Electronic Supplementary Material (ESI) for Green Chemistry.

Supplementary Information

Diformylxylose as a New Polar Aprotic Solvent Produced from Renewable Biomass

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1. Solvation properties of DFX and Other Solvents

The Kamlet-Abboud-Taft solvatochromic parameters of the reference solvents shown in the polarity maps of the main article are given here (Table S1).

Table S1. Kamlet-Abboud-Taft Parameters of DFX and various solvents.

Solvent	α	β	π^*	Reference
Acetone	0.08	0.48	0.71	1
Acetonitrile	0.35	0.37	0.80	2
1-Butanol	0.73	0.85	0.61	3
2-butanone	0.06	0.48	0.67	4
Chloroform	0.20	0.10	0.58	5
CPME	0.00	0.53	0.42	1
Cyclohexane	0.00	0.00	0.00	3
Cyclopentanone	0.00	0.52	0.76	4
Cyrene	0.00	0.61	0.93	6
Dichloromethane	0.13	0.10	0.82	4
Dibutyl ether	0.00	0.46	0.27	4
Diethyl ether	0.00	0.47	0.27	4
1,4-dioxane	0.00	0.37	0.55	4
DMAc	0.00	0.76	0.88	4
DMF	0.00	0.69	0.88	4
DMSO	0.00	0.74	1.00	3
Ethanol	0.83	0.77	0.62	3
Ethyl acetate	0.00	0.45	0.55	4
Ethyl lactate	0.69	0.52	0.82	1
Ethylene carbonate	0.00	0.32	0.99	7
Glycerol triacetate	n/a	n/a	0.63	1
Glycerol	1.21	0.51	0.62	1
GVL	0.00	0.60	0.83	1
Isopropanol	0.76	0.84	0.48	1
Methanol	0.93	0.66	0.58	1
2-Me-THF	0.00	0.58	0.53	1
NBP	0.00	0.92	0.77	8
Nitrobenzene	0.00	0.30	1.01	4
NMP	0.00	0.75	0.90	7
Propylene carbonate	0.00	0.38	0.90	7
Sulfolane	0.00	0.39	0.98	4
THF	0.00	0.55	0.58	3
Toluene	0.00	0.12	0.50	9
Triethylamine	0.00	0.7	0.08	3
Water	1.17	0.18	1.09	4
DFX	0.00	0.82	0.92	this work

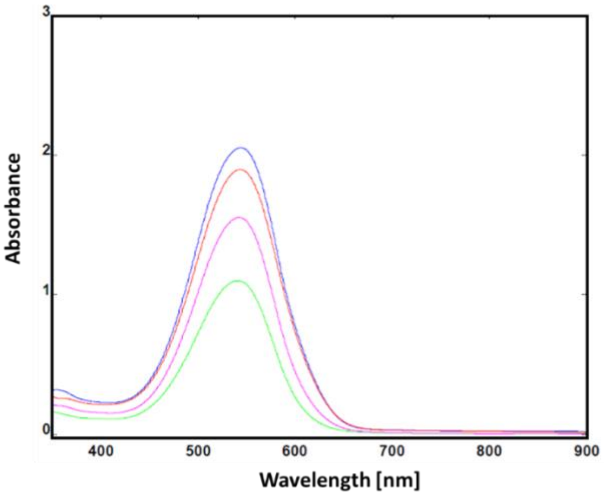

Figure S1. Absorption spectra of Nile Red in Diformylxylose at 4 different concentrations of Nile Red, ranging from 10^{-3} to 10^{-4} M.

Table S2.

Solvent	Maximum average wavelength in DENA, nm	Standard Deviation	Relative standard deviation, %	Wavenumber, kK	Calculated π*
DMSO	411.7	1.53	0.37	24.29	1.00
Cyclohexane	362.8	4.01	1.11	27.56	0.00
1,4-dioxane	387.7	0.58	0.15	25.80	0.54
DFX	407.3	3.51	0.86	24.55	0.92

Table S3.

Solvent	Maximum average wavelength in NA, nm	Standard Deviation	Relative standard deviation, %	Wavenumber, kK	Calculated β
DMSO	387.5	0.5	0.13	25.81	0.76
Cyclohexane	324.5	0.87	0.27	30.82	0.00
1,4-dioxane	353.3	2.52	0.71	28.30	0.33
DFX	385.8	3.88	1.01	25.92	0.82

Table S4. Hansen Solubility Parameters of the solvents within DFX's interaction sphere of a radius of 4 MPa½ and their distance to DFX data point in 3D Hansen space.

