Endocrine activities of phthalate alternatives; assessing the safety profile of furan dicarboxylic acid esters using a panel of human cell based reporter gene assays

Barbara M. A. van Vugt-Lussenburg,*[a] Daan S. van Es,*[b] Matthijs Naderman,[a] Jerome le Notre,[b] Frits van der Klis,[b] Abraham Brouwer,[a,c] and Bart van der Burg[b]

[a.] *BioDetection Systems bv, Science Park 406, 1098XH Amsterdam.*
[b.] *Wageningen Food and Biobased Research (WFBR), Bornse Weilanden 9, 6708WG, Wageningen, The Netherlands.*
[c.] *VU University, Department of Animal Ecology, Amsterdam, the Netherlands.*

Electronic Supporting Information

Selection of Chemicals

The chemicals selected for this study are shown in ESI table 1. The selection was based on several criteria, such as:

Expected toxicological effects (e.g. for known endocrine disrupting substances (EDC) like bisphenols and certain ortho-phthalate esters); Isomerism, in order to investigate the effect of positional isomers; Synthetic accessibility (can the substance be synthesised in required purity with acceptable effort); Commercial availability; where possible commercial materials were used.

ESI Table 1: all substances selected for the current study

CAS no	Name	Abbreviation	Reason for inclusion
620-92-8	Bisphenol F	BPF	Assay selection: known EDC
80-05-7	Bisphenol A	BPA	Assay selection: known EDC
140-66-9	4-tert-octylphenol	4-t-OP	Assay selection: known EDC
104-40-5	4-Nonylphenol	4-NP	Assay selection: known EDC
4376-18-5	Monomethyl phthalate	MMP	Reference: Potential DMP metabolite
131-70-4	Monobutyl phthalate	MBP	Reference: Potential BBP metabolite
2528-16-7	Monobenzyl phthalate	MBzP	Reference: Potential BBP metabolite
4376-20-9	Mono(2-ethylhexyl) phthalate	MEHP	Reference: known EDC; DEHP metabolite
131-11-3	Dimethyl pthtalate	DMP	Reference. Was used as solvent Comparison set diMe esters
1459-93-4	Dimethyl isophthalate	DMIP	Reference Monomer/feedstock for polyesters (PETI), resins and plasticisers Comparison set diMe esters
120-61-6	Dimethyl terephthalate	DMT	Reference: Monomer/feedstock for polyesters like PET and for TA plasticisers (occupational exposure) Comparison set diMe esters
84-66-2	Diethyl phthalate	DEP	Reference; short chain phthalate diester Comparison set diEt esters
636-53-3	Diethyl isophthalate	DEIP	Reference; short chain phthalate diester Comparison set diEt esters
636-09-9	Diethyl terephthalate	DET	Reference; short chain phthalate diester Comparison set diEt esters
84-74-2	Di(n-butyl) phthalate	DBP	Reference phthalate: short chain phthalates are known for tox effects/ endocrine disruptors
84-69-5	Diisobutyl phthalate	DIBP	Reference phthalate: short chain phthalates are known for tox effects/ endocrine disruptors Comparison set di-iBut esters
85-68-7	Butylbenzyl phthalate	BBP	Reference phthalate: short chain phthalates are known for tox effects/ endocrine disruptors

