Building bio-Profiles for common catalytic reactions

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Supplementary Information

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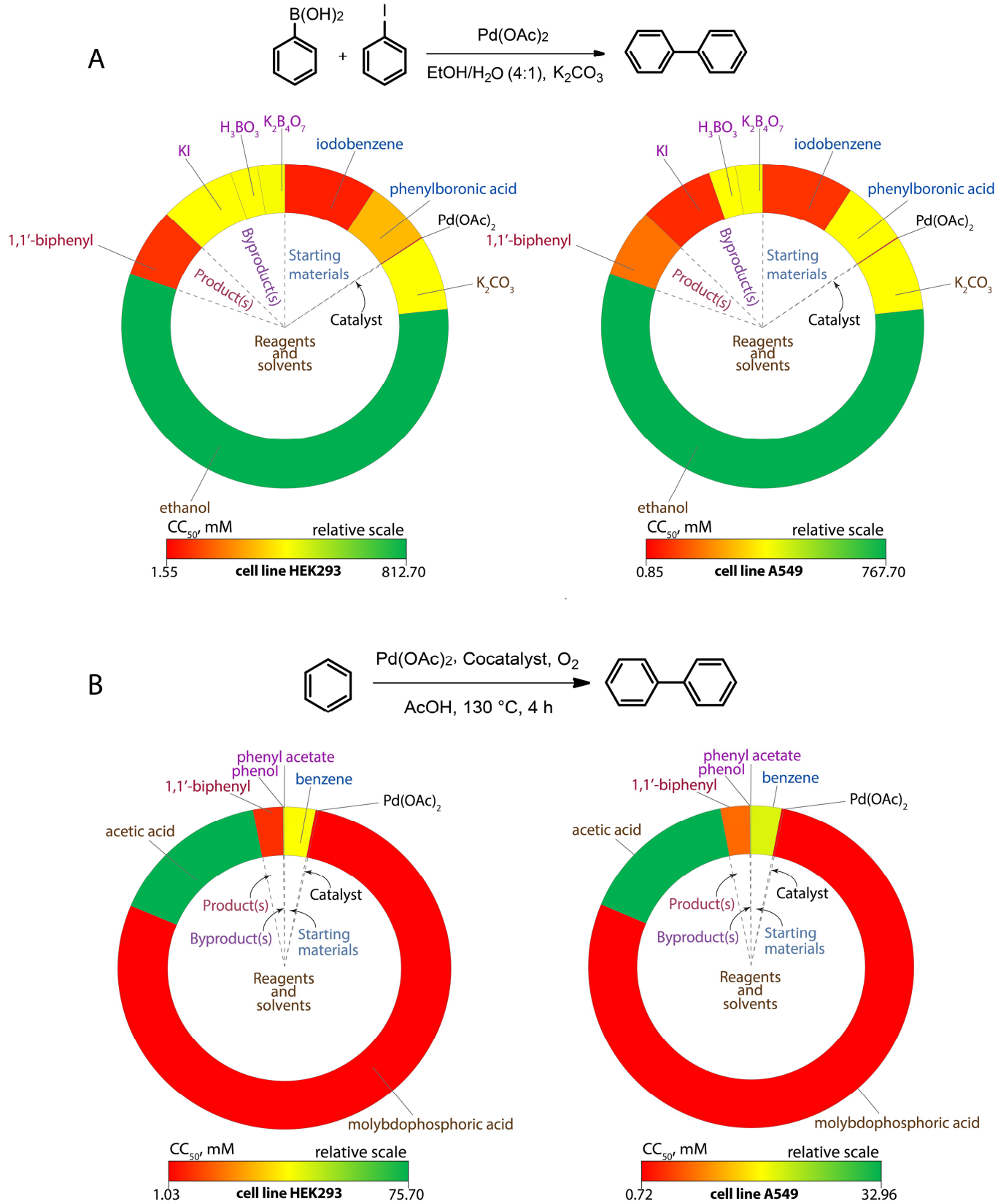


Fig. S1. Bio-Profiles for Suzuki and oxidative C-C coupling reactions. Synthesis of 1,1'-biphenyl from (A) iodobenzene and phenylboronic acid, and (B) benzene are used as exemplary reactions. The area of the sectors in the diagrams corresponds to the amounts (g) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The exact values used for bio-Profiles are provided in Table 1.

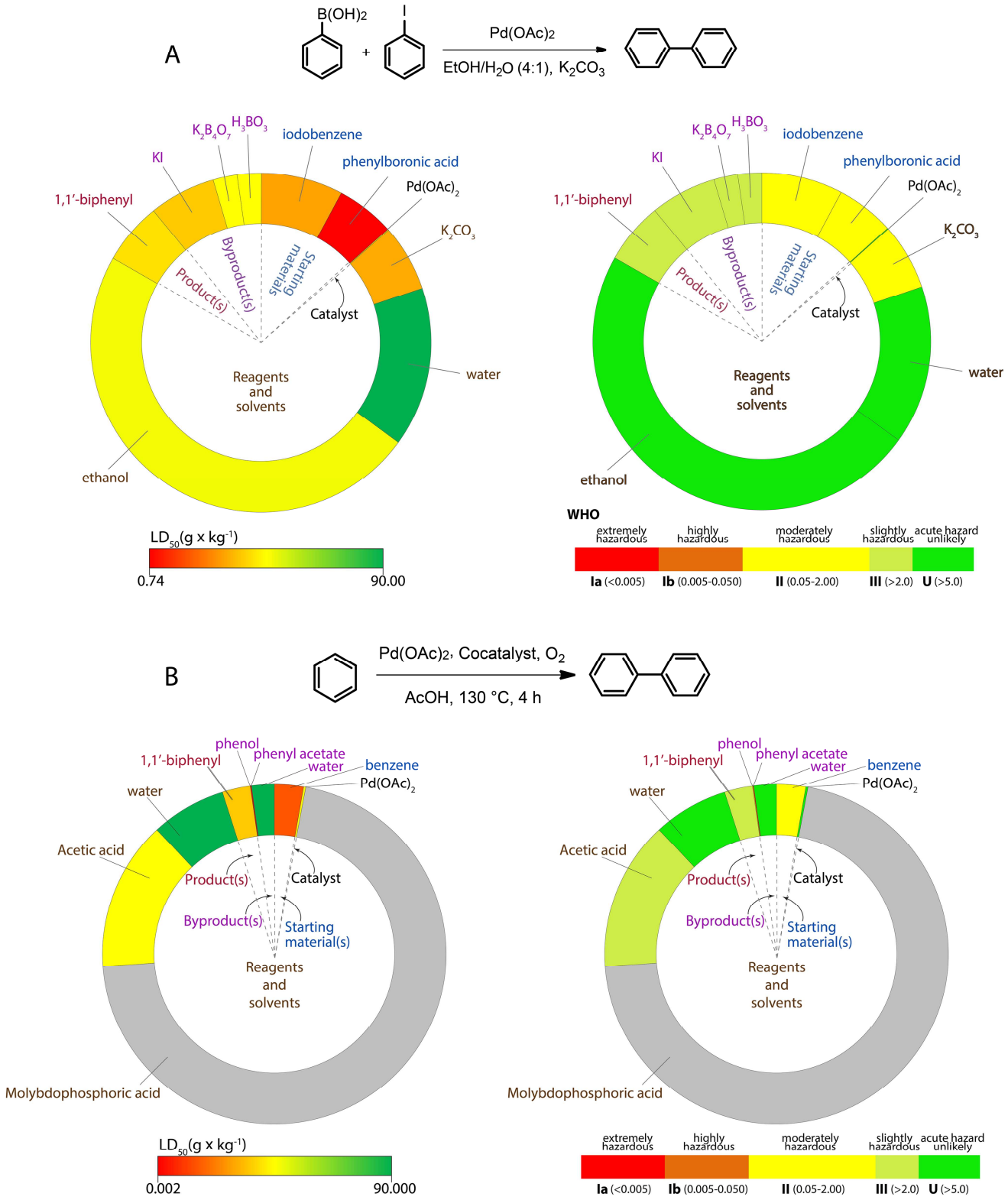
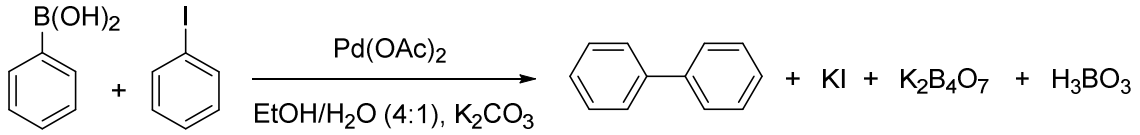


Fig. S2. Tox-Profiles for Suzuki and oxidative C-C coupling reactions. Synthesis of 1,1'-biphenyl from (A) iodobenzene and phenylboronic acid, and (B) benzene are used as exemplary reactions. The area of the sectors in the diagrams corresponds to the amounts (g) of the compounds. The color of the sectors corresponds to the actual values of LD_{50} (oral, rat) of the substances (left, see the relative toxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow) or the WHO toxicity rating (right, see the scales below the diagrams). The gray color corresponds to "no data available". The exact values used for bio-Profiles are provided in Table S1 and Table S2. Adapted and reproduced with permission from [1].

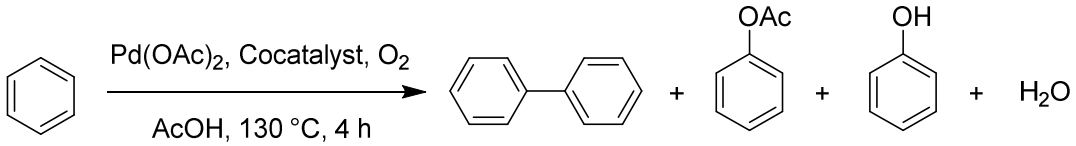
Table S1. Synthesis of 1,1'-biphenyl: Method A



Substances	LD_{50} (oral, rat), $g \cdot kg^{-1}$ b.w.	Amount in reaction, g[b]
Starting materials		
Iodobenzene	1.749	0.2040
Phenylboronic acid	0.740	0.1460
Reagents, solvents, catalysts		
$Pd(OAc)_2$	>5.100	0.0022
K_2CO_3	1.870	0.1660
Water	>90.000	0.3990
Ethanol	7.060	1.2630
Product(s)		
1,1'-Biphenyl	2.140	0.1540
Byproduct(s)		
KI	>2.000	<0.1660
$K_2B_4O_7$	>2.500[a]	<0.0600
H_3BO_3	2.660	<0.0600

[a] Data for $K_2B_4O_7 \cdot 4H_2O$.
[b] The product yield is considered as 100%.