Solvent	***Hansen Solubility Parameters, MPa½***			***Distance***
	δD	***δP***	***δH***	
DFX	17.9	9.0	7.6	0
Dimethyl isosorbide	17.6	7.1	7.5	1.99
Dichloromethane	17.0	7.3	7.1	2.53
Cyclohexanone	17.8	8.4	5.1	2.58
1,4-dioxane	17.1	6.8	7.8	2.73
1,3-dioxolane	18.1	6.6	9.3	2.97
Isophorone	17.0	8.0	5.0	3.32
NMP	18.0	12.3	7.2	3.33
THF	16.8	5.7	8.0	3.99

2. Model Reactions

1.1 Alkylation (Menshutkin reaction)

Table S5. Rate constant values for the alkylation (Menshutkin) reaction used to construct the linear solvation energy relationship depicted in Figure 4.

Solvent	**α**	***β***	***π****	**k*10^3, M^{-1}*s^{-1}**	**ln(k), M^{-1}*s^{-1}**
CPME	0.00	0.53	0.42	0.48	-7.64
Isopropanol	0.76	0.84	0.48	0.52	-7.57
1,4-dioxane	0.00	0.37	0.55	0.63	-7.38
Acetonitrile	0.35	0.37	0.80	0.96	-6.95
GVL	0.00	0.60	0.83	1.18	-6.75
DFX	0.00	0.82	0.92	1.26	-6.67
DMSO	0.00	0.74	1.00	1.57	-6.46
NMP	0.00	0.75	0.90	1.43	-6.55
Butanone	0.06	0.48	0.67	0.93	-6.98
DMF	0.00	0.69	0.88	1.34	-6.61

