# **Supporting Information**

# Rational and Statistical Approaches in Enhancing the Yield of Ethylene Carbonate in Urea Transesterification with Ethylene Glycol over Metal Oxides

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#### 1. XRD: Hydrotalcite precursors of mixed metal oxides

Figure S1 shows the X-ray diffraction patterns of the as-synthesized materials. As-synthesized Zn-Al, Mg-Al, and Mg-Fe materials showed d-spacing values and reflection peaks which are characteristic to hydrotalcite materials as indicated in JCPDS file No. 14-0191 (sharp intense reflections of (003), (006) planes in the angle region  $(2\theta < 25^{\circ})$ , broad reflections of (012), (015) and (018) planes in the middle angle region  $(2\theta = 30-50^{\circ})$  and sharp reflections of (110), (113) and (116) planes in the high angle region  $(2\theta = 55-65^{\circ})$ ). The XRD pattern of as-synthesized Zn-Fe is notably different from the other hydrotalcite materials, but it is similar to SO<sub>4</sub>-LDH reported by Zhang et al.<sup>1</sup> The difference stems from the anion in the structure caused by the use of NaCO<sub>3</sub> for Zn-Fe synthesis instead of NaOH for the other materials. We observed that hydrotalcite structure cannot be formed with NaOH for Zn-Fe and the incorporation of CO<sub>3</sub><sup>-</sup> anion in Zn-Fe matrix was apparently necessary to form ordered layered material for this combination of cations.



Figure S1. XRD patterns of hydrotalcite precursors. Characteristic layered double hydroxide (LDH) phase is indicated with ♦ symbol.

# 2. XRD: Single metal oxides and hydrotalcite-derived mixed metal oxides

For the single metal oxides, the XRD pattern of ZnO was well characterized by the hexagonal wurtzite phase with characteristic peaks at 31.7, 34.2, and 36.1° (JCPDS: 36-1451). MgO showed clearly the cubic periclase phase ( $2\theta = 36.7$ , 42.8, 62.1°, JCPDS: 45-0946) and Fe<sub>2</sub>O<sub>3</sub> was crystallized in the hematite phase ( $2\theta = 24.5$ , 33.2, 35.7, 40.9, 49.5, 54.1, 62.5, 64.1°, JCPDS: 33-0664). Al<sub>2</sub>O<sub>3</sub> showed low crystallinity with characteristic peaks of  $\gamma$  phase ( $2\theta = 37.0$ , 45.6 and 67.1°, JCPDS: 29-0063).

After calcination at 725 K, the hydrotalcite structure (Figure S1) was destroyed with formation of new phases as shown in Figure S2. Zn-Al and Zn-Fe mixed oxides revealed the presence of

hexagonal ZnO phase. For Mg-Al and Mg-Fe mixed oxides, the cubic periclase phase of MgO was well recognized. In all Al- and Fe-containing materials, there was no aluminum oxide and iron oxide phases detected, implying the well incorporation and thus high dispersion of these metal ions in the oxide structures.

The XRD pattern of Zn-Fe reveals the reflections of zinc franklinite (ZnFe<sub>2</sub>O<sub>4</sub>), which is a single phase spinel-type structure consistent with that of the JCPDS card (22-1012), in addition to the hexagonal ZnO phase. The characteristic reflections of (111), (220), (311), (400), (422), (511), and (440) of the spinel structure were well recognized. This is in contrast to the results of Mg-Fe which showed mainly the reflections of cubic periclase phase of MgO and no such single mixed phase could be identified.



Figure S2. XRD patterns of calcined metal and mixed oxides. The symbols indicate the following crystal phases: ● hexagonal wurtzite phase of ZnO, ▼ cubic periclase phase of MgO and ◆ Franklinite ZnFe<sub>2</sub>O<sub>4</sub>.

### 3. Multivariate Curve Resolution (MCR)

MCR is a modern chemometric method for the resolution of multiple component responses in unknown unresolved reaction mixtures.<sup>2</sup> The MCR technique has the target to decompose matrix **D** into the pure contributions of the components of the reaction into the following matrices.

$$\mathbf{D}_{(r \times c)} = \mathbf{C}_{(r \times n)} \mathbf{S}_{(n \times c)}^{\mathrm{T}} + \mathbf{E}_{(r \times c)}$$

The experimental data are disposed in the matrix **D**. Rows r are the spectra at different times, n represents wavelength (since we apply MCR for time-resolved IR spectra) and columns c are the IR absorbance at different wavelength. **C** contains the concentration profiles of resolved compounds, **S** is the corresponding spectra matrix, and **E** represents unexplained variance (errors) in the data set.