Table S2. Synthesis of 1,1'-biphenyl: Method B



Substances	LD_{50} (oral, rat), $g \cdot kg^{-1}$ b.w.	Amount in reaction, g[a]
Starting materials		
Benzene	0.93000	0.3861
Reagents, solvents, catalysts		
$Pd(OAc)_2$	>5.10000	0.0292
Molybdophosphoric acid	no data	10.0000
Acetic acid	3.31000	2.0000
Water	>90.00000	1.0000
Product(s)		
1,1'-Biphenyl	2.14000	0.3727
Byproduct(s)		
Phenol	0.31700	0.0075
Phenyl acetate	0.00163	0.0095
Water	>90.00000	0.3000

[a] The conversion is considered as 100%.

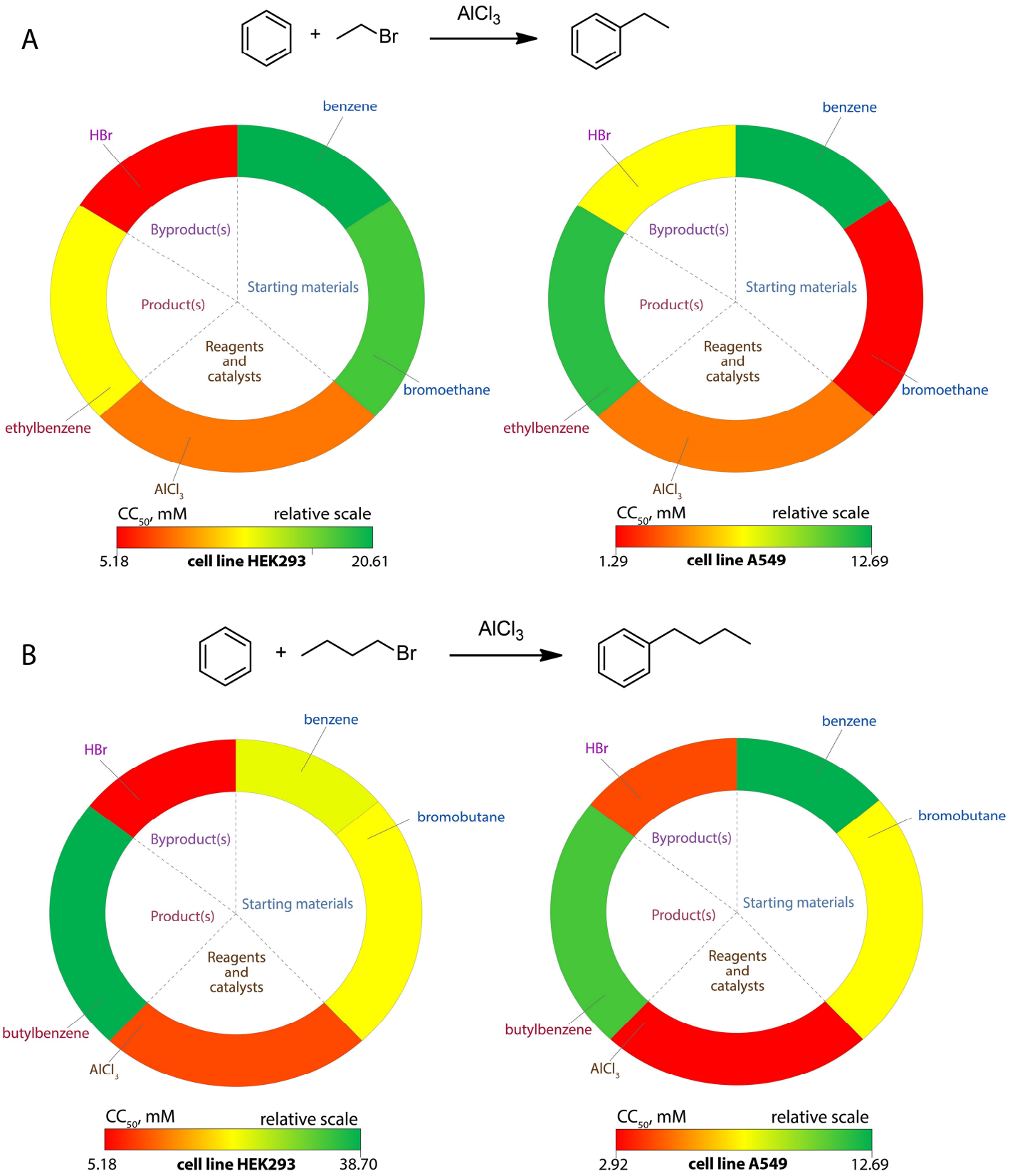


Fig. S3. Bio-Profiles for Friedel-Crafts reaction. Syntheses of (A) ethylbenzene from benzene and bromoethane and (B) butylbenzene from benzene and bromobutane are used as exemplary reactions. The area of the sectors in the diagrams corresponds to the amounts (g) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The exact values used for bio-Profiles are provided in Table 2.

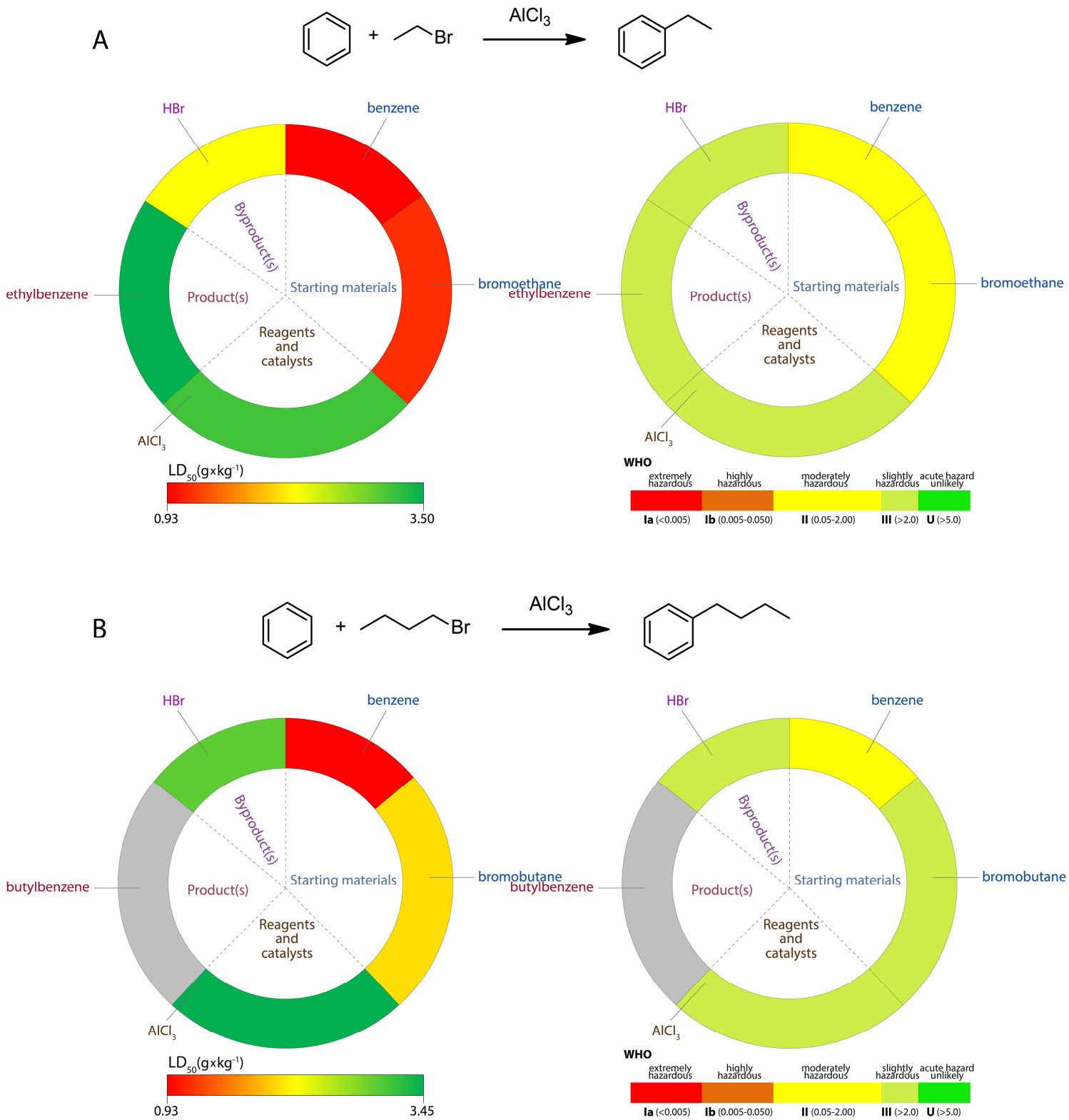
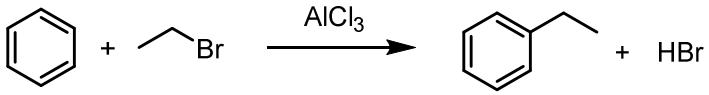


Fig. S4. Tox-Profiles for Friedel-Crafts reaction. Syntheses of (A) ethylbenzene from benzene and bromoethane and (B) butylbenzene from benzene and bromobutane are used as exemplary reactions. The area of the sectors in the diagrams corresponds to the amounts (g) of the compounds. The color of the sectors corresponds to the actual values of LD_{50} (oral, rat) of the substances (left, see the relative toxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow) or the WHO toxicity rating (right, see the scales below the diagrams). The gray color corresponds to "no data available". The exact values used for bio-Profiles are provided in Table S3 and Table S4. (A) is adapted and reproduced with permission from [1].

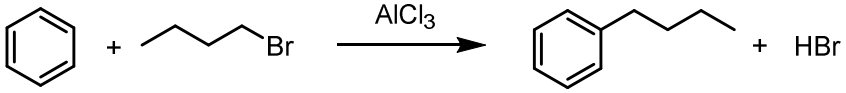
Table S3. Synthesis of ethylbenzene from benzene and bromoethane



Substances	**LD_{50} (oral, rat), g·kg^{-1} b.w.**	**Amount in reaction, g[a]**
Starting materials		
Benzene	0.93	0.0780
Bromoethane	1.35	0.1090
Reagents, solvents, catalysts		
$AlCl_3$	3.45	0.1335
Product(s)		
Ethylbenzene	3.50	0.1060
Byproduct(s)		
HBr	3.30	0.0810

[a] The product yield is considered as 100%.