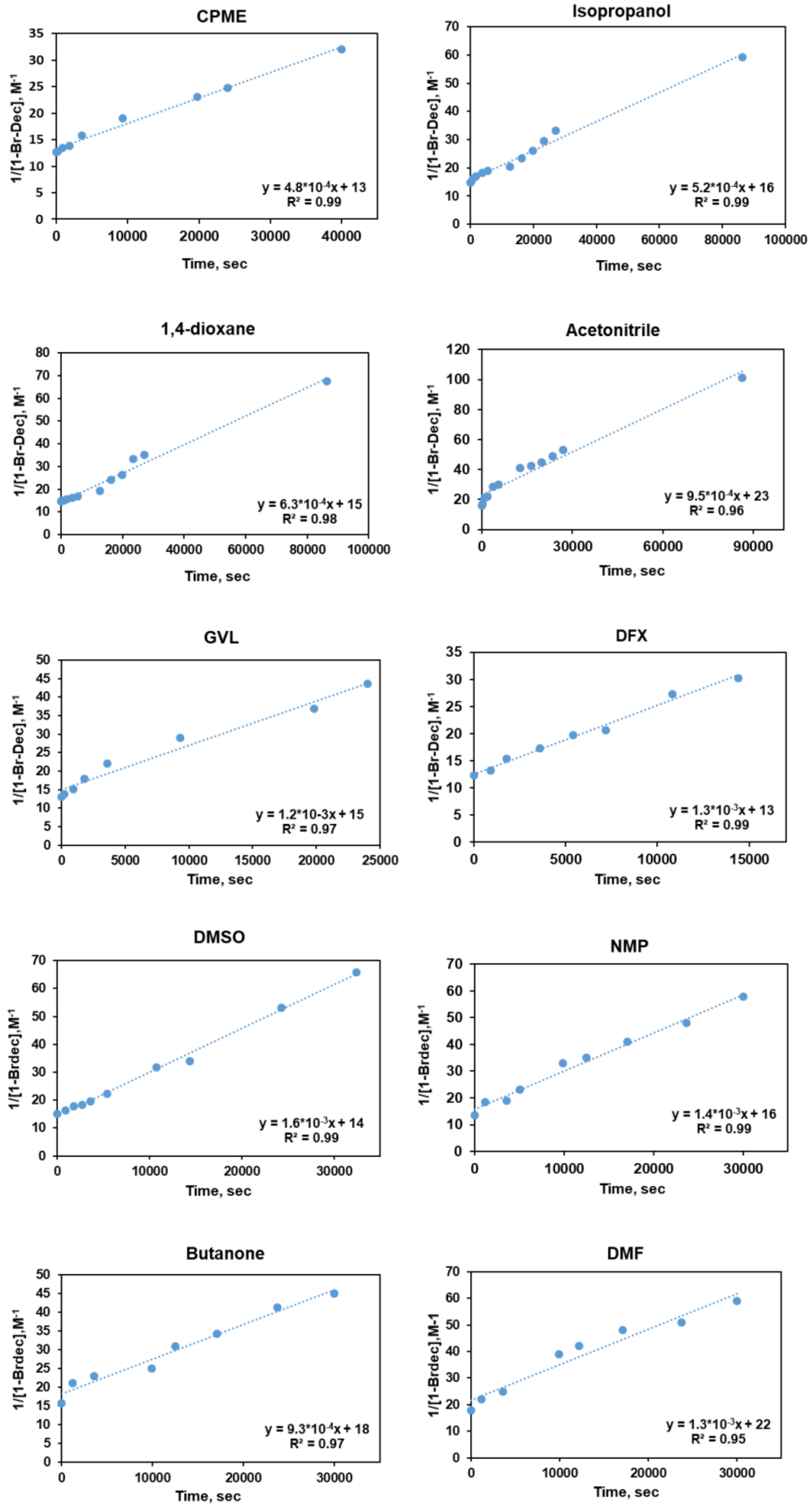

Figure S2. The plots of 1/concentration of 1-bromodecane as a function of time in different solvents, corresponding to second-order reaction kinetic. The slope represents a rate constant.

1.2 Hydrogenation of cinnamaldehyde

Table S6. Conversion of cinnamaldehyde for the hydrogenation reaction, selectivity, corresponding HSP, and hydrogen gas solubility of various solvents.

Solvent	Conversion, %	Selectivity, %			Hansen Solubility Parameters, MPa½			H_2 mole fraction * 10^4 *
		HCAL	PPL	COL	*δD*	*δP*	*δH*	
cyclohexane	98.5	85.3	14.7	0.0	16.8	0.0	0.2	4.14
diethyl ether	91.3	88.7	11.3	0.0	14.5	2.9	4.6	3.46
methanol	90.4	56.4	32.1	11.5	14.7	12.3	22.3	1.61
dibutyl ether	86.2	90.6	9.4	0.0	15.2	3.4	3.2	n/a
IPA	81.45	68.6	31.4	0.0	15.8	6.1	16.4	4.61
THF	69.5	81.3	18.7	0.0	16.8	5.7	8	2.74
1,4-dioxane	55.03	91.9	8.1	0.0	17.1	6.8	7.8	1.84
DMF	40.7	79.3	20.7	0.0	17.4	13.7	11.3	1.47
DMSO	22.6	93.0	7.0	0.0	18.4	16.4	10.2	0.76
DFX	15	88.6	11.4	0.0	17.9	9.0	7.6	n/a

*H_2 mole fraction values were taken from Young C. L. Hydrogen and deuterium. Solubility Data Series, (1981), 5, 428-429.