84-61-7	Dicyclohexyl phthalate	DCP	Reference phthalate: short chain phthalates are known for tox effects/ endocrine disruptors
84-75-3	Di(n-hexyl) phthalate	DHP	Reference phthalate: short chain phthalates are known for tox effects/ endocrine disruptors
117-84-0	Di(n-octyl) phthalate	DOP	Reference phthalate: isomer of DEHP; shows effects of linear alcohols
117-81-7	Di(2-ethylhexyl) phthalate	DEHP	Reference phthalate: primary industrial benchmark. Comparison set diEtHex esters
137-89-3	Di(2-ethylhexyl) isophthalate	DEHIP	Reference phthalate: used to study isomer effects. Comparison set diEtHex esters
6422-86-2	Di(2-ethylhexyl) terephthalate	DEHT	Reference phthalate: commercialised as 'non-phthalate' plasticiser. Comparison set diEtHex esters
28553-12-0	Diisononyl phthalate	DINP	Reference phthalate: industrial benchmark; long chain derivative, alternative to DEHP
26761-40-0	Diisodecyl phthalate	DIDP	Reference phthalate: industrial benchmark; long chain derivative, alternative to DEHP. Comparison set di-iDec esters
4282-33-1	Dimethyl-3,4-Furandicarboxylic acid	DM-34FDCA	Test substance; for isomer comparison. Comparison set diMe esters
4282-32-0	Dimethyl-2,5-Furandicarboxylic acid	DM-25FDCA	Test substance; Monomer/feedstock for polyesters like PET and for FDCA plasticisers (occupational exposure). Comparison set diMe esters
1710-13-0	Dimethyl-2,4-Furandicarboxylic acid	DM-24FDCA	Test substance; for isomer comparison. Comparison set diMe esters
53662-83-2	Diethyl-2,5-furandicarboxylate	DEF	Test substance; potential monomer/feedstock for polyesters like PET and for FDCA plasticisers (occupational exposure). Comparison set diEt esters
-	Di(isobutyl)furan-2,5-dicarboxylate	DIBF	Test substance; solid substance; interesting for tox effect comparison to short chain phthalates of the butyl series. Comparison set di-iBut esters
158099-01-5	Di(2-ethylhexyl)furan-2,5-dicarboxylate	DEHF	Test substance; plasticising performance similarity to 2-EH phthalates; possible functional alternative to DEHP/DEHT. Comparison set diEtHex esters
-	Di(isodecyl)furan-2,5-dicarboxylate	DIDF	Test substance; possible functional alternative to DIDP. Comparison set di-iDec esters
88-99-3	Phthalic acid	PA	Reference. Fully hydrolysed diacid, expected intermediate hydrophilic metabolite; isomer effect; Monomer for resins. Comparison set free acids
121-91-5	Isophthalic acid	IPA	Reference. Fully hydrolysed diacid, expected intermediate hydrophilic metabolite; isomer effect Monomer/feedstock for polyesters (PETI), resins and plasticisers. Comparison set free acids
100-21-0	Terephthalic acid	TA	Reference. Fully hydrolysed diacid, expected intermediate hydrophilic metabolite (monoesters are also hydrolysis metabolites, yet more lipohilic) Monomer for PET and for TA plasticisers (occupational exposure). Comparison set free acids
3387-26-6	3,4-Furandicarboxylic acid	34FDCA	Test substance; Fully hydrolysed diacid, expected intermediate hydrophilic metabolite; isomer effect Comparison set free acids
3238-40-2	2,5-Furandicarboxylic acid	25FDCA	Test substance; Fully hydrolysed diacid, expected intermediate hydrophilic metabolite; main target substance Monomer/feedstock for polyesters like PEF and for FDCA plasticisers (occupational exposure). Comparison set free acids
4282-28-4	2,4-Furandicarboxylic acid	24FDCA	Test substance; Fully hydrolysed diacid, expected intermediate hydrophilic metabolite; isomer effect. Comparison set free acids

Synthesis of derivatives

All chemicals were used as received from commercial chemical suppliers (e.g. Sigma Aldrich, VWR, etc). 2,5-FDCA for diester synthesis, was a gift from Archer Daniels Midland (ADM). Exxal 10®, isodecanol isomeric mixture, was a gift from Exxon-Mobil.

GC-MS analysis was performed on an Interscience Trace GC Ultra GC with AS3000 II auto sampler (He carrier gas, flow 1mL/min, split flow 20 mL/min; Restek GC column Rxi-5ms 30 30 m x 0.25 mm x 0.25 µm; GC program: hold 3 min at 50 °C, ramp 7.5 °C/min, final temperature 330 °C) connected to an Interscience Trace DSQ II XL quadrupole mass selective detector (EI, mass range 35-500 Dalton, 150 ms sample speed).

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III spectrometer operating at 400.17 MHz (1H) and 100.62 MHz (13C).

Differential Scanning Calorimetry (DSC) was performed on a Perkin Elmer Diamond series DSC. The temperature range used was -90 °C up to 20 °C at a heating rate of 10 °C/min after holding at -90 ºC for 1 minute.