The model corresponds to the general Lambert-Beer law; therefore it fits in elaborating ATR-IR data matrix. In MCR, the common first step is a preliminary estimation of the number of involved components (*n*) in the studied system using singular value decomposition and an evaluation of  $S^{T}$  or C. Afterward, these initial results are used to perform the constrained alternating least squares method in such a way to optimize them through an iterative process. At each cycle, a new estimation of  $S^{T}$  and C is calculated by solving alternatingly the two following least squares matrix equations:

$$\mathbf{S}^{\mathrm{T}} = (\mathbf{C})^{+}\mathbf{D}$$
$$\mathbf{C} = \mathbf{D}(\mathbf{S}^{\mathrm{T}})^{+}$$

Where  $(S^T)^+$  and  $(C)^+$  are the pseudoinverse of the  $S^T$  and C matrices, respectively. We have used MCR implemented in The Unscrambler® version 10.2 (CAMO Software).

# 4. Catalytic results for comprising reactions of urea transesterification with EG

Catalyst	Х <sub>2-НС</sub> / %	S <sub>EC</sub> / %	$S_{2-Ox} / %$	S <sub>DEG</sub> / %	S <sub>3-(2-EtOH)-2-Ox</sub> / %	S <sub>tea</sub> / %
blank	2.6	100	0	0	0	0
Al <sub>2</sub> O <sub>3</sub>	16.4	100	0	0	0	0
ZnO	66.5	90.7	0	0	0	9.3
MgO	93.8	76.4	0	9.1	0	14.5
Fe <sub>2</sub> O <sub>3</sub>	5.3	87.3	0	12.7	0	0
Zn-Al	48.6	100	0	0	0	0
Zn-Fe	24.7	100	0	0	0	0
Mg-Al	100	65.4	6.3	28.3	0	0
Mg-Fe	88.6	80.6	11.5	7.8	0	0

Table S1. Product selectivity and 2-HC conversion in the reaction of 2-HC in EG.

**Table S2.** Product selectivity and 2-Ox conversion in the reaction of 2-Ox with EG

Catalyst	X2-0x / %	S <sub>3-(2-EtOH)-2-Ox</sub> / %	S <sub>TEA</sub> / %
<u> </u>	17 (	01.6	0.4
blank	17.6	91.6	8.4
Al <sub>2</sub> O <sub>3</sub>	25.8	96.7	3.2
ZnO	23.0	98.2	1.8
MgO	33.7	97.4	2.5
Fe <sub>2</sub> O <sub>3</sub>	57.0	63.7	36.2
Zn-Al	28.6	94.4	5.6
Zn-Fe	12.4	90.8	9.1
Mg-Al	31.3	96.2	3.8
Mg-Fe	35.3	94.1	5.9

# 5. Kinetic study and kinetic modeling

### General assumptions

The kinetic study of reactions identified in this work was performed using the information of the matrix **C**, containing the profile concentrations (A<sub>i</sub>) of kinetically differentiable species (i.e. the involved reactants and products) extracted by MCR. The concentrations of identified chemical species were normalized ( $C_i = \frac{A_i}{A_{i,0}}$ ) to facilitate the modeling from the IR data obtained.

Kinetic study was performed with the followed assumptions and practical considerations

- 1. Constant volume of the reaction solution
- 2. Isothermal
- 3. No mass transfer limitations
- 4. No explicit influence of catalyst surface
- 5. We considered investigated component (urea, 2-HC, EC, 2-Ox) isolated, due to excess of other reactant (EG).
- 6. Concentration profiles of first 120 min were considered to calculate reaction order and k values to extract kinetic parameters more characteristic for the reaction towards the product side with minimized influence of possible products-catalyst interactions.

# Reaction of urea with EG



Reaction was assumed irreversible and all urea was assumed to lead to 2-HC after the reaction with EG. Based on the concentration profiles, it was identified that the reaction is a second order, whose rate is proportional to the square of the concentration of urea.  $\frac{dC_{urea}}{dt} = -k_{urea}C_{urea}^2$ Integrated rate law describes the concentration of the reactant at a given time as follows.

$$\frac{1}{C_{urea}} = \frac{1}{C_{urea,o}} + k_{urea}t$$

According to the integrated rate law for a second-order reaction, a plot of  $\frac{1}{C_{urea}/c_{urea,0}}$  versus t is

a straight line, as shown in part (b) in Figure S3.



