

Establishing the main determinants of the environmental safety of catalytic fine chemical synthesis with catalytic cross-coupling reactions

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Table S1. Experimental data for Sonogashira reactions used in this work.

Substance	Mw, g·mol ⁻¹	Amount in reaction, mmol ^a	24-h CC ₅₀ , mM ^b		
			CaCo-2	FRSN	HEK293T
<i>Starting materials</i>					
Phenylacetylene	102.14	1.00	13.907 (11.268-16.545)	19.513 (11.123-27.902)	28.960 (18.033-39.887)
1-Ethynyl-3-nitrobenzene	147.13	1.00	2.492 (0.798-4.186)	5.524 (2.102-8.946)	4.441 (2.164-6.718)
Iodobenzene	204.01	1.00	3.349 (1.595-5.104)	3.333 (1.915-4.750)	9.543 (6.517-12.568)
Bromobenzene	157.01	1.00	5.546 (4.449-6.643)	4.803 (1.874-7.732)	17.497 (12.613-22.380)
Chlorobenzene	112.55	1.00	8.274 (7.014-9.533)	6.300 (1.317-11.284)	36.047 (30.006-42.087)
1-Iodo-4-nitrobenzene	249.01	1.00	>20 ^c	>20 ^c	>35 ^c
1-Bromo-4-nitrobenzene	202.01	1.00	>2 ^c	>10 ^c	>4 ^c
1-Chloro-4-nitrobenzene	157.55	1.00	>16 ^c	11.846 (3.789-19.904)	>33 ^c
1-Iodo-4-methoxybenzene	234.04	1.00	23.464 (15.107-31.821)	11.793 (10.574-13.013)	34.293 (27.562-41.023)
1-Bromo-4-methoxybenzene	187.04	1.00	7.915 (4.567-11.263)	6.500 (2.858-10.143)	24.195 (13.868-34.522)
<i>Catalysts</i>					
Pd(OAc) ₂	224.50	0.01	1.035 (0.421-1.650)	0.709 (0.510-0.908)	1.096 (0.640-1.553)
PdCl ₂	177.33	0.01	0.698 (0.522-0.875)	0.385 (0.305-0.465)	0.724 (0.347-1.102)
Pd(acac) ₂	304.64	0.01	0.037 (0.026-0.049)	0.007 (0.005-0.009)	0.014 (0.009-0.019)
CuI	190.45	0.01	0.479 (0.237-0.722)	0.306 (0.140-0.472)	0.623 (0.397-0.850)
CuBr	143.45	0.01	0.197 (0.134-0.260)	0.164 (0.093-0.235)	0.195 (0.165-0.225)
<i>Reagents</i>					
Et ₃ N	101.19	1.00	29.270 (17.623-40.917)	119.525 (103.494-135.556)	38.997 (30.689-47.304)
Et ₂ NH	73.138	1.00	13.785 (3.492-24.077)	23.963 (18.375-29.552)	11.255 (1.261-21.249)
<i>Solvents</i>					
DMF	73.09	25.83 (12.92) ^d	>35 ^c	>34 ^c	>139 ^c
NMP	99.13	20.78 (10.39) ^d	144.300 (108.218-180.382)	118.167 (86.989-149.345)	192.500 (161.918-223.082)
H ₂ O	18.02	110.80 (55.40) ^d	>11000 ^e	>11000 ^e	>11000 ^e
<i>Products</i>					
Diphenylacetylene	178.23	1.00	>11 ^c	19.790 (10.992-28.588)	>24 ^c
1-Nitro-4-(phenylethynyl)benzene	223.23	1.00	>10 ^c	>11 ^c	>10 ^c
1-Nitro-3-((4-nitrophenyl)ethynyl)benzene	268.23	1.00	10.101 (6.978-13.224)	0.535 (0.169-0.902)	11.360 (10.679-12.041)
1-((4-Methoxyphenyl)ethynyl)-3-	253.26	1.00	5.150 (1.163-9.136)	9.493 (4.860-14.127)	2.317 (1.175-3.459)

nitrobenzene					
<i>Byproducts</i>					
Et ₃ N·HI	229.104	1.00	17.823 (12.807-2.839)	55.937 (40.497-71.376)	56.670 (42.050-71.290)
Et ₃ N·HBr	182.104	1.00	27.290 (14.732-39.848)	53.413 (51.322-55.505)	72.057 (61.478-82.636)
Et ₃ N·HCl	137.6	1.00	>19 ^c	>86 ^c	>39 ^c
Et ₂ NH·HI	201.05	1.00	9.903 (6.404-13.401)	66.827 (60.219-73.434)	87.748 (71.546-103.949)
Et ₂ NH·HBr	154.05	1.00	38.833 (27.087-50.580)	42.133 (31.963-52.304)	>36 ^c
Et ₂ NH·HCl	109.60	1.00	>13 ^c	>95 ^c	80.518 (70.500-90.535)

^a 100% conversion is considered. For clarity, maximal possible amount of byproduct was used in calculations. ^b 95% confidence intervals are shown in parentheses. ^c The exact value could not be measured due to technical difficulties (insufficient solubility in the cultural media). ^d The amount in a 1 : 1 mixture with water (for DMF and NMP) or with DMF or NMP (for water) is provided in the parentheses. ^e Estimated in accordance with the maximal dilution of cultural media with deionized water that did not affect the viability of cells.