Melting points were measured using a Mettler Toledo MP80 Melting Point System.

Di(2-methylpropyl)furan-2,5-dicarboxylate (DIBF) synthesis **method 1**.

In a 1 L round-bottom flask, under a positive pressure of nitrogen, and strong magnetic stirring, were introduced the substrate 2,5-FDCA (100.0 g, 0.64 mol), 2-methyl-1-propanol (236 mL, 2.56 mol) and methanesulfonic acid (MSA, 1.0 ml, 2.5 mol%). Additional 2-methyl-1-propanol (20 mL) was placed in the Dean-Stark trap and the white slurry was heated at 130 °C. After 24 h, 23 mL of water was collected in the Dean-Stark trap (theoretical 23 mL). After reaction, a clear slightly brown crude solution was obtained. During cooling down to room temperature a white solid crystalized in the flask. The solid was filtered over a Büchner funnel, washed with ethanol, and dried under vacuum to afford the product (109.7 g, 71% yield) as a white solid.

^{1}H NMR (400.2 MHz, RT, $CDCl_3$): δ = 7.18 (s, 2H), 4.10 (d, 4H, J = 6.7 Hz), 2.06 (nontuplet, 2H, J = 6.7 Hz), 0.98 (d, 12H, J = 6.7 Hz); ^{13}C NMR (100.6 MHz, RT, $CDCl_3$): δ = 158.1, 146.9, 118.1, 71.3, 27.8, 19.0; MS (EI): m/z (%) = 268 ($[M]^+$, <1), 213 (13), 196 (5), 195 (45), 158 (6), 156 (100), 140 (9), 139 (93), 95 (9), 94 (7), 66 (7), 57 (26), 56 (43), 41 (18), 39 (8). m.p.: 88-89 °C.

Di(2-ethylhexyl)furan-2,5-dicarboxylate (DEHF) synthesis **method 1**

In a 1 L round-bottom flask, under a positive pressure of nitrogen, and strong magnetic stirring, were introduced the substrate 2,5-FDCA (82.8 g, 0.53 mol), 2-ethylhexanol (250 mL, 1.59 mol) and methanesulfonic acid (MSA, 0.9, 2.5 mol%). Additional 2-ethylhexanol (20 mL) was placed in the Dean-Stark trap and the white slurry was heated at 160 °C. After 10 h, 19 mL of water was collected in the Dean-Stark trap (theoretical 19 mL). Excess 2-ethylhexanol was removed under reduced pressure (high vacuum and heating) to afford a light brown crude. The crude product was purified by flash

chromatography over silica gel (elution: ether/petroleum ether = 1/9, Rf = 0.5) giving the product (133.9 g, 66% yield) as a pale yellow oil.

^{1}H NMR (400.2 MHz, RT, $CDCl_3$): δ = 7.15 (s, 2H), 4.10 (ddd, 4H, J = 15.6, 9.7, 3.5 Hz), 1.68 (heptuplet, 2H, J = 6.1 Hz), 1.42-1.26 (m, 16H), 0.92-0.85 (m, 12H); ^{13}C NMR (100.6 MHz, RT, $CDCl_3$): δ =158.1, 146.9, 118.0, 67.8, 38.8, 30.3, 28.8, 23.7, 22.8, 13.9, 10.9; MS (EI): m/z (%) = 380 ([M]$^{+}$, <1), 269 (9), 251 (9), 157 (100), 140 (11), 139 (87), 113 (33), 112 (58), 95 (9), 94 (7), 84 (24), 83 (41), 82 (10), 71 (37), 70 (90), 69 (22), 57 (49), 56 (18), 55 (35), 43 (20), 41 (28).