Table S4. Synthesis of butylbenzene from benzene and bromobutane



Substances	**LD_{50} (oral, rat), g·kg^{-1} b.w.**	**Amount in reaction, g[a]**
Starting materials		
Benzene	0.930	0.0780
Bromobutane	2.761	0.1370
Reagents, solvents, catalysts		
$AlCl_3$	3.450	0.1335
Product(s)		
Butylbenzene	no data	0.1340
Byproduct(s)		
HBr	3.300	0.0810

[a] The product yield is considered as 100%.

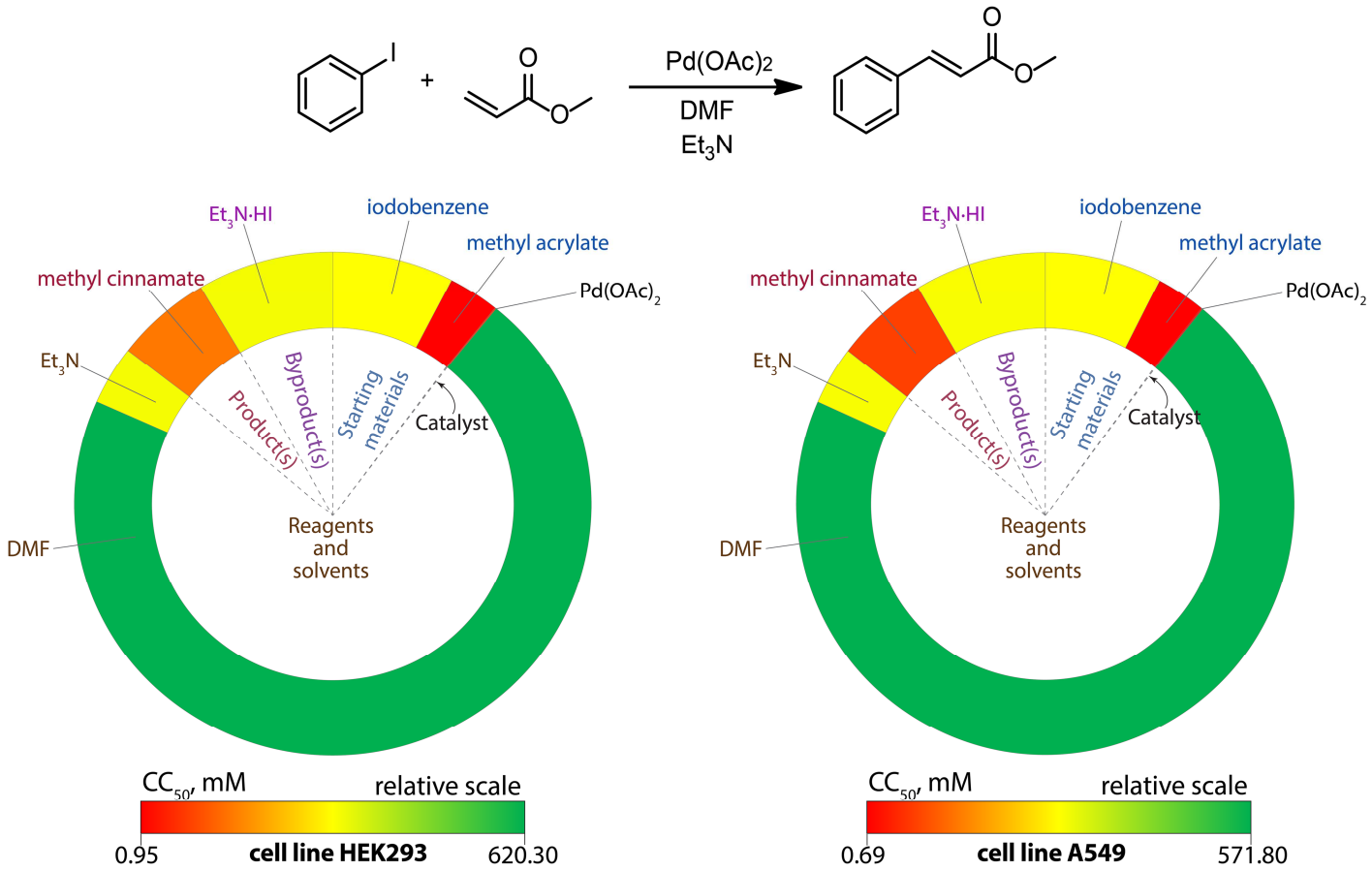


Fig. S5. Bio-Profiles for Heck reaction. Synthesis of methyl cinnamate from iodobenzene and methyl acrylate is used as an exemplary reaction. The area of the sectors in the diagrams corresponds to the amounts (g) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The exact values used for bio-Profiles are provided in Table 3.

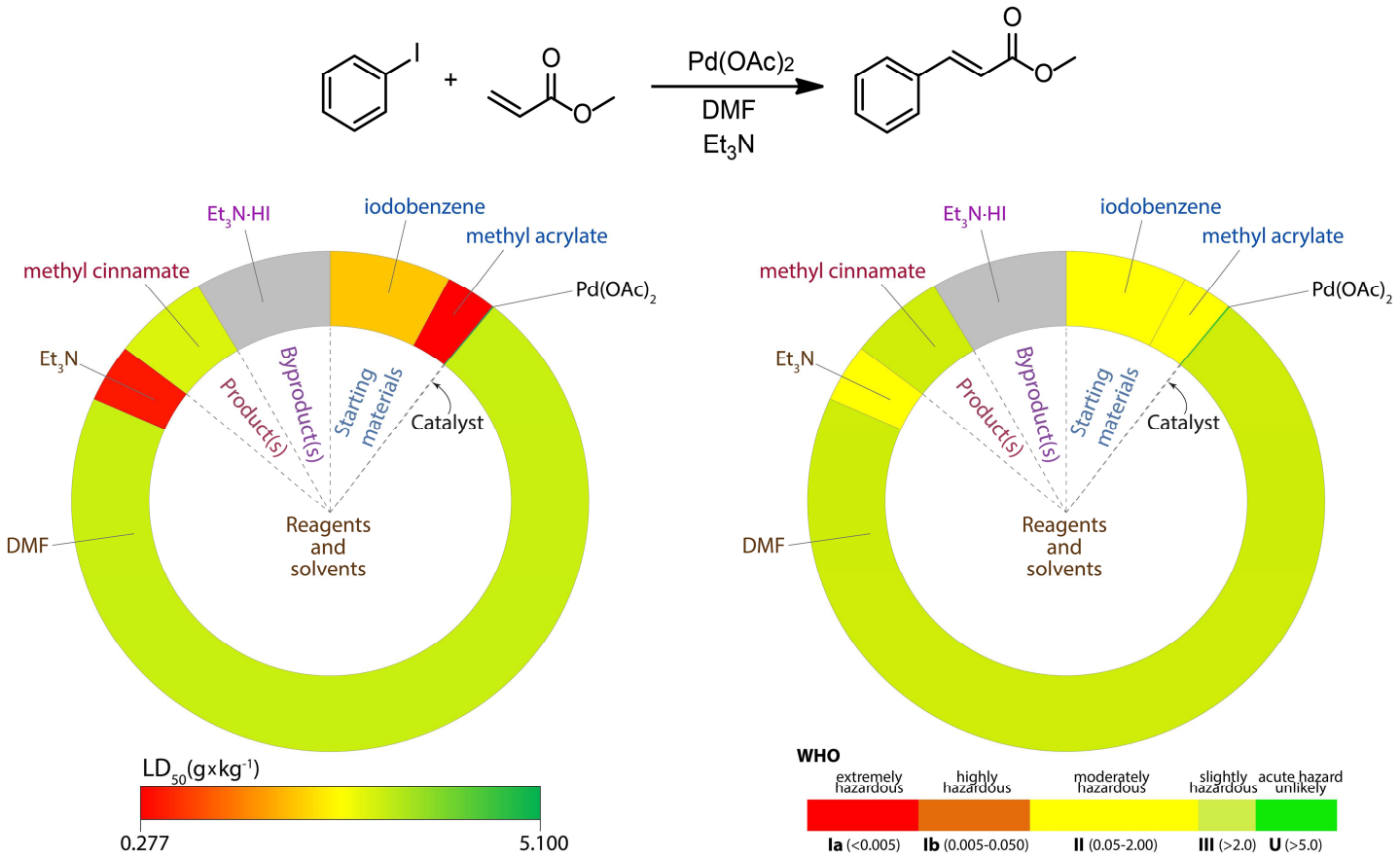
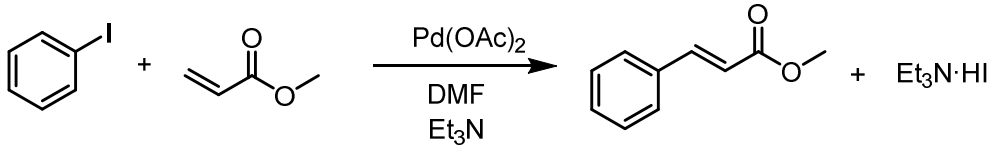


Fig. S6. Tox-Profiles for Heck reaction. Synthesis of methyl cinnamate from iodobenzene and methyl acrylate is used as an exemplary reaction. The area of the sectors in the diagrams corresponds to the amounts (g) of the compounds. The color of the sectors corresponds to the actual values of LD_{50} (oral, rat) of the substances (left, see the relative toxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow) or the WHO toxicity rating (right, see the scales below the diagrams). The gray color corresponds to "no data available". The exact values used for bio-Profiles are provided in Table S5.

Table S5. Synthesis of butyl cinnamate



Substances	**LD_{50} (oral, rat), g·kg^{-1} b.w.**	**Amount in reaction, g[a]**
Starting materials		
Iodobenzene	1.749	0.2040
Methyl acrylate	0.277	0.0860
Reagents, solvents, catalysts		
$Pd(OAc)_2$	>5.100	0.0022
Dimethylformamide	2.800	1.9000
Triethylamine	0.460	0.1010
Product(s)		
Methyl cinnamate	2.610	0.1620
Byproduct(s)		
Triethylamine hydroiodide	no data	0.2290

[a] The product yield is considered as 100%.

