

Electronic Supporting Information

An innovative catalytic pathway for the synthesis of acyl furans: the cross-ketonization of methyl 2-furoate with carboxylic acids

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Chapter S1: detailed description of ZrO₂ and Ce/Zr/O synthesis

Zirconia (ZrO₂) was synthesized as follows: ZrOCl₂·8H₂O was dissolved in deionized water to obtain 250 mL of a 0.5 mol/L solution, which was slowly added dropwise to 500 mL of aqueous NH₃ (5 mol_{Zr}/L) under vigorous stirring. The pH of the resulting suspension remained above 11 until the end of the addition of the metal precursor. The precipitate was aged for 1 hour under stirring, filtered over a Buchner funnel, and washed with 2 L of distilled water for each 3 g of material to remove adsorbed chloride, nitrate, and ammonium ions. Finally, the resulting wet solid was dried at 120°C overnight and calcined at 550°C for 4 hours with a heating rate of 5 °C/min.

Ceria-zirconia (Ce/Zr/O) was synthesized as follows: ZrOCl₂·8H₂O and CeCl₃·H₂O were dissolved in deionized water to obtain 200 mL of a solution containing 0.25 mol/L of Zr⁴⁺ and 0.25 mol/L of Ce³⁺ (Ce/Zr ratio = 1), which was slowly added dropwise to 400 mL of aqueous NH₃ (5 mol/L) under vigorous stirring. The pH of the resulting suspension remained above 11 until the end of the addition of the metal precursor. The precipitate was aged for 1 hour under stirring, filtered over a Buchner funnel, and washed with 2 L of distilled water for each 3 g of material to remove adsorbed chloride, nitrate, and ammonium ions. Finally, the resulting wet solid was dried at 120°C overnight and calcined at 400°C for 4 hours with a heating rate of 5 °C/min.

Chapter S2: detailed description of H₂-TPR and TGA experiments

H₂-TPR: All experiments were carried out on 0.2 g of sample using a Micromeritics Autochem II 2920 instrument equipped with a TCD detector. The sample was heated up from room temperature to calcination temperature at a rate of 10 °C/min to clean surface of the material from physisorbed and chemisorbed molecules by flowing a 5 % O₂/He mixture (30 mL/min). The final temperature was kept for 60 min. After cooling down to 50 °C in a pure He flow (30 mL/min), the sample was flown with a 5% H₂/Ar mixture (50 mL/min) for 30 minutes to allow stabilization of the TCD detector signal. Then, the sample was heated up from 50 °C to calcination temperature at a rate of 10 °C/min and the final temperature was kept for 60 min. In order to remove any traces of water before the TCD detector, the effluents from the samples were flown through a cold trap filled with a 3Å molecular sieve kept at room temperature.

TGA: All experiments were carried out with 5-10 mg of sample using a NETZSCH TG 209 F1 thermogravimetric analyser. To quantify the mass of carbon deposited over catalysts surface during the catalytic tests, the samples were heated up from room temperature to 600 °C in a 20 mL/min flow of air at a heating rate of 10 °C/min. The final temperature was kept for 30 minutes.