Di(2-ethylhexyl)furan-2,5-dicarboxylate (DEHF) synthesis **method 2**

A 2L 3-neck round-bottom flask was placed in a heating mantle and equipped with a mechanical stirrer, a Dean-Stark trap with reflux condenser, a temperature controller and an N_2-inlet. The flask was charged with 2,5-FDCA (189.4 g, 1.21 mol, ADM), 2-ethylhexanol (632 g, 4.85 mol, >99.6 %, Aldrich) and methanesulfonic acid (MSA, 2.91 g, 0.03 mol, anhydrous, Aldrich). The resulting white suspension was heated to 160 °C under stirring (500 rpm), while a stream of nitrogen was bubbled through the reaction mixture. At 130 °C, water formation started, as was observed in the Dean-Stark trap. After 9 h (including additional MSA addition), > 80% of the theoretical amount of water was obtained, and the reaction mixture was allowed to cool down to RT.

The resulting suspension was filtered over a type-3 glass filter, giving a slightly yellow clear solution, which was washed with sat. $NaHCO_3$-solution (1 L) to remove MSA. The resulting hazy organic phase was washed twice with brine to give a clear organic phase. The organic layer was subsequently dried over $MgSO_4$ and filtered over a type-3 glass filter to give a clear, slightly yellow solution. Decoloration was achieved using activated carbon (20 g) for 1 h at RT. After filtration over Celite, a slightly yellow clear liquid product was obtained.

Next, excess 2-ethylhexanol was removed under reduced pressure (0.5 mbar, 140 °C) giving the product (343 g, 74% yield) as a yellow liquid.

NMR and GC-MS analyses same as for method 1.

Di(isodecyl)furan-2,5-dicarboxylate (DIDF) synthesis **method 1**.

In a 1 L round-bottom flask, under a positive pressure of nitrogen, and strong magnetic stirring, were introduced the substrate 2,5-FDCA (67.9 g, 0.44 mol), isodecanol (256 mL, 1.31 mol), *o*-xylene (200 ml) and methanesulfonic acid (MSA, 0.7, 2.5 mol%). Additional isodecanol (20 mL) was placed in the Dean-Stark trap and the white slurry was heated at 175 °C. After 12 h, 7 mL of water was collected in the Dean-Stark trap (theoretical 16 mL). The reaction mixture was subsequently cooled down to room temperature, and another 0.7 mL of MSA was added and heating was resumed at 185 °C for 6 h (the collected water volume reached 11.6 mL). Next, excess isodecanol was removed under reduced pressure (high vacuum and heating) to afford a light brown crude. The crude product was purified by flash chromatography over silica gel (elution: ether/petroleum ether = 1/9, Rf = 0.35) giving the product (124.1 g, 65% yield) as a pale yellow oil.

Since Exxal 10® is a complex mixture of C9, C10, C11 alcohols, the proton and carbon NMR spectra of the isolated product are too complicated to be described in detail. MS (EI): m/z (%) = 437 ([M]+, <1),

297 (14), 157 (41), 141 (59), 140 (46), 139 (52), 112 (65), 111 (39), 99 (22), 98 (31), 97 (50), 85 (77), 84 (53), 83 (81), 71 (86), 70 (69), 57 (96), 56 (31), 55 (92), 43 (66), 41 (43).

Di(2-ethylhexyl) phthalate (DEHP) synthesis **method 2**.

A 2 L 3-neck round-bottom flask was placed in a heating mantle and equipped with a mechanical stirrer, a Dean-Stark trap with reflux condenser, a temperature controller and an N_2-inlet. The flask was charged with phthalic acid (244 g, 1.47 mol, ACS reagent, >99.5%, Sigma Aldrich), 2-ethylhexanol (765.1 g, 5.87 mol, >99.6 %, Aldrich) and methanesulfonic acid (MSA, 3.53 g, 0.037 mol, anhydrous, Sigma Aldrich). The resulting white suspension was heated to 140 ℃ under stirring (300 rpm), while a stream of nitrogen gas was bubbled through the reaction mixture. At 120 ℃ water formation started, as was observed in the Dean-Stark trap, and at 140 ℃ the mixture started to reflux. After 20 min. at 140 ℃, the reaction mixture turned from a white suspension into a clear light yellow solution. After 80 min., the temperature was increased to 150 ℃. After 6 h, the theoretical amount of water (52.9 g) was obtained, and the reaction mixture was allowed to cool down to RT.

