

Supporting Information

Ecotoxicological assessment of biomass-derived furan platform chemicals using aquatic and terrestrial bioassays

Stella Parmaki^a, Marlen I. Vasquez^{a, b}, Maria Patsalou^a, Rafael F. A. Gomes^c, Svilen P. Simeonov,^{c, d} Carlos A. M. Afonso^c and Michalis Koutinas^{a, *}

^a Department of Chemical Engineering, Cyprus University of Technology, 30 Archbishop Kyprianou Str., 3036, Limassol, Cyprus

^b European University of Technology, 30 Archbishop Kyprianou Str., 3036, Limassol, Cyprus

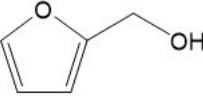
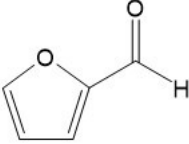
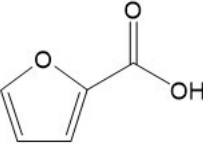
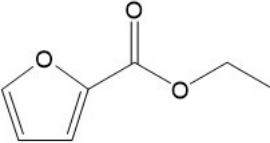
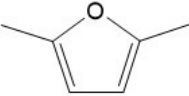
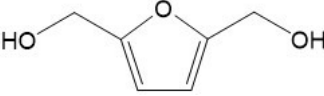
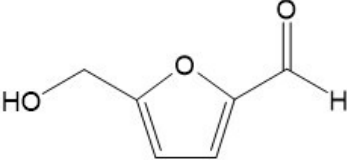
^c Research Institute for Medicines (iMed.Ulisboa), Faculty of Pharmacy, Universidade de Lisboa, Av. Prof. Gama Pinto, 1649-003, Lisbon, Portugal

^d Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Acad. G. Bonchev str., bl. 9, 1113, Sofia, Bulgaria

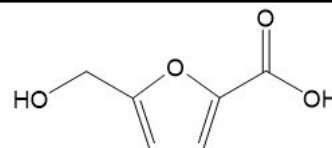
* Corresponding author.

E-mail address: michail.koutinas@cut.ac.cy (M. Koutinas).

Table S1. Chemical structure, purity and synthesis (if applicable) of the compounds applied in the study.

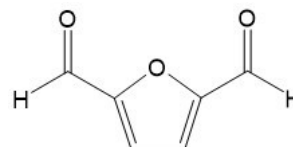
Chemical compound (common name)	Chemical structure	Details
furan-2-yl-methanol (Furfuryl alcohol)		Alfa Aeser, Ref. A10968, distilled under vacuum ^a
furan-2-carbaldehyde (Furfural)		Alfa Aeser, Ref. A16167, distilled under vacuum ^a
furan-2-carboxylic acid or 2-furoic acid (FA)		Sigma Aldrich, Ref. F20505
ethyl 2-furoate or ethyl furan-2-carboxylate (EFA)		Alfa Aeser, Ref. A13909
2,5-dimethylfuran (DMF)		Sigma Aldrich, Ref. 177717
furan-2,5-diylmethanol or 2,5-bis(hydroxymethyl)furan (DHMF)		Prepared and purified following the method described by the authors ^{1,a}
5-hydroxymethyl furfural or 5-(hydroxymethyl)furan-2-carbaldehyde (HMF)		Prepared and purified following the method described by the authors ^{1,a}

5-(hydroxymethyl)furan-2-carboxylic acid
(HMFA)



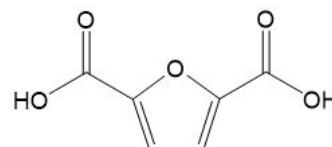
Prepared and purified following the method described by the authors^{1,a}

2,5-furandicarboxaldehyde or furan-2,5-dicarbaldehyde
(DFA)



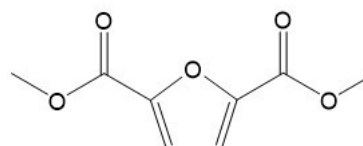
Prepared and purified following the method described by the authors^{2-4,a}

2,5-furandicarboxylic acid or furan-2,5-dicarboxylic acid
(FDCA)