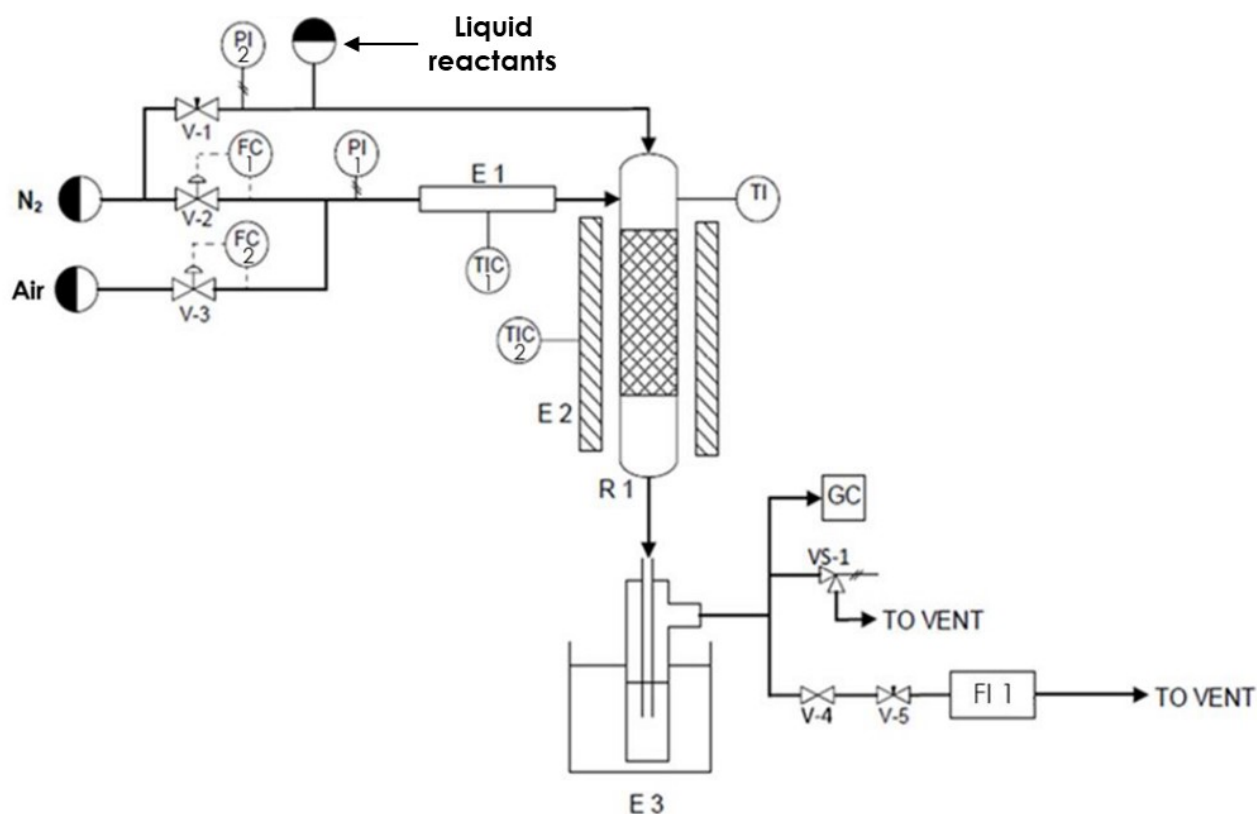


Figure S1: Schematic illustration of the gas-phase plant and the analytical system used to carry out the catalytic tests. Symbols: PI = pressure indicator, FC = mass flow meter, TIC-1 = temperature controller 1 (N_2 and air inlet), TI = temperature indicator (catalytic bed), TIC2 = temperature controller 2 (reactor furnace).

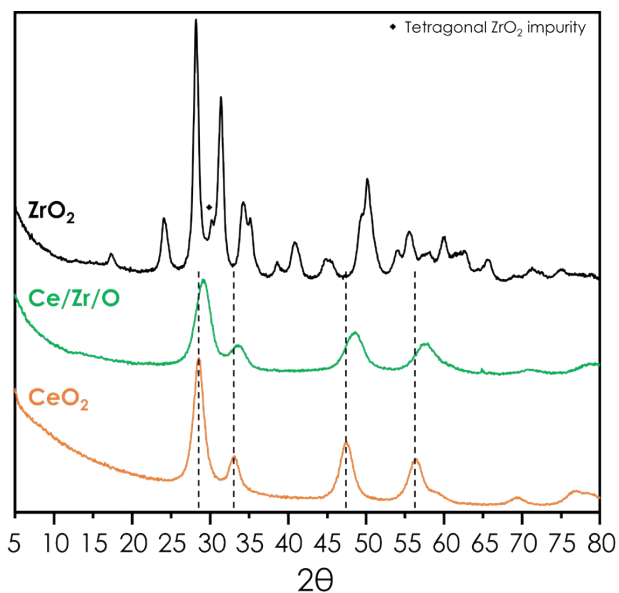


Figure S2: powder XRD diffraction patterns of (from top to bottom): ZrO_2 , $Ce/Zr/O$ and CeO_2 .

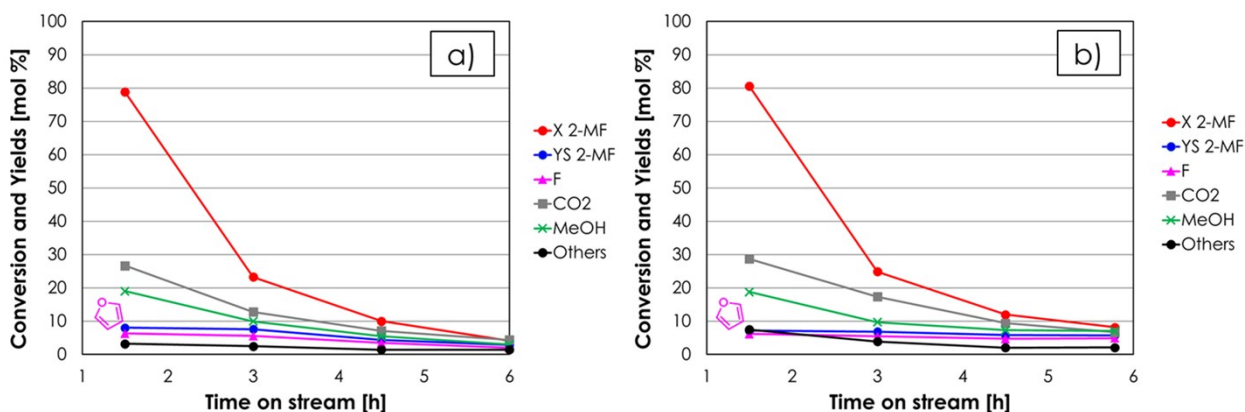


Figure S3: results of tests carried out to assess the stability of 2-MF as a function of the time on stream without catalyst (a) and over ZrO_2 (b). Reaction conditions: temperature = $350\text{ }^\circ\text{C}$, 2-MF = 1 mol % in N_2 , contact time = $\tau = 1\text{ s}$, GHSV = 1722 h^{-1} , 1 mL of ZrO_2 . Symbols: 2-methyl furoate conversion (X 2-MF), sum of yields (YS 2-MF), furan yield (F); carbon dioxide yield (CO_2), methanol yield (MeOH), sum of yields of unknown by-products (Others).