The resulting slightly yellow clear solution was washed with sat. $NaHCO_3$-solution (1 L) to remove MSA. The resulting hazy organic phase was washed twice with brine to give a clear organic phase. The organic layer was subsequently dried over $MgSO_4$ and filtered over a type-3 glass filter to give a clear, slightly yellow solution. Decoloration was achieved using activated carbon (25 g) for 1 h at RT. After filtration over Celite, a slightly yellow clear liquid product was obtained.

Next, excess 2-ethylhexanol was removed under reduced pressure (0.5 mbar, 140 °C) giving the product as a pale yellow (100 Hazen, Dr. Lange LICO 100 universal colorimeter) liquid.

NMR and GC-MS analyses confirmed DEHP, with over 98% purity.

2,4-FDCA and its dimethyl ester were prepared according to ref [1].

ESI Table 2: All CALUX data; left the selected assays, right the non-selected non-responsive assays. Results are presented as lowest effect concentrations (LEC) in LogM. - = no activity observed; X = Not Assessed.

Entry Number	CAS	substance	Cytotox	ERα	AR-anti	PR-anti	GR-anti	TRβ-anti	PPARα	PPARγ	AhR	AP1	ESRE	Nrf2	p53 GENTOX		ERα-anti	AR	PR	GR	TRβ	RAR	LXR	PAH	Hif1α	TCF	NFκB	p21
1		Reference substance	-6.6	-12.2	-7.7	-11.0	-9.5	-6.9	-9.7	-7.7	-12.3	-9.5	-7.5	-5.4	-9													
2	620-92-8	Bisphenol F	-	-6.6	-5.4	-4.8	-	X	-	-	-	-	-4.7	-	-3.3		-	-	-	-	-	-	-	-	-	-	-	-
3	80-05-7	Bisphenol A	-4.0	-7.7	-6.8	-5.5	-4.5	-4.2	-	-	-	-	-4.3	-	X		-	-	-	-	-	-	X	-	-	-	-	-
4	140-66-9	4-tert-Octylphenol	-5.5	-7.2	-6.0	-6.1	-	-	-	-	-	-	-	-4.5	-		-	-	-	-	-	-	-	X	-	-	-	-
5	104-40-5	4-Nonylphenol	-4.9	-5.1	-5.8	-5.5	-	-	-	-	-	-	-4.6	-	X		-	-	-	-	-	-	-	-	-	-	-	-
6	4376-18-5	Monomethyl phthalate	-	-	-	-	-	X	-	-	-	-	-	-	X		-	-	-	-	-	-	-	-	-	-	X	-
7	131-70-4	Monobutyl phthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
8	2528-16-7	Monobenzyl phthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
9	4376-20-9	Mono(2-ethylhexyl) phtalate	-3.5	-	-	-	-	-	-5.5	-4.7	-	-	-	-	-3.2		-	-	-	-	-	-	-	-	-	-	-	-
10	131-11-3	Dimethyl pthtalate	-	-	-4.7	-3.6	-	-	-	-	-	-	-	-	-		X	X	X	X	X	X	X	X	X	X	X	X
11	1459-93-4	Dimethyl isophthalate	-	-3.3	-3.1	-	-	-	-	-	-	-	-	-	-		X	X	X	X	X	X	X	X	X	X	X	X
12	120-61-6	Dimethyl terephthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
13	84-66-2	Diethyl phthalate	-3.5	-4.0	-5.0	-4.3	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
14	636-53-3	Diethyl isophthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		X	X	X	X	X	X	X	X	X	X	X	X
15	636-09-9	Diethyl terephthalate	-	-	-4.0	-	-	-	-	-	-	-	-	-	-		X	X	X	X	X	X	X	X	X	X	X	X
16	84-74-2	Dibutyl phthalate	-	-5.2	-4.7	-4.5	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
17	84-69-5	Diisobutyl phthalate	-4.5	-5.3	-5.0	-5.0	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
18	84-75-3	Di(n-hexyl) phthalate	-3.5	-5.0	-5.0	-5.5	-4.5	X	-	-	-4.0	-4.2	-	-	X		-	-	-	-	-	-	-	-	-	-	-	-