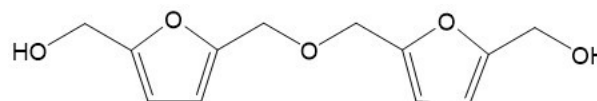
Prepared and purified following the method described by the authors^{2-4,a}

dimethyl furan-2,5-dicarboxylate
(DFDC)



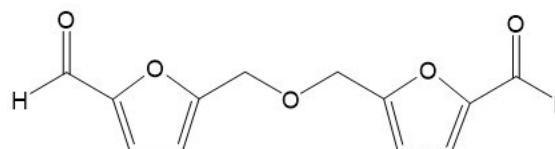
Prepared and purified following the method described by the authors for dimethyl ester^{5,a}

(5,5'-(oxybis(methylene))bis(furan-5,2-diyl))dimethanol
(OBMFA)



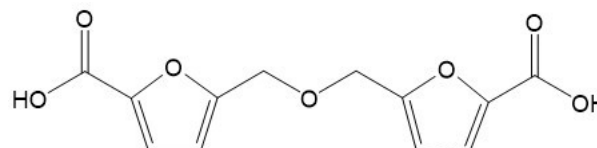
Prepared and purified following the method described by the authors for the monoreduction of aldehyde^{2,a}

5,5'-(oxybis(methylene))bis(furan-2-carbaldehyde)
(OBMF)



Prepared and purified following the method described by the authors^{2-6,a}

5,5'-(oxybis(methylene))bis(furan-2-carboxylic acid)
(OBCA)



Prepared and purified following the method described by the authors for the monooxidation of aldehyde^{2,a}

^a Purity (> 97 %) determined by ¹H NMR (Bruker Fourier 300)

Table S2: Ecotoxicological effects of furan compounds in different organisms.

Chemical name	Organism scientific name	Organism common name	Concentration	Endpoint	Exposure time	Reference
Freshwater algae						
Furfuryl alcohol	<i>Chlorococcales</i>	Green algae	1000 mg L ⁻¹	EC ₁₀	1 d	ECOTOX ⁷
			> 1000 mg L ⁻¹	EC ₅₀	1 d	ECOTOX ⁷
Furfural	<i>Anabaena flosaquae</i>	Blue-green algae	61 (39-93) mg L ⁻¹	EC ₅₀	4 d	ECOTOX ⁷
			12 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
	<i>Chlorococcales</i>	Green algae	84 mg L ⁻¹	EC ₁₀	1 d	ECOTOX ⁷
			570 mg L ⁻¹	EC ₅₀	1 d	ECOTOX ⁷
			<i>Navicula pelliculosa</i>	Diatom	32 (23-45) mg L ⁻¹	EC ₅₀
	<i>Raphidocelis subcapitata</i>	Green algae	5.8 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
			19.9 mg L ⁻¹	EC ₅₀	3 d	Zuriaga et al. ⁸
43 (39-48) mg L ⁻¹			EC ₅₀	4 d	ECOTOX ⁷	
HMF	<i>Raphidocelis subcapitata</i>	Green algae	16.5 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
			110.2 (106.8-115.5) mg L ⁻¹	EC ₅₀	3 d	Muralidhara et al. ⁹
Freshwater crustaceans						
Furfuryl alcohol	<i>Daphnia magna</i>	Water flea	63 mg L ⁻¹	EC ₀	1 d	ECOTOX ⁷
			110 ± 2 mg L ⁻¹	EC ₅₀	1 d	Zuriaga et al. ⁸
			328 mg L ⁻¹	EC ₅₀	1 d	ECOTOX ⁷
			4000 mg L ⁻¹	EC ₁₀₀	1 d	ECOTOX ⁷
			31 mg L ⁻¹	LC ₀	1 d	ECOTOX ⁷
			115 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			500 mg L ⁻¹	LC ₁₀₀	1 d	ECOTOX ⁷
Furfural	<i>Daphnia magna</i>	Water flea	13 mg L ⁻¹	EC ₀	1 d	ECOTOX ⁷
			29 mg L ⁻¹	EC ₅₀	1 d	ECOTOX ⁷
			31 ± 1 mg L ⁻¹	EC ₅₀	2 d	Zuriaga et al. ⁸
			51 mg L ⁻¹	EC ₁₀₀	1 d	ECOTOX ⁷

