Supporting Information for

Continuous Flow Aerobic Alcohol Oxidation Using a Heterogeneous Ru(OH)$_x$/Al$_2$O$_3$ Catalyst

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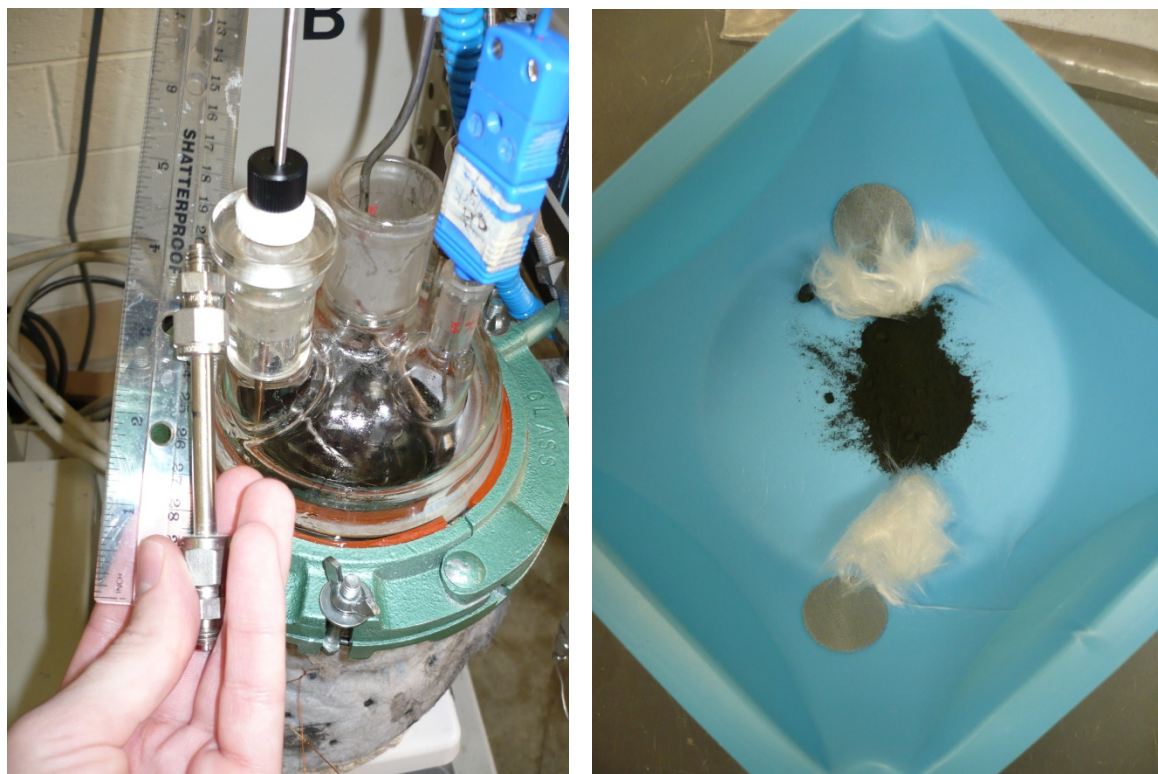[b]Department of Chemistry, University of Wisconsin-Madison, Madison Wisconsin, 53706

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Figures of Packed Bed Reactor (PBR)

**Figure S1:** Left: picture of assembled packed bed reactor next to the heating bath.

Right: Ordering and appearance of materials packed inside the reactor tube.

Physical Parameters of PBRs

Table S1: Physical parameters for the PBRs used in this study.

| Reactor	A	B
Mass $Ru(OH)_x/Al_2O_3$	1.25 g	20.8 g
Mass Ru	29 mg	480 mg
PBR O.D.	¼"	½"
PBR Length	6"	12"
PBR Volume	2.5 mL	28.6 mL
Volume % Solid	20	21
Volume % Liquid	> 75	> 74
Volume % Gas	< 5	< 5
Peripheral Tubing Volume	3.3 mL	13 mL