**Figure S3.** Determination of order and rate constant for the reaction of urea with EG in the presence of Zn-Fe catalyst. The straight line in (b) is expected for a second-order reaction.

The slope of straight line gives us reaction rate constant, which is shown as  $k'_{urea} = k_{urea} \cdot C_{urea,0}$ . The rate constant values are summarized and listed in Table S3

Catalyst	blank	Al <sub>2</sub> O <sub>3</sub>	ZnO	MgO	Fe <sub>2</sub> O <sub>3</sub>	Zn-Al	Zn-Fe	Mg-Al	Mg-Fe
$k'_{\rm urea} \cdot 10^3 / \min^{-1}$	7.5	8.9	14.6	15.4	10.8	16.9	18.4	14.4	19.4
R <sup>2</sup>	0.979	0.994	0.987	0.982	0.988	0.991	0.987	0.961	0.990

**Table S3.** Rate constants k for reaction between urea and EG.

Reaction of 2-HC with EG



Non-reversibility of the reactions was assumed. The concentration profiles suggest an apparent first order reaction. In other words, the reaction rate is directly proportional to the concentration of 2-HC.

$$\frac{\mathrm{dC}_{2-\mathrm{HC}}}{\mathrm{dt}} = -\mathrm{k}_{2-\mathrm{HC}}\mathrm{C}_{2-\mathrm{HC}}$$

The integrated rate law for the reaction can be written using logarithmic.

$$\ln(C_{2-HC}) = \ln(C_{2-HC,0}) - k_{2-HC}t$$



**Figure S4.** Determination of order and rate constant for the reaction of 2-HC in EG in the presence of Zn-Fe catalyst. The straight line in (b) is expected for a first-order reaction.

As expected, the plot of the natural logarithm of 2-HC versus time is linear as shown in Figure S4 (b) taking Zn-Fe as an example. The slope of straight line gives the reaction rate constant  $k_{2-}$ <sub>HC</sub>, which was calculated for all catalysts and the results are listed in Table S4.

It is important to mention that there was no kinetic resolution between EC and 2-Ox; therefore, it was not possible to separate these two species by MCR. To obtain the respective concentration profile, experimentally obtained selectivity values towards EC (plus the secondary product) and toward 2-Ox (plus the secondary products) were used to scale the concentration values obtained for the mixture of EC and 2-Ox. In other words,  $C_{EC}$  and  $C_{2-Ox}$  were calculated as follows.

$$C_{EC} = C_{products} \cdot S_{EC}$$
$$C_{2-Ox} = C_{products} \cdot S_{2-Ox}$$

where 
$$S_{EC} = \frac{[EC]}{[EC] + [2 - Ox] + [DEG] + [TEA] + [3 - (2 - EtOH) - 2 - Ox]}$$
, and  
 $S_{2-Ox} = \frac{[2 - Ox]}{[EC] + [2 - Ox] + [DEG] + [TEA] + [3 - (2 - EtOH) - 2 - Ox]}$ 

Finally, the reaction rate constants of 2-HC to EC or 2-Ox were scaled as follow.

$$k_{2-HC \rightarrow EC} = S_{EC} \cdot k_{2-HC}$$
$$k_{2-HC \rightarrow 2-Ox} = S_{2-HC} \cdot k_{2-HC}$$

These rate constants were used for kinetic modeling and in fitting as shown later.

Table S4. Rate constants for the reaction of 2-HC in EG

Catalyst	blank	Al <sub>2</sub> O <sub>3</sub>	ZnO	MgO	Fe <sub>2</sub> O <sub>3</sub>	Zn-Al	Zn-Fe	Mg-Al	Mg-Fe
$k_{2-\text{HC}} \cdot 10^3 / \text{min}^{-1}$	0.2	0.4	1.3	2.4	0.5	0.8	0.6	2.4	2.4
<b>R</b> <sup>2</sup>	0.966	0.972	0.995	0.963	0.986	0.940	0.988	0.787	0.929

# Reaction of EC with EG



The reaction was assumed irreversible and was best matching apparently as a first order on EC concentration.

$$\frac{dC_{EC}}{dt} = -k_{EC}C_{EC}$$
$$ln(C_{EC}) = ln(C_{EC,0}) - k_{EC}t$$



**Figure S5.** Determination of order and rate constant for the reaction of EC with EG in the presence of Zn-Fe catalyst. The straight line in (b) is expected for a first-order reaction.

The plot of the natural logarithm of EC versus time is linear as shown in Figure S5 (b) taking Zn-Fe as an example. The slope of the straight line gives the reaction rate constant  $k_{\text{EC}}$ , which was calculated for all catalysts and results are summarized in Table S5.

