml) to make 25 ml solution and **2** was a 1.42 M aqueous solution of NaOH. Two feeds were pumped at 65.449 µl·min^{-1} respectively (residence time: 90 sec). **1** and **2** were mixed by using a PEEK T-mixer (0.5 mm i.d.) prior to entering PTFE capillary reactor 1 (**R1**, 0.1963 ml internal volume, 1 mm i.d.) that was submerged within a heating oil bath maintained at 75 °C. Fig. S1 shows the UV-vis spectra for calibration of *p*-nitrophenol in buffer pH 8 for degradation reaction. The crude product was collected at steady state, diluted with phosphate buffer pH = 8 and analyzed for yield using UV-Vis (**Fig. S2**). In order to verify any instrumental or human error caused during analysis, the breakdown of paraoxon was also monitored using ^{1}H-NMR (**Fig. S3**). The reactor mixture was collected, neutralized with 1M HCl solution to pH = 7, extracted with ethyl acetate and solvent was evaporated under vacuum and analyzed for conversion using ^{1}H-NMR (**Fig. S3b**). The yield of paraoxon was double checked by both UV-Vis and ^{1}H-NMR henceforth confirming the complete degradation occurred at 90 s of residence time. **Fig. S2a** and **S2b** are the data obtained by collecting 8 µl of the reaction mixture, and in **Fig. S2c** and **S2d**, 5 µl of the reaction mixture was collected and diluted with 30 ml phosphate buffer (pH = 8).

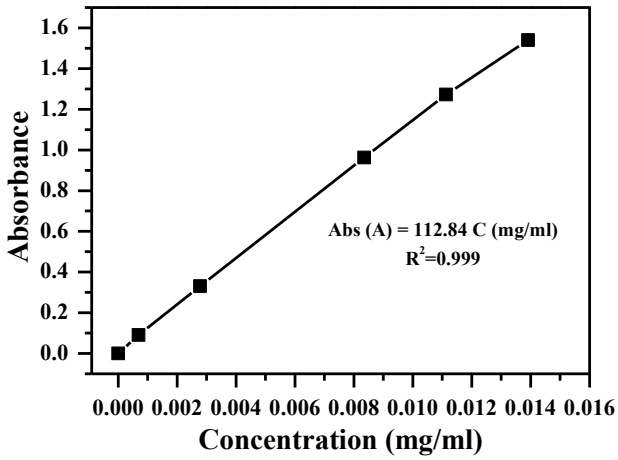


Fig. S1 UV-Vis spectra for calibration curve of *p*-nitrophonol (NP) in buffer pH 8

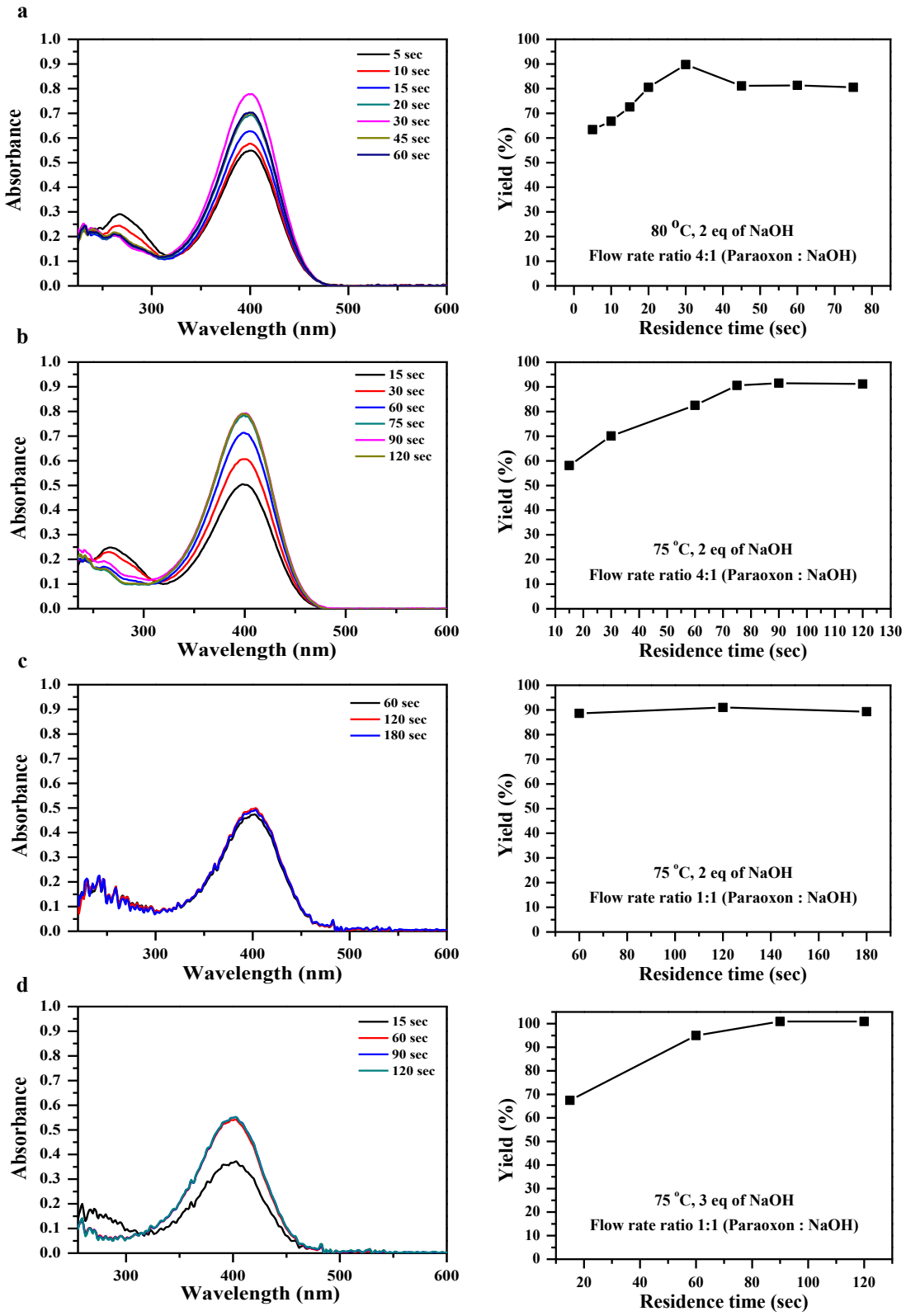


Fig. S2 UV-Vis spectra for degradation of paraoxon at various conditions

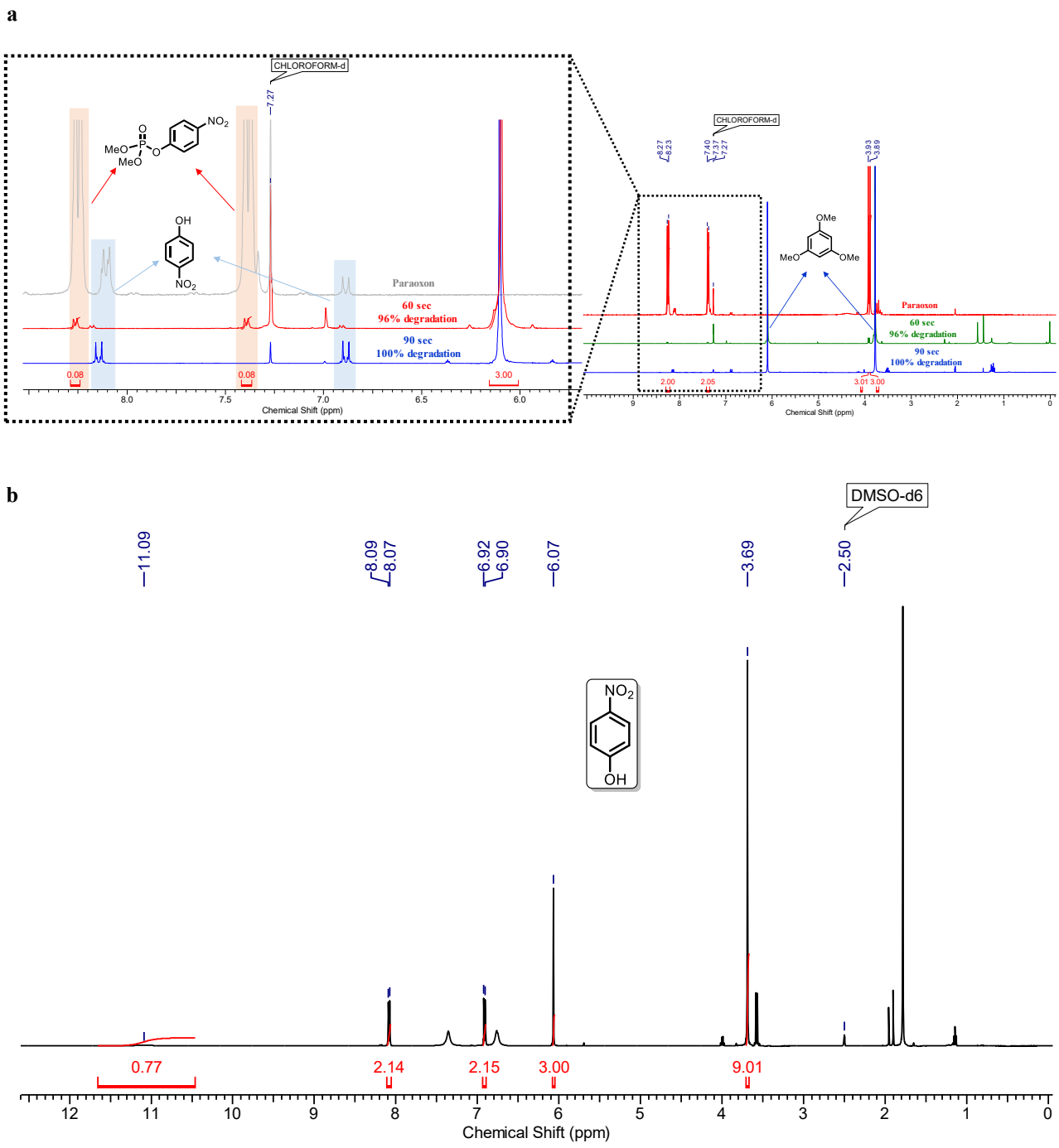


Fig. S3 (a) Crude ^{1}H NMR spectra showing conversion for degradation of paraoxon w.r.t to residence time and **(b)** crude ^{1}H NMR yield using 1,3,5-trimethoxy benzene as an internal standard for 90 s of residence time in DMSO-d6

1.3 General Procedure for alkaline hydrolysis of CWA simulant under Batch condition:

To compare how the degradation reaction rate of paraoxon could be accelerated at microreactor, we proceeded further experiment using flask. Paraoxon (37 µL, 0.2023 mmoles, 1 equivalent) was dissolved in CH_3CN:H_2O (0.25 mL : 0.11 mL) to make total volume of 0.4 mL, followed by addition of 1N NaOH (0.6 mL, 3 equivalents) and the resulting solution was stirred in a vial. The effect of temperature (25 ºC ~ 80 ºC) and the retention time parameters were studied by sampling the crude reaction mixture after regular interval of time. After degradation reaction, the crude mixture was diluted with phosphate buffer pH = 8 and was further analyzed for yield using UV-Vis (**Fig. S4**). Thus, confirming in batch the complete degradation occurred at 80 ºC for a reaction time of 10 min.