Liquid and Gas + Liquid RTD curves for the large and the small reactor. RTD curves generated for the other reactor as well as the fit using the nCSTR model are presented in Figures S2-S4.
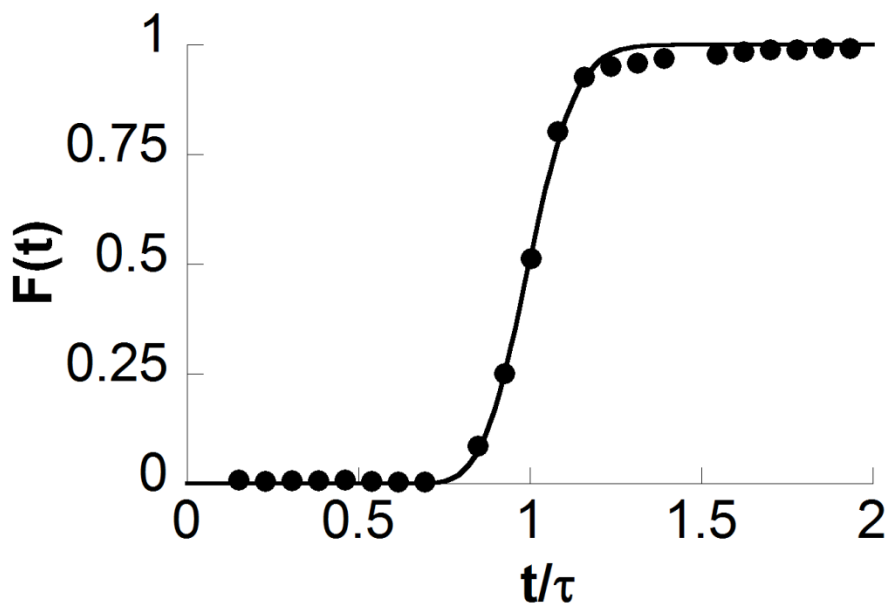
Figure S2: RTD of liquid flow through PBR A. 1.25 g $Ru(OH)_x/Al_2O_3$, 0.5 mL/min liquid flow of 0.002 to 0.004 M phenanthrene in toluene. nCSTR model fit with n = 85 and τ = 8.6 min.
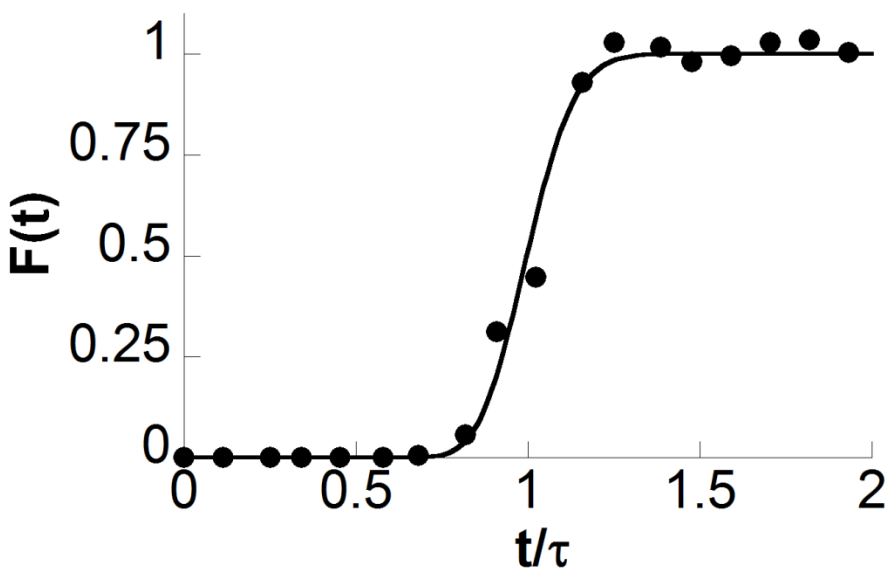