Table S5. Rate constants for reaction between EC and EG

Catalyst	blank	Al <sub>2</sub> O <sub>3</sub>	ZnO	MgO	Fe <sub>2</sub> O <sub>3</sub>	Zn-Al	Zn-Fe	Mg-Al	Mg-Fe
$k_{\rm EC} \cdot 10^3 / {\rm min}^{-1}$	0.3	0.5	0.5	1.6	2.4	0.4	0.4	2.3	1.7
<b>R</b> <sup>2</sup>	0.924	0.905	0.966	0.991	0.994	0.939	0.966	0.939	0.931

Reaction of 2-Ox with EG



The reactions were assumed irreversible and found to follow first order kinetics.

$$\frac{dC_{2-Ox}}{dt} = -k_{2-Ox}C_{2-Ox}$$
$$\ln(C_{2-Ox}) = \ln(C_{2-Ox,0}) - k_{2-Ox}t$$

The plot of the natural logarithm of reactant concentration versus time is linear as shown in Figure S6 (b) taking Zn-Fe as an example.



**Figure S6.** Determination of order and rate constant for the reaction of 2-Ox with EG in the presence of Zn-Fe catalyst. The straight line in (b) is expected for a first-order reaction.

The slope of the straight line gives the reaction rate constant  $k_{2-\text{Ox}}$ , which was calculated for all catalysts and the results are summarized in Table S6.

Catalyst	blank	Al <sub>2</sub> O <sub>3</sub>	ZnO	MgO	Fe <sub>2</sub> O <sub>3</sub>	Zn-Al	Zn-Fe	Mg-Al	Mg-Fe
$k_{2-\text{Ox}} \cdot 10^3 / \text{min}^{-1}$	0.4	0.5	0.7	0.8	1.5	0.7	0.7	0.8	0.6
<b>R</b> <sup>2</sup>	0.850	0.979	0.959	0.956	0.997	0.926	0.904	0.956	0.930

Table S6. Rate constants for the reaction between 2-Ox and EG

# Kinetic modelling and fitting

Commonly, time-dependent concentration profiles of a chemical reaction can be modeled by a set of time-dependent ordinary differential equations in the form of  $\sum_{i} \frac{d}{dt} C_i(t) = f(t, C_i(t), k)$  where  $C_i(t)$  represents the concentrations of chemical species i at a time t.

Assuming the consecutive-parallel character of urea transesterification reaction and the above kinetic studies, we have set up a set of the rate equations.

$$\frac{dC_{urea}}{dt} = -k_{urea} \cdot C_{urea}^2$$
$$\frac{dC_{2-HC}}{dt} = k_{urea} \cdot C_{urea}^2 - k_{2-HC} \cdot C_{2-HC}$$
$$\frac{dC_{EC}}{dt} = k_{2-HC \rightarrow EC} \cdot C_{2-HC} - k_{EC} \cdot C_{EC}$$
$$\frac{dC_{2-Ox}}{dt} = k_{2-HC \rightarrow 2-Ox} \cdot C_{2-HC} - k_{2-Ox} \cdot C_{2-Ox}$$

After solving the differential equations simultaneously, concentration profiles of all four species can be obtained. An example of the solution for Zn-Fe (using the obtained k values obtained from the above studies) using the above equations is shown in Figure S7.



**Figure S7.** Calculated concentration profiles in urea transesterification for Zn-Fe based on k values obtained above from the comprising reactions.

Based on the set of differential equations, the kinetic rate constants can be fitted to the concentration profiles observed experimentally. We minimized the sum of squared errors to find rate constants from obtained kinetic model.

Prior to fitting, urea concentration was normalized by the initial concentration;  $C_{urea,n} = \frac{C_{urea}}{C_{urea,0}}$ . Concentrations of EC and 2-Ox obtained after MCR analysis were normalized using the final experimental concentrations:

$$C(t)_{i,n} = \frac{C(t)_i}{C_{i,\text{final}}} \cdot \frac{C_{i,\text{final}}^{exp}}{\sum C_{i,\text{final}}^{exp}} (1 - C_{\text{urea},n}^{\text{final}})$$

where

$$\sum C_{i,\text{final}}^{\exp} = C_{2-\text{HC},\text{final}}^{\exp} + C_{\text{EC},\text{final}}^{\exp} + C_{2-\text{Ox},\text{final}}^{\exp} + C_{\text{DEG},\text{final}}^{\exp} + C_{\text{TEA},\text{final}}^{\exp} + C_{3-(2-\text{EtOH})-2-\text{Ox},\text{final}}^{\exp}$$

The concentration profile of 2-HC was calculated by subtracting normalized concentrations of other products found in the IR monitoring:  $C_{2-HC,n} = 1 - C_{urea,n} - C_{EC,n} - C_{2-Ox,n}$ .