			10 mg L ⁻¹	EC ₀	1 d	ECOTOX ⁷
			10 mg L ⁻¹	EC ₀	2 d	ECOTOX ⁷
			20.4 (16.4-25.2) mg L ⁻¹	EC ₅₀	2 d	ECOTOX ⁷
			56 mg L ⁻¹	EC ₁₀₀	1 d	ECOTOX ⁷
			56 mg L ⁻¹	EC ₁₀₀	2 d	ECOTOX ⁷
			25 mg L ⁻¹	LC ₀	1 d	ECOTOX ⁷
			36 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			52 mg L ⁻¹	LC ₁₀₀	1 d	ECOTOX ⁷
			39 (35-43) mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷
			13 (11-15) mg L ⁻¹	LC ₅₀	3 d	ECOTOX ⁷ , TOXNET ¹⁰
			18 mg L ⁻¹	LOEC	2 d	ECOTOX ⁷
			3.7 mg L ⁻¹	LOEC	21 d	ECOTOX ⁷
			3.7 mg L ⁻¹	LOEC	21 d	ECOTOX ⁷
			10 mg L ⁻¹	NOEC	2 d	ECOTOX ⁷
			1.9 mg L ⁻¹	NOEC	21 d	ECOTOX ⁷
			1.9 mg L ⁻¹	NOEC	21 d	ECOTOX ⁷
			5.7 mg L ⁻¹	NOEL	2 d	ECOTOX ⁷
	<i>Gammarus pseudolimnaeus</i>	Scud	11.89 (9.18-15.4) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
HMF	<i>Daphnia magna</i>	Water flea	> 500 mg L ⁻¹	EC ₅₀	1 d	Muralidhara et al. ⁹
			36.5 (30.0-45.1) mg L ⁻¹	EC ₅₀	2 d	Muralidhara et al. ⁹
			55.3 (50.3-60.9)	EC ₅₀	2 d	Swart et al. ¹¹
			62 (53-78) mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			34 (27-43) mg L ⁻¹	LC ₅₀	3 d	ECOTOX ⁷ , TOXNET ¹⁰
Freshwater fish						
Furfuryl alcohol	<i>Leuciscus idus ssp. melanotus</i>	Carp	113 mg L ⁻¹	LC ₀	2 d	ECOTOX ⁷
			226 mg L ⁻¹	LC ₀	2 d	ECOTOX ⁷
			701 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷
			1356 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷
			1495 mg L ⁻¹	LC ₁₀₀	2 d	ECOTOX ⁷

			1700 mg L ⁻¹	LC ₁₀₀	2 d	ECOTOX ⁷
	<i>Pimephales promelas</i>	Fathead minnow	7240 mg L ⁻¹	EC ₅₀	2 h	ECOTOX ⁷
Furfural	<i>Cyprinodon variegatus</i>	Sheepshead minnow	14 (12-15) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			4.2 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
	<i>Gambusia affinis</i>	Western mosquitofish	44 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			24 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷ , TOXNET ¹⁰
			24 mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷ , TOXNET ¹⁰
	<i>Lepomis macrochirus</i>	Bluegill	5.8 mg L ⁻¹	EC ₅₀	4 d	Zuriaga et al. ⁸
			32 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			16 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷ , TOXNET ¹⁰
			5.8 (3.2-9) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			3.2 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
	<i>Leuciscus idus ssp. melanotus</i>	Carp	12 mg L ⁻¹	LC ₀	2 d	ECOTOX ⁷
			29 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷
			46 mg L ⁻¹	LC ₁₀₀	2 d	ECOTOX ⁷
	<i>Oncorhynchus mykiss</i>	Rainbow trout	3.62 mg L ⁻¹	EC ₅₀	4 d	Zuriaga et al. ⁸
			3.06 (2.14-4.53) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			0.56 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
	<i>Pimephales promelas</i>	Fathead minnow	726 mg L ⁻¹	EC ₅₀	2 h	ECOTOX ⁷
			20.6 mg L ⁻¹	EC ₅₀	4 d	Zuriaga et al. ⁸
			> 50 mg L ⁻¹	LC ₅₀	1 h	ECOTOX ⁷ , TOXNET ¹⁰
			48 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			> 50 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			37 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷ , TOXNET ¹⁰
			32 mg L ⁻¹	LC ₅₀	3 d	ECOTOX ⁷ , TOXNET ¹⁰
			33 mg L ⁻¹	LC ₅₀	3 d	ECOTOX ⁷ , TOXNET ¹⁰
			16.1 (13.4-19.3) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			21.02 (16.79-26.35) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			32 mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷ , TOXNET ¹⁰
			0.095 mg L ⁻¹	LOEC	32 d	ECOTOX ⁷