Figure S3: Liquid RTD with gas and liquid flow through PBR A. 1.25 g Ru(OH)$_x$/Al$_2$O$_3$, 0.05 mL/min liquid flow of 0.01 M tetradecane to 0.01 M tetradecane and 0.01 M phenanthrene in toluene and 4 sccm gas flow (8 % O$_2$ in N$_2$) at 11 bar and 80 °C. nCSTR model fit with n = 83 and τ = 44 min.
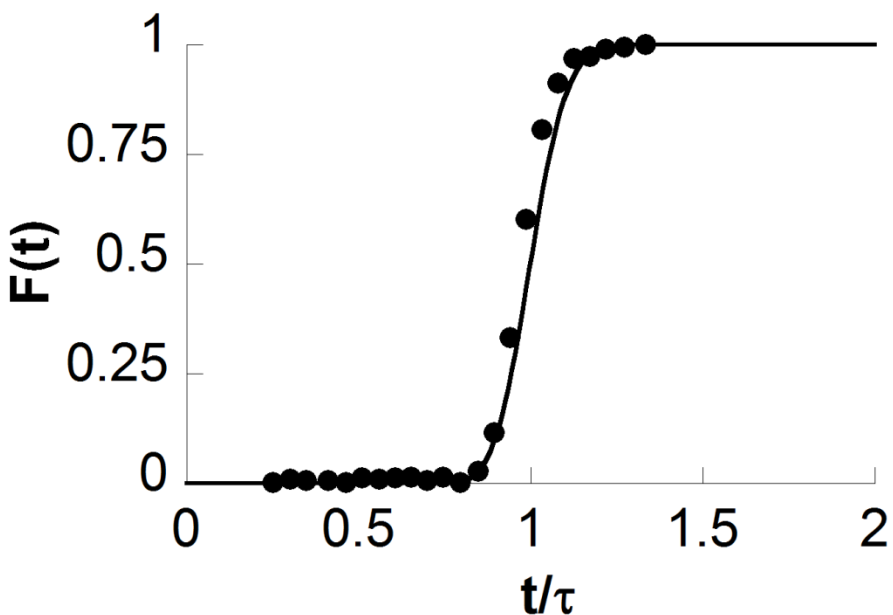
Figure S4. RTD of liquid flow through PBR B. 20.8 g $Ru(OH)_x/Al_2O_3$, 2 mL/min liquid flow of