Thus obtained reaction rate constants of overall reactions (i.e. by means of fitting) are compared with the rate constants obtained from the kinetic studies of reaction steps ("single reaction", Table S7). The major differences were observed for the k values of the reaction of 2-HC. This implies that the reaction rate of 2-HC is significantly different when the reaction is initiated with 2-HC itself or starting from urea. The results have been interpreted as selective blocking of acidic sites by urea and promoted conversion of 2-HC by basic sites. The latter can lead to higher rate in conversion, but this does not necessarily impact the catalytic performance positively depending on promoted reaction pathways as discussed in the main text.

**Table S7**. Comparison of reaction rate constants. The rate constants obtained by fitting are shown with the range of 95% confidence interval.

Catalyst	k'urea · 10	<sup>3</sup> / min <sup>-1</sup>	<i>k</i> 2-нс·1	0 <sup>3</sup> / min <sup>-1</sup>	kec·10	<sup>3</sup> / min <sup>-1</sup>	k2-0x · 10	<sup>3</sup> / min <sup>-1</sup>
	single reaction	fitting	single reaction	fitting	single reaction	fitting	single reaction	fitting
blank	7.5	6.7±0.1	0.2	1.0±0.1	0.3	0.5±0.3	0.4	0
Al <sub>2</sub> O <sub>3</sub>	8.9	8.6±0.2	0.4	1.1±0.1	0.5	0	0.5	0
ZnO	14.6	10.5±0.4	1.3	13.9±0.8	0.5	1.6±0.3	0.7	3.2±1.1
MgO	15.4	13.6±0.4	2.4	7.1±0.2	1.6	1.0±0.1	0.8	4.0±1.7
Fe <sub>2</sub> O <sub>3</sub>	10.8	9.8±0.1	0.5	1.1±0.1	2.4	2.2±0.5	1.5	0
Zn-Al	16.9	13.5±0.5	0.8	8.2±0.3	0.4	1.5±0.2	0.7	4.0±2.0
Zn-Fe	18.4	14.8±0.5	0.6	10.4±0.4	0.4	1.6±0.2	0.7	0
Mg-Al	14.4	11.7±0.7	2.4	6.2±0.4	2.3	6.7±2.3	0.8	0.7±0.5
Mg-Fe	19.4	17.9±0.8	2.4	18.2±1.1	1.7	1.5±0.2	0.6	2.6±0.8

The normalized concentration profiles obtained by MCR analysis and fitted profiles are compared in Figure S8.





Figure S8. Comparison of experimental and fitted concentration profiles.



Figure S9. XRD patterns of (a) calcined Zn-Fe mixed oxides and (b) calcined tri-metallic mixed oxides. The symbols indicate the following crystal phases: ● hexagonal wurtzite phase of ZnO, ▼ cubic periclase phase of MgO and ♦ Franklinite ZnFe<sub>2</sub>O<sub>4</sub>.

Catalyst	NH <sub>3</sub> uptake / μmol·g <sup>-1</sup>	CO <sub>2</sub> uptake / μmol·g <sup>-1</sup>	A/B	BET surface area / m <sup>2</sup> ·g <sup>-1</sup>
Zn <sub>1</sub> -Fe <sub>2</sub>	0.070	0.75 0.094		25
Zn3-Fe1	0.056	0.44	0.127	21
Zn <sub>6</sub> -Fe <sub>1</sub>	0.016	0.12 0.133		16
Zn9-Fe1	0.011	0.15	0.071	12
Zn1.5-Mg1.5-Fe1	0.100	6.77	0.015	102
Zn3-Al0.5-Fe0.5	0.086	1.50	0.057	52

**Table S8.** NH<sub>3</sub>- and CO<sub>2</sub>-TPD results, A/B ratio, BET surface area of Zn–Fe and tri-metallic mixed oxides

Table S9. Catalytic results of the Zn–Fe and tri-metallic mixed oxides.