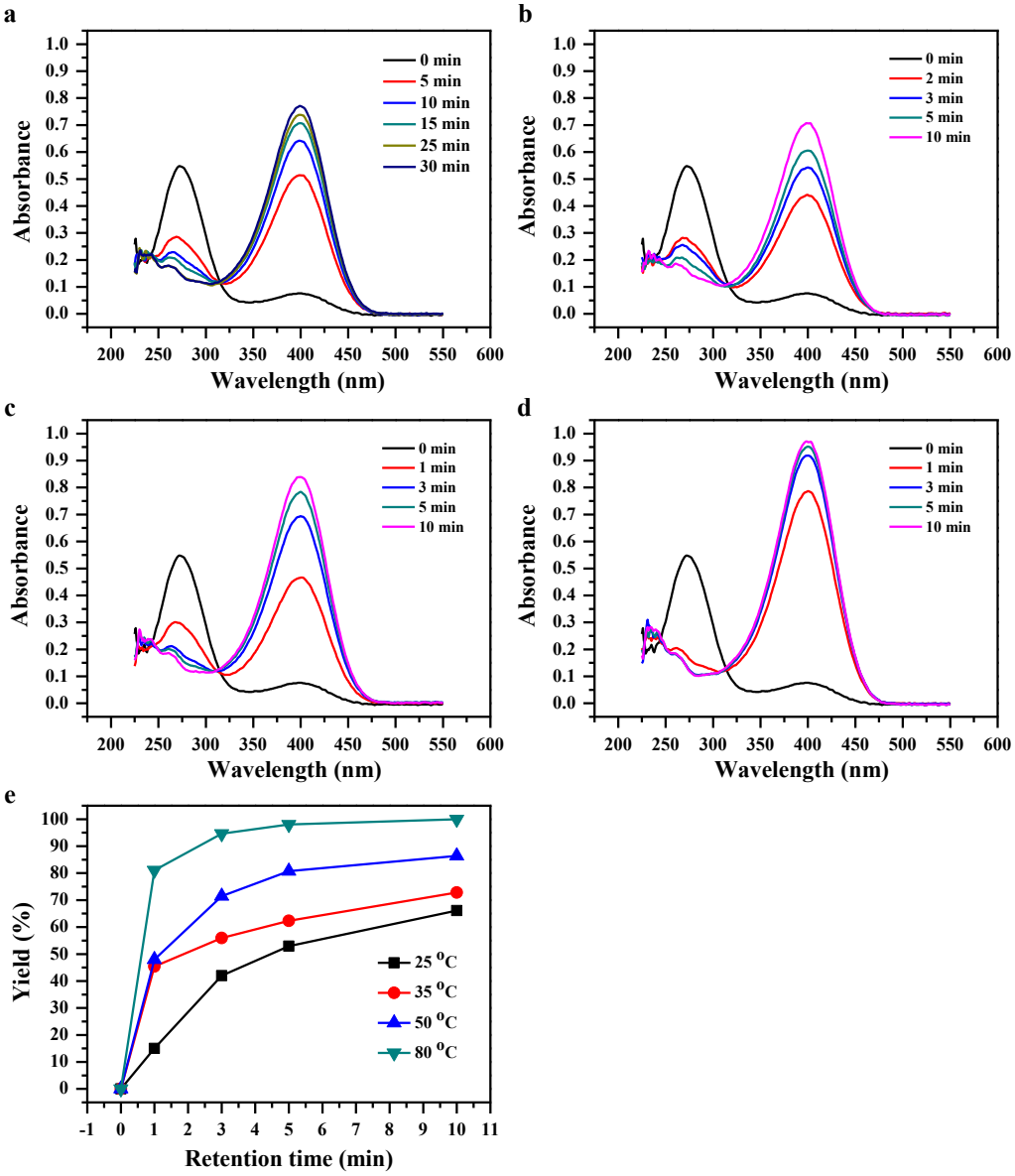


Fig. S4 Degradation of paraoxon at batch reactor under different temperature. (**a**) 25 ºC, (**b**) 35 ºC, (**c**) 50 ºC, (**d**) 80 ºC and (**e**) yield tendency of paraoxon degradation

1.4 Fabrication of TPM for kilogram scale degradation of paraoxon and multi-step synthesis of paracetamol:

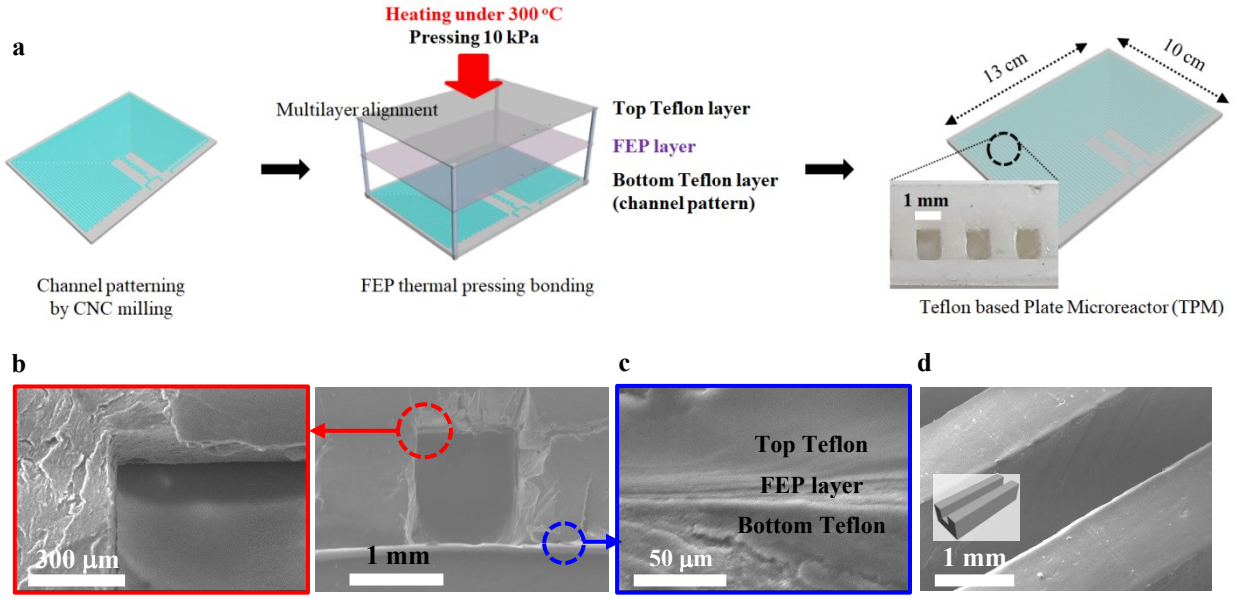


Fig. S5 (a) Scheme for fabrication of Teflon based plate microreactor (TPM) by one-step thermal bonding process of stacked patterned Teflon plates and FEP adhesive layer at 300 °C. SEM images of cross section for (**b)** TPM channel, (**c)** interface between Teflon and FEP layers after the thermal compression bonding and (**d)** Teflon channel patterned by CNC milling.

A Teflon based Plate microreactor was designed and fabricated to allow a high throughput production and operate toxic chemical reaction by selection of material with excellent chemical resistance and strong bonding process. We patterned the Teflon plate (thickness: 2 mm) by CNC milling and the adhesion between the patterned Teflon plates was proceeded by a fluoroethylene propylene film (thickness: 50 µm) as a kind of fluoropolymer. The FEP film with a softening point at 260 ~ 280 °C was laser ablated to make holes for alignment and inlets of reagents. To stack the patterned Teflon plates and FEP adhesive film, 4 corners of each layer holed with 1.5 mm diameter were passed through metal pins (diameter: 1.5 mm, length: 6 cm). The exactly aligned Teflon plates were placed between flat metal plates and were thermal bonded at 300 °C under 10 kPa for 7 h (heating rate: 1.5 °C·min^{-1}). Under these conditions, the softened FEP film between the Teflon plates improved the reliability of the hermetic seal at 300 °C by modulating the pressure (10 kPa) applied at the interface and tended to seal the patterned channel with no leak by slow cooling for 20 h. After fabrication process, the cross-sectional morphology of TPM channel was observed by SEM to confirm that the shape of the Teflon-based channel was not deformed during the thermal compress bonding step as seen in **Fig. S5a** and **S5d**. In addition, the sandwiched FEP film was strongly adhered between two Teflon plates without delamination and the bonding durability was maintained even at chemically corrosive conditions under pressure. Deformation of the channel occurred in the process of obtaining the TPM channel cross section through mechanical cutting.

1.5 Numbering-up TPM platform setup for scale-up degradation of paraoxon:

Three sets of TPM modules, designated as TPM 1, TPM 2 & TPM 3, was assembled in series by using PTFE tubing and a flangeless fitting. All TPM modules has identical microchannel design (width 1 mm, height 1 mm) but somewhat different volume for TPM 1 of 3.5 ml, TPM 2 and 3 of 4.25 ml due to different mixing channel length at each inlet. Two HPLC pumps (SP-930D, Younglin, Korea) were used to inject the solution of 0.473 M paraoxon (58.5 g, 236.71 mmol) dissolved in 500 ml CH_3CN : H_2O (316.2 ml : 141.5 ml) and 1.42 M aqueous solution of NaOH (500 ml, 28.4 g, 710 mmol) (**Fig. S8**). The individual flow rates of each HPLC pump was set at 4 $ml \cdot min^{-1}$, thus resulting in a 90 s residence time. Every TPM is set as 75 ^oC for complete degradation of paraoxon. In order to set a heating module and a frame fixture for interfacing with tight tubing connection, two aluminum metal plates (14 × 14 cm) was drilled to make holes for inlets, outlet at the corner and alternative cylindrical hole at center of plate side for inserting a cartridge type of rod heater (diameter: 1 cm, Rs 340, S.M. Enterprise). Heating module consist of a k-type thermocouple (SCASS-125G-6, Omega Engineering Korea) for sensing the heat by connecting to NX2 Proportional-Integral-Differential (PID) based temperature controller (Hanyoung NUX) to feedback the output signal depend on the current temperature of the TPM. The output value was converted to the high voltage current entering the heater by a thyristor power regulator (WYU-DG 25 SI, Woonyoung Co., Ltd). Counter pressure generated from the evaporation of acetonitrile was balanced using 40 psi back pressure regulator (BPR) for better reproducibility of results over a long run. After reaching steady state, a product was collected from the outlet of the TPM 3. To confirm complete degradation of paraoxon, the small product sample was extracted by diethyl ether (5 ml x 3) and was analyzed using ^{1}H-NMR (**Fig. S10)**.