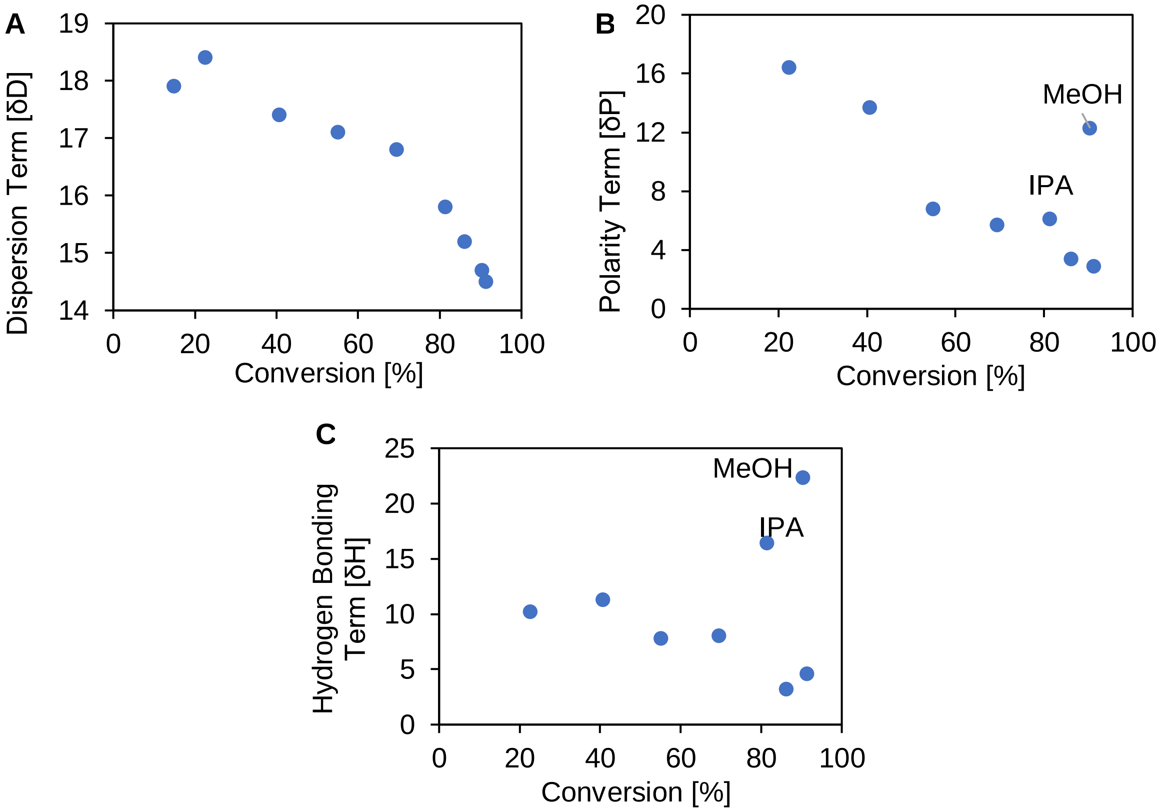

Figure S3. HSP parameters (**A** – *δD;* ***B*** **–** *δP;* ***C*** **–** *δH***)** of the studied solvent as a function of the conversion of cinnamaldehyde for the model hydrogenation reaction.

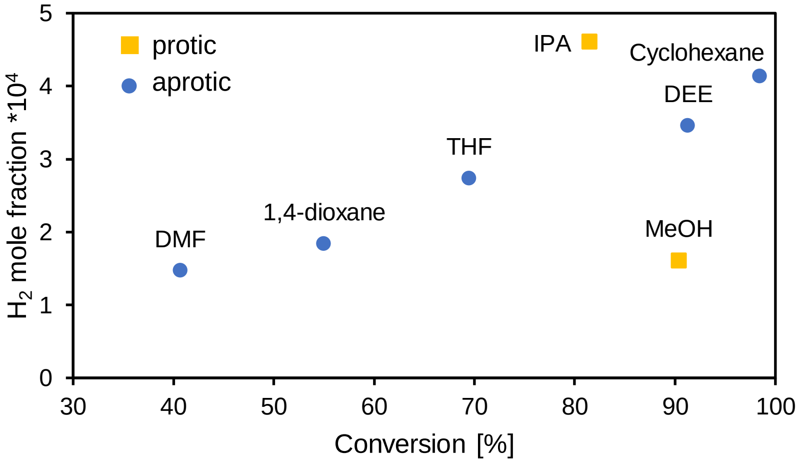

Figure S4. Solubility of the hydrogen gas in the selected solvents at 298K and 1 atm as a function of the conversion of cinnamaldehyde for the model hydrogenation reaction.

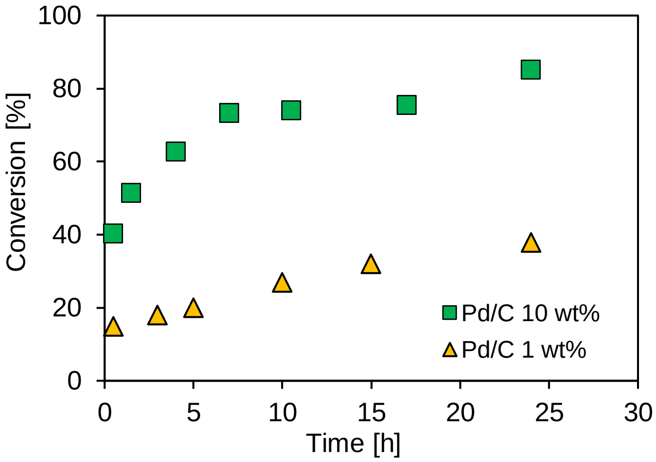

Figure S5. Conversion of DFX as a function of time at different Pd/C catalyst loadings.

1.3 Heck reaction

Table S7. Rate constant values for the model Heck reaction used to construct the linear solvation energy relationship depicted in Figure 6.