Catalyst	Y(EC) / mmol·g <sub>cat</sub> <sup>-1</sup>	S(EC) / %	S(2-Ox) / %	S(DEG) / %	S(3-(2-EtOH)-2-Ox) / %	S(TEA) / %
Zn <sub>1</sub> -Fe <sub>2</sub>	26.8	88.5	2.5	8.5	0	0.5
Zn3-Fe1	25.9	91.5	5.1	3.5	0	0
Zn <sub>6</sub> -Fe <sub>1</sub>	25.6	88.2	2.8	7.1	0	1.8
Zn9-Fe1	25.8	91.2	3.2	5.4	0.1	0
Zn1.5-Mg1.5-Fe1	16.3	52.7	4.1	42.6	0	0.5
Zn3-Al0.5-Fe0.5	20.2	93.6	3.3	3.1	0	0

# 7. Design of Experiments (DoE)

Our general strategy in DoE was based on a preliminary evaluation of all factors and possible interactions between factors using Fractional Factorial Experimental Design,<sup>3</sup> followed by an optimization of the significant factors using Central Composite Design.<sup>3b, 4</sup> All reactions were run in the batch reactor under the same condition using the same chemicals. As a catalyst Zn-Fe mixed oxide was chosen, due to its excellent catalytic performance. The complete set of experiments was performed in a random order, to avoid systematic error. The experimental design procedures implemented in The Unscrambler® version 10.2 from Camo software were used.

### Screening design

For Fractional Factorial Design, appropriate variables and their levels have to be selected. We have selected representative experimental parameters, namely EG/urea molar ratio, temperature, time and catalyst loading. For screening design, we evaluated a wide range of variables to obtain a clear picture of how these factors affect EC yield and selectivity. Two levels (extremes; upper and lower limits) were chosen for each of variables, named as "high" and "low". Temperature range was 393-443 K, initial EG/urea loading was in the range 4-10, amount of catalyst was varied from 1-3 wt% of EG, and time was restricted in 2-12 h. With these four design variables at high and low values each of them 2<sup>4-1</sup> experiments are required to resolve all effects by factors and factor interactions with resolution IV. Four response variables were evaluated: EC yield and selectivity, and selectivities of main side product 2-Ox and the secondary reaction product of EC (DEG). The obtained values are displayed in Table S10.

Design variables	Levels of de	sign variables
EG/urea ratio	4	10
Temperature	393 K	443 K
Time	2 h	12 h
Amount of the catalyst	1 wt% of EG	3 wt% of EG
Response variables	Range of ob	tained results
Y(EC)	0.1 mmol·g <sub>cat</sub> <sup>-1</sup> ·mmol <sub>urea</sub> <sup>-1</sup>	10.9 mmol·g <sub>cat</sub> <sup>-1</sup> ·mmol <sub>urea</sub> <sup>-1</sup>
S(EC)	26.8%	100%
S(2-Ox)	0%	19.9%
S(DEG)	0%	47.1%

Table S10. Levels of design and response variables obtained by screening experimental design.

To obtain a clear picture of the precision and the accuracy of the model and also to estimate experimental error, three center points (points, for which the value of every design variable is set at its mid-level) were evaluated. These considerations led to a set of 11 reactions which were performed in the batch reactor under the same conditions. The results of the catalytic runs are summarized in Table S11

Name	EG/ urea	Temp. / K	Time / h	Amount of catalyst /	Y <sub>EC</sub> / mmol·g <sub>cat</sub> -1·mmol <sub>urea</sub> -1	Sec / %	S2-Ox / %	Sdeg / %
				wt%				
1	4	393	2	1	0.219	100	0	0
ad	10	393	2	3	0.126	100	0	0
bd	4	443	2	3	3.64	80.1	0	18.3
ab	10	443	2	1	10.9	92.4	3.1	4.5
cd	4	393	12	3	7.031	95.7	2.4	1.5
ac	10	393	12	1	7.38	100	0	0
bc	4	443	12	1	4.71	26.8	19.9	47.1
abcd	10	443	12	3	3.029	55.7	6.1	36.8
cp01	7	418	7	2	6.52	93.7	3.4	2.9
cp02	7	418	7	2	5.38	86.5	5.9	6.5
cp03	7	418	7	2	4.95	79.5	7.5	10.6

Table S11. Results of a set of experiments suggested by screening design

The detailed analysis of variance is presented in Table S12. P-values and F-ratio show how well model fits responses – the lower p-values, the higher the probability, meaning that model would be adequate. For instance, p-values of  $Y_{EC}$  0.03 mean, that the model is valid with the significance level of 97%. According to p-values, all models seem adequate, although the significance level of the model for S(DEG) is less than 95%.