1.6 Stability test of Teflon based Plate Microreactor:

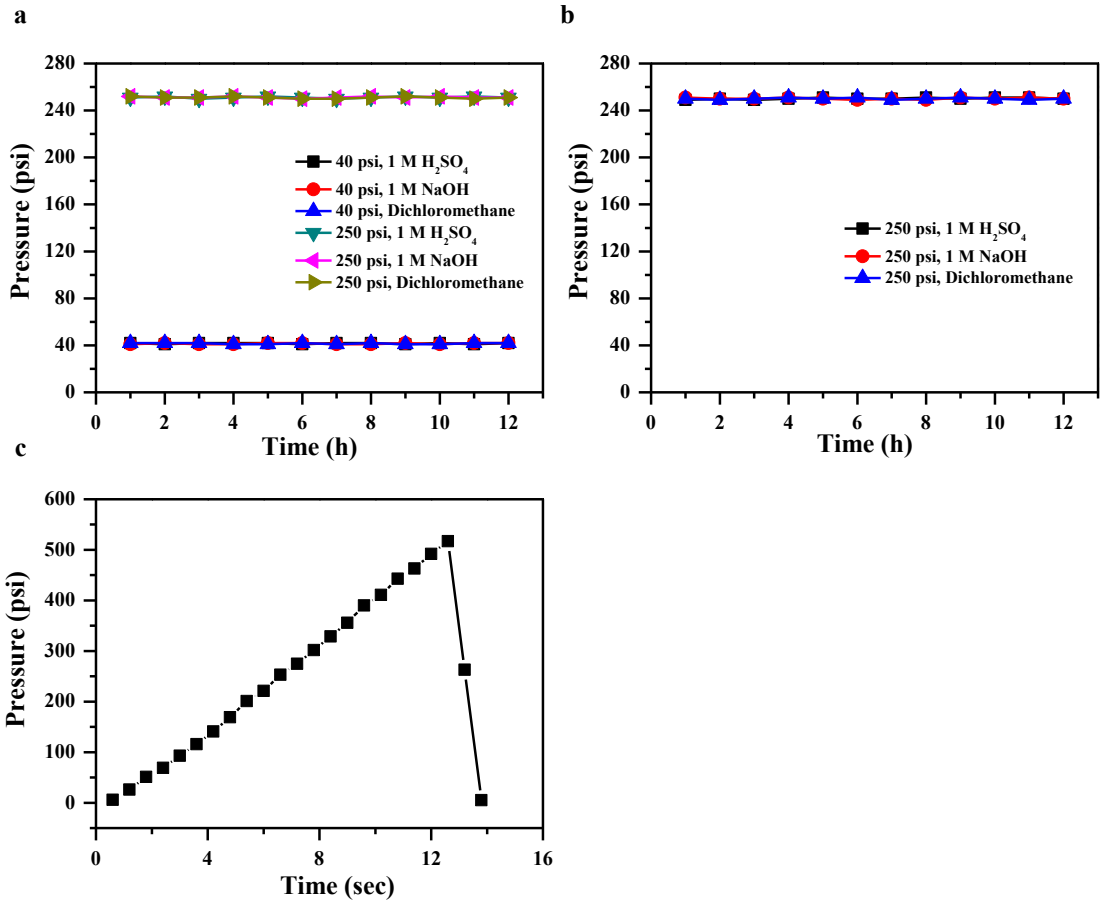


Fig. S6 Chemical stability test of TPM in various harsh conditions: strong acid, base and chlorinated solvent under high pressure (**a)** 25 °C, (**b)** 100 °C and (**c)** mechanical stability test by checking the maximum withstanding pressure of TPM.

To confirm the stability of TPM, we prepared 400 ml of 1 M H_2SO_4 acid, 1 M NaOH base and dichloromethane which are candidates to be able to corrode the reactor. Test solvents were injected at a flow rate of 0.55 ml·min^{-1} to the TPM (width: 1mm, height: 1mm, volume 4.25 ml) with applying pressure to the entire reactor using a back pressure regulator of 40 psi and 250 psi at different temperature (25 °C and 100 °C). When the reactor is damaged by the toxicity of the solvent it will induce a leakage, therefore the pressure will drop. By checking each cases of pressure inside of reactor for 12 h using HPLC pump which can read the pressure at inlet of device, we confirmed that TPM can be operated with no defect even exposed in toxic substances under high pressure for long time. After chemical resistance test, the maximum pressure tolerance of the TPM was experimentally verified by closing the outlet and injecting water into the inlet at a flow rate of 1 ml·min^{-1}. The pressure inside of TPM was gradually increased and eventually the burst pressure was approximately 3.56 MPa (517 psi).

1.7 Computational fluid dynamic simulation of TPM 1, 2 and 3:

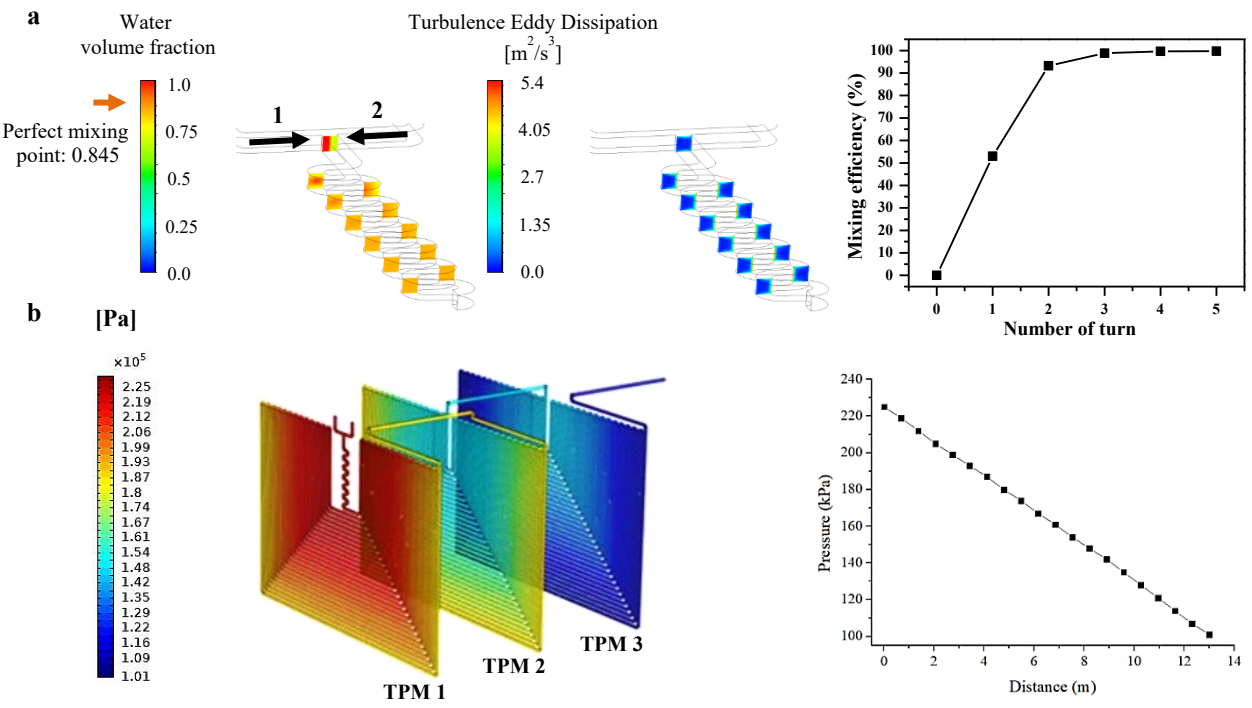


Fig. S7 Computational fluid dynamics (CFD) simulation of serpentine micromixers near inlet of TPM 1. (**a)** Calculated mixing efficiency by volume fraction contour of acetonitrile depend on channel cross section A, B, C and D in TPM 1. (**b)** Visualization on pressure drop induced along flow path (total length: 12 m) of three-parallelized TPM platform.

To decompose paraoxon in large quantities, we connected each TPM reactors in series. Here, we checked how well the reactants were mixed and what value the pressure drop occurred according to channel distance through computational fluid dynamic simulation. In order to quantify the degree of mixing of two different fluids depending on the channel geometry, the volume fraction of water was considered along the flow. The mixing degree of three fluids was quantified by the mixing efficiency[2, 3].

$$\eta = 1 - \sigma/\sigma_{max}$$

where

$$\sigma = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(C_i - C_{in})^2}$$

σ is the standard deviation of concentration at cross-section, **N** is the number of nodes at the channel cross-section, c_{in} is the local concentration at a sample node of channel cross-section **i**, $\boldsymbol{c_{in}}$is the average concentration at the inlet, and $\boldsymbol{\sigma_{max}}$ is the maximum standard deviation of concentration. It can be assumed that high mixing efficiency is attained when the volume fraction of water reach nearly 0.845. To sufficiently dissolve paraoxon, we mixed acetonitrile and water with volume fraction of 0.31. Base on the calculated turbulence eddy dissipation, the fluid flow forms a vortex at the same time as the fluid is pulled to the left or right as it passes through the serpentine-shaped microchannel. As a result, the complete mixing of two reagents was achieved by taking only 75 ms at total flow rate 8 ml·min^{-1} on flowing 10 mm serpentine-shaped channel from the mixing start zone. When reactants are injected into the reactors connected in series at a high flow rate, there may be a problem in the stability of the process due to the pressure at inlets. Therefore the pressure drop was also analyzed through CFD. When the liquids flowed at 8 ml·min^{-1} to the reactors, a total pressure drop of 124 kPa (18 psi) occurred, however it was sufficiently controlled through a high pressure HPLC pump.

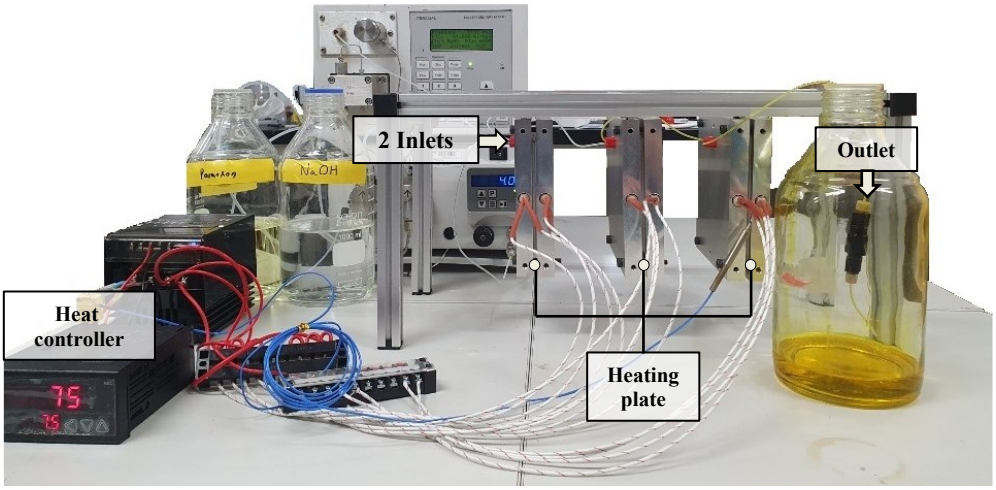


Fig. S8 Scale-up degradation of Paraoxon in a numbering-up system of "Teflon based Plate Microreactor" (TPM1 to 3) platform

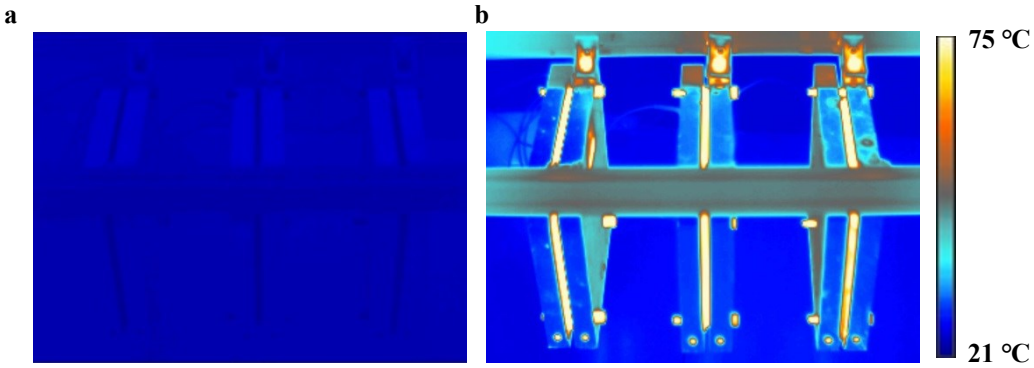


Fig. S9 Temperature profile of three-parallelized TPM set-up integrated with heating module, taken by IR imaging. (**a)** Thermal image at 21 °C and (**b)** 75 °C, heated TPM between two metal plates.

