Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Evaluating the toxicity of biomass derived platform chemicals

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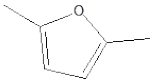
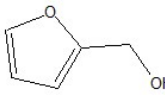
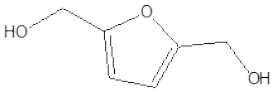
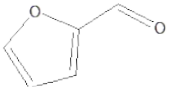
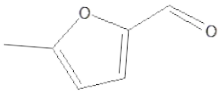
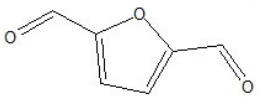
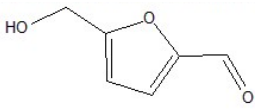
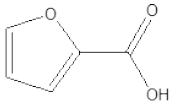
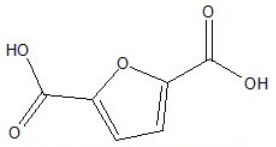
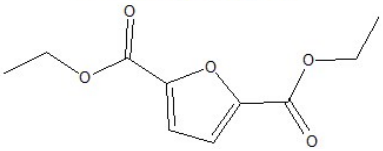
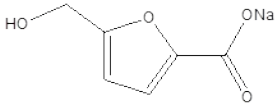
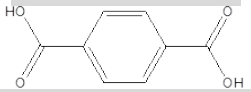
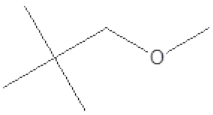
Table A1. Chemical structure, purity and synthesis (if applicable) of the compounds.

Chemical compound (common name)	Code name	Chemical structure	Details
2,5-Dimethylfuran	**1**		Aldrich, Ref. 177717, 99 %
Furan-2-yl-methanol (furfuryl alcohol)	**2**		Aldrich, Ref. 18112, 98 %, distilled under vacuum, >98 %[e]
Furan-2,5-diyldimethanol (DHMF)	**3**		Prepared following the method described by us and purified by silica flash chromatography using EtOAc/Hexane,[a] ≥ 97 %[d,e]
Furan-2-carbaldehyde (furfural)	**4**		Aldrich, Ref. 18.591-4, 99 %, distilled under vacuum, 99 %[c]
5-Methylfuran-2-carbaldehyde (5-methylfurfural)	**5**		Alfa Aesar, Ref. A13264, 98%
Furan-2,5-dicarbaldehyde	**6**		Prepared following the method described by us, the resulting crude mixture was purified by flash chromatography with Et_2O/Hexane and the collected solid was further recrystallized from hexane/EtOAc, [a] 99 %[c]
5-(Hydroxy-methyl)furan-2-carbaldehyde (5-hydroxymethyl-furfural)	**7**		Prepared following the method described by us and purified by column chromatography with silica gel (hexane/ethyl acetate 1:1),[a] 98 %[c]
2-furoic acid	**8**		Aldrich, Ref. F20505, 98 %
Furan-2,5-di-carboxylic acid (dehydromucic acid, FDCA)	**9**		Prepared following the method described by us and purified by precipitation,[a] ≥ 97 %[c]
Diethyl furan-2,5-dicarboxylate	**10**		Prepared following the method described by us and purified by silica flash chromatography using EtOAc/Hexane,[b] ≥ 97 %[d]
Sodium 5-(hydroxymethyl)furan-2-carboxylate (HMFA)	**11**		Prepared following the method described by us and purified crystallization with ethanol/ethyl acetate 1:50) (100 mL),[a] 99 %[c]

5-(((Tertbutyl-dimethylsilyl)-oxy)methyl)-furan-2-carbaldehyde	**12**		Prepared following the method described by us and purified by distillation (100ºC/0.8 mbar),[a] 98 %[c]
Terephtaldehyde	**13**		Aldrich, Ref. 86410, ≥98 %
Terephthalic acid	**14**		Alfa Aesar, Ref. A12527, ≥98 %
4-Oxopentanoic acid (levulinic acid)	**15**		Aldrich, Ref. L2009, 98 %
Ethyl 4-oxopentanoate (ethyl levulinate)	**16**		Aldrich, Ref. W244201, ≥98 %
Hexane-1,6-diol	**17**		Aldrich, Ref. H11807, 97%
***Tert*-butylmethyl ether** (MTBE)	**18**		Aldrich, Ref. 179787, , ≥98 %