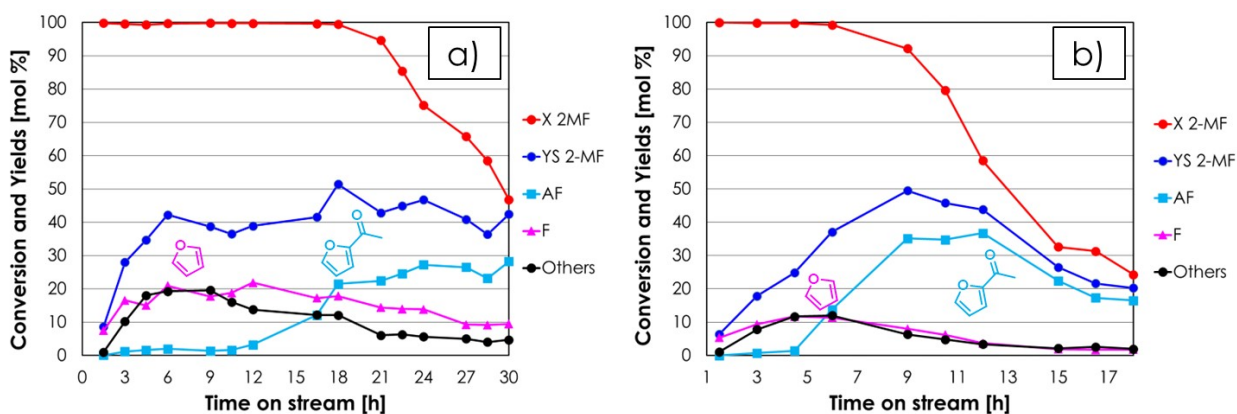


Figure S4: Results of the cross-ketonization between 2-MF and AA as a function of the time on stream in respect to 2-MF over CeO_2 (a) and $Ce/Zr/O$ (b). Reaction conditions: temperature = $350\text{ }^\circ\text{C}$, 2-MF/EA/ N_2 = 0.4/1.6/98 mol %, contact time = $\tau = 1\text{ s}$, GHSV = 1722 h^{-1} , 1 mL of catalyst. Symbols: 2-methyl furoate conversion (X 2-MF), sum of yields (YS 2-MF), acetyl furan yield (AF), furan yield (F), sum of yields of unknown by-products (Others).

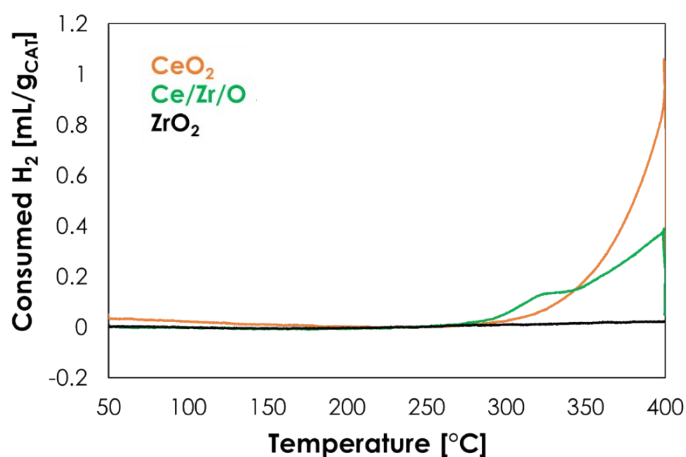


Figure S5: temperature programmed reduction profiles for CeO_2 , $Ce/Zr/O$ and ZrO_2 as a function of the temperature.