Solvent	**α**	***β***	***π****	**k*10^3, M^{-1}*s^{-1}**	**ln(k), M^{-1}*s^{-1}**
CPME	0.00	0.53	0.42	0.006	-12.04
1,4-dioxane	0.00	0.37	0.55	0.012	-11.30
Cyclopentanone	0.00	0.52	0.76	0.038	-10.17
Triacetin	n/a	n/a	0.63	0.032	-10.36
GVL	0.00	0.60	0.83	0.135	-8.91
DFX	0.00	0.82	0.92	0.088	-9.34
DMSO	0.00	0.74	1.00	0.171	-8.68
NMP	0.00	0.75	0.90	0.235	-8.35
DMF	0.00	0.69	0.88	0.641	-7.35

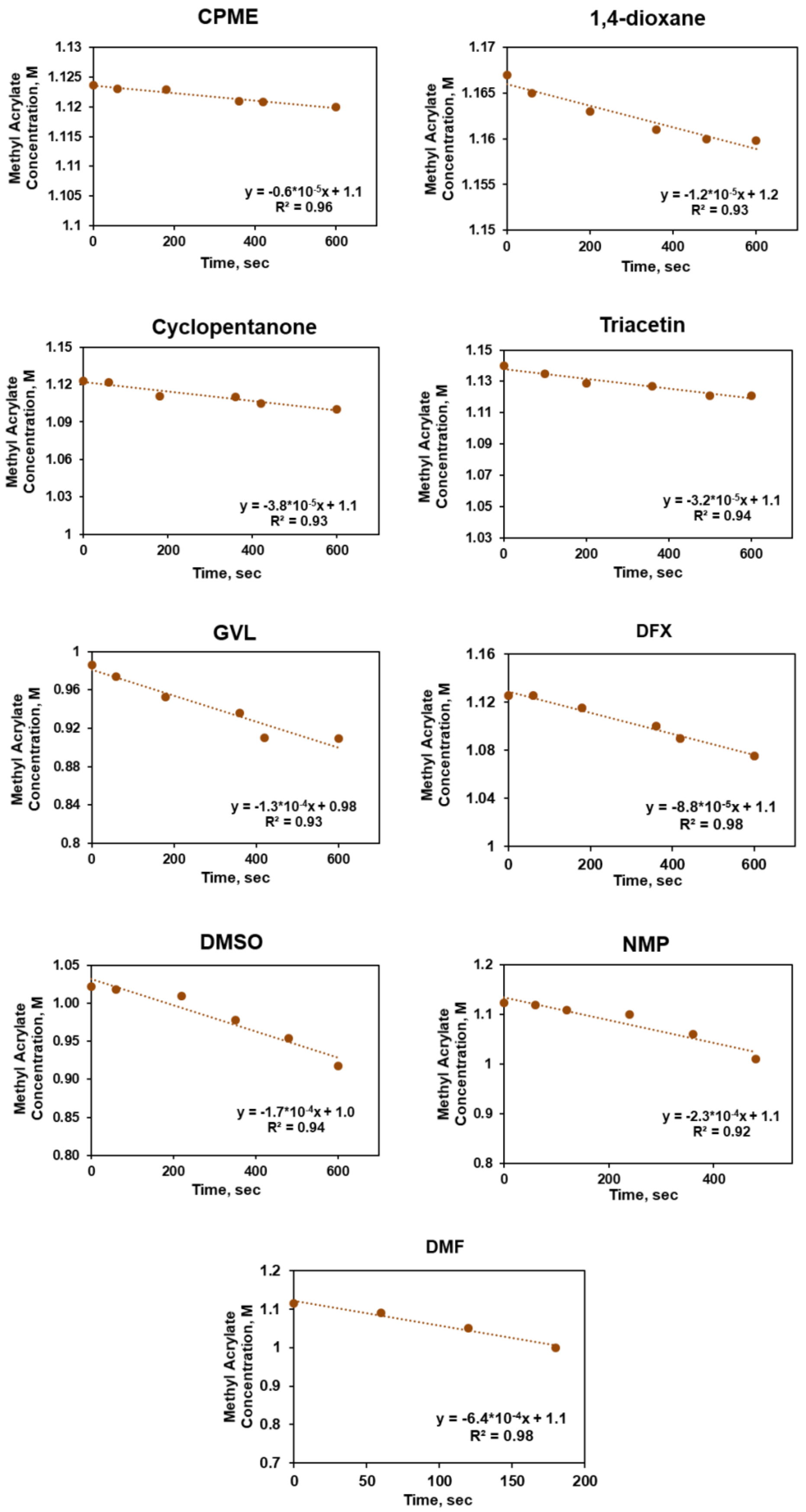

Figure S6. The plots of concentration of methyl acrylate as a function of time in different solvents. The slope represents the initial rate.