[a] R. F. M. Frade, J. A. S. Coelho, S. P. Simeonov and C. A. M. Afonso, *Toxicology Research*, 2014, **3**, 311-314. [b] J. A. S. Coelho, A. F. Trindade, V. Andre, M. Teresa Duarte, L. F. Veiros and C. A. M. Afonso, *Organic & Biomolecular Chemistry*, 2014, **12**, 9324-9328. [c] The HPLC purity was determined by comparing the integration area of the main signal with other observed minor peaks and are represented in the chromatograms by relative area. Retention times were determined by using the mobile phase gradient from 1:99 to 90:10 in 50 min. The HPLC analysis was performed on Dionex P680 pump, Dionex UVD 340S diode array detector, detection at 275 and 225 nm, manual injector with 20 μL loop, column HICHROM C18, 250x4.6mm, or Kromasil 100, C18, 250x4.6mm. Mobile phase gradient from 1:99 to 50:50 for 40 min acetonitrile:water, and then 50:50 for the time indicated in the chromatogram, flow 1 mL/min. [d] Not detected impurities by ^{1}H NMR using Bruker AMX 300 or Bruker AMX 400 using $CDCl_3$, D_2O or DMSO-d_6 as solvents and $(CH_3)_4Si(^{1}H)$ as internal standard. [e] Purity estimated by GC-MS. The GC–MS analyses were performed on Gas Chromatograph Mass Spectrometer-QP2010S, *Shimadzu* by using the column TRB-5MS-Teknokroma (30 m × 0.25 mm × 0.25 μm). GC program: column oven $T_{initial}$=: 50.0 °C, T_{final}=: 250.0 °C, slope = 5ºC/min ; injection temperature: 250 °C; pressure: 77.9 kPa, total flow: 17.7 mL/min; column flow: 1.34 mL/min; linear velocity: 42.0 cm/sec; purge flow: 3.0 mL/min split ratio: 10.0, high press. inj. pressure: 100.0 kPa, high press. inj. time: 1.00 min. MS program: start

time: 3.00 min; end time: 50.00 min; event time: 0.50 s; scan speed: 666; start: m/z = 40.00; end: m/z = 350.00.

Table A2. Median effective concentration (EC_{50}) values, in mM, and respective confidence intervals (c. i.) at 95 %, obtained with *Vibrio fischeri* (Microtox system) after 5, 15 and 30 minutes of exposure to different furans and derivatives.

Code name	Chemical structure	EC_{50} at 5 min (mM) (95 % c. i.)	EC_{50} at 15 min (mM) (95 % c. i.)	EC_{50} at 30 min (mM) (95 % c. i.)
1		**0.349** (0.196 – 0.501)	**0.253** (0.154 – 0.352)	**0.244** (0.173 – 0.315)
2		**1.704** (1.122 – 2.296)	**1.337** (0.941 – 1.724)	**1.031** (0.772 – 1.296)
3		**2.453** (2.039 – 2.875)	**2.391** (2.078 – 2.695)	**2.266** (1.930 – 2.6023)
4		**3.531** (2.344 – 4.417)	**2.656** (1.958 – 3.344)	**1.958** (1.479 – 2.448)
5		**0.778** (0.671 – 0.886)	**0.861** (0.758 – 0.964)	**0.973** (0.855 – 1.091)
6		**0.316** (0.215 – 0.417)	**0.172** (0.122 – 0.2236)	**0.184** (0.101 – 0.267)
7		**3.230** (2.651 – 3.810)	**3.056** (2.548 – 3.556)	**3.087** (2.262 – 3.905)
8		**0.139** (0.132 – 0.147)	**0.138** (0.128 – 0.146)	**0.133** (0.127 – 0.139)
9		**0.067** (0.060 – 0.074)	**0.062** (0.055 – 0.069)	**0.061** (0.053 – 0.069)
10		**0.364** (0.285 – 0.443)	**0.403** (0.317 – 0.491)	**0.437** (0.372 – 0.505)
11		**8.116** (6.220 – 10.012)	**6.622** (5.006 – 8.232)	**5.994** (4.634 – 7.354)
12		**0.015** (0.014 – 0.016)	**0.017** (0.017 – 0.018)	**0.023** (0.020 – 0.025)
13		**0.063** (0.050 – 0.075)	**0.057** (0.051 – 0.064)	**0.050** (0.045 – 0.055)

14		**n.d.*** **not toxic**	**n.d.*** **not toxic**	**n.d.*** **not toxic**
15		**0.229** (0.220 – 0.239)	**0.240** (0.228 – 0.250)	**0.245** (0.234 – 0.254)
16		**1.757** (1.431 – 2.083)	**3.271** (2.167 – 4.368)	**4.819** (2.889 – 6.750)
17		**7.627** (5.381 – 9.873)	**9.347** (6.212 – 12.475)	**10.068** (6.025 – 14.119)
18		**0.234** (0.167 – 0.300)	**0.236** (0.149 – 0.323)	**0.240** (0.111 – 0.367)