0.002 to 0.004 M phenanthrene in toluene. nCSTR model fit with $n = 144$ and $\tau = 18$ min.


Results of ICP-AES Analysis

Table S2: Ru content of catalysts and solutions from 12 g reaction with 2-thiophene methanol.

| $Ru(OH)_x/Al_2O_3$ Catalyst	Wt. % Ru
Newly Prepared	2.3 ± 0.1
Post-Reaction	2.4 ± 0.1
Indirect post-reaction Ru loss	$< 10^{-5}$ over 80 h operation
[Ru] in reactor effluent	3 ppb

Batch time courses
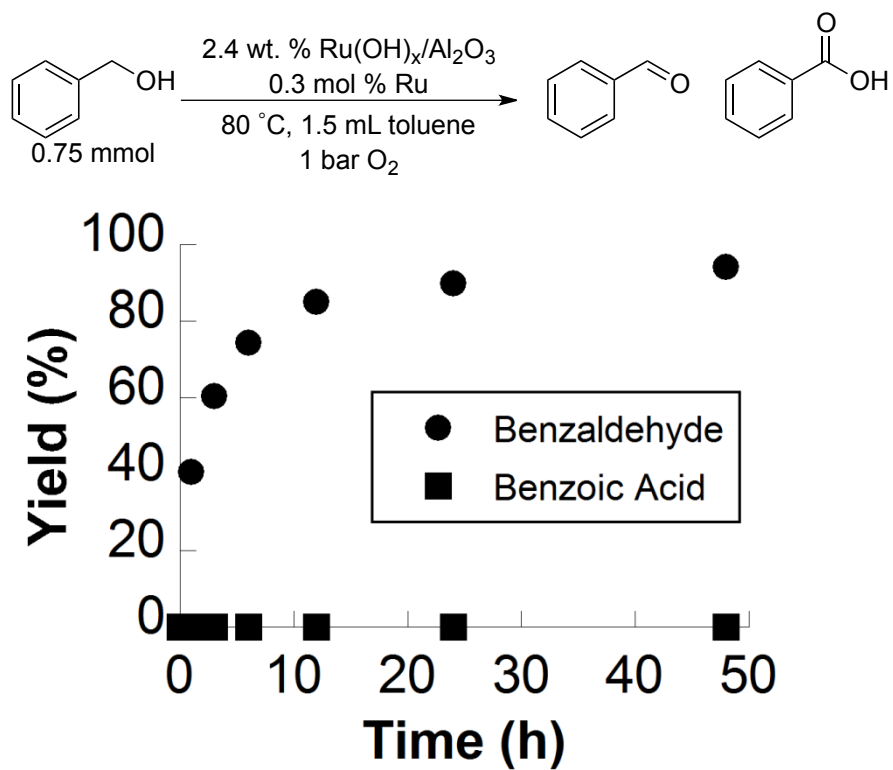
Figure S5. Yield vs. time of benzaldehyde and benzoic acid from reaction of benzyl alcohol with 0.3 mol % Ru.
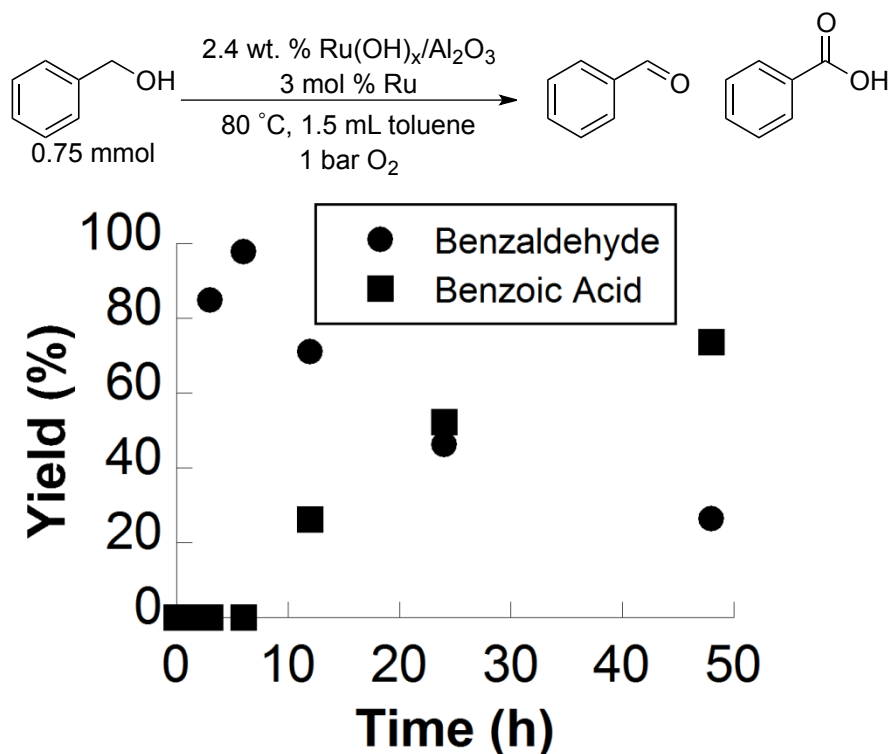
Figure S6. Yield vs. time of benzaldehyde and benzoic acid from reaction of benzyl alcohol with 3 mol % Ru.