2. Toxicological Assessment using the Ames Test

The experimental procedure was based on manufacturer's guidelines.[10] Briefly, TA100 and TA98 bacterial strains were grown overnight and diluted until OD_{600} was 0.1 (for TA98) or 0.05 (for TA100). In a 24-well plate, samples containing grown bacteria and negative controls (water), positive controls (4-nitroquinoline-N-oxide (4-NQO) for TA100, 2-nitrofluorene (2-NF) for TA98, 2-Aminoanthracene (2-AA) when S9 mix is added), sterility controls, 5-serial dilutions of the DFX water solution (80, 40, 20, 10, 5, 2.5 mg/ml) were prepared and incubated at 37°C for 100 min in a medium including sufficient histidine to initiate cell division. After the exposure, these samples were diluted in Reversion Media absent histidine in a second 24-well plate, then aliquoted into three 384-well plates and incubated at 37°C for 48 h. After this, plats were scored visually: yellow wells indicated bacterial growth as they had undergone reverse mutation and could produce the histidine needed for their growth; purple wells indicated no reverse mutation of His+ biopathway in bacteria as they couldn't grow without histidine. The number of yellow wells was calculated and averaged to obtain the mean number of revertants (Figure S4). Baseline and positive criteria were then calculated in accordance with the manufacturer's guide.

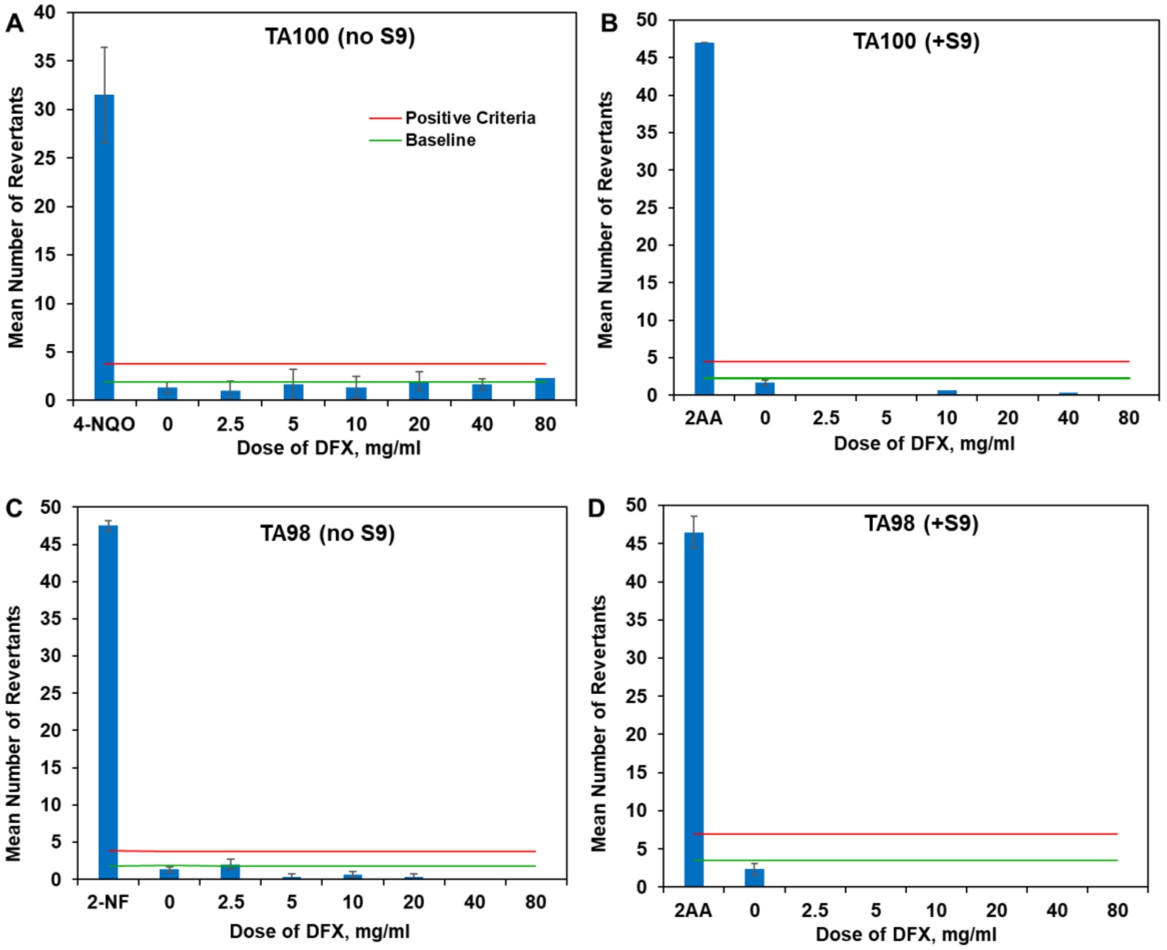

Figure S7. Results of the Ames test on DFX using Salmonella TA100 **(A,B)** and TA98 **(C,D)** strains in comparison with the positive control (4-Nitroquinoline-N-oxide (4-NQO) for TA100 strain; 2-Nitrofluorene (2-NF) for TA98 strain; 2-Aminoanthracene (2-AA) when S9 mix was added) and negative control (water) with S9 **(B,D)** and without **(A,C)**. Error bars represent standard error of the mean. The green line was a calculated baseline, incorporating the average of negative control data and the standard deviation. The red line represents a positive criterion for the consideration of the tested compound as a mutagen (≥2x baseline).