From the analysis of effects, it is also clear that most significant factors influencing selectivity of products are temperature and time. Neither EG/urea ratio nor catalyst loading had considerable effects on the response variables. Interaction of two variables – time and temperature was found to be the most significant to influence Y(EC). Interaction of temperature and time is also significant factor for selectivity of EC, 2-Ox and DEG.

			4			)		
ANOVA	Y(E	C)	S(E	C)	S(2-	Ox)	S(D	EG)
Summary	F-ratio	p-value	F-ratio	p-value	F-ratio	p-value	F-ratio	p-value
Model	12.06	0.032	13.36	0.028	9.44	0.046	7.94	0.058
Variables								
EG/urea (A=BCD)	3.76	0.15	4.82	0.11	4.41	0.12	1.84	0.26
Temperature (B=ACD)	6.23	0.087	46.26	0.006	18.07	0.023	31.17	0.01
Time (C=ABD)	5.74	0.096	20.75	0.02	16.24	0.027	11.04	0.04
Amount of the catalyst (D=ABC)	69.6	0.052	0.35	0.59	5.38	0.10	0.07	0.80
EG/urea*temp (AB=CD)	3.14	0.17	3.18	0.17	1.78	0.27	1.44	0.31
EG/urea*time (AC=BD)	7.97	0.066	1.01	0.38	9.52	0.054	0.012	0.92
temp*time (BC=AD)	47.85	0.0062	17.17	0.02	10.66	0.047	10.01	0.05

Table S12. ANOVA Summary for response variables for screening design

Interaction between variables can also be represented graphically by plotting parameters against one of the variables overlaid with a second one. If the lines run in parallel, there is an independence of these variables, but if the lines are divert this indicates the presence of interaction between them. Figure S10 displays interaction of variables "time" and "temperature" for parameters Y(EC), S(EC), S(2-Ox) and S(DEG). A positive interaction between two variables means that when one variable increases the effect exerted by the second variable increases. From the plots it is clear that these variables have strong negative interaction in case of EC yield. For product selectivity positive interaction between "time" and "temperature" was observed. The presence of such interaction implies that different optimum reaction times would exist at different temperatures, which is completely ignored in the single-factor-at-a-time method, where the interdependence of factors would have been missed.



Figure S10. Time-temperature interaction graphs for screening study

After identifying the important variables, we initiated optimization study applying Central Composite Design in order to obtain response surface and optimum values for temperature and time.

# **Optimization design**

As it was shown previously, screening design is linear, which means it only has two levels. They connect all points with straight lines and a mathematical optimum cannot be modelled. The model of the reaction can be refined with a more detailed second non-linear study, such as response surface study (RSM) which is used in this work. The points in the RSM model were

chosen according to Central Composite Design. In this case, results of experiments performed in optimization design were analysed independently from results of screening design, i.e. previous values were not used. The factors investigated in this study were the only important ones identified earlier, i.e. reaction time and temperature.

Central Composite Design was performed to examine important factors and finally generate response surfaces for the EC yield and selectivity as a function of two selected parameters (reaction time and temperature). Since we set the defined limits for the two variables, Inscribed Central Composite Design was applied to explore the design space over the central point which requires 5 levels (possible values) of each variable. Two variables at five levels and two center samples were used, giving in total 10 experiments. The values of the variables are listed in Table S13.

Design variables	Levels of des	sign variables		
Temperature	393 K 443 K			
Time	2 h	12 h		
Response variables	Range of obtained results			
Y(EC)	$0.9 \text{ mmol} \cdot \text{g}_{\text{cat}}^{-1} \cdot \text{mmol}_{\text{urea}}^{-1}$	2.9 mmol $\cdot$ g <sub>cat</sub> <sup>-1</sup> $\cdot$ mmol <sub>urea</sub> <sup>-1</sup>		
S(EC)	67%	100%		

Table S13. Levels of design and response variables obtained with optimization design.

The other experimental variables were fixed at the optimum values previously defined: EG/urea ratio 10 and the catalyst amount of 3 wt% of EG. The summary of performed experiments in optimization design is shown in Table S14.