Efforts to achieve on-stream catalyst regeneration

Benzoic acid is presumed to arise from the hydration of benzaldehyde to form the hemiacetal. To decrease the rate of benzaldehyde hydration we looked at solvents with higher water solubilities to decrease the activity of the water. The initial rate of benzyl alcohol oxidation was compared under different amounts of added water to the reaction rate with no added water (rate0) (Figure S7). Non-polar solvents (toluene, ethyl acetate) show very rapid decrease in rate with added water, while more polar solvents (acetonitrile, DMSO) show more stable activity with increasing concentrations of water.
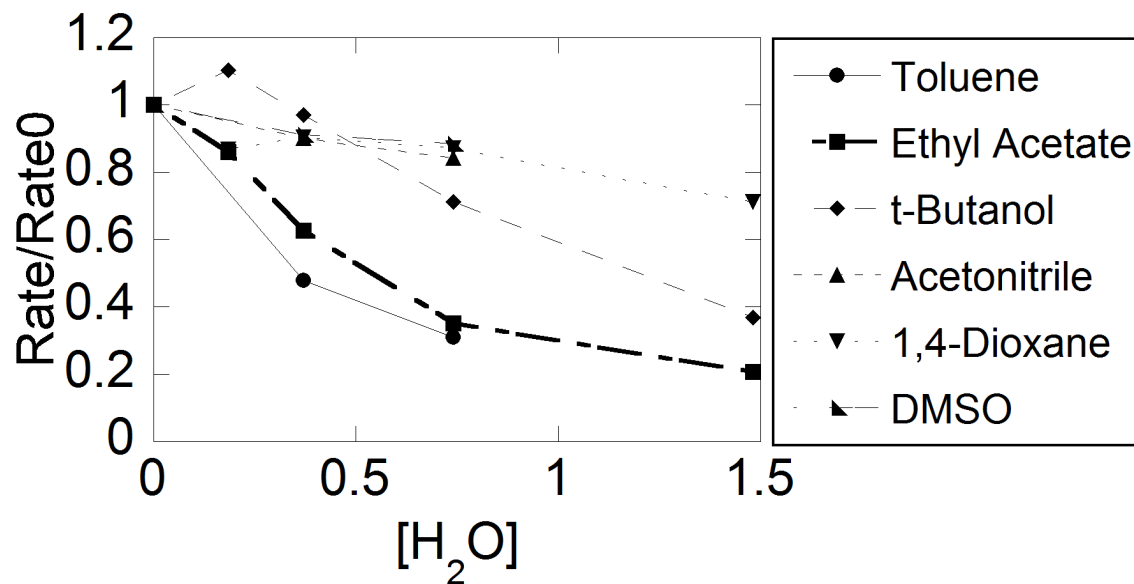
Figure S7. Water poisoning effect on initial rate in various solvents. 0.15 M benzyl alcohol, 3.3 mol % Ru as Ru(OH)$_x$/Al$_2$O$_3$, 60 ˚C, 1 bar O$_2$, 1.5 mL solvent. Rates determined from disappearance of benzyl alcohol at short times using GC. Rate0 is rate with no added water.

In addition to the water poisoning of various solvents, there is a change in base rate (rate0) for different solvents under standard reaction conditions (shown as TOF in Figure S8). Dimethyl carbonate (DMC) was chosen for additional screening as a polar aprotic solvent with initial rates similar to toluene.
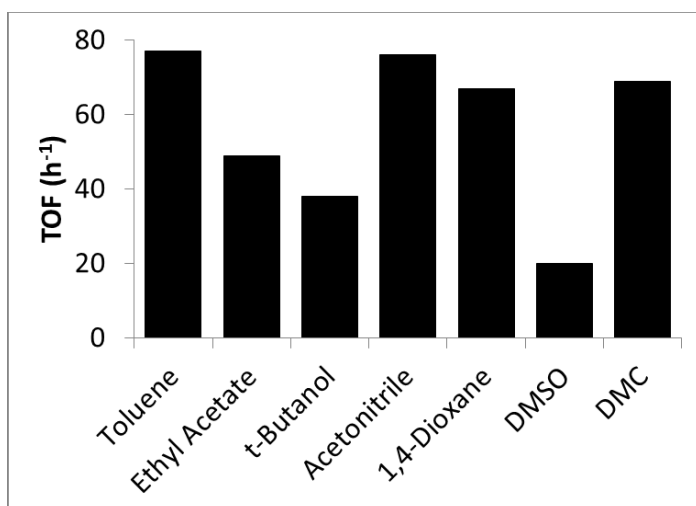
Figure S8. TOF of benzyl alcohol in various solvents. 0.15 M benzyl alcohol, 3.3 mol % Ru as Ru(OH)$_x$/Al$_2$O$_3$, 60 ˚C, 1 bar O$_2$, 1.5 mL solvent. Rates determined from disappearance of benzyl alcohol at short times using GC.