Table S6. Experimental data used for construction of bio-Profiles for 1,1'-biphenyl synthesis

Substances	Amount in reaction		HEK293		A549	
	g	mmol	24-h CC_{50}, mM[b]	NC	24-h CC_{50}, mM[b]	NC
Reaction A-A-A[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$Pd(OAc)_2$	0.0022	0.01	1.55 (1.43-1.67)	0.006	0.85 (0.76-0.94)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.74**		**1.19**	
Reaction A-B-A[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.74**		**1.19**	
Reaction A-C-A[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdBr_2$	0.0027	0.01	1.24 (1.13-1.35)	0.008	0.82 (0.74-0.90)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.74**		**1.19**	
Reaction A-D-A[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142

Reagents, solvents, catalysts						
PdI_2	0.0036	0.01	1.79 (1.60-1.98)	0.006	1.22 (1.10-1.34)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.74**		**1.19**	
Reaction A-B-B[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.81**		**1.14**	
Reaction A-C-B[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdBr_2$	0.0027	0.01	1.24 (1.13-1.35)	0.008	0.82 (0.74-0.90)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.81**		**1.14**	
Reaction A-D-B[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
PdI_2	0.0036	0.01	1.79 (1.60-1.98)	0.006	1.22 (1.10-1.34)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474

$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.81**		**1.14**	
Reaction B-A-A[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$Pd(OAc)_2$	0.0022	0.01	1.55 (1.43-1.67)	0.006	0.85 (0.76-0.94)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.62**		**0.52**	
Reaction B-B-A[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.62**		**0.52**	
Reaction B-C-A[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdBr_2$	0.0027	0.01	1.24 (1.13-1.35)	0.008	0.82 (0.74-0.90)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.63**		**0.52**	
Reaction B-D-A[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461

Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
PdI_2	0.0036	0.01	1.79 (1.60-1.98)	0.006	1.22 (1.10-1.34)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.62**		**0.52**	
Reaction B-B-B[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.72**		**0.64**	
Reaction B-C-B[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdBr_2$	0.0027	0.01	1.24 (1.13-1.35)	0.008	0.82 (0.74-0.90)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.72**		**0.64**	
Reaction B-D-B[a]						
Starting materials						
Bromobenzene	0.1570	1.00	3.24 (2.93-3.55)	0.309	2.17 (1.99-2.35)	0.461
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
PdI_2	0.0036	0.01	1.79 (1.60-1.98)	0.006	1.22 (1.10-1.34)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						

KBr	0.119	1.00	89.48 (81.37-97.59)	0.011	67.12 (61.63-72.61)	0.015
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.72**		**0.64**	
Reaction C-A-A[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$Pd(OAc)_2$	0.0022	0.01	1.55 (1.43-1.67)	0.006	0.85 (0.76-0.94)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.52**		**0.47**	
Reaction C-B-A[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.52**		**0.47**	
Reaction C-C-A[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdBr_2$	0.0027	0.01	1.24 (1.13-1.35)	0.008	0.82 (0.74-0.90)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.52**		**0.47**	
Reaction C-D-A[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
PdI_2	0.0036	0.01	1.79 (1.60-1.98)	0.006	1.22 (1.10-1.34)	0.008

K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.52**		**0.47**	
Reaction C-B-B[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.63**		**0.59**	
Reaction C-C-B[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdBr_2$	0.0027	0.01	1.24 (1.13-1.35)	0.008	0.82 (0.74-0.90)	0.012
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.63**		**0.59**	
Reaction C-D-B[a]						
Starting materials						
Chlorobenzene	0.1125	1.00	2.51 (2.25-2.77)	0.398	1.92 (1.73-2.11)	0.521
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
PdI_2	0.0036	0.01	1.79 (1.60-1.98)	0.006	1.22 (1.10-1.34)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
NMP	1.6480	16.62	79.16 (71.70-86.62)	0.210	58.61 (52.49-64.73)	0.284
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KCl	0.0745	1.00	319.76 (289.80-349.72)	0.003	247.15 (224.32-269.98)	0.004
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.63**		**0.59**	

[a] The product yield is considered as 100%. The first, second and third letters in the reaction names correspond to the type of starting material, catalyst, and solvent, respectively. Starting material: A, iodobenzene, B, bromobenzene, C, chlorobenzene; catalyst: A, $Pd(OAc)_2$; B, $PdCl_2$; C, $PdBr_2$; D, PdI_2. Solvent: A, ethanol; B, *N*-methylpyrrolidone (NMP). The compounds being varied in the reactions are also highlighted in different colors. [b] 95% confidence intervals are shown in parentheses. [c] Not tested. [d] CC_{50} for $Na_2B_4O_7$, which is supposed to be similar to that for $K_2B_4O_7$, is used.

Table S7. Experimental data used for construction of bio-Profiles for 1,1'-biphenyl synthesis by using water/surfactant method

Substances	**Amount in reaction**		**HEK293**		**A549**	
	g	**mmol**	**24-h CC_{50}, mM**[b]	**NC**	**24-h CC_{50}, mM**[b]	**NC**
Reaction A-B-C[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
SDS	0.0721	0.25	2.62 (2.35-2.89)	0.095	1.44 (1.28-1.60)	0.174
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.08**	
Reaction A-B-D[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
TBAB	0.0806	0.25	7.85 (7.09-8.61)	0.032	3.96 (3.54-4.38)	0.063
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.09**	
Reaction A-B-E[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
TBAC	0.0695	0.25	24.57 (22.36-26.78)	0.010	12.29 (10.95-13.63)	0.020
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008

H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.09**	
Reaction A-B-F						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
$Oct_1(Me)_3NCl$	0.0520	0.25	3.16 (2.82-3.48)	0.079	1.99 (1.79-2.20)	0.126
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.08**	
Reaction A-B-G[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
PEG-400	0.1000	0.25	874.21 (795.85-952.57)	0.0003	416.78 (377.99-455.57)	0.0006
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.09**	
Reaction A-B-H[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
PEG-10000	2.5000	0.25	84.43 (76.32-92.54)	0.003	39.83 (36.65-43.01)	0.006
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.09**	

Reaction A-B-I[a]						
Starting materials						
Iodobenzene	0.2040	1.00	3.37 (3.06-3.68)	0.297	2.39 (2.18-2.60)	0.418
Phenylboronic acid	0.1460	1.20	12.14 (11.08-13.20)	0.099	8.45 (7.69-9.21)	0.142
Reagents, solvents, catalysts						
$PdCl_2$	0.0018	0.01	1.72 (1.55-1.89)	0.006	1.23 (1.10-1.36)	0.008
K_2CO_3	0.1660	1.20	20.89 (19.63-22.15)	0.057	10.49 (9.51-11.47)	0.115
Water	0.3990	22.15	-[c]	-[c]	-[c]	-[c]
PEG-35000	8.75	0.25	28.96 (26.31-31.61)	0.009	15.49 (13.87-17.11)	0.016
Toluene	0.8670	9.41	12.97 (11.79-14.15)	0.725	11.83 (10.87-12.79)	0.795
Ethanol	1.2630	27.41	812.70 (797.02-828.38)	0.034	767.70 (749.11-786.29)	0.036
Product(s)						
1,1'-Biphenyl	0.1540	1.00	4.50 (4.03-4.97)	0.222	4.26 (3.68-4.84)	0.234
Byproduct(s)						
KI	0.1660	1.00	16.08 (15.27-16.89)	0.062	2.11 (1.74-2.48)	0.474
$K_2B_4O_7$	0.0600	0.26	38.50 (36.96-40.04)[d]	0.007	31.24 (30.12-32.36)[d]	0.008
H_3BO_3	0.0600	0.97	27.70 (26.25-29.15)	0.035	10.24 (9.26-11.22)	0.095
bio-Factor			**0.90**		**1.09**	

[a] The product yield is considered as 100%. The first, second and third letters in the reaction names correspond to the type of starting material, catalyst, and solvent/surfactant, respectively. Surfactant: C, SDS (sodium dodecylsulfate); D, TBAB (tetrabutylammonium bromide); E, TBAC (tetrabutylammonium chloride); F, $Oct_1(Me)_3NCl$ (octyltrimethylammonium chloride); G, PEG-400; H, PEG-10000; I, PEG-35000. The compounds being varied in the reactions are also highlighted in different colors. [b] 95% confidence intervals are shown in parentheses. [c] Not tested. [d] CC_{50} for $Na_2B_4O_7$, which is supposed to be similar to that for $K_2B_4O_7$, is used.

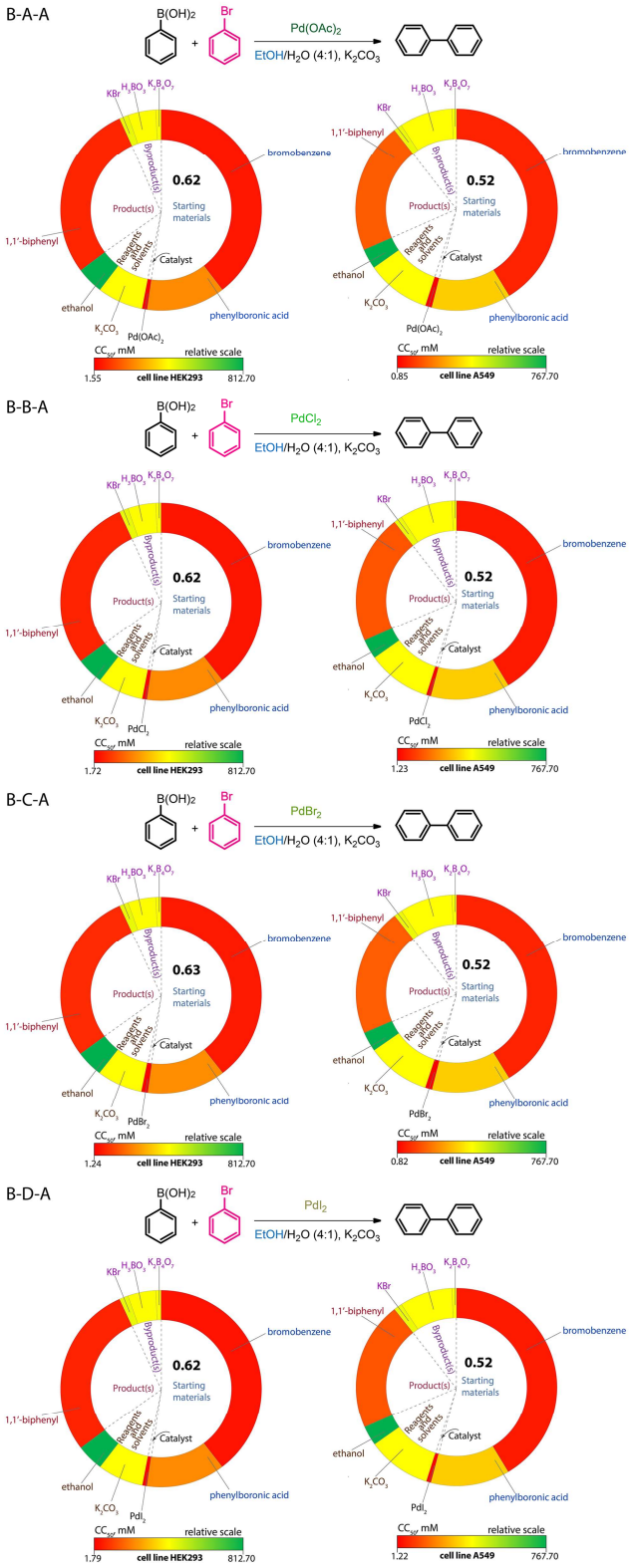


Fig. S7. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various catalysts. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, bromobenzene (B)), catalyst ($Pd(OAc)_2$ (A), $PdCl_2$ (B), $PdBr_2$ (C), PdI_2 (D)), and solvent (in this case, ethanol (A)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