Name	Temp / K	Time / h	Yec /	Sec /	Sox /	Sdeg /
	_		mmol·g <sub>cat</sub> <sup>-1</sup> ·mmol <sub>urea</sub> <sup>-1</sup>	%	%	%
Cube1	400.3	3.5	1.01	96.7	3.3	0
Cube2	435.6	3.5	4.07	82.1	7.2	8.9
Cube3	400.3	10.5	2.75	98.7	0	1.3
Cube4	435.6	10.5	3.36	59.8	27.6	10.0
Axial	393	7	1.35	100	0	0
A(low)						
Axial	443	7	2.75	67.1	21.7	9.3
A(high)						
Axial	418	2	3.54	86.1	8.3	5.2
B(low)					_	
Axial	418	12	1.91	98.4	0	1.6
B(high)		_	/			
cp01	418	7	2.76	92.8	3.7	3.3
cp02	418	7	2.82	93.5	2.7	3.8

**Table S14.** Results of experiments in optimization design.

The model generated by optimization design for EC selectivity is approximation of reality which is demonstrated in ANOVA table (Table S15). Significance level of the model (p-value) is 0.05 indicating that the model is useful. On the other hand, probability for the model of EC yield to be significant is quite low, 87% according to the p-value 0.13. This implies the lower level of confidence for estimating the optimum experimental condition for EC yield using the model.

ANOVA Summary	Y(EC)		S(EC)	
-	F-ratio	p-value	F-ratio	p-value
Model	6.70	0.13	19.28	0.05
Temperature (A)	25.54	0.03	91.45	0.01
Time (B)	5.64	0.14	13.07	0.06
Temp*time (AB)	8.89	0.09	11.57	0.07
Temp*temp (AA)	1.92	0.3	11.48	0.07
Time*time (BB)	0.13	0.75	0.63	0.51
Temp*temp*temp (AAA)	23.42	0.04	97.04	0.01
Time*time*time (BBB)	8.22	0.10	13.80	0.06

Table S15. ANOVA summary of the response variables of optimization design

The results of the optimization study are depicted at the response surfaces where the optima are clearly visualized. Figures S11 and S12 show the response surfaces of the two variables: EC yield and selectivity, respectively. Analysing these 3D plots following general conclusions can be drawn:

- The higher the temperature and the shorter the reaction time, the better EC yield.
- The lower the temperature, the higher EC selectivity.

Optima in EC yield and selectivity are clearly defined on the response surfaces: 5.2 mmolg<sub>cat</sub><sup>-1</sup>·mmol<sub>urea</sub><sup>-1</sup> yield when at 438.8 K in 2 h, and 118% EC selectivity at 395 K after 12 h. Although the analysis of variance indicated that predicted model for Y(EC) has a relatively low significance level, the model of S(EC) appears to be adequate (p-values around 0.05) as mentioned above.



Figure S11. Response surface of Y(EC)



Figure S12. Response surface of S(EC)

To substantiate both generated models, verification experiments were performed under the two conditions (predicted by  $S_{EC}$  model and  $Y_{EC}$  model) using the Zn-Fe mixed oxide. Both reaction conditions were highly favorable for the EC synthesis. The first condition resulted in an excellent EC selectivity (99.6%) and a good EC yield (16 mmol·g<sub>cat</sub><sup>-1</sup>), while the second case led to a highest obtained EC yield (28.59 mmol·g<sub>cat</sub><sup>-1</sup>) and a good EC selectivity (93.3%). These are considerable improvements compared to the EC yield and selectivity obtained in our standard condition (423 K and 6 h) which yielded 25.9 mmol<sub>EC</sub>·g<sub>cat</sub><sup>-1</sup> with 91.5% EC selectivity.

The obtained EC yield for the latter case was lower than that predicted by the model (44.09 mmol $\cdot$ g<sub>cat</sub><sup>-1</sup>). The deviation from the model is likely due to the high complexity of underlying parameters influencing EC yield. Since the investigated reaction of urea transesterification with EG is consecutive and parallel with additional side reactions, it is not an easy task to predict precisely the yield of the target product. Nevertheless, the generated models are found to be useful approximation of the EC yield and selectivity, well predicting a set of parameters that yield excellent catalytic results.

#### References

- 1. Zhang, H.; Wen, X.; Wang, Y. X., J. Solid State Chem. 2007, 180, 1636-1647.
- 2. Tauler, R., Chemometr. Intell. Lab. 1995, 30, 133-146.
- (a) Araujo, P. W.; Brereton, R. G., *TrAC, Trends Anal. Chem.* 1996, *15*, 26-31; (b) Massart D. L.; Vandeginste B. G. M.; Buydens L. M. C.; De Jong S.; Lewi P. J.; Smeyers-Verbeke, J., *Handbook of Chemometrics and Qualimetrics: Part A.* Elsevier: Amsterdam, 1997; Vol. 20A.
- 4. Araujo, P. W.; Brereton, R. G., TrAC, Trends Anal. Chem. 1996, 15, 63-70.