Entry Number	CAS	substance	Cytotox	ERα	AR-anti	PR-anti	GR-anti	TRβ-anti	PPARα	PPARγ	AhR	AP1	ESRE	Nrf2	p53 GENTOX		ERα-anti	AR	PR	GR	TRβ	RAR	LXR	PAH	Hif1α	TCF	NFκB	p21
19	84-61-7	Dicyclohexyl phthalate	-4.5	-5.3	-	-5.4	-5.1	X	-	-	NA	X	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
20	85-68-7	Butylbenzyl phthalate	-3.9	-6.3	-5.6	-5.5	-	-	-	-4.5	-3.7	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
21	117-81-7	Di(2-ethylhexyl) phthalate (synthesized)	-	-3.9	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	X	-	-	-	-
22	117-81-7	Di(2-ethylhexyl) phthalate (commercial)	-	-4.0	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	X	-	-	-	-
23	137-89-3	Di(2-ethylhexyl) isophthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		X	X	X	X	X	X	X	X	X	X	X	X
24	6422-86-2	Di(2-ethylhexyl) terephthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		X	X	X	X	X	X	X	X	X	X	X	X
25	117-84-0	Dioctyl phthalate	-	-	-	-	-	X	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
26	28553-12-0	Diisononyl phthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-
27	26761-40-0	Diisodecyl phthalate	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-	-

ESI Table 3. CALUX assay panel results for di-substituted phthalates (bold) versus furans, arranged by order of increasing chain length. Results are presented as lowest effect concentrations (LogM). - = no activity observed up to 1E-3M. N/A: not applicable; DIBF and DIDF have not been CAS-registered.

Entry Number	CAS	substance	Abbreviation	Cytotox	ERα	AR-anti	PR-anti	GR-anti	TRβ-anti	PPARα	PPARγ	AhR	AP1	ESRE	Nrf2	p53 GENTOX
28	131-11-3	**Dimethyl phthtalate**	**DMP**	-	-	-4.7	-3.6	-	-	-	-	-	-	-	-	-
29	1459-93-4	**Dimethyl isophthalate**	**DMIP**	-	-3.3	-3.1	-	-	-	-	-	-	-	-	-	-
30	120-61-6	**Dimethyl terephthalate**	**DMT**	-	-	-	-	-	-	-	-	-	-	-	-	-
31	4282-33-1	Dimethyl-3,4-furandicarboxylate	DM-3,4-FDCA	-	-	-	-	-	-	-	-	-	-	-	-	-
32	4282-32-0	Dimethyl-2,5-furandicarboxylate	DM-2,5-FDCA	-	-	-	-	-	-	-	-	-	-	-	-	-
33	1710-13-0	Dimethyl-2,4-furandicarboxylate	DM-2,4-FDCA	-	-	-	-	-	-	-	-	-	-	-	-	-
34	84-66-2	**Diethyl phthalate**	**DEP**	-3.5	-4.0	-5.0	-4.3	-	-	-	-	-	-	-	-	-
35	636-53-3	**Diethyl isophthalate**	**DEIP**	-	-	-	-	-	-	-	-	-	-	-	-	-
36	636-09-9	**Diethyl terephthalate**	**DET**	-	-	-4.0	-	-	-	-	-	-	-	-	-	-
37	53662-83-2	Diethyl-2,5-furandicarboxylate	DEF	-	-	-	-	-	-	-	-	-	-	-	-	-
38	84-69-5	**Diisobutyl phthalate**	**DIBP**	-4.5	-5.3	-5.0	-5.0	-	-	-	-	-	-	-	-	-
39	N/A	Diisobutyl-2,5-furandicarboxylate	DIBF	-	-4.3	-	-	-	-	-	-	-	-	-	-	-
40	117-81-7	**Di(2-ethylhexyl) phthalate**	**DEHP (synthesized)**	-	-3.9	-	-	-	-	-	-	-	-	-	-	-
41	117-81-7	**Di(2-ethylhexyl) phthalate**	**DEHP (commercial)**	-	-4.0	-	-	-	-	-	-	-	-	-	-	-
42	137-89-3	**Di(2-ethylhexyl) isophthalate**	**DEHIP**	-	-	-	-	-	-	-	-	-	-	-	-	-
43	6422-86-2	**Di(2-ethylhexyl) terephthalate**	**DEHT**	-	-	-	-	-	-	-	-	-	-	-	-	-
44	158099-01-5	Di(2-ethylhexyl)-2,5-furandicarboxylate	DEHF (method 1)	-	-	-	-	-	-	-	-	-	-	-	-	-
45	158099-01-5	Di(2-ethylhexyl)-2,5-furandicarboxylate	DEHF (method 2)	-	-	-	-	-	-	-	-	-	-	-	-	-
46	26761-40-0	**Diisodecyl phthalate**	**DIDP**	-	-	-	-	-	-	-	-	-	-	-	-	-
47	N/A	Diisodecylfuran-2,5-dicarboxylate	DIDF	-	-	-	-	-	-	-	-	-	-	-	-	-
48	100-21-0	**Terephthalic acid**	**TA**	-	-	-	-	-	-	-	-	-	-	-	-	-
49	88-99-3	**Phthalic acid**	**PA**	-	-	-	-	-	-	-	-	-	-	-	-	-
50	121-91-5	**Isophthalic acid**	**IPA**	-	-	-	-	-	-	-	-	-	-	-	-	-
51	4282-28-4	2,4-Furandicarboxylic acid	2,4-FDCA	-	-	-	-	-	-	-	-	-	-	-	-	-
52	3238-40-2	2,5-Furandicarboxylic acid	2,5-FDCA	-	-	-	-	-	-	-	-	-	-	-	-	-
53	3387-26-6	3,4-Furandicarboxylic acid	3,4-FDCA	-	-	-	-	-	-	-	-	-	-	-	-	-