We studied in-situ catalyst regeneration and prevention of catalyst activity loss using various bases. Screening various inorganic and organic bases as reaction additives in batch (

Table S3) was done in batch reactions to determine how bases affected the overall reaction rate and yield. Li_2CO_3, Na_2CO_3, NaH_2PO_4, and LiOH did not detrimentally impact the reaction prompting investigation into their effect on catalyst stability.

**Table S3:** Effect of added base on reaction yield in dimethyl carbonate.[a]

Entry	Base Identity	Yield (%) at 30 min	Yield (%) at 120 min
1	None[b]	66	100
2	None	38	97
3	**Li_2CO_3**	**33**	**98**
4	**Na_2CO_3**	**42**	**98**
5	$NaHCO_3$	20	95
6	$KHCO_3$	23	96
7	LiOAc	44	29
8	NaOAc	8	45
9	KOAc	5	12
10	**NaH_2PO_4**	**41**	**97**
11	Na_2HPO_4	35	98
12	Na_3PO_4	26	98
13	Et_3N	16	72
14	KOtBu	0	19
15	NaOMe	5	42
16	**LiOH**	**39**	**95**
17	NaOH	20	56
18	KOH	0	18

[a]Yields from GC using an internal standard. 0.15 M substrate in 1.5 mL dimethyl carbonate, 0.05 M tetradecane, 2.3 wt. % $Ru(OH)_x/Al_2O_3$ (3.3 mol % Ru), 1 bar O_2, 80 °C, 1 equivalent base to substrate. [b]toluene.

Determination of impact these four bases (runs 3, 4, 10, 16) had on retention of catalyst activity was done using batch reuse experiments. Each catalyst was recovered, rinsed, and re-evaluated for activity with fresh substrate and dimethyl carbonate without additional base. Initial rates (r_k) were compared to the initial rate of the deactivated DMC-only sample (r_2), and the difference in rates for used catalysts was scaled by the difference between the fresh and deactivated catalyst (eq (S1). With this scaling positive numbers denote the base improved catalyst stability and by how much, while negative numbers denote that the base had a negative impact on catalyst stability. A F(r) value of 1.0 would indicate complete retention of fresh catalyst activity.

$$F(r) = \frac{r_k - r_2}{r_0 - r_2} \qquad \text{(S1)}$$

The four best bases from initial screening were compared for catalyst stability (Figure S9). NaH_2PO_4 shows additional loss of activity, while the other three show a small improvement or no change.
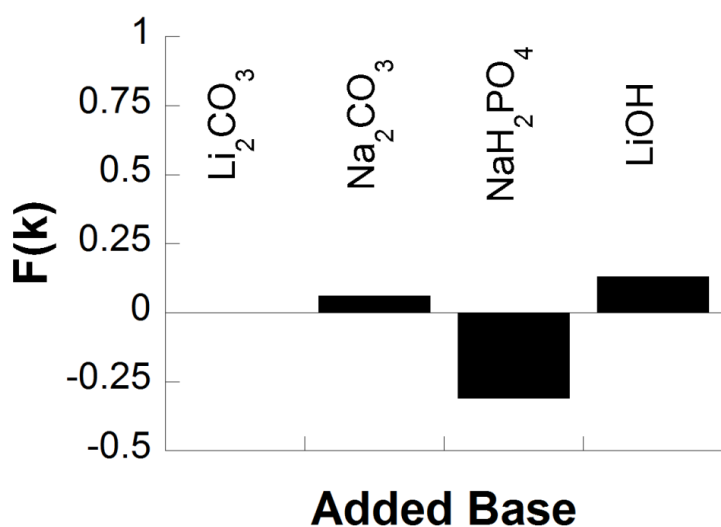
Figure S9: Fractional activity retained after 33 turnovers with different bases. 0.15 M substrate in 1.5 mL dimethyl carbonate, 0.05 M tetradecane, 2.3 wt. % $Ru(OH)_x/Al_2O_3$ (3.3 mol % Ru), 1 bar O_2, 80 °C, 1 equivalent base to substrate.