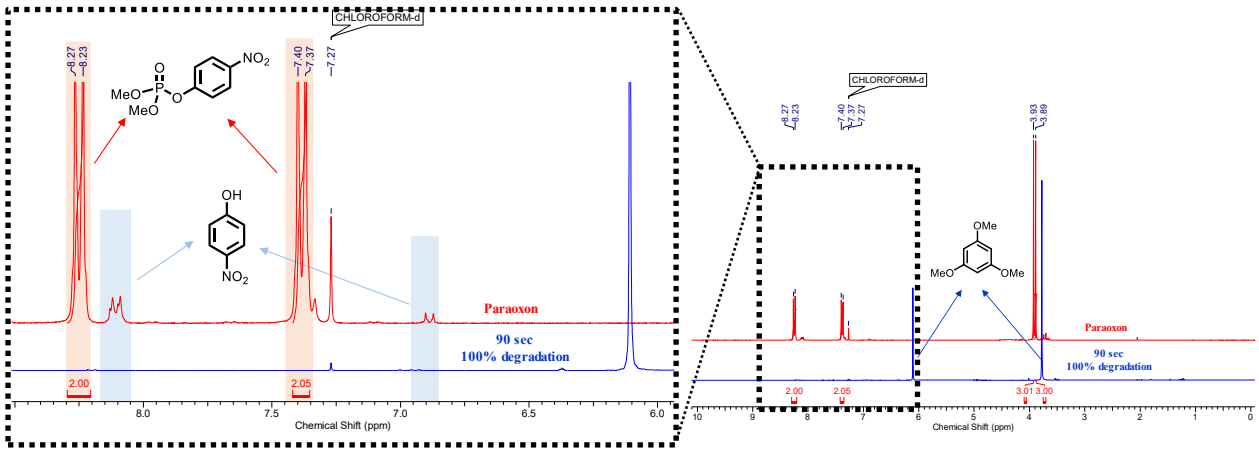
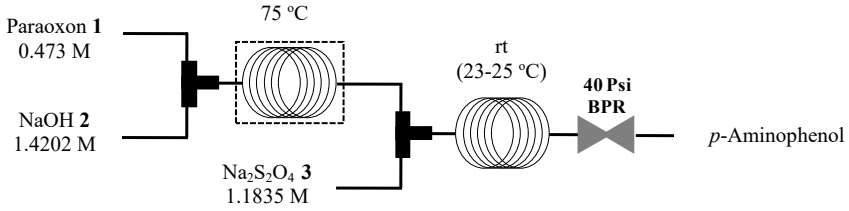


Fig. S10 Crude ^{1}H NMR spectra in $CDCl_3$ showing conversion for degradation of paraoxon using TPM platform

1.8 General procedure for reduction of *p*-nitrophenol byproduct generated from degradation of paraoxon under flow condition:

The continuous-flow system (**Scheme S2**) comprised of 3 separate feeds. After mixing **1** and **2**, the crude reaction mixture coming from **R1** at a total flowrate of 130.898 µl·min^{-1} was further mixed with **3** consisting of 1.1835 M aqueous solution of $Na_2S_2O_4$, through a PEEK T-mixer (0.5 mm i.d.) before entering **R2** (0.3927 ml internal volume, 1 mm i.d.) which was maintained at room temperature. In order to get complete reduced product, 40 psi BPR was connected at the outlet so as to counterbalance the pressure generated due to evaporation of acetonitrile from **R1**. After the steady state, reactor mixture was collected, diluted with phosphate buffer pH = 8 and analyzed for yield and conversion using UV-Vis (**Fig. S11a**). Similarly, reactor mixture was collected, diluted with sat. $NaHCO_3$ solution and extracted with ethyl acetate and solvent was evaporated under vacuum and analyzed for conversion using ^{1}H-NMR (**Fig. S11c**). The 3% error in yield by UV-Vis (**Table S1**) and ^{1}H NMR (**Fig. S11c**) can be accounted due to instrumental or human handling error. An amount of 5 µl of the reaction solution was sampled and was diluted with 30 ml buffer (pH 8.0) and the yields were determined based on the absorbance at 400 nm was determined using UV spectrophotometry (**Fig. S11b**).



Scheme S2. Continuous-flow two-step process for degradation of paraoxon, reduction of *p*-nitrophenol in a capillary

	% Yield of *p*-NP by $Na_2S_2O_4$				
t_R (sec)	1 eq (0.236 M)	2 eq (0.473 M)	3 eq (0.710 M)	4 eq (0.947 M)	5 eq (1.185 M)
60	13.9	53.8	77.1	94.1	95.7
90	14.0	62.5	79.8	95.4	97.6
120	14.2	74.7	90.3	96.5	97.8

Table S1. Optimization on reduction yields of *p*-NP at different equivalents of $Na_2S_2O_4$

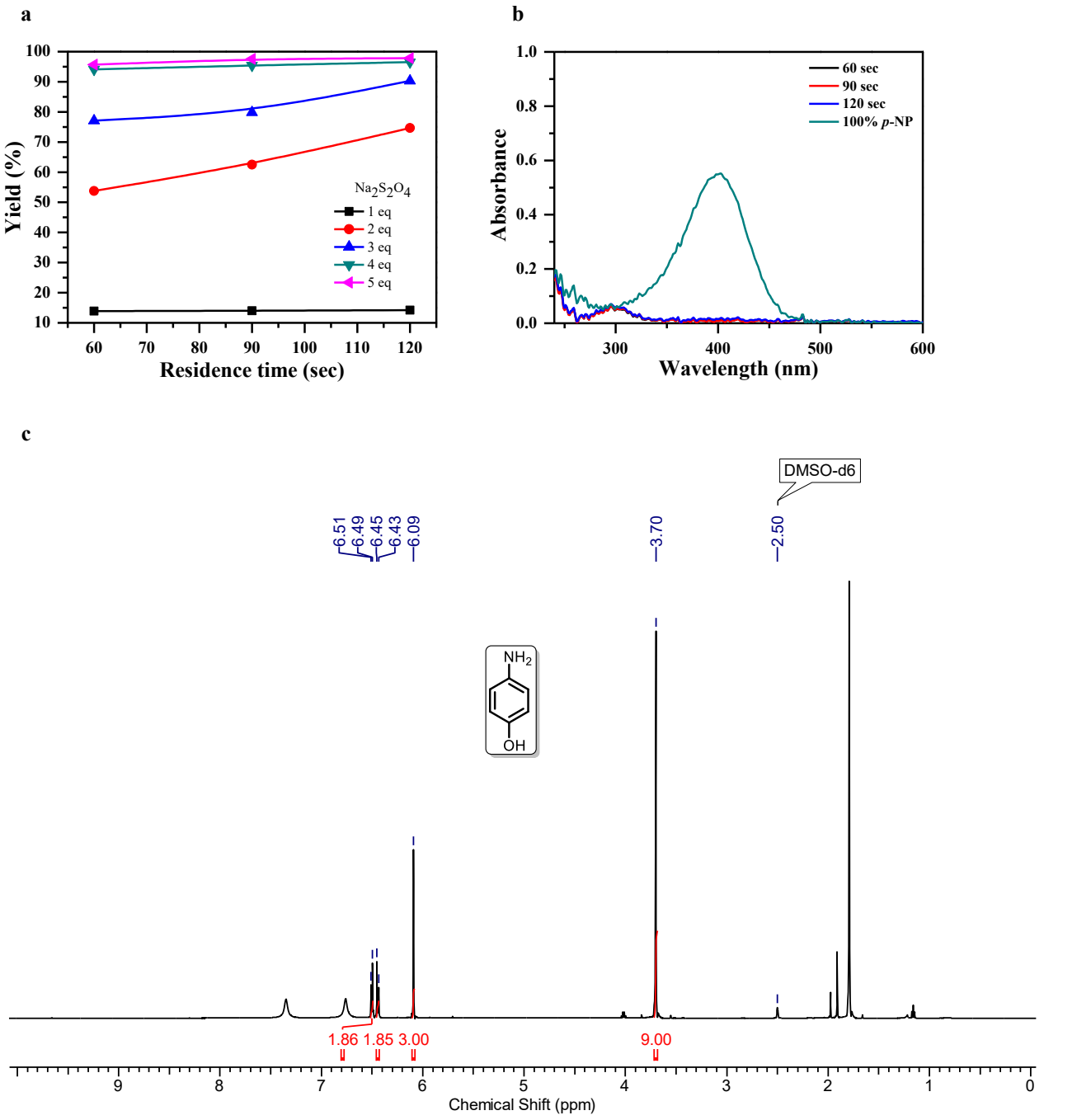
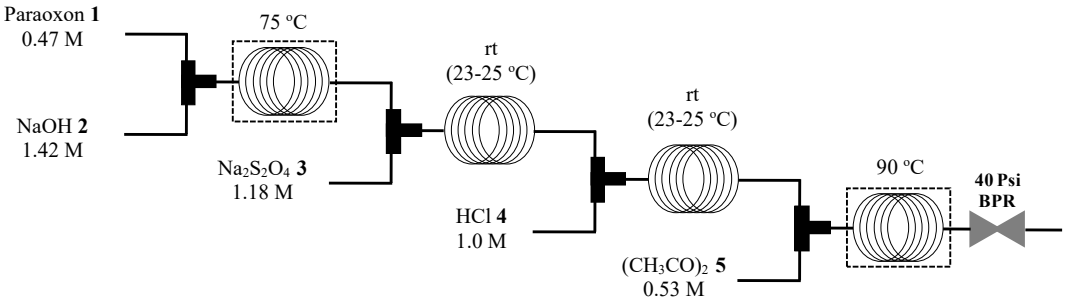


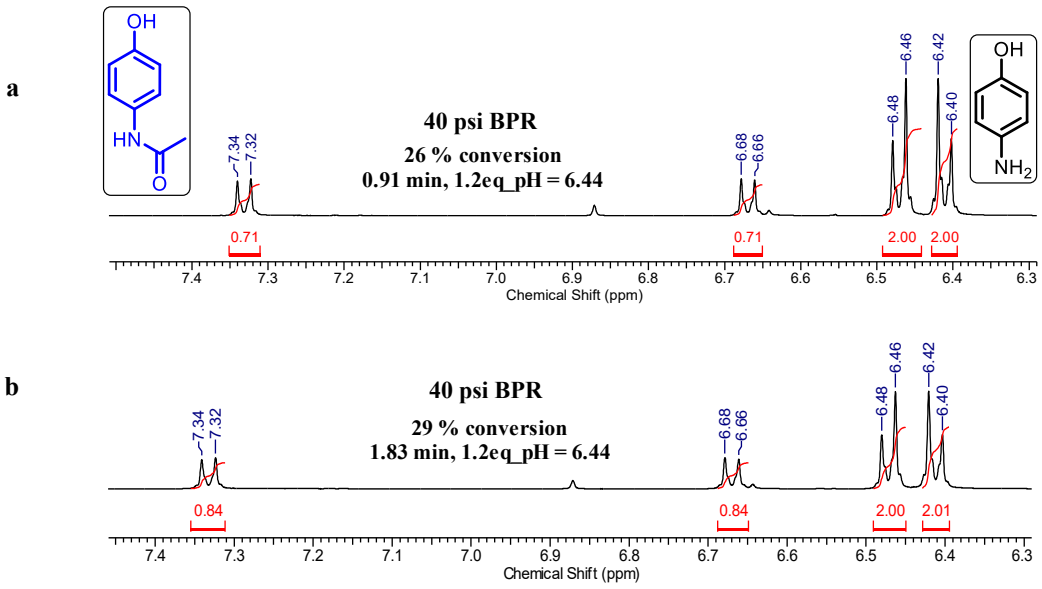
Fig. S11 (a), (b) UV-Vis spectra of samples obtained at 2nd reduction step at different conditions. **(c)** 1H-NMR spectra to determine the yield of p-aminophenol using 1,3,5-trimethoxy benzene as an internal standard at 90 s of residence time in DMSO-d6.