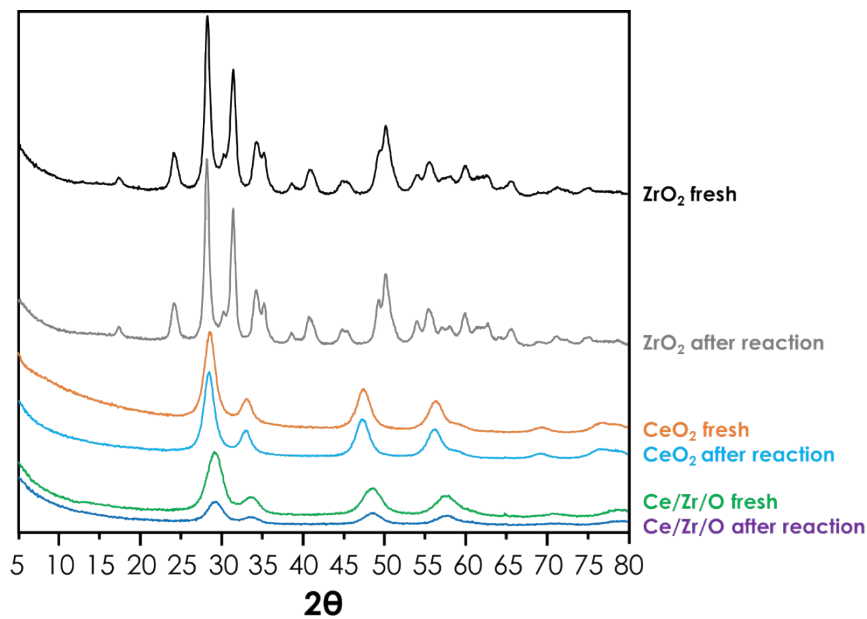


Figure S6: powder XRD diffraction patterns of (from top to bottom): ZrO_2 fresh, ZrO_2 after reaction, CeO_2 fresh, CeO_2 after reaction, $Ce/Zr/O$ fresh and $Ce/Zr/O$ after reaction.

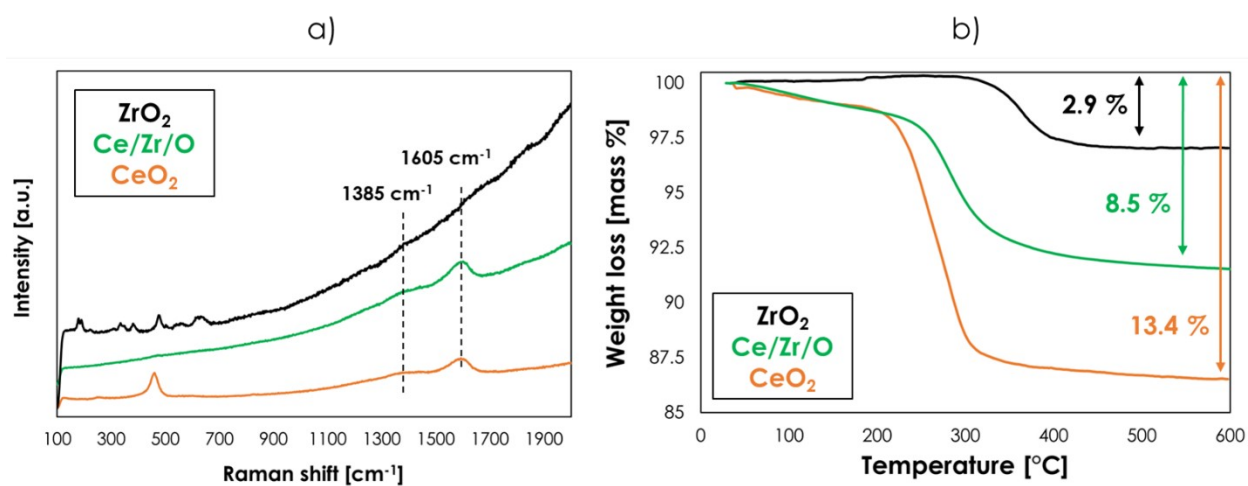


Figure S7: Raman spectra (a) and TGA analysis (b) of ZrO_2 , $Ce/Zr/O$ and CeO_2 after reaction.