***n.d.-** value of EC_{50} not defined due to the very low solubility in water of the compound.

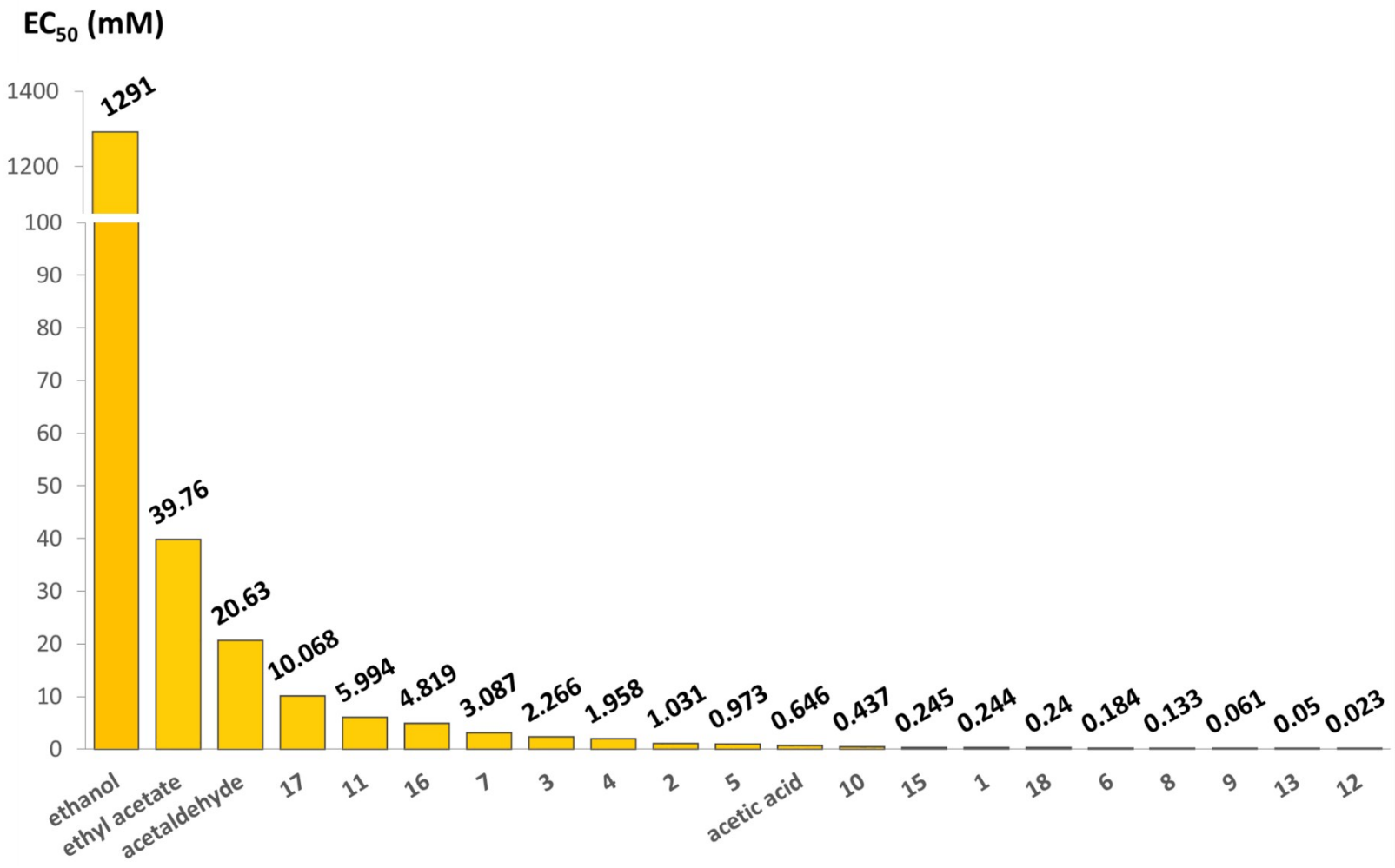


Figure A1. EC_{50} results (in mM units) obtained for the chemical compounds tested in this work.