1.9 General procedure for synthesis of paracetamol under flow condition:

The continuous-flow system (**Scheme S3**) comprised of 5 separate feeds. The crude reaction mixture coming after degradation and reduction from **R1** and **R2** at a total flow rate of 261.8 µl·min^{-1} was further mixed with **4** consisting of 1.0 M aqueous solution of HCl, at a flow rate of 87.26 µl·min^{-1}. After attaining proper pH, the reaction mixture was mixed with **5** consisting of 0.53 M solution of acetic anhydride in CH_3CN, using a PEEK T-mixer (0.5 mm i.d.) before entering **R3** (3.48 ml internal volume, 1 mm i.d.) which was submerged in water bath maintained at 90 °C. The outlet was connected to 40 psi BPR, so as to increase the vapor pressure of acetonitrile and stabilize the system for uniform flow (**Fig. S13**). After the steady state, reactor mixture was collected, diluted with sat. $NaHCO_3$ solution and extracted and solvent was evaporated under vacuum with ethyl acetate and analyzed for conversion using ^{1}H-NMR (**Fig. S12**). The crude ^{1}H NMR yield was calculated using 1,3,5-trimethoyxy benzene as an internal standard (**Fig. S14**). The final compound on purification using column chromatograhpy (100–200 mesh silica gel, gradient elution: 50% to 100% EtOAc in hexanes) afforded paracetamol as an off-white solid in 81% yield. ^{1}H NMR (500MHz, DMSO-d6) δ = 9.66 (s, 1 H), 9.16 (s, 1 H), 7.35 (d, J = 8.8 Hz, 2 H), 6.69 (d, J = 8.7 Hz, 2 H), 1.99 (s, 3 H); ^{13}C NMR (75MHz, DMSO-d6) δ = 167.6, 153.2, 131.1, 120.9, 115.1, 23.8.



Scheme S3. One-flow process of three-step degradation, reduction and paracetamol synthesis in a capillary



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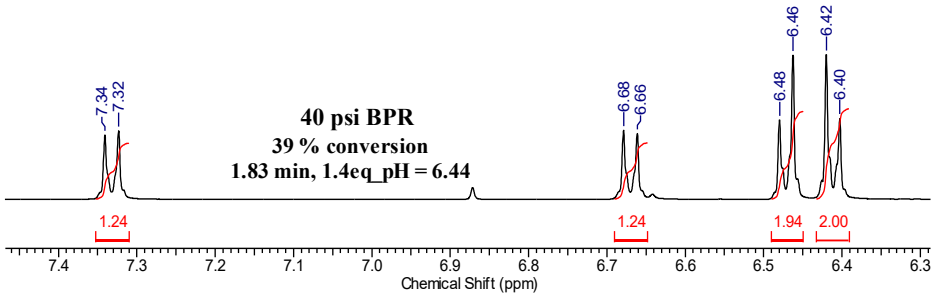
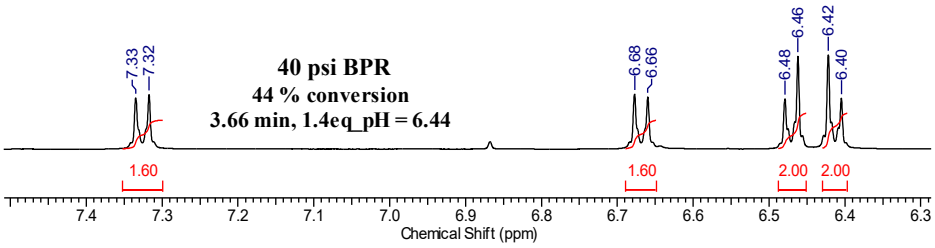
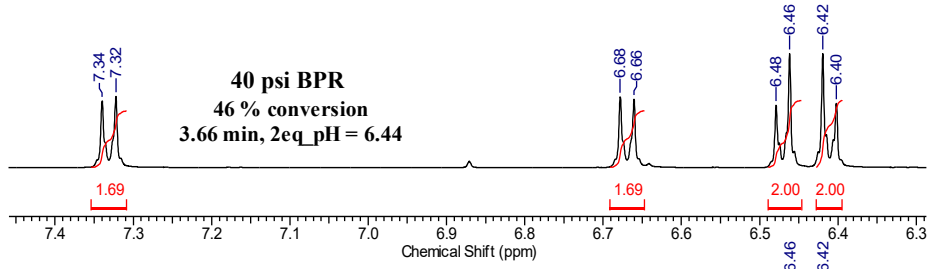

7.34
7.32
6.68
6.66
6.46
6.42
6.48
6.40
40 psi BPR
39 % conversion
1.83 min, 1.4eq_pH = 6.44
1.24
1.24
1.94
2.00
Chemical Shift (ppm)

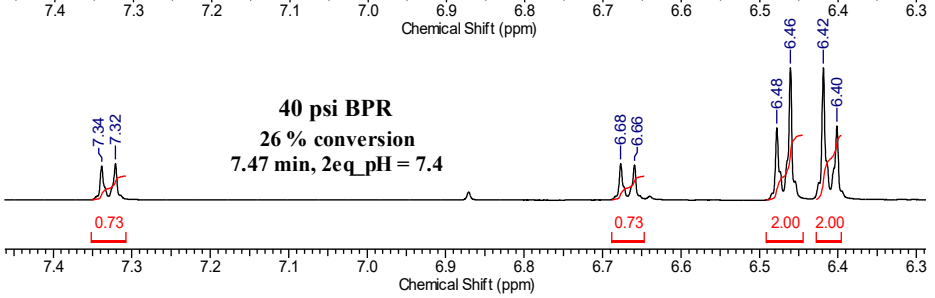
d


7.33
7.32
6.68
6.66
6.46
6.42
6.48
6.40
40 psi BPR
44 % conversion
3.66 min, 1.4eq_pH = 6.44
1.60
1.60
2.00
2.00
Chemical Shift (ppm)

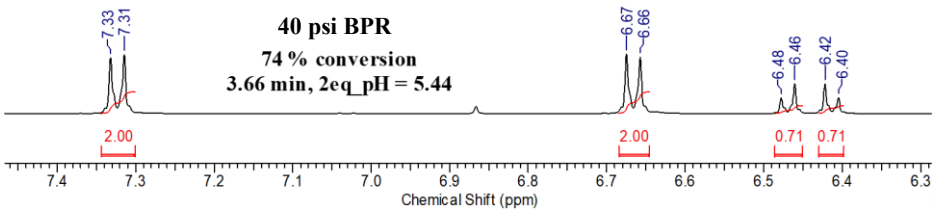
e


7.34
7.32
6.68
6.66
6.46
6.42
6.48
6.40
40 psi BPR
46 % conversion
3.66 min, 2eq_pH = 6.44
1.69
1.69
2.00
2.00
Chemical Shift (ppm)

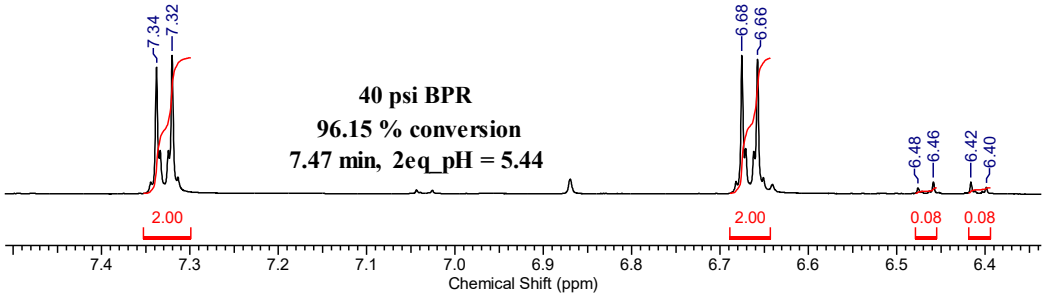
f


7.34
7.32
6.68
6.66
6.46
6.42
6.48
6.40
40 psi BPR
26 % conversion
7.47 min, 2eq_pH = 7.4
0.73
0.73
2.00
2.00
Chemical Shift (ppm)

g


7.33
7.31
6.67
6.66
6.48
6.46
6.42
6.40
40 psi BPR
74 % conversion
3.66 min, 2eq_pH = 5.44
2.00
2.00
0.71
0.71
Chemical Shift (ppm)

h


7.34
7.32
6.68
6.66
6.48
6.46
6.42
6.40
40 psi BPR
96.15 % conversion
7.47 min, 2eq_pH = 5.44
2.00
2.00
0.08
0.08
Chemical Shift (ppm)