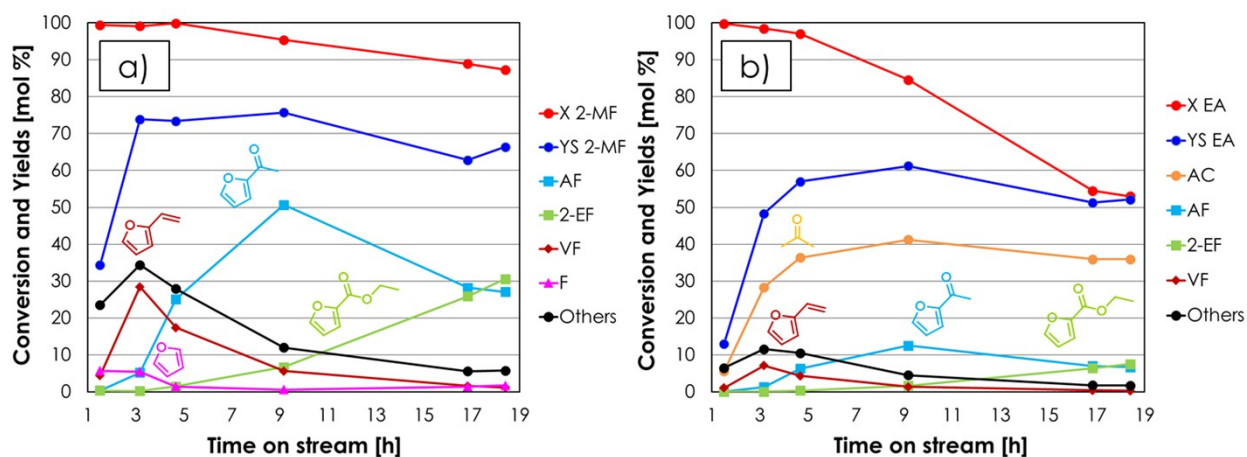


Figure S8: Results of the cross-ketonization between 2-MF and EA as a function of the time on stream in respect to 2-MF (a) and EA (b). Reaction conditions: temperature = 350 °C, 2-MF/EA/N₂ = 0.4/1.6/98 mol %, contact time = $\tau = 1$ s, GHSV = 1722 h⁻¹, 1 mL of ZrO₂. Symbols: a) 2-methyl furoate conversion (X 2-MF), sum of yields (YS 2-MF), acetyl furan yield (AF), 2-ethyl furoate yield (2-EF), furan yield (F), vinyl furan yield (VF), sum of yields of unknown by-products (Others); b) ethyl acetate conversion (X EA), sum of yields (YS EA), acetone yield (AC), acetyl furan yield (AF), 2-ethyl furoate yield (2-EF), vinyl furan yield (VF), sum of yields of unknown by-products (Others).

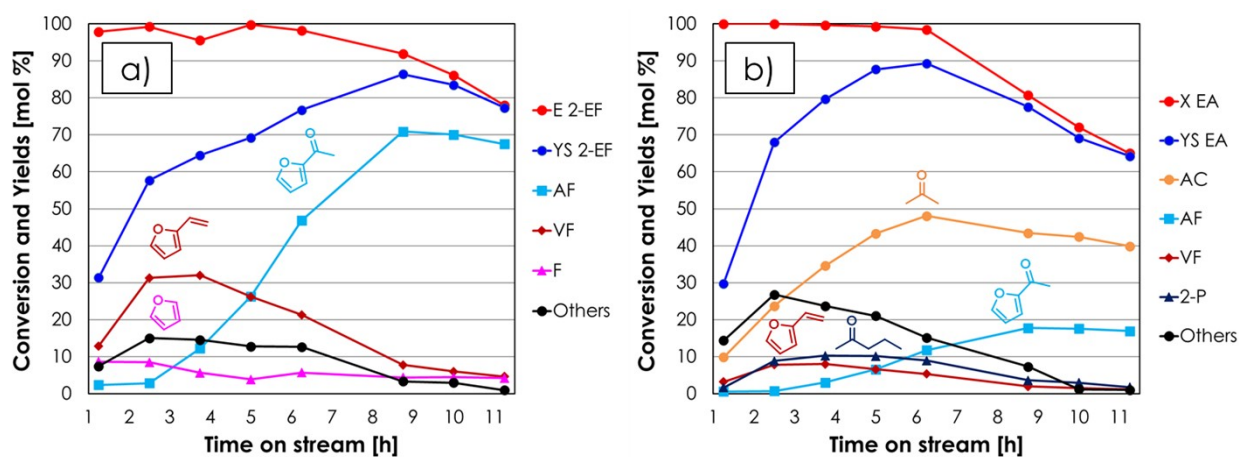


Figure S9: Results of the cross-ketonization between 2-EF and EA as a function of the time on stream in respect to 2-EF (a) and EA (b). Reaction conditions: temperature = 350 °C, 2-EF/EA/N₂ = 0.4/1.6/98 mol %, contact time = $\tau = 1$ s, GHSV = 1722 h⁻¹, 1 mL of ZrO₂. Symbols: a) 2-ethyl furoate conversion (X 2-EF), sum of yields (YS 2-EF), acetyl furan yield (AF), 2-ethyl furoate yield (2-EF), furan yield (F), vinyl furan yield (VF), sum of yields of unknown by-products (Others); b) ethyl acetate conversion (X EA), sum of yields (YS EA), acetone yield (AC), acetyl furan yield (AF), vinyl furan yield (VF), 2-pentanone yield (2-P), sum of yields of unknown by-products (Others).

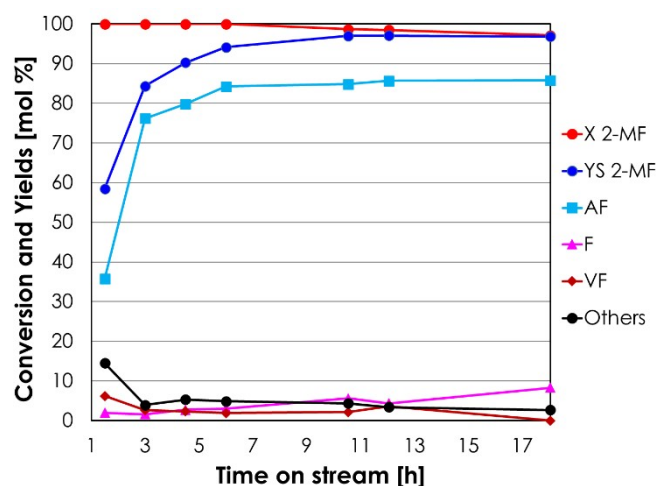


Figure S10: Results of the cross-ketonization between 2-MF and AA as a function of the time on stream in respect to 2-MF. Reaction conditions: temperature = 350 °C, 2-MF/AA/N₂ = 1/9/90 mol %, contact time = $\tau = 1$ s, GHSV = 1722 h⁻¹, 1 mL of ZrO₂. Symbols: 2-methyl furoate conversion (X 2-MF), sum of yields (YS 2-MF), acetyl furan yield (AF), furan yield (F), vinyl furan yield (VF), sum of yields of unknown by-products (Others).