ESI table 4: overview of literature values for solubilities of ortho-phthalate esters at 20-22°C; bold substances are part of this study.

Phthalate		molecular weight	solubility (μgL^{-1})	Solubility (M)	logM
DMP	dimethyl	194.2	$4.2\ 10^{6}$ [2]	$2.16\ 10^{-2}$	-1.66
DEP	diethyl	222.2	$1.1.\ 10^{6}$ [2] $9.4\ 10^{5}$ [3]	$4.95\ 10^{-3}$ $4.23\ 10^{-3}$	-2.31 -2.37
DBP	Di(n-butyl)	278.4	$1.1\ 10^{4}$ [2] $1.5\ 10^{4}$ [3]	$3.95\ 10^{-5}$ $5.39\ 10^{-5}$	-4.40 -4.27
DIBP	diisobutyl	278.4	$2.0\ 10^{4}$ [2]	$7.18\ 10^{-5}$	-4.14
BBP	butylbenzyl	312.4	$2.7\ 10^{3}$ [2]	$8.64\ 10^{-6}$	-5.06
DHP	Di(n-hexyl)	334.4	520 [3] 70 [4] 50 [2, 5]	$1.56\ 10^{-6}$ $2.09\ 10^{-7}$ $1.50\ 10^{-7}$	-5.81 -6.68 -6.83
DOP	Di(n-octyl)	390.6	0.5 [2, 5] 0.4 [4]	$1.28\ 10^{-9}$ $1.02\ 10^{-9}$	-8.89 -8.99
DEHP	di(2-ethylhexyl)	390.6	17 [3] 3 [2] 1.9 [4]	$4.35\ 10^{-8}$ $7.68\ 10^{-9}$ $4.86\ 10^{-9}$	-7.36 -8.11 -8.31
DNP	Di(n-nonyl)	418.6	0.13 [4]	$3.11\ 10^{-10}$	-9.51
DINP	diisononyl	418.6	< 1 [2] 0.61 [4]	$1.46\ 10^{-9}$	-8.84
DDP	Di(n-decyl)	446.6	0.2 [5] 0.05 [4]	$4.48\ 10^{-10}$ $1.12\ 10^{-10}$	-9.35 -9.95
DIDP	diisodecyl	446.6	< 1 [2] 0.17 [4]	$9.81\ 10^{-10}$	-9.42

Note that there is an inverse relationship between phthalate solubility and temperature; e.g. for DBP solubility drops from 14.6 mg/L at 25°C to 5.5 mg/L at 35°C; while cell assays are performed at an incubation temperature of 37°C[3].

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