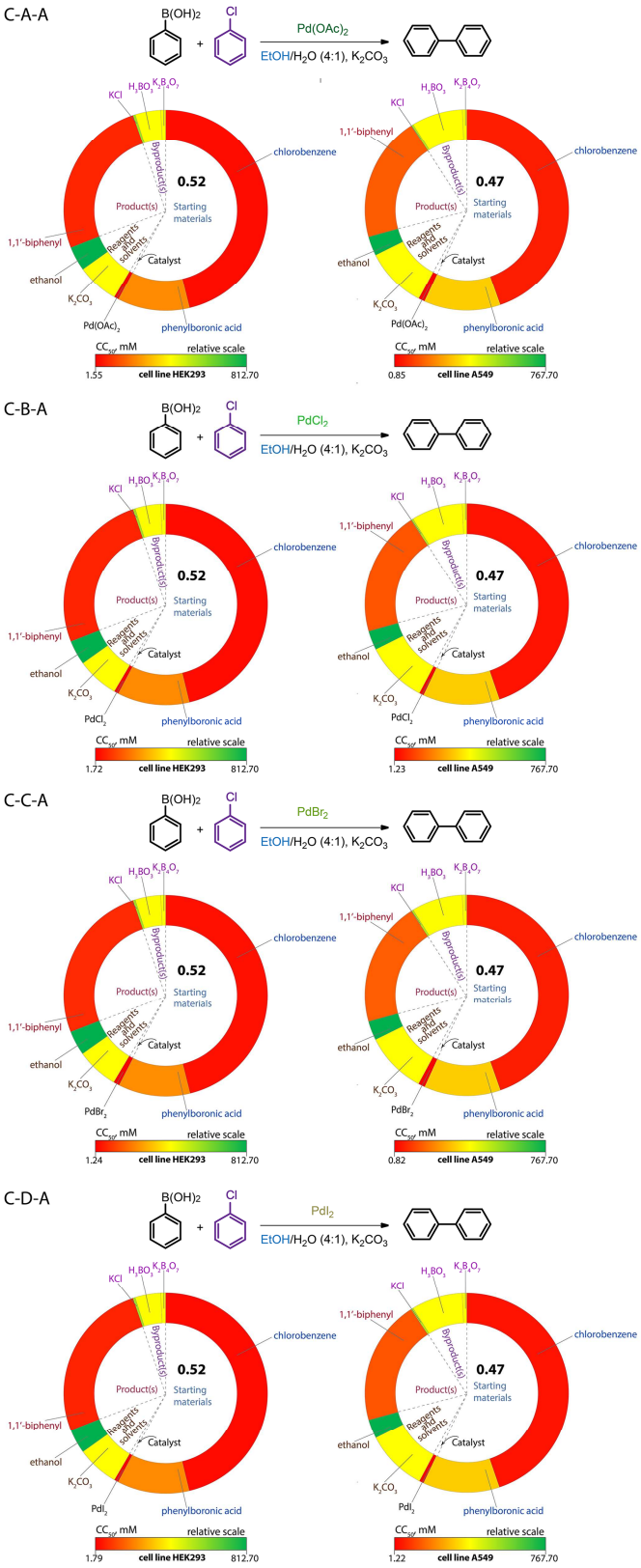


Fig. S8. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various catalysts. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, chlorobenzene (C)), catalyst ($Pd(OAc)_2$ (A), $PdCl_2$ (B), $PdBr_2$ (C), PdI_2 (D)), and solvent (in this case, ethanol (A)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

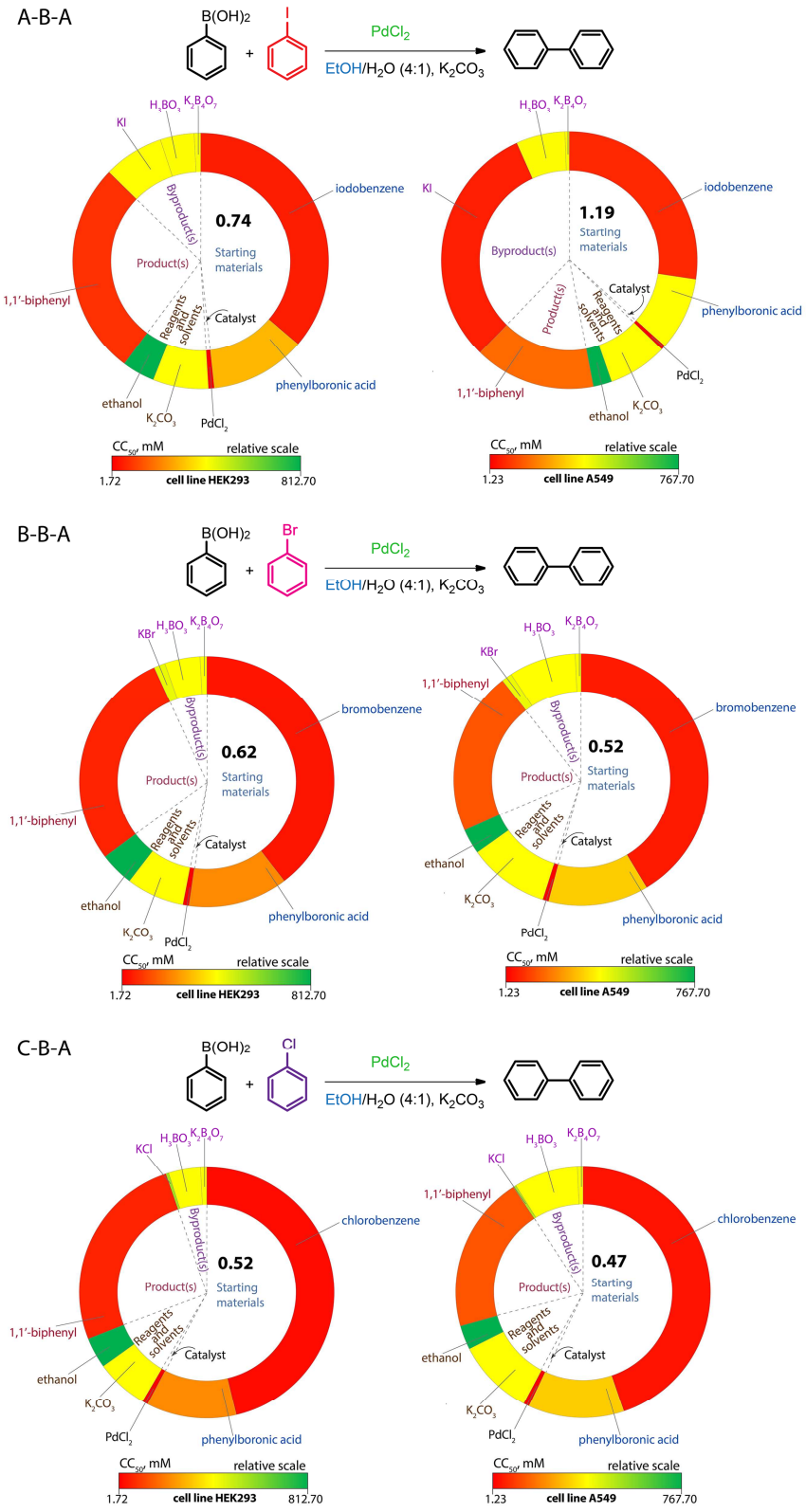


Fig. S9. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various starting materials. The first, second and third letters in the reaction names correspond to the type of starting material (iodobenzene (A), bromobenzene (B), chlorobenzene (C)), catalyst (in this case, $PdCl_2$ (B)), and solvent (in this case, ethanol (A)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