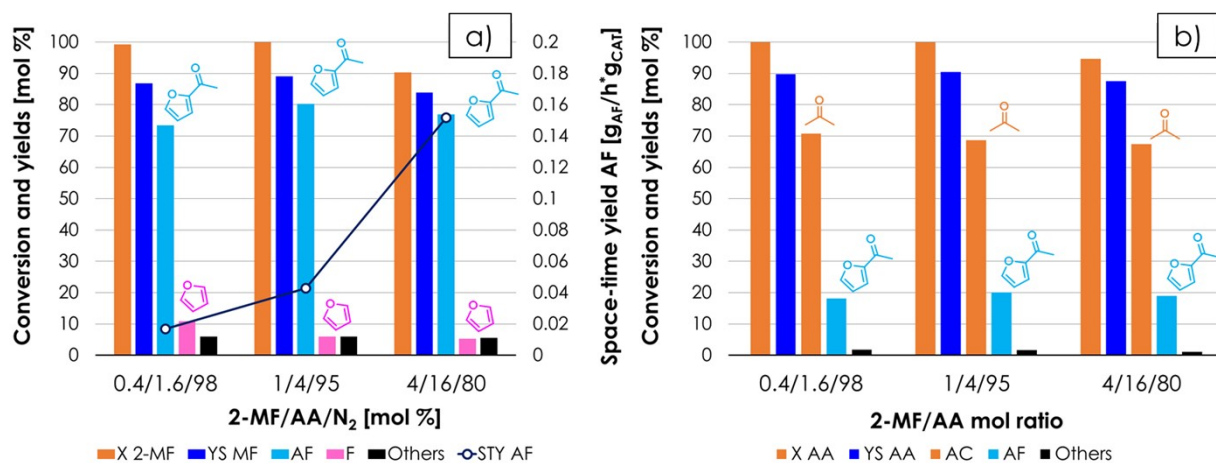


Figure S11: Results of the cross-ketonization between 2-MF and AA as a function of the feed concentration in respect to 2-MF (a) and AA (b). Reaction conditions: temperature = 350 °C, 2-MF/AA mol ratio = 4, total organic fraction in feed = variable, contact time = $\tau = 1$ s, GHSV = 1722 h⁻¹, 1 mL of ZrO₂. Symbols: a) 2-methyl furoate conversion (X 2-MF), sum of yields (YS 2-MF), acetyl furan yield (AF), furan yield (F), sum of yields of unknown by-products (Others), Space-time yield of AF (STY AF, right y-axis); b) acetic acid conversion (X AA), sum of yields (YS AA), acetone yield (AC), acetyl furan yield (AF), sum of yields of unknown by-products (Others).

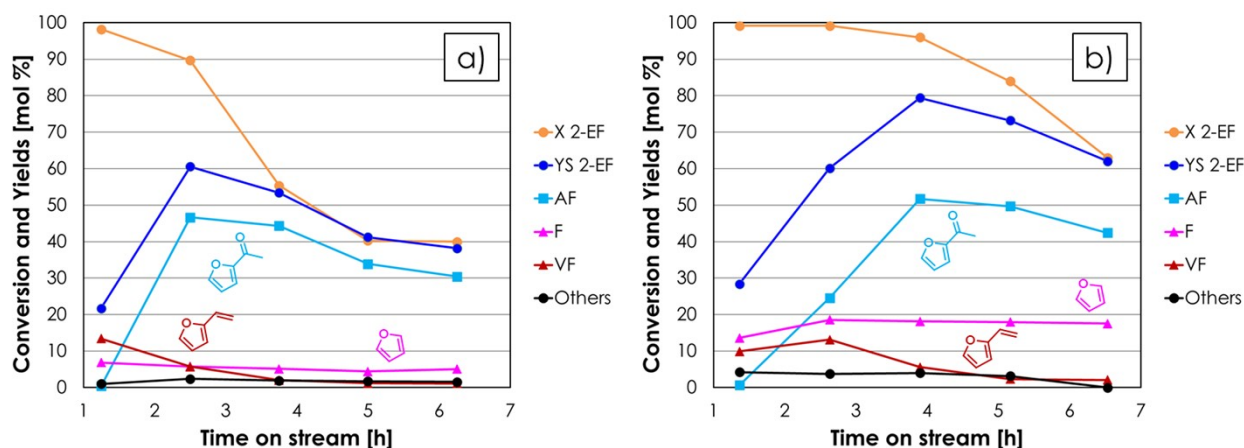


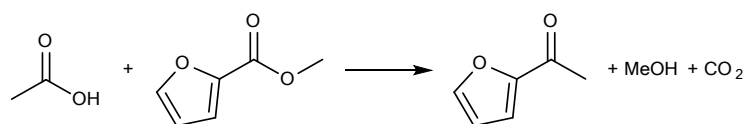
Figure S12: Results of the cross-ketonization between 2-EF and EA as a function of the time on stream in respect to 2-EF at 350 °C (a) and 375 °C (b). Reaction conditions: 2-EF/EA/N₂ = 1/1/98 mol %, contact time = $\tau = 1$ s, GHSV = 1722 h⁻¹, 1 mL of ZrO₂. Symbols: 2-ethyl furoate conversion (X 2-EF), sum of yields (YS 2-EF), acetyl furan yield (AF), furan yield (F), vinyl furan yield (VF), sum of yields of unknown by-products (Others).