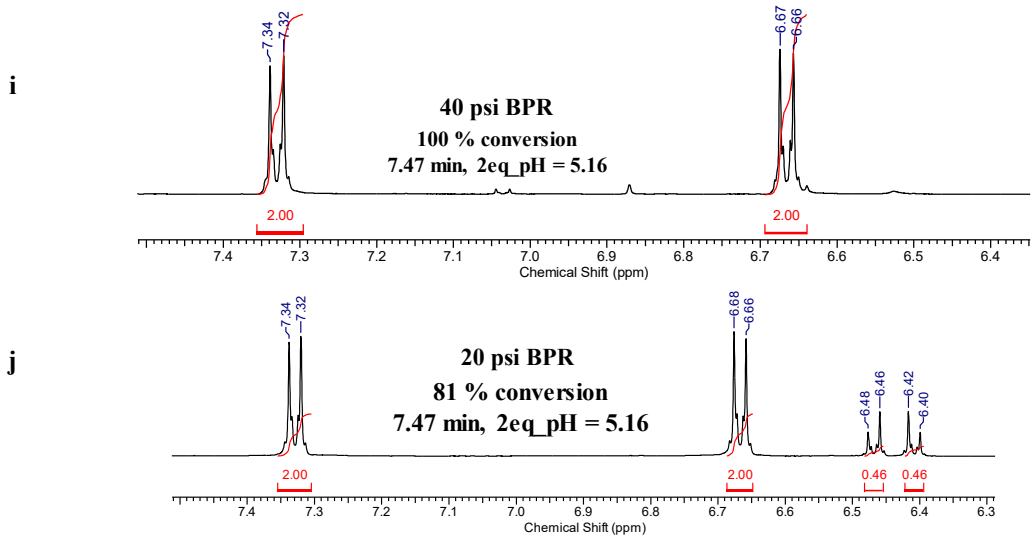
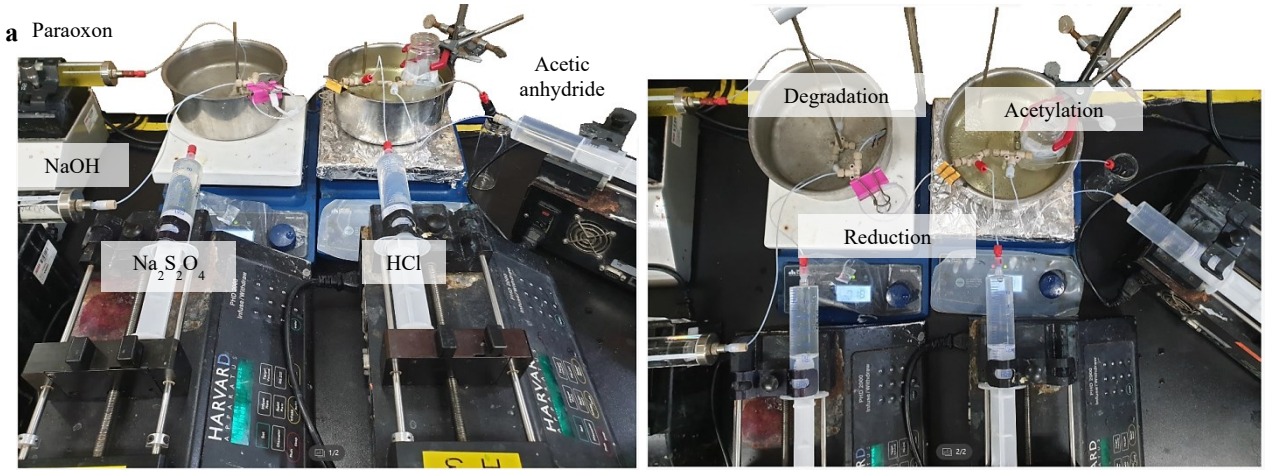


Fig. S12 ^{1}H NMR spectra for effect of pH, stoichiometry and pressure on paracetamol synthesis step



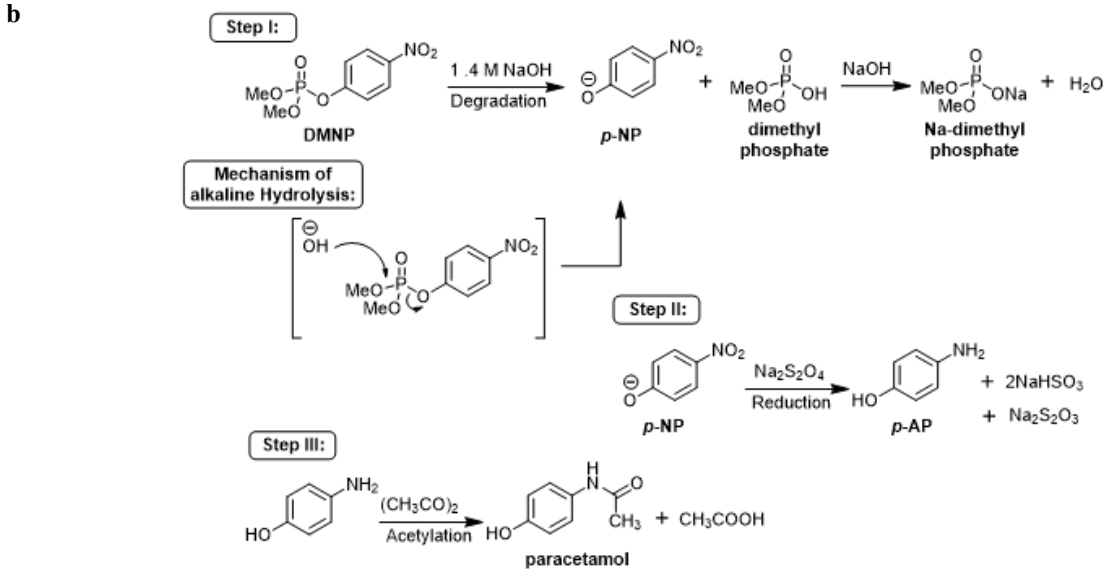


Fig. S13 (a) Experimental setup for one-flow three-step degradation, reduction and paracetamol synthesis in a capillary. (**b)** Mechanism for degradation of paraoxon along with product and byproducts formed in overall three step reaction process

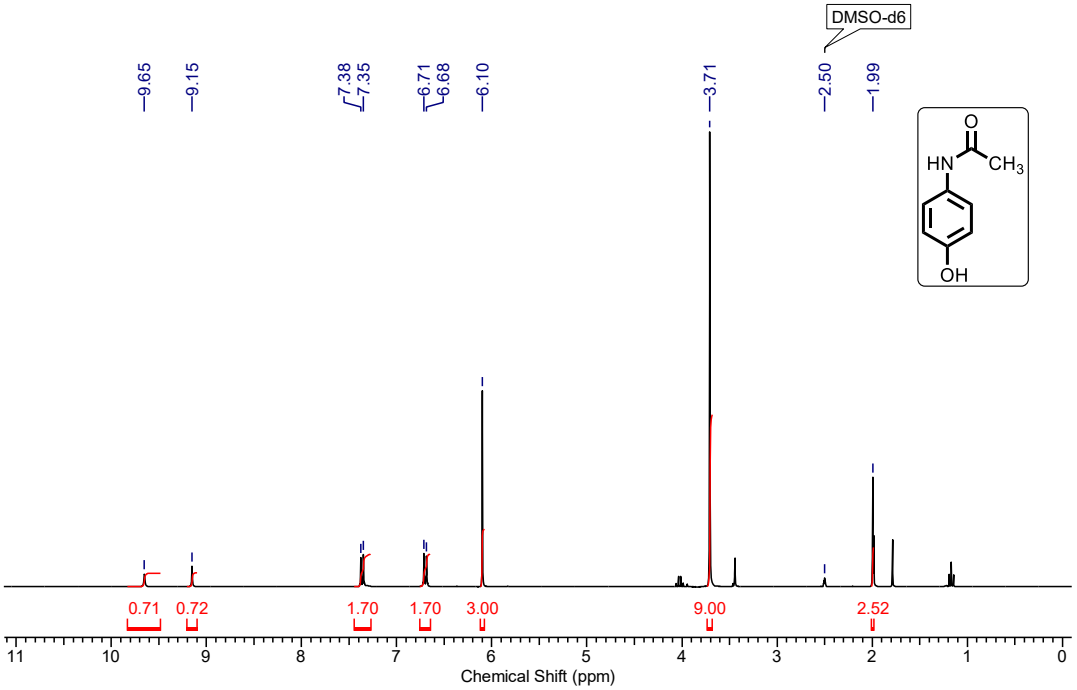


Fig. S14 Crude ^{1}H-NMR yield to determine the yield of Paracetamol using 1,3,5-trimethoxy benzene as an internal standard at 7.5 min of residence time in DMSO-d6.

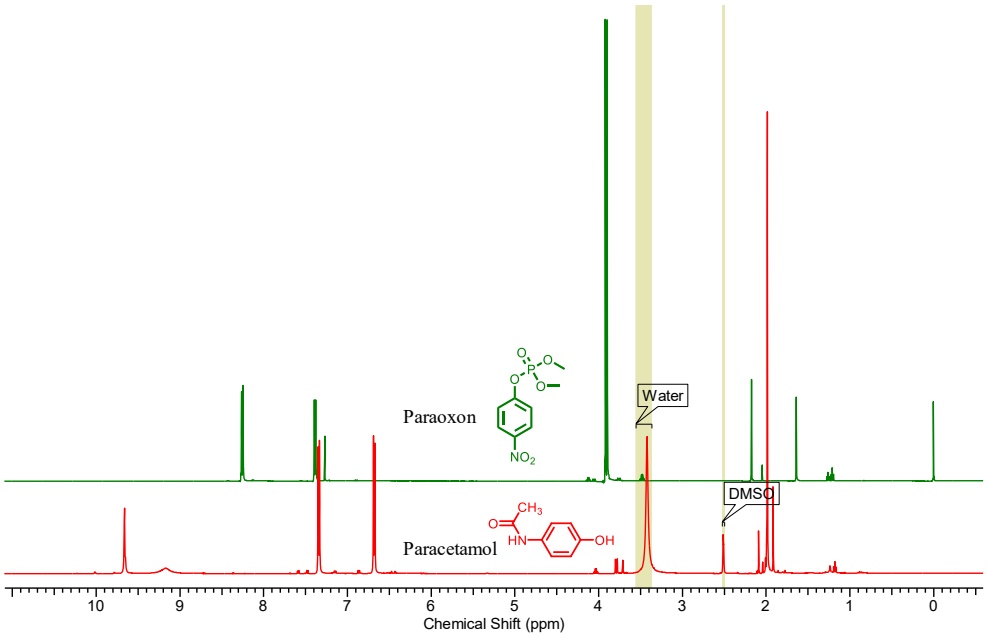


Fig. S15 Comparison of crude ^{1}H-NMR of Paraoxon and Paracetamol, showing impurity profile of paracetamol after multi-step reaction