3. Optimization of the DFX synthesis

In order to assess the overall performance of the new synthetic route, conversion of xylose, yield of DFX and furfural were calculated using data from high-performance liquid chromatography (HPLC) analysis at different time points (Figure S.5). There are several general trends observable for this synthesis. The conversion of xylose was higher compared to original synthesis, starting with more than 80% even after 5 min of reaction (Figure S.5, B, D), even though the overall yield of DFX was almost the same (around 70-75%) (Figure S.5, A, B, D). In addition, the yield of furfural was almost negligible in the new synthesis, meaning that much less degradation of xylose occurred during the reaction. Finally, if the same amount of solvent used for the new synthesis had been used in the old procedure, then the yield of DFX would have fallen to less than 50%, which confirms the need to use much higher volumes of solvent in the past procedures to maintain yields.

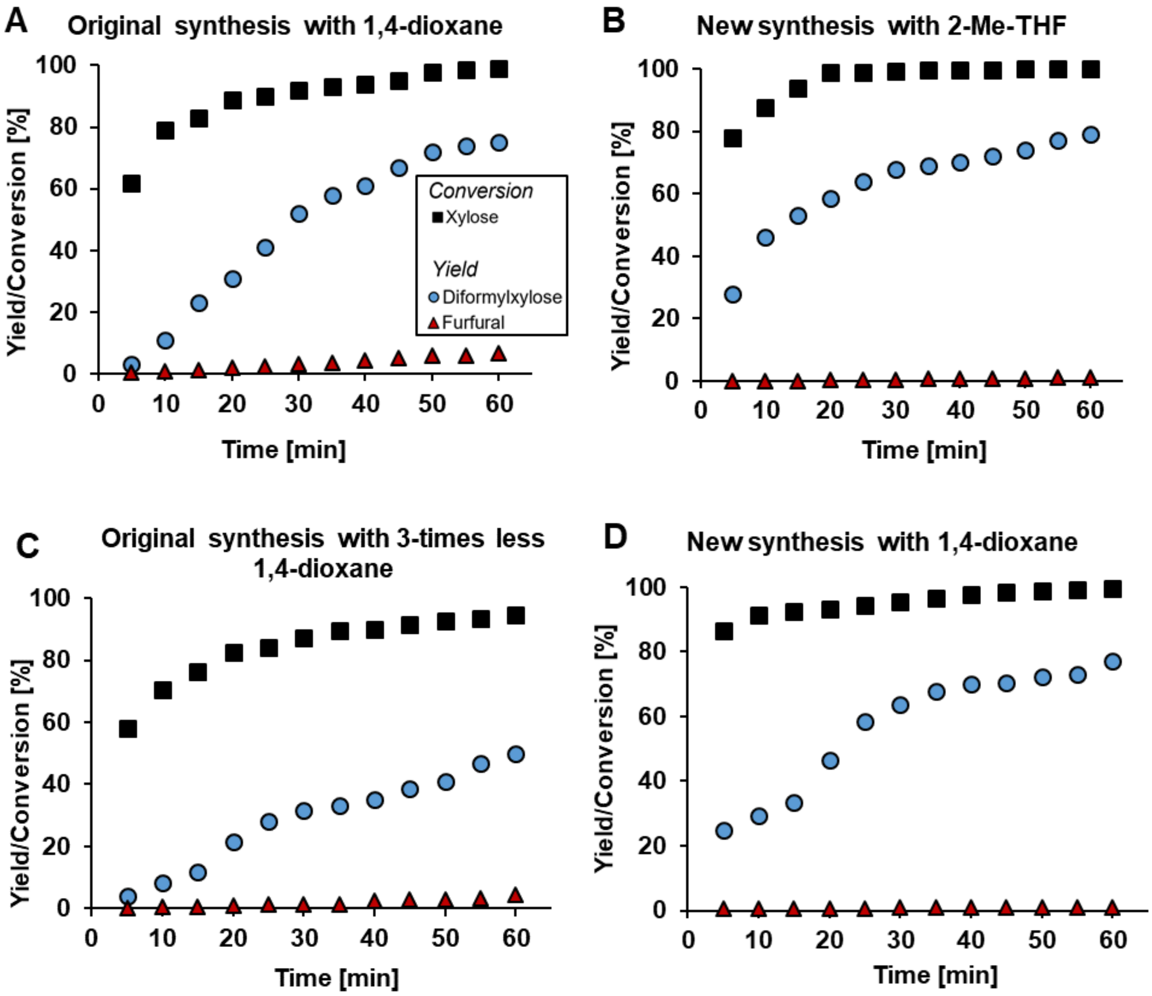

Figure S8. Optimization of reaction conditions for the direct synthesis of diformylxylose in 1,4-dioxane **(A,C,D)** or 2-Me-THF **(B)** at 80°C using the previous **(A,C)** and new procedure **(B, D).**

4. Stability of DFX

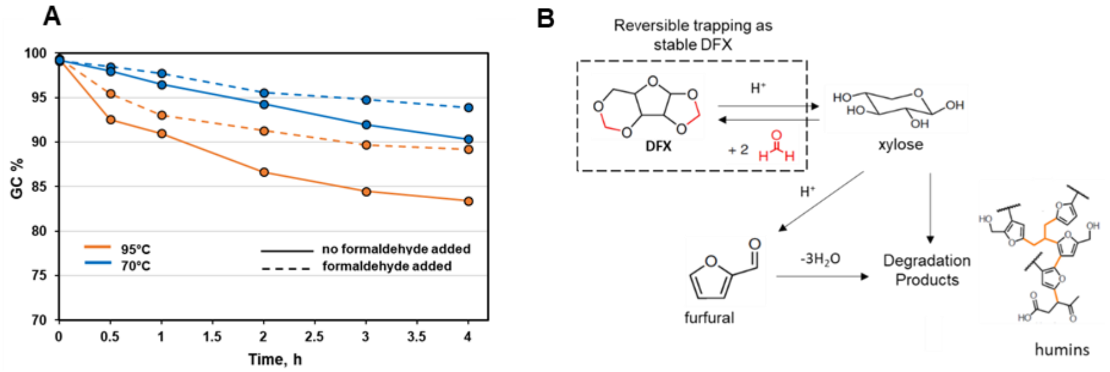

Figure S9. A. Stability of pure diformylxylose at 2.75 wt.% (0.8M) HCl, 95 or 70°C with formaldehyde added (dashed line), or without any formaldehyde present (straight line). **B.** DFX stabilization with formaldehyde.