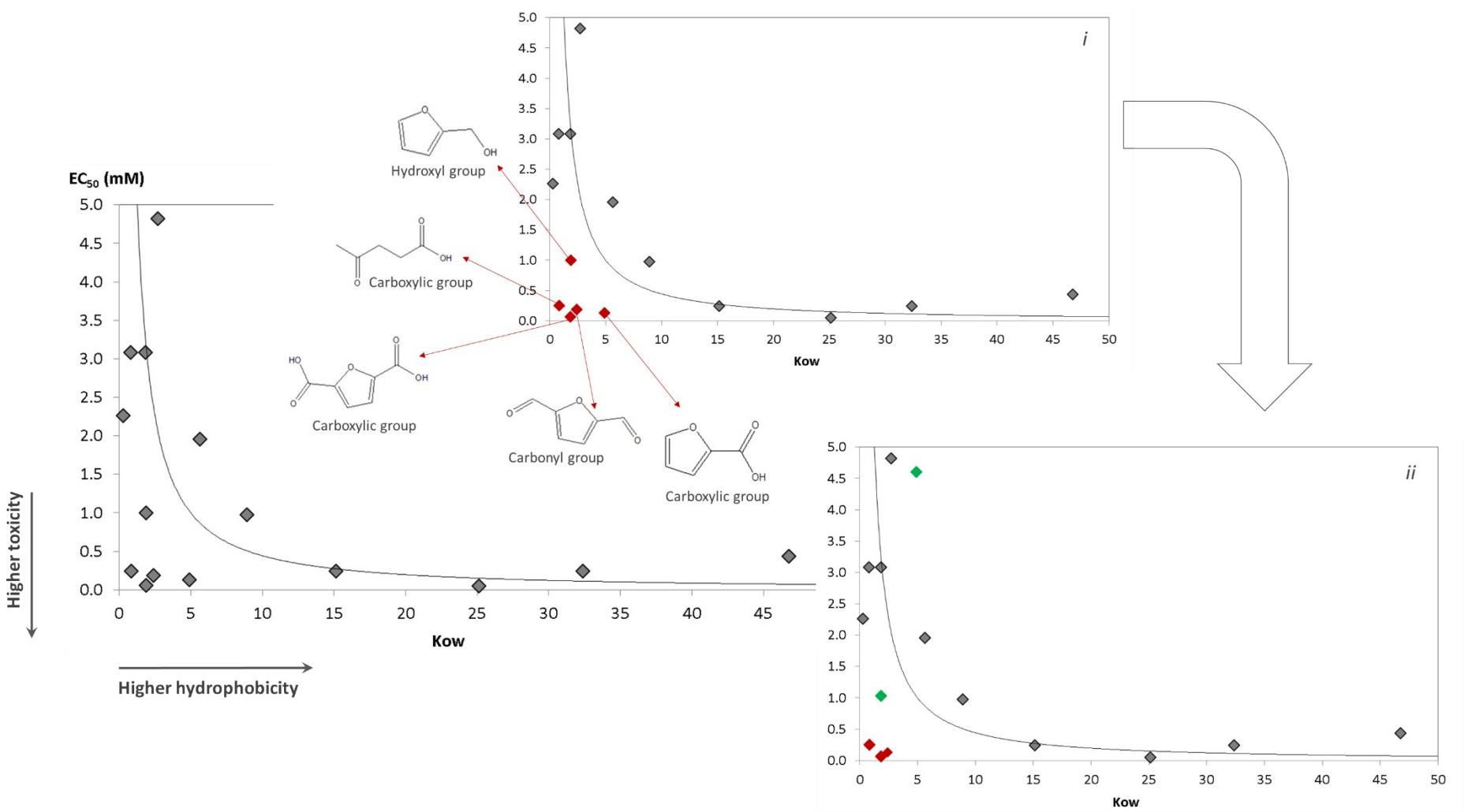

EC50 (mM)
Kow
Higher toxicity
Higher hydrophobicity
Hydroxyl group
Carboxylic group
Carboxylic group
Carbonyl group
Carboxylic group
i
ii
Kow
Kow

Figure A2. Correlation between the values of median effective concentration (EC_{50}), in mM, obtained after 30 minutes of exposure between the compounds under study and the marine bacteria *Vibrio fischeri* and the octanol-water partition coefficient (K_{ow}). The insets are representing the compounds with an exceptional behavior to the relation (red diamonds) and the respective chemical structures identified: before neutralization (i) and after neutralization (ii). The reader should note that the green diamonds are representing the compounds with exceptional behavior that after neutralization are following the tendency between the toxicity and octanol-water partition coefficient.