Chapter S3: detailed description of E-factors calculation

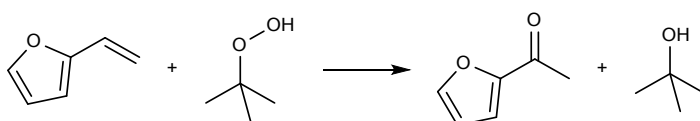
The following contribution to the total E-factor were considered:

- Unreacted reactants: $E_R = [(\text{mass of unreacted reactants}) / (\text{mass of AF})]$: for the references where the actual conversion of the reactants was given, the mass of the unreacted reactants was not considered as waste because it was assumed that they could be separated and recycled. For the references where the actual conversion of reactants was not given and only the AF yield is known, it was assumed that only the desired reaction occurs (e.g., AF selectivity = 100 %) but the mass of unreacted reactants was considered waste.
- By-product: $E_{BP} = [(\text{mass of by-products}) / (\text{mass of AF})]$: the mass of by-products (e.g., tert-BuOH, AA) for the literature references was considered waste and was calculated from the stoichiometry of the reactions depicted in Figure S1. For the cross-ketonization processes, the mass of MeOH, CO₂, H₂O and the carbon loss were considered waste, while AC and F (for the synthesis of AF) and 12-tricosanone (12-T) and F (for the synthesis of 2-dodecanoyl furan, DF) were considered valuable products once separated from the product.
- Reaction solvent: $E_S = [(\text{mass of reaction solvent}) / (\text{mass of AF})]$: it was assumed that 90 % of the solvent could be separated and recovered, thus only 10 % of the mass of the reaction solvent used as reaction medium was considered waste.
- Catalyst and Co-catalysts: $E_{CAT} = [(\text{mass of catalyst and co-catalyst}) / (\text{mass of AF})]$: for the references describing continuous processes either in the liquid or the gas phase, and for the references where it was demonstrated that the catalyst could be reused several times, the mass of catalyst and co-catalysts was not considered waste. Otherwise, the mass of catalyst used was considered waste.

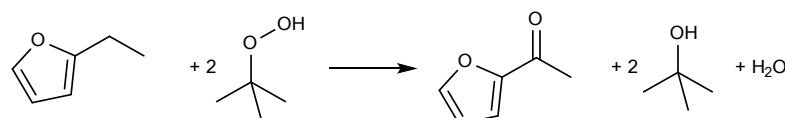
- Work-up: $E_w = [(mass\ of\ work\text{-}up\ waste) / (mass\ of\ AF)]$: for the references where information about the work-up were given, only the waste resulting from catalyst separation, recovery, and washing before re-use were considered. It was assumed that 90 % of the solvents used could be recovered; also, only the mass of salt was considered as a waste when aqueous solution were used. Work-up operations required to purify further the crude product were not considered in the calculation of E-factors.



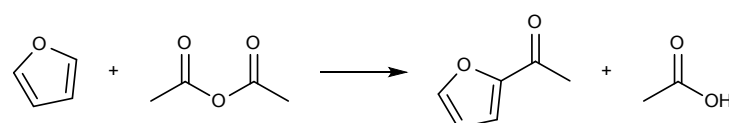
cross-ketonization, AE = 59 %



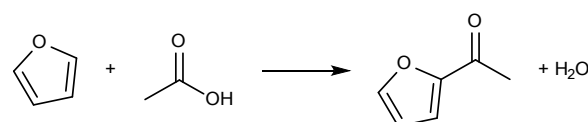
Wacker-type oxidation, AE = 60 %



Oxidation, AE = 40 %



Friedel-Crafts acylation with AAN, AE = 65 %



Friedel-Crafts acylation with AA, AE = 86 %

Figure S13: Processes proposed in the literature for the synthesis of AF.

Table S1: Comparison between the environmental factors (E) of the cross-ketonization pathway towards AF and the other methods reported in the literature.

synthetic pathway	process type	Catalyst	Solvent	E_R	E_{BP}	E_S	E_{Cat}	E_w	E_{Tot}	note	Ref.
	C, GP, Ht	ZrO ₂	/	0.30	1.74 (2.50)	0.00	6.59	0	1.74 (2.50)	a	this work
cross-ketonization	B, LP, Ht	FeO	C ₁₂ H ₂₆	1.62	4.77	14.61	1.29	/	14.61 (19.38)	b	27
	B, LP, Ht	MgO	C ₁₂ H ₂₆	0	0.77	2.32	0.25	/	2.32 (3.09)	c	28