Table S8. Stability of DFX under basic conditions.

Base	Temperature, °C	Reaction (Y/N)			DFX degradation, %		
		0.5h	24h	48h	0.5h	24h	48h
NEt_3	80	Y	Y	Y	3	4	5
K_2CO_3	80	Y	Y	Y	2	3	7
	110	Y	Y	Y	2	5	13
KOAc	80	**N**	**N**	**N**	0	2	3
	110	Y	Y	Y	1	3	5
Pyridine	80	**N**	**N**	**N**	0	0	0
	110	**N**	Y	Y	0	3	6
NaOH	80	Y	Y	Y	0	9	17
	110	Y	Y	Y	3	11	21
$CsCO_3$	80	Y	Y	Y	1	4	8
	110	Y	Y	Y	1	7	11

*Reaction (Y/N) refers to the observation of a color change compared to the control solution.

Visual color change compared to a control solution of pure DFX indicated some reactions were occurring. After 0.5h, 24h, 48h of exposure, the samples were injected in GC-FID and GC-MS and the area of DFX was compared with that of the control sample using decane as the internal standard.

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Abbreviations

2-AA – 2-Aminoanthracene

2-Me-THF – 2-Methyltetrahydrofuran

2-NF – 2-Nitrofluorene

4-NQO – 4-Nitroquinoline-N-oxide

COL – Cinnamylalcohol

CPME – Cyclopentyl methyl ether

DFX – Diformylxylose

DMAc – N, N-Dimethylacetamide

DMF – N, N-Dimethylformamide

DMSO – Dimethyl sulfoxide

GVL – γ-Valerolactone

HCAL – Hydrocinnamaldehyde

HSP – Hansen Solubility Parameters

IPA – Isopropanol

MeCN – Acetonitrile

NBP – N-butylpyrrolidinone

NMP – N-Methyl-2-pyrrolidone

PPL – 3-Phenylpropanol

THF – Tetrahydrofuran