			0.426 mg L ⁻¹	LOEC	33 d	ECOTOX ⁷
			0.915 mg L ⁻¹	LOEC	33 d	ECOTOX ⁷
			0.915 mg L ⁻¹	LOEC	33 d	ECOTOX ⁷
			0.624 mg L ⁻¹	MATC	33 d	ECOTOX ⁷
			< 0.426 mg L ⁻¹	MATC	33 d	ECOTOX ⁷
			0.624 mg L ⁻¹	MATC	33 d	ECOTOX ⁷
			0.038 mg L ⁻¹	NOEC	32 d	ECOTOX ⁷
			0.426 mg L ⁻¹	NOEC	33 d	ECOTOX ⁷
	<i>Poecilia reticulata</i>	Guppy	10.6 mg L ⁻¹	EC ₅₀	14 d	Zuriaga et al. ⁸
	<i>Rasbora heteromorpha</i>	Harlequinfish, red rasbora	31 mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷ , TOXNET ¹⁰
			23 mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷ , TOXNET ¹⁰
DMF	<i>Pimephales promelas</i>	Fathead minnow	71.1 (62-81.6) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
Freshwater worms						
Furfural	<i>Meloidogyne javanica</i>	Javanese root-knot nematode	13.0 uL L ⁻¹	EC ₅₀	2 d	ECOTOX ⁷
			39.4 uL L ⁻¹	EC ₅₀	5 d	ECOTOX ⁷
Marine algae						
Furfural	<i>Skeletonema costatum</i>	Diatom	24 (17-33) mg L ⁻¹	EC ₅₀	4 d	ECOTOX ⁷
			13 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷
Marine bacteria						
Furfuryl alcohol	<i>Aliivibrio fischeri</i>		167 ± 57.5 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			131 ± 38.4 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
			101 ± 25.65 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
			116 ± 9 mg L ⁻¹	EC ₅₀	30 min	Zuriaga et al. ⁸
Furfural	<i>Aliivibrio fischeri</i>		339 ± 84.5 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			255 ± 66.5 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
			188 ± 46.5 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
			454 ± 5 mg L ⁻¹	EC ₅₀	30 min	Zuriaga et al. ⁸
FA	<i>Aliivibrio fischeri</i>		15.6 ± 0.85 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			15.4 ± 1.05 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴

			14.9 ± 0.7 mg L ⁻¹	EC ₅₀	30min	Ventura et al. ⁴
DMF	<i>Aliivibrio fischeri</i>		33.5 ± 14.65 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			24.3 ± 9.5 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
DHMF	<i>Aliivibrio fischeri</i>		23.4 ± 6.8 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
			314 ± 53.5 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			306 ± 39.5 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
HMF	<i>Aliivibrio fischeri</i>		290 ± 43 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
			407 ± 73 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			385 ± 63.5 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
DFA	<i>Aliivibrio fischeri</i>		389 ± 103.5 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
			39.2 ± 12.5 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			21.3 ± 6.25 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
FDCA	<i>Aliivibrio fischeri</i>		22.8 ± 10.3 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
			10.4 ± 1.1 mg L ⁻¹	EC ₅₀	5 min	Ventura et al. ⁴
			9.66 ± 1.14 mg L ⁻¹	EC ₅₀	15 min	Ventura et al. ⁴
			9.57 ± 1.25 mg L ⁻¹	EC ₅₀	30 min	Ventura et al. ⁴
Marine crustaceans						
Furfural	<i>Americamysis bahia</i>	Opossum shrimp	8.76 (6.84-11.2) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			10.57 (7.94-14.07) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			14.1 mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
		15 (12-19) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷	
		3.8 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷	
		10 mg L ⁻¹	LC ₀	1 d	ECOTOX ⁷	
	<i>Chaetogammarus marinus</i>	Amphipod	18 mg L ⁻¹	LC ₀	1 d	ECOTOX ⁷
			10 mg L ⁻¹	LC ₀	2 d	ECOTOX ⁷
			10 mg L ⁻¹	LC ₀	3 d	ECOTOX ⁷
			10 mg L ⁻¹	LC ₀	4 d	ECOTOX ⁷
			40 (32-50) mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷
			51 (42-61) mg L ⁻¹	LC ₅₀	1 d	ECOTOX ⁷