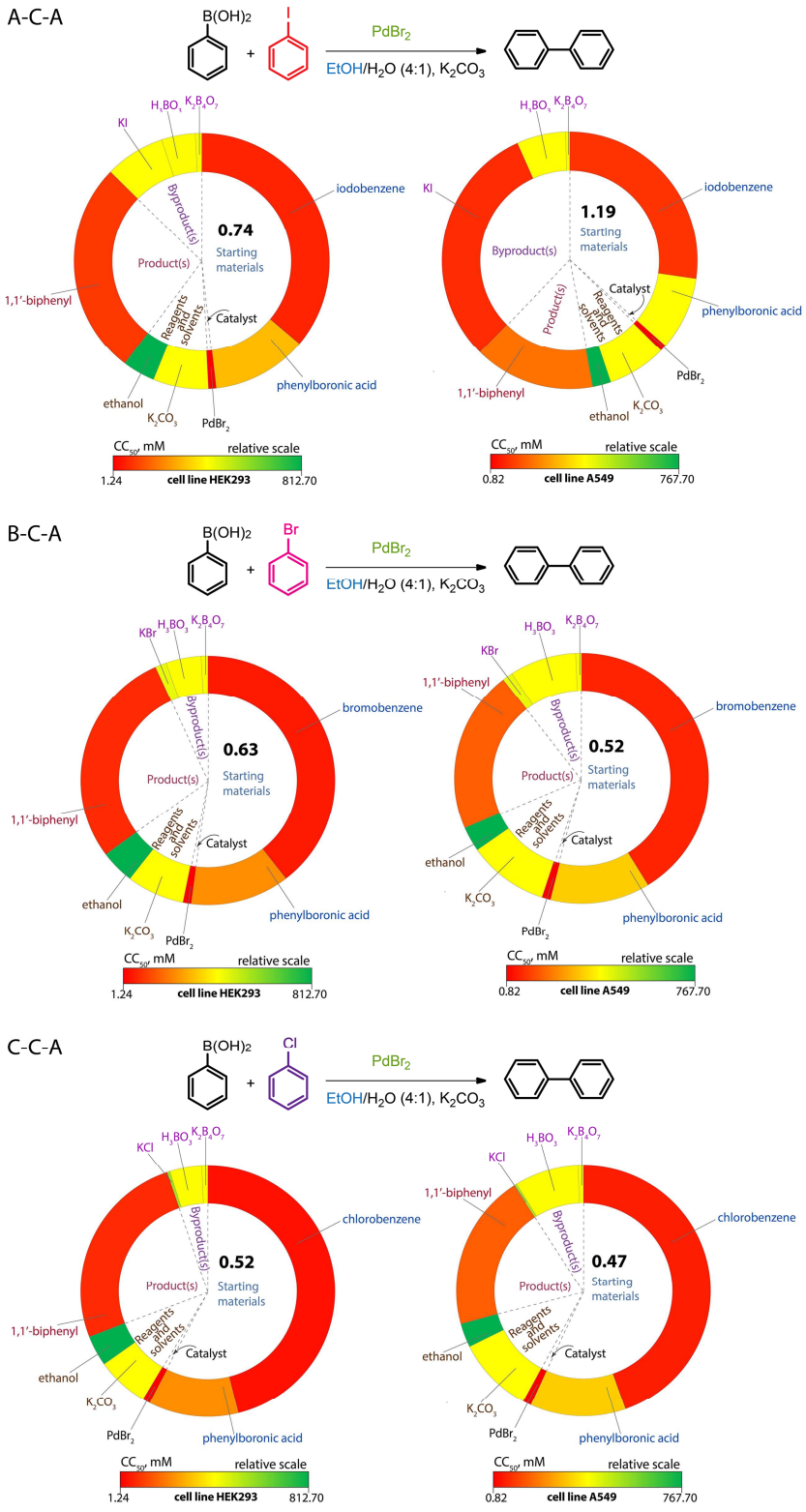


Fig. S10. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various starting materials. The first, second and third letters in the reaction names correspond to the type of starting material (iodobenzene (A), bromobenzene (B), chlorobenzene (C)), catalyst (in this case, $PdBr_2$ (C)), and solvent (in this case, ethanol (A)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

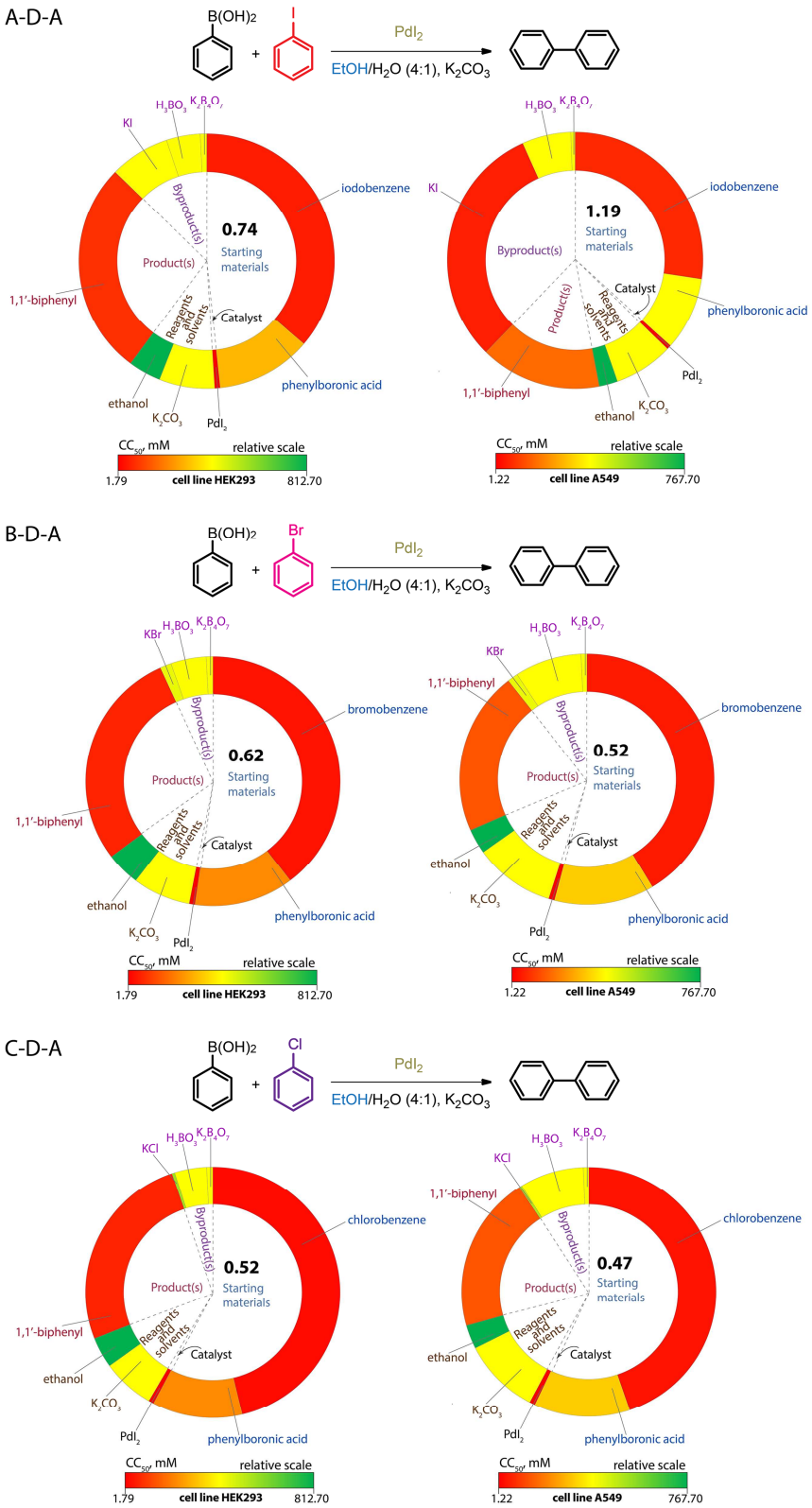


Fig. S11. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various starting materials. The first, second and third letters in the reaction names correspond to the type of starting material (iodobenzene (A), bromobenzene (B), chlorobenzene (C)), catalyst (in this case, PdI_2 (D)), and solvent (in this case, ethanol (A)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

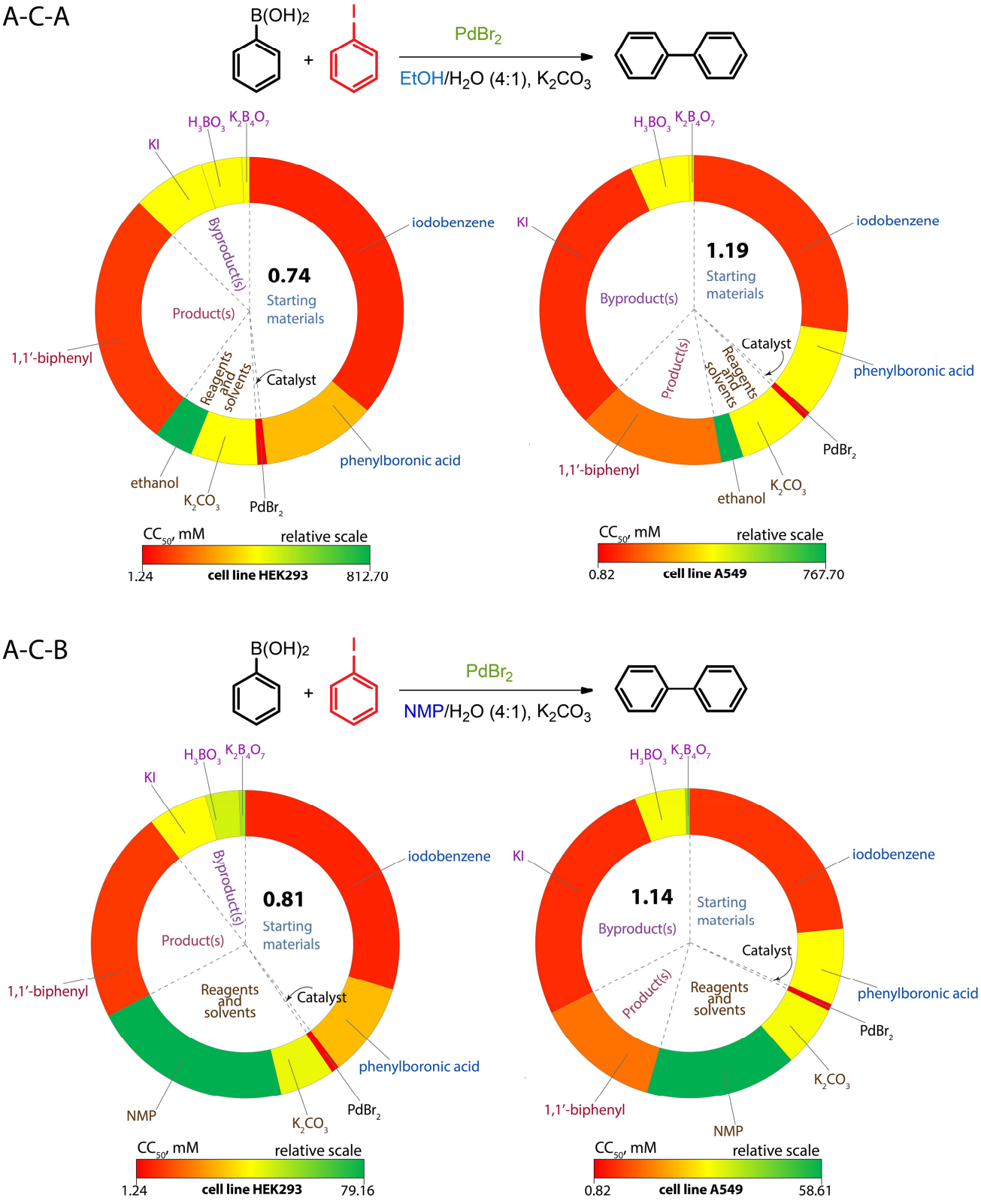


Fig. S12. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various solvents. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, iodobenzene (A), catalyst (in this case, $PdBr_2$ (C)), and solvent (ethanol (A) or *N*-methylpyrrolidone (B)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