1.10 Simulation analysis on the mixing efficiency of various introductory channel designs of TPM 4 and 5:

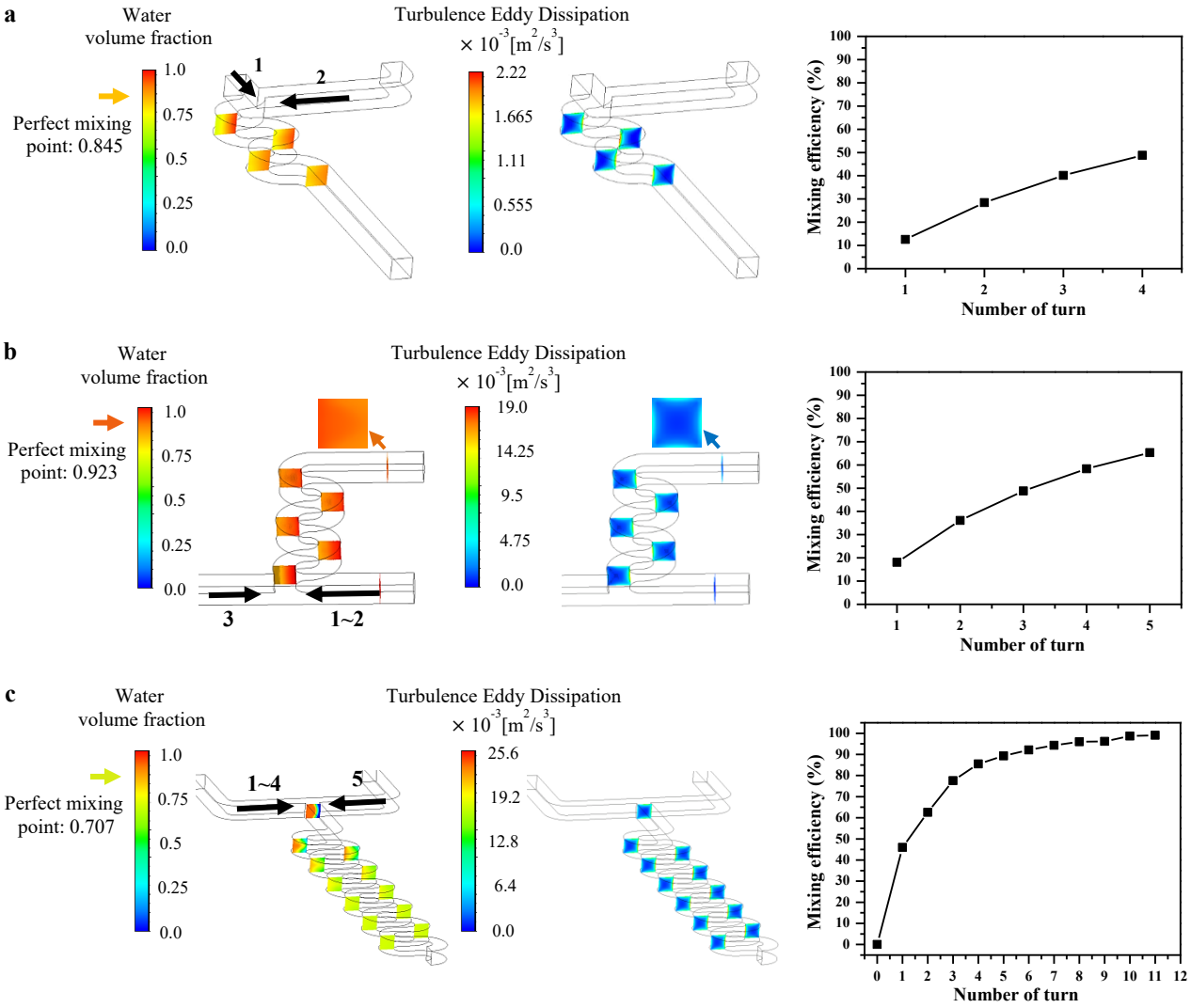


Fig. S16 Computational fluid dynamics (CFD) simulation of serpentine micromixers of TPM 4 and 5. **C**alculated mixing efficiency by volume fraction contour of water depend on channel cross in **(a)** first mixer, **(b)** second mixer in TPM 4 and **(c)** one mixer in TPM 5.

(i) **Mixer 1 in TPM 4A:** In case of multistep reaction for synthesizing paracetamol, **1** and **2** are injected into the TP M 4A at the same flow rate (0.06545 ml/min). **1** is dissolved in H_2O/ACN mixture (69:31 vol %) and **2** is dissol ved in H_2O. From the point where the two reactants collide, the total flow rate is 0.131 ml/min, where the densit y of the mixture is 936.3 kg/m^3 and the viscosity is 0.3502 mPa·s at 75 ºC. Therefore, the calculated Renolyds n umber is 5.84 and the De number is 4.129.

(ii) **Mixer 2 in TPM 4B:** After degradation step at TPM 4A, the crude mixture (**1~2**) flow along the channel with fl ow rate of 0.131 ml/min and start to mix with **3** which has flow rate of 0.131 ml/min for the reduction step. From the point where the two mixture collide, the total flow rate is 0.262 ml/min, where the density of the mixture is 951.23 kg/m^3 and the viscosity is 0.3646 mPa·s. Therefore, the calculated Renolyds number is 11.4 and the De number is 8.06

As a result of recalculating the two static mixers built into the TPM 4 through simulation, the mixing efficiency remained at 48~65% due to the low fluidized bed flow phenomenon. However, this result is likely to be a very similar phenomenon as when we carried out the reaction using a capillary reactor because Re is same (When capillary reactor and TPM 4~5 are used, all flow rate, hydraulic diameter, temperature and pressure conditions are same). For that reason, if the total residence time is the same, the reaction yield was measured the same.

(iii) **Mixer 3 in TPM 5:** After degradation & reduction step at TPM 4, the crude mixture (**1**~**3**) flow along the capillary tube outlet with flow rate of 0.262 ml/min and mix with **4** solution which flow rate is 0.08726 ml/min at T-junction. Flow rate of overall crude mixture (**1**~**4**) before injecting TPM 5 is 0.349 ml/min. Total liquid mixture (**1**~**5**) flows in the TPM 5 at a total flow rate of 0.465 ml/min, where the density of the mixture is 891.989 kg/m^3 and the viscosity is 2658 mPa·s at 95 ^{o}C. Therefore, the calculated Renolyds number is 26.0 and the De number is 18.38. When the mixing efficiency by the static mixer built into the TPM 5 was calculated, it was confirmed that the fluid was completely mixed when it passed a total of 10 serpentine-shape microchannel.

1.11 One-flow recycling of paraoxon degradation for synthesis of paracetamol in a TPM platform:

Two sets of TPM modules, designated as TPM 4 & TPM 5, were integrated by assembling with flow connection for three-step recycling process for the conversion of organic byproducts generated from paraoxon to a value-added-chemical, paracetamol. All TPM modules has identical microchannel design (width 1 mm, height 1 mm) but somewhat different volume for TPM4-A of 0.2 ml and TPM4-B of 0.4 ml in one chip and TPM 5 of 3.5 ml. All connections were made using PTFE tubing, PEEK T-mixer and a flangeless fitting. Four syringe pumps were used to inject **1** to **5** (**Fig. S18a**). The individual flow rates of each pump was set corresponding to the optimized residence time by referring to the pre-optimized reaction condition. The temperature of TPM 4 and 5 was maintained at 75 °C and 90 °C respectively, using two heating modules. Counter pressure generated from the evaporation of acetonitrile was balanced using 40 psi back pressure regulator (BPR) for better reproducibility of results over a long run. After the steady state, reactor mixture was collected, diluted with sat. $NaHCO_3$ solution and extracted with ethyl acetate and analyzed for yield and conversion using ^{1}H-NMR in presence of 1,3,5-trimethoyxy benzene as an internal standard (**Fig. S18b**).

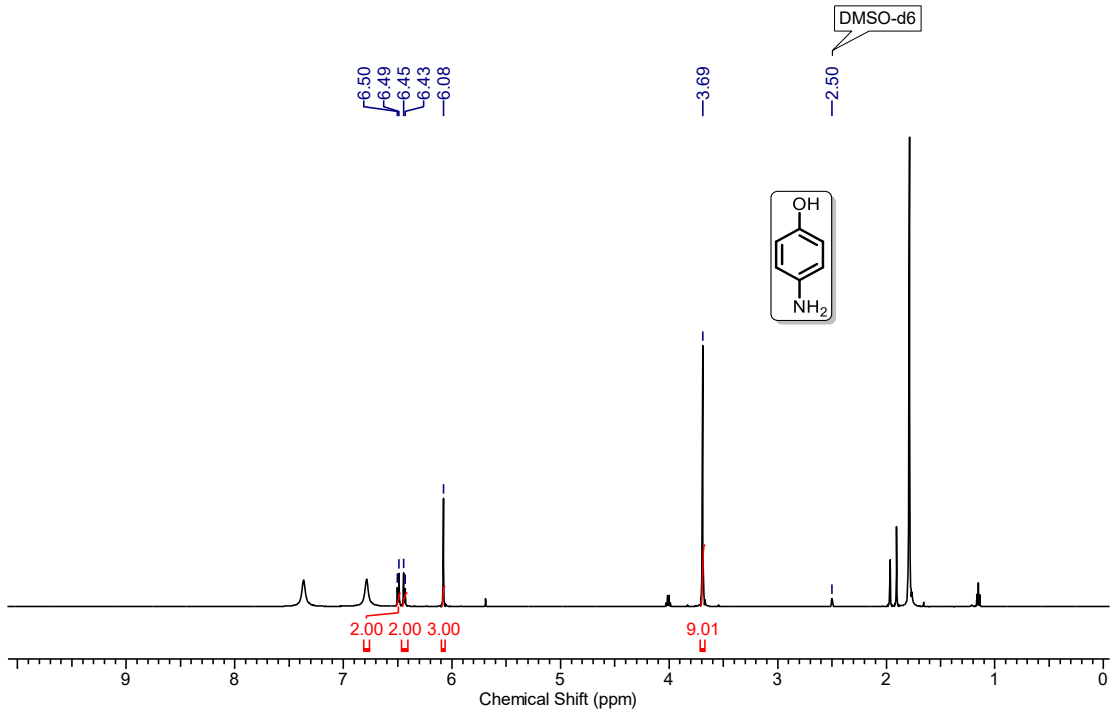
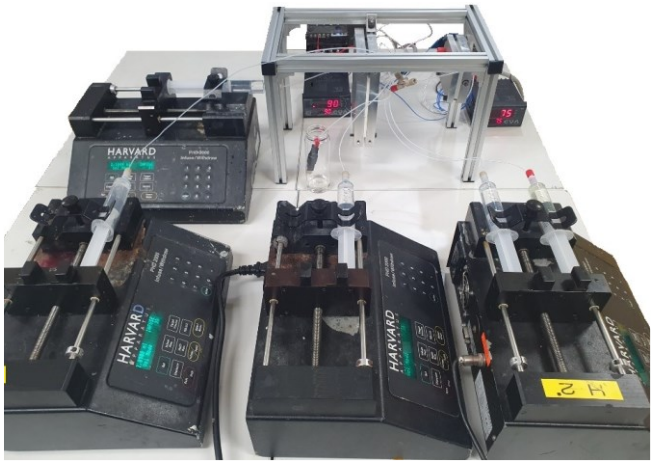


Fig. S17 Crude ^{1}H NMR to determine the yield of reduction reaction at 75 °C using TPM 4 using 1,3,5-trimethoxy benzene as an internal standard at 90 s of residence time in DMSO-d6

a



b

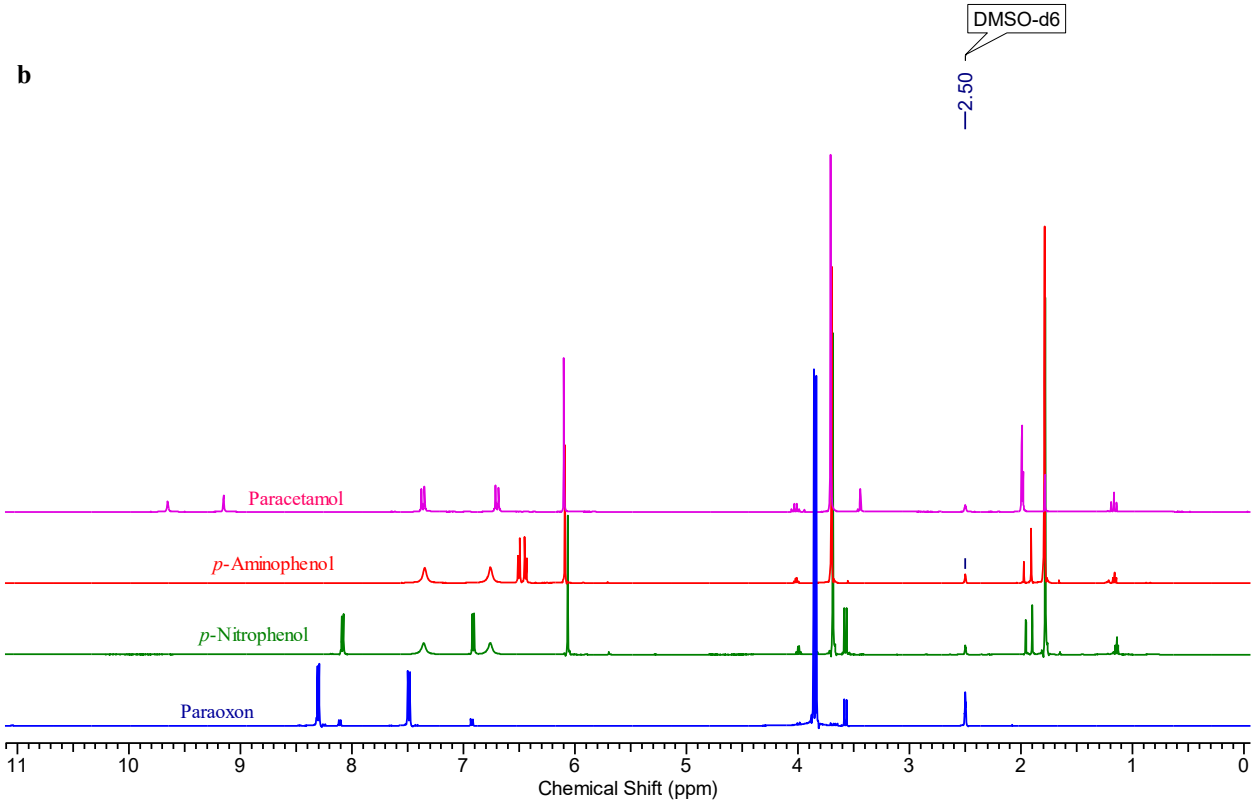


Fig. S18 (**a**) Experimental setup of two-parallelized TPM platform for one-flow three-step degradation, reduction and paracetamol synthesis. (**b**) Stacked crude ^{1}H-NMR spectra in DMSO-d6 of crude reaction mixture from TPM 4 and TPM 5