			24 (20-29) mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷
			30 (24-38) mg L ⁻¹	LC ₅₀	2 d	ECOTOX ⁷
			19 (16-23) mg L ⁻¹	LC ₅₀	3 d	ECOTOX ⁷
			23 (18-28) mg L ⁻¹	LC ₅₀	3 d	ECOTOX ⁷
			15 (13-19) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			21 (17-27) mg L ⁻¹	LC ₅₀	4 d	ECOTOX ⁷
			> 56 mg L ⁻¹	LC ₁₀₀	1 d	ECOTOX ⁷
			56 mg L ⁻¹	LC ₁₀₀	2 d	ECOTOX ⁷
			32 mg L ⁻¹	LC ₁₀₀	3 d	ECOTOX ⁷
			56 mg L ⁻¹	LC ₁₀₀	3 d	ECOTOX ⁷
			32 mg L ⁻¹	LC ₁₀₀	4 d	ECOTOX ⁷
			5.6 mg L ⁻¹	LOEC	4 d	ECOTOX ⁷
			10 mg L ⁻¹	LOEC	4 d	ECOTOX ⁷
			< 5.6 mg L ⁻¹	NOEC	4 d	ECOTOX ⁷
			5.6 mg L ⁻¹	NOEC	4 d	ECOTOX ⁷
Marine molluscs						
Furfural	<i>Crassostrea virginica</i>	American or virginia oyster	18 (14-22) mg L ⁻¹	EC ₅₀	4 d	ECOTOX ⁷
			5 mg L ⁻¹	NOEL	4 d	ECOTOX ⁷

References

- 1 R. F. A. Gomes, Y. N. Mitrev, S. P. Simeonov and C. A. M. Afonso, *ChemSusChem*, 2018, **11**, 1612–1616.
- 2 C. Martins, D. O. Hartmann, A. Varela, J. A. S. Coelho, P. Lamosa, C. A. M. Afonso and C. Silva Pereira, *Microbial Biotechnolog*, 2020, **13**, 1983–1996.
- 3 R. F. M. Frade, J. A. S. Coelho, S. P. Simeonov and C. A. M. Afonso, *Toxicol Res (Camb)*, 2014, **3**, 311–314.
- 4 S. P. M. Ventura, P. Morais, J. A. S. Coelho, T. Sintra, J. A. P. Coutinho and C. A. M. Afonso, *Green Chemistry*, 2016, **18**, 4733–4742.

- 5 J. M. J. M. Ravasco, C. M. Monteiro, F. Siopa, A. F. Trindade, J. Oble, G. Poli, S. P. Simeonov and C. A. M. Afonso, *ChemSusChem*, 2019, **12**, 4629–4635.
- 6 N. Stanev, J. C. M. Bordado, C. A. M. Afonso and S. P. Simeonov, *ChemCatChem*, 2018, **10**, 5406–5409.
- 7 United States Environmental Protection Agency (US EPA), *ECOTOX Knowledgebase* <http://www.epa.gov/ecotox/>
- 8 E. Zuriaga, B. Giner, M. P. Ribate, C. B. García and L. Lomba, *Environ Toxicol Chem*, 2018, **37**, 1014–1023.
- 9 A. Muralidhara, A. Bado-Nilles, G. Marlair, V. Engelen, C. Len and P. Pandard, *Biofuels, Bioproducts and Biorefining*, 2019, **13**, 464–470.
- 10 National Institutes of Health (NIH), *TOXNET database* <https://www.nlm.nih.gov/toxnet/index.html>
- 11 E. Swart, T. E. Boer, G. Chen, R. Vooijs, C. A. M. Gestel, N. M. Straalen and D. Roelofs, *Environmental Pollution*, 2019, **252**, 399–408.