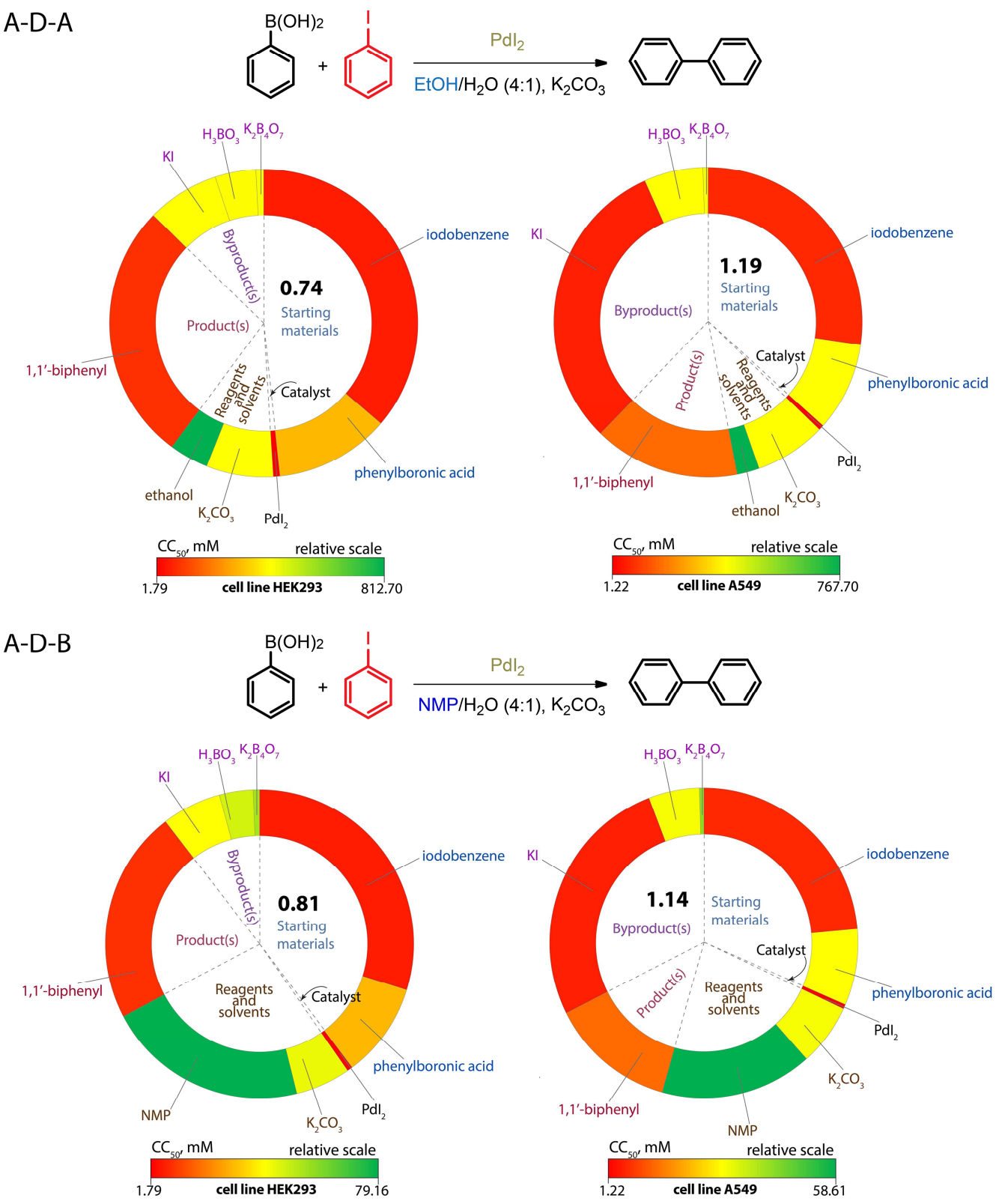


Fig. S13. Bio-Profiles for routes of synthesis of 1,1’-biphenyl with various solvents. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, iodobenzene (A), catalyst (in this case, PdI_2 (D)), and solvent (ethanol (A) or *N*-methylpyrrolidone (B)). The area of the sectors in the diagrams corresponds to the “normalized cytotoxicity” (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

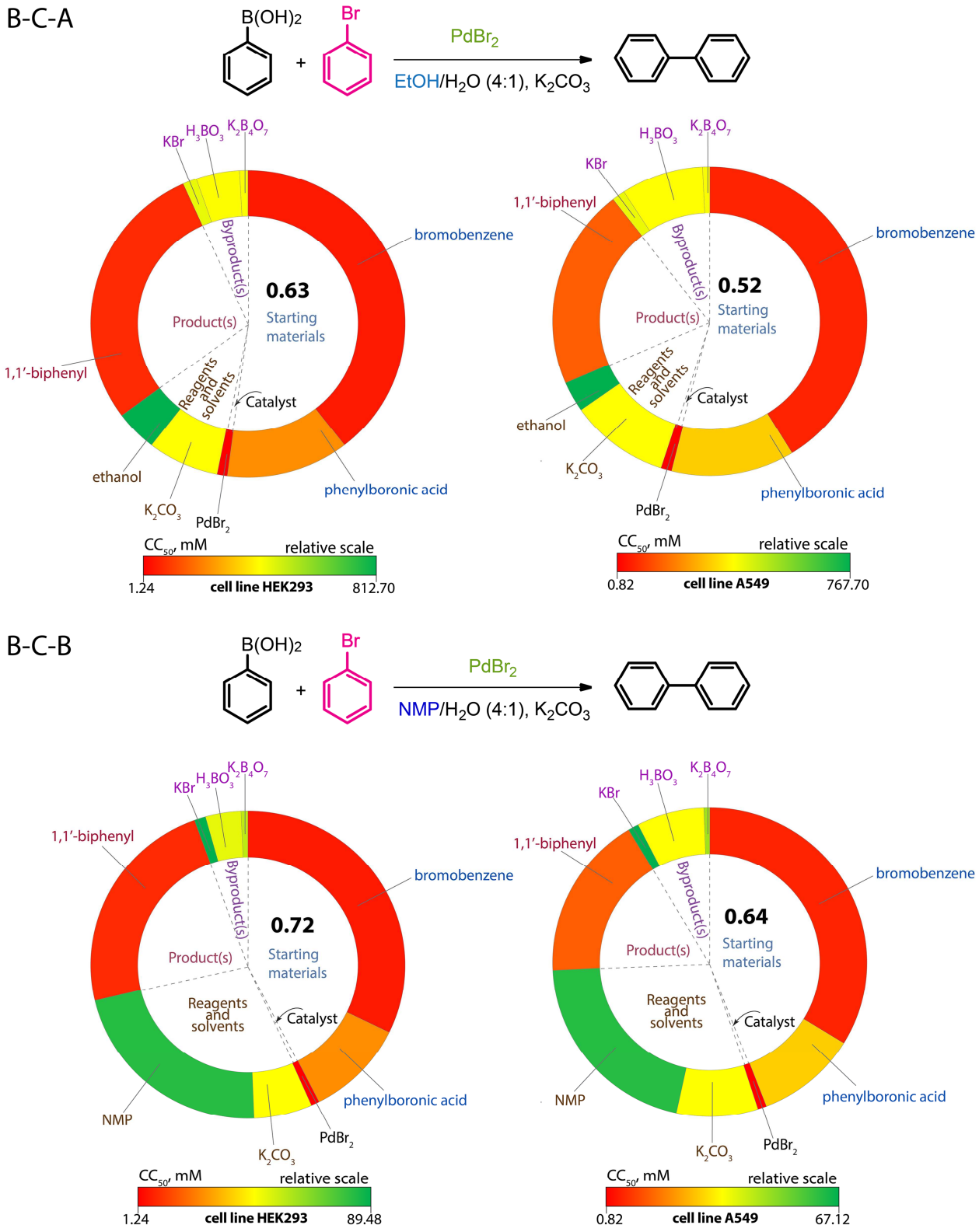


Fig. S14. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various solvents. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, bromobenzene (B), catalyst (in this case, $PdBr_2$ (C)), and solvent (ethanol (A) or *N*-methylpyrrolidone (B)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