Wacker oxidation	B, LP, Hm	Pd(II)(aPmic)(CH ₃ CN) ₂ (BF ₄) ₂	CH ₃ CN	2.00	0.67	2.55	0.13	/	5.35	d	65
oxidation	B, LP, Hm	Cu(OOCCH ₃) ₂ + H ₃ PMo ₁₂ O ₄₀	CH ₃ CN/H ₂ O	1.91	1.35	0.54	0.33	37.05	40.85	e	66
	B, LP, Ht	FePW ₁₂ O ₄₀ /g-C ₃ N ₄	CH ₃ CN	1.98	1.35	10.98	0.14	/	14.31	f	67
acylation	B, LP, Hm	Sn(CF ₃ SO ₃) ₂	CH ₃ NO ₂	1.21	0.55	1.18	0.22	5.51	8.67	g	68
		Zn(CF ₃ SO ₃) ₂	CH ₃ NO ₂	1.13	0.55	1.72	0.57	2.89	6.86	h	69
	B, LP, Ht	Sc(CF ₃ SO ₃) ₃ / terpyridine dendrimer ligand	CH ₃ CN	0.95	0.54	4.12	0.39	33.5	39.11	i	70
		HBEA (Si/Al = 12)	neat	4.26	0.54	/	0.19	/	4.99	j	71
		graphite / CH ₃ SO ₃ H	neat	0.02	/	/	3.56	54.5	58.08	k	72
		AIPW ₁₂ O ₄₀ / TFAAN	neat	0.07	/	/	1.42	6.86	8.35	l	73
		Fe ³⁺ exchanged K10 montmorillonite	neat	2.23	0.54	/	0.50	0	2.77	m	74
		Al ₂ O ₃ / TFAAN	neat	0.39	/	/	15.80	21.49	37.68	n	75
		sulfated TiO ₂	neat	0.57	0.54	/	1.91	/	3.02	o	76
		C, LP, Ht	HBEA (Si/Al = 27.6)	neat	5.05	0.54	/	5.89	0	0.54	p
C, GP, Ht	HZSM-5	/	0.86	0.81	/	4.58	0	1.67	q	64	

C = continuous, B = batch, GP = gas-phase, LP = liquid-phase, Ht = heterogeneous catalyst, Hm = homogeneous catalyst, E = environmental factor, R = unreacted reagent, BP = by-products, S = solvent, CAT = catalyst, W = work-up, TBHP = tert-butyl hydroperoxide, EF = ethyl furan, AAN = acetic anhydride, TFAAN = trifluoroacetic anhydride, DF = 2-dodecanoyl furan, 12-T = 12-tricosanone, F = furan.

^a The value of E_{BP} between brackets is the one calculated assuming that also AC and F are waste; continuous process, no work-up.

^b The value of E_{BP} between brackets is the one calculated assuming that also 12-T and F are waste; quantitative information not available; qualitative information: AF is extracted with DMSO, then the catalyst is filtered and washed with hexane before re-use.

^c The value of E_{BP} between brackets is the one calculated assuming that also 12-T and F are waste; quantitative information not available; qualitative information: AF is extracted with DMSO, then the catalyst is filtered and washed several time with chloroform before calcination at 600 °C and re-use.

^d quantitative information not available; qualitative information: homogeneous Pd(II) catalyst is separated by chromatography (waste: silica gel, ethyl acetate, petroleum ether).

^e aqueous H₃PMo₁₂O₄₀ is separated by extracting the reaction mixture with ethyl acetate, dichloromethane and ethanol, then is dried and re-used (waste: ethyl acetate, dichloromethane and ethanol).

^f quantitative information not available; qualitative information: reaction is quenched with saturated aqueous NH₄Cl solution, then the catalyst is filtered and washed with ethyl acetate before re-use (waste: NH₄Cl, ethyl acetate).

^g Sn(CF₃SO₃)₂ is separated by extraction with 10 mL of saturated aqueous NaHCO₃ (waste: NH₄Cl).

^h Zn(CF₃SO₃)₂ is separated by extraction with 10 mL of saturated aqueous NaHCO₃ (waste: NH₄Cl).

ⁱ Sc(CF₃SO₃)₃ / terpyridine dendrimer ligand is precipitated, filtered and washed with 18 mL of diethyl ether before re-use.

^j no information on work-up were given.

^k graphite is separated from the product and washed twice with 20 mL of chloroform before re-use. the E_{CAT} contribution consider only the mass of CH₃SO₃H co-catalyst (waste = chloroform, methanesulfonic acid).

^l AIPW₁₂O₄₀ is separated by filtration and washing with 20 mL of diethyl ether (waste : Et₂O); the E_{CAT} contribution consider only the mass of TFAAN co-catalyst (waste = diethyl ether, methanesulfonic acid).

^m quantitative information not available; qualitative information: the catalyst is separated by centrifugation after adding ethyl acetate (waste = ethyl acetate).

ⁿ Al₂O₃ is separated and washed with 50 mL of diethyl ether (waste = diethyl ether).

^o no information on work-up were given.

^p continuous process, no work-up.

^q continuous process, no work-up.