2. References

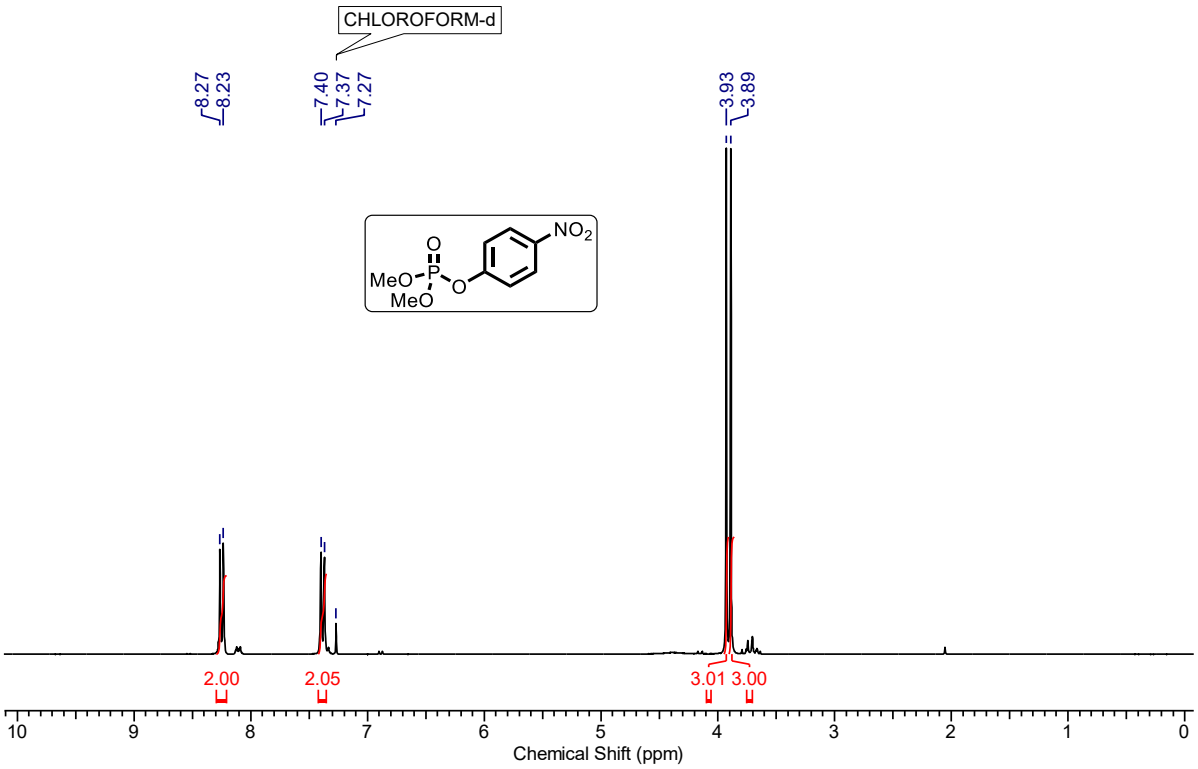
1 D. You, F. Ham and P. Moin. *Phs. Fluids,* **2008***,* 20, 101515.

2 H. Kim, K.-I. Min, K. Inoue, D. J. Im, D.-P. Kim and J.-I. Yoshida. *Science,* **2016***,* 352 (6286), 691– 694.

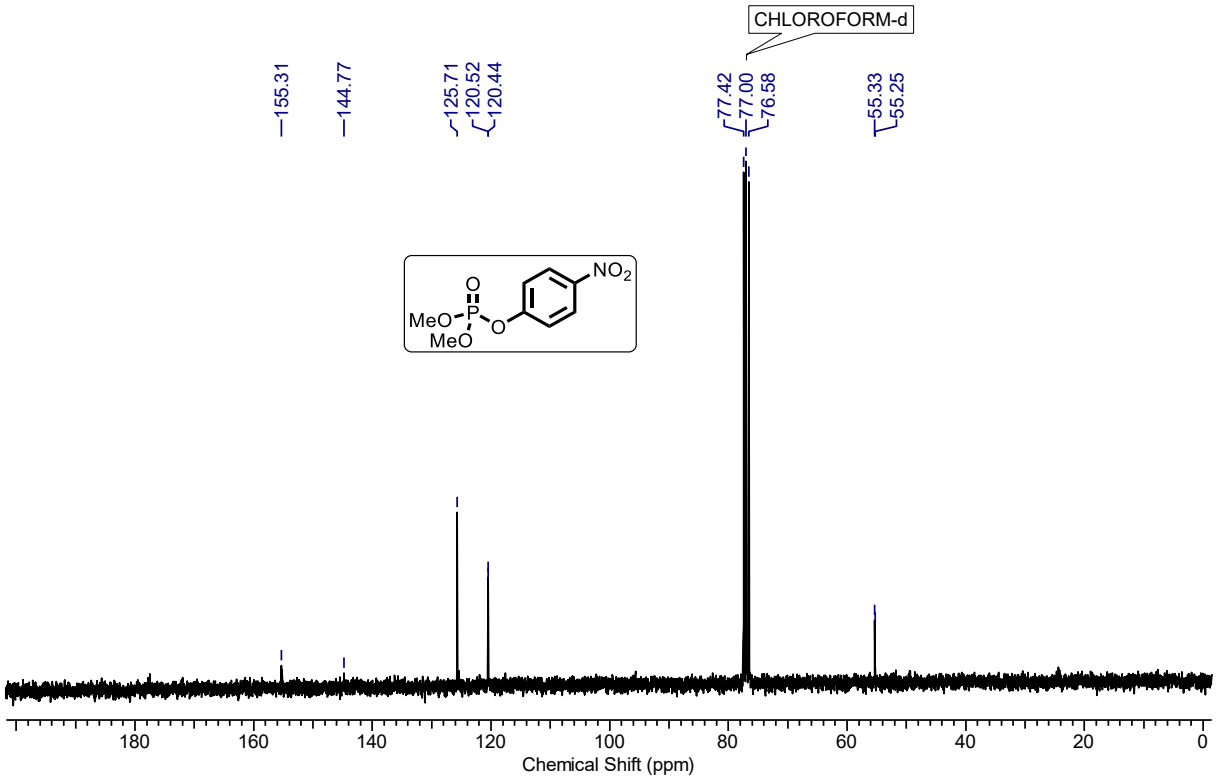
3 V. Viktorov, M. R. Mahmud and C. Visconte. *Eng. Appl. Comput. Fluid Mech.* **2016***,* 10 (1), 183–193.

3. ^{1}H and ^{13}C NMR copies

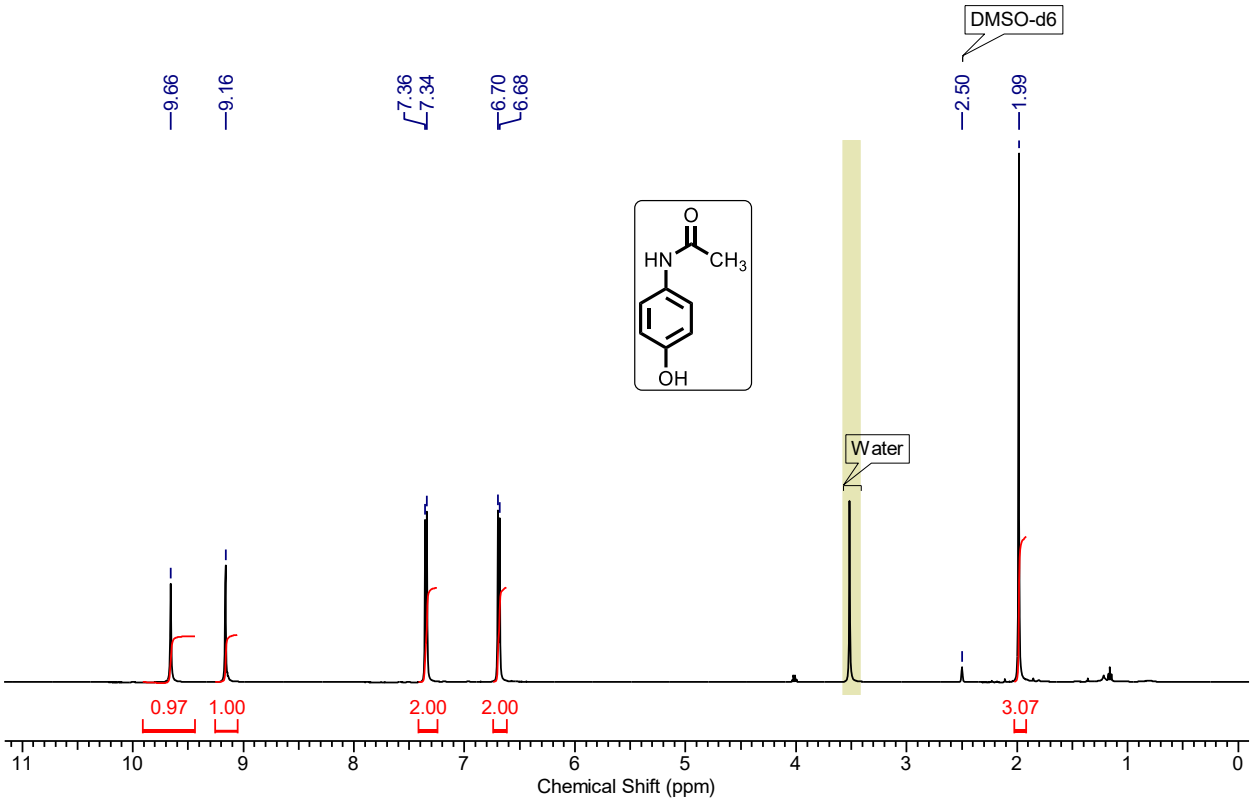
Paraoxon ^{1}H-NMR in $CDCl_3$



Paraoxon ^{13}C-NMR in $CDCl_3$



Paracetamol ^{1}H-NMR in DMSO-d6



Paracetamol ^{13}C-NMR in DMSO-d6