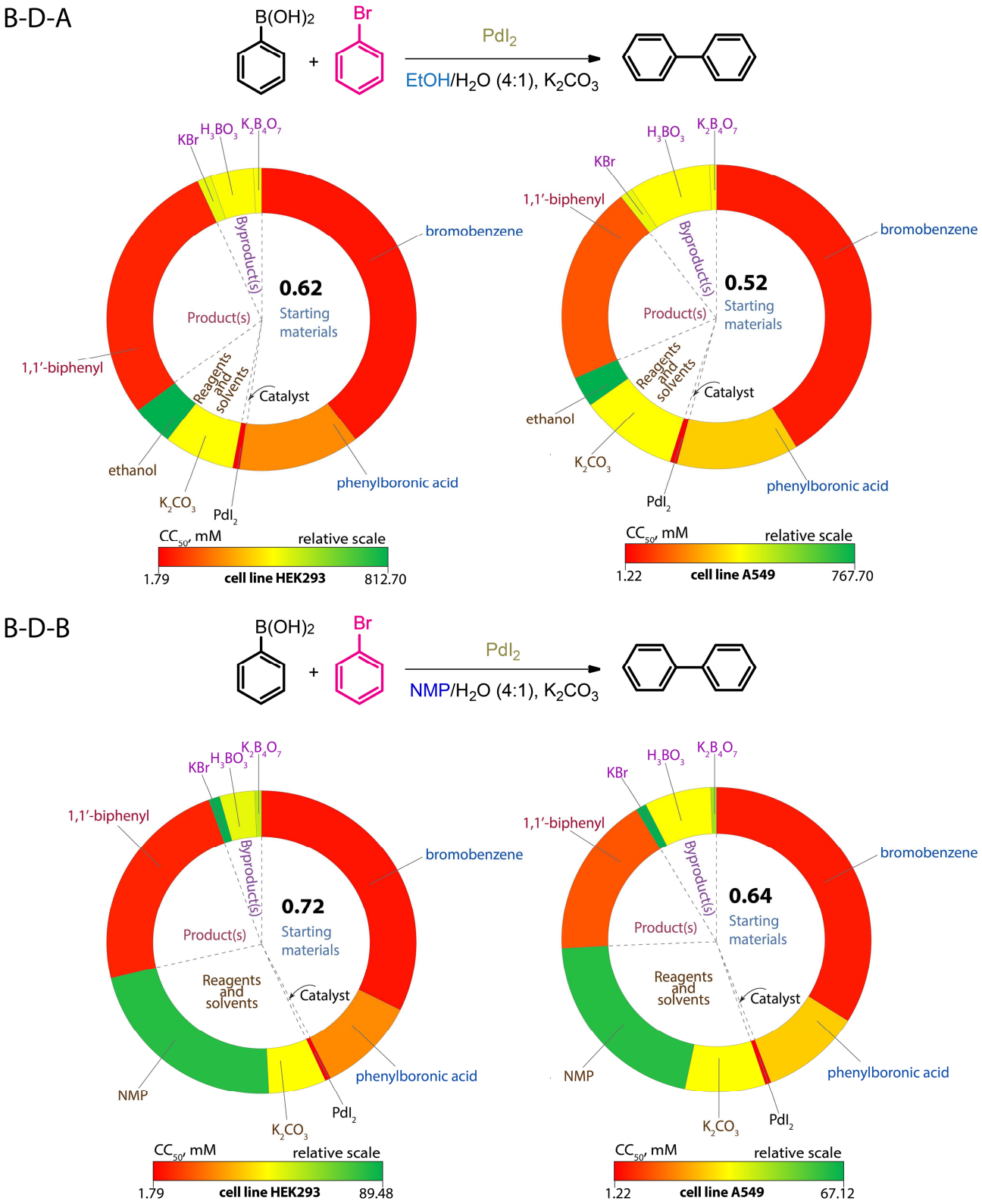


Fig. S15. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various solvents. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, bromobenzene (B), catalyst (in this case, PdI_2 (D)), and solvent (ethanol (A) or *N*-methylpyrrolidone (B)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

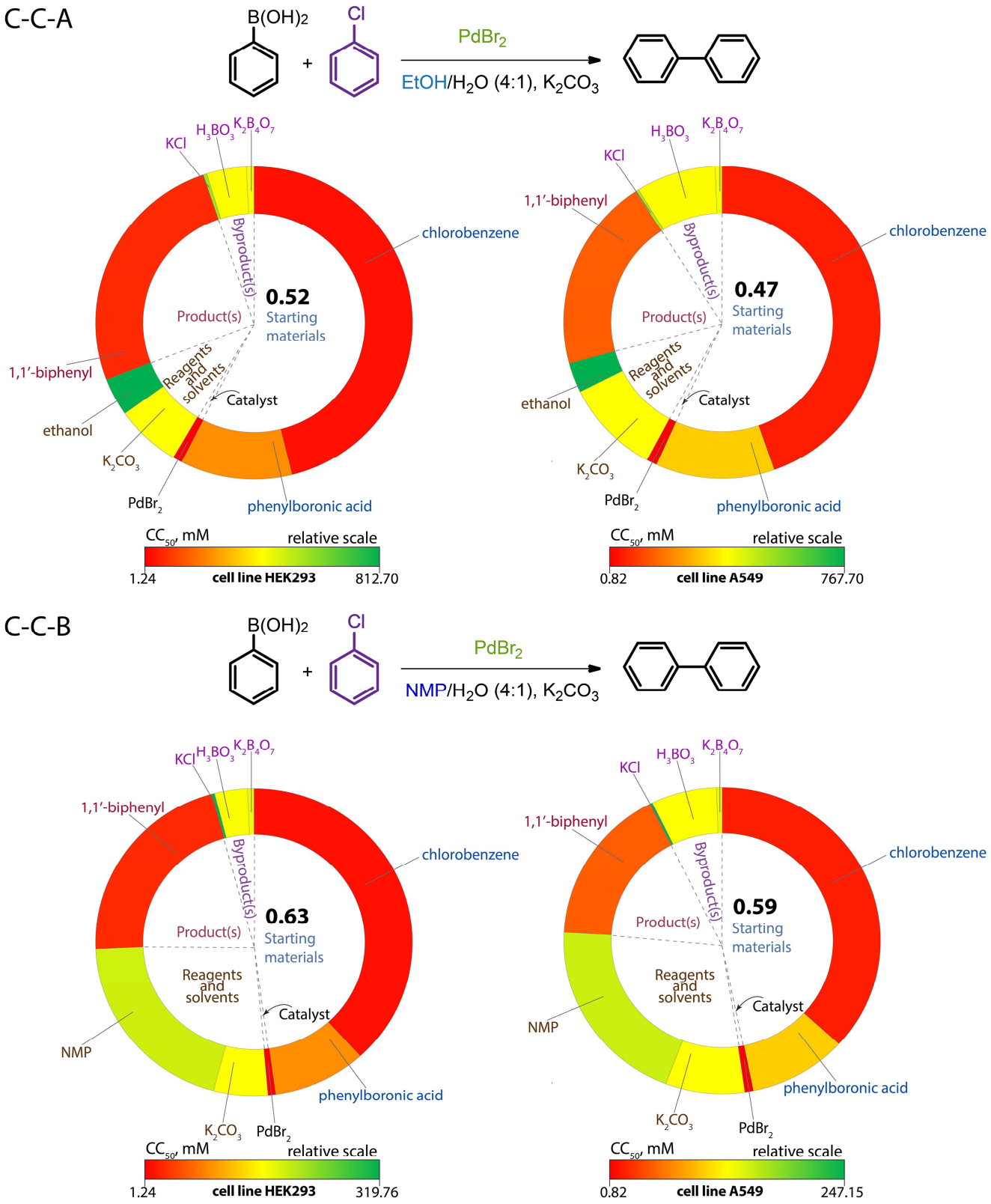


Fig. S16. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various solvents. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, chlorobenzene (C), catalyst (in this case, $PdBr_2$ (C)), and solvent (ethanol (A) or *N*-methylpyrrolidone (B)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

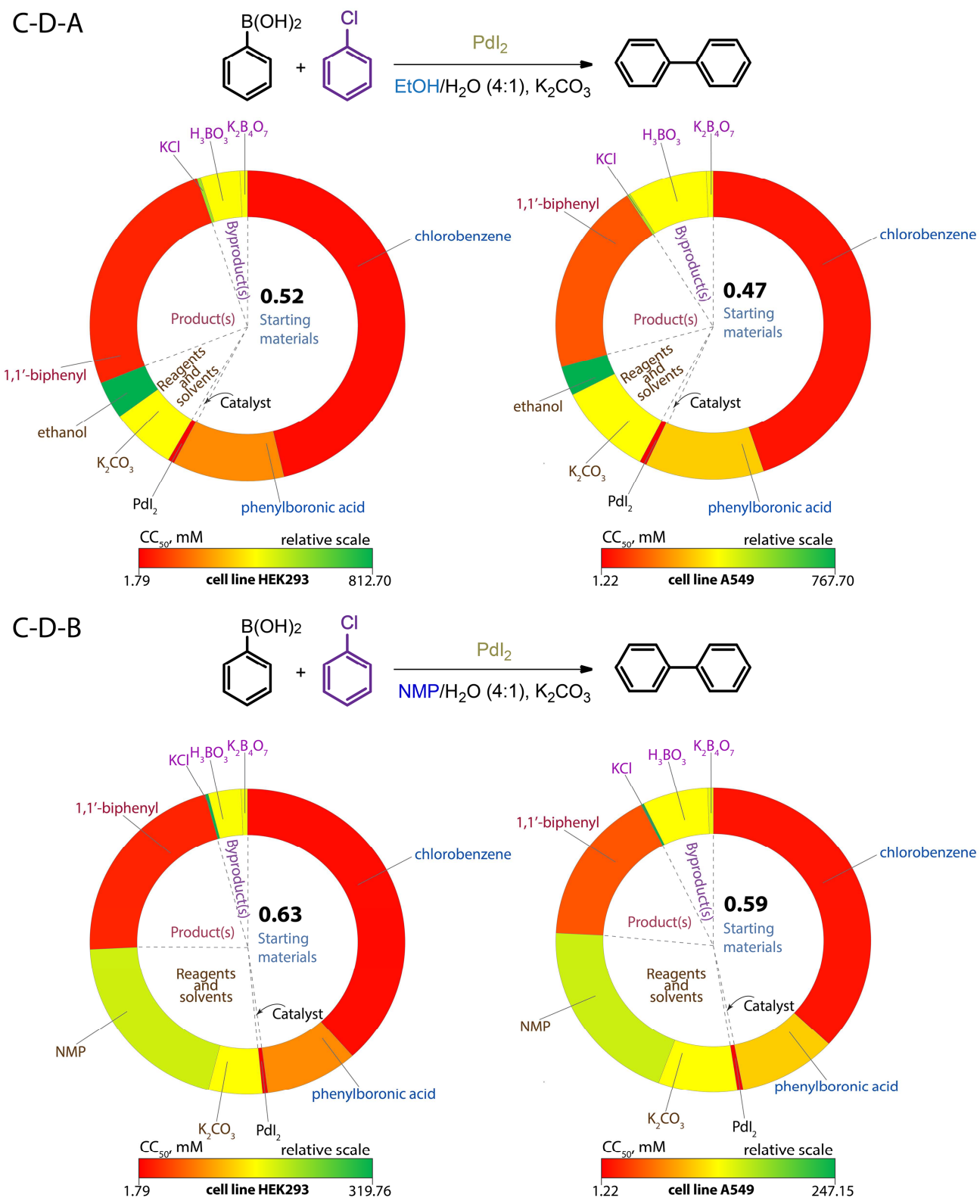


Fig. S17. Bio-Profiles for routes of synthesis of 1,1'-biphenyl with various solvents. The first, second and third letters in the reaction names correspond to the type of starting material (in this case, chlorobenzene (C), catalyst (in this case, $PdCl_2$ (D)), and solvent (ethanol (A) or *N*-methylpyrrolidone (B)). The area of the sectors in the diagrams corresponds to the "normalized cytotoxicity" (NC) of the compounds. The color of the sectors corresponds to the actual values of CC_{50} of the substances in a given cell line (see the relative cytotoxicity scales under the diagrams; the least toxic substance is shown in green, the most toxic is in red, and the other substances are of intermediate shades of red, orange and yellow). The calculated bio-Factors are shown inside the diagrams. See Table S6 for details.

References

1. K. S. Egorova, A. S. Galushko and V. P. Ananikov, *Angew. Chem. Int. Ed.*, 2020, **59**, 22296-22305.