Table S2. Experimental data for Mizoroki-Heck reactions used in this work.

Substance	Mw, g·mol ⁻¹	Amount in reaction, mmol ^a	24-h CC ₅₀ , mM ^b		
			CaCo-2	FRSN	HEK293T
<i>Starting materials</i>					
Styrene	104.15	1.00	10.416 (6.474-14.357)	12.773 (8.254-17.292)	46.606 (17.818-75.394)
4-Chlorostyrene	138.59	1.00	3.882 (2.711-5.052)	2.007 (1.169-2.845)	12.073 (9.238-14.909)
4-Fluorostyrene	122.14	1.00	4.961 (2.751-7.171)	3.959 (1.003-6.914)	18.634 (8.087-29.181)
Iodobenzene	204.01	1.00	3.349 (1.595-5.104)	3.333 (1.915-4.750)	9.543 (6.517-12.568)
Bromobenzene	157.01	1.00	5.546 (4.449-6.643)	4.803 (1.874-7.732)	17.497 (12.613-22.380)
Chlorobenzene	112.55	1.00	8.274 (7.014-9.533)	6.300 (1.317-11.284)	36.047 (30.006-42.087)
1-Iodo-4-nitrobenzene	249.01	1.00	>20 ^c	>20 ^c	>35 ^c
1-Bromo-4-nitrobenzene	202.01	1.00	>2 ^c	>10 ^c	>4 ^c
1-Chloro-4-nitrobenzene	157.55	1.00	>16 ^c	11.846 (3.789-19.904)	>33 ^c
1-Iodo-4-methoxybenzene	234.04	1.00	23.464 (15.107-31.821)	11.793 (10.574-13.013)	34.293 (27.562-41.023)
1-Bromo-4-methoxybenzene	187.04	1.00	7.915 (4.567-11.263)	6.500 (2.858-10.143)	24.195 (13.868-34.522)
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Pd(OAc) ₂	224.50	0.01	1.035 (0.421-1.650)	0.709 (0.510-0.908)	1.096 (0.640-1.553)
PdCl ₂	177.33	0.01	0.698 (0.522-0.875)	0.385 (0.305-0.465)	0.724 (0.347-1.102)
Pd(acac) ₂	304.64	0.01	0.037 (0.026-0.049)	0.007 (0.005-0.009)	0.014 (0.009-0.019)
<i>Reagents</i>					
Et ₃ N	101.19	1.00	29.270 (17.623-40.917)	119.525 (103.494-135.556)	38.997 (30.689-47.304)
Et ₂ NH	73.138	1.00	13.785 (3.492-24.077)	23.963 (18.375-29.552)	11.255 (1.261-21.249)
<i>Solvents</i>					
DMF	73.09	25.83	>35 ^c	>34 ^c	>139 ^c
NMP	99.13	20.78	144.300 (108.218-180.382)	118.167 (86.989-149.345)	192.500 (161.918-223.082)
<i>Products</i>					
(E)-Stilbene	180.25	1.00	>58 ^c	>33 ^c	>58 ^c
(E)-4-Nitrostilbene	225.25	1.00	>10 ^c	22.287 (20.685-23.888)	>9 ^c
(E)-4-Chlorostilbene	214.69	1.00	5.634 (2.796-8.473)	2.336 (0.891-3.782)	8.409 (2.821-13.998)
(E)-4-Chloro-4'-nitrostilbene	259.69	1.00	>6 ^c	>13 ^c	>13 ^c
(E)-4-Fluoro-4'-nitrostilbene	243.24	1.00	>2 ^c	18.167 (15.695-20.638)	>15 ^c
(E)-4-Methoxystilbene	210.28	1.00	>34 ^c	33.720 (26.234-41.206)	>8 ^c
<i>Byproducts</i>					
Et ₃ N·HI	229.104	1.00	17.823 (12.807-2.839)	55.937 (40.497-71.376)	56.670 (42.050-71.290)
Et ₃ N·HBr	182.104	1.00	27.290 (14.732-39.848)	53.413 (51.322-55.505)	72.057 (61.478-82.636)

Et ₃ N·HCl	137.6	1.00	>19 ^c	>86 ^c	>39 ^c
Et ₂ NH·HI	201.05	1.00	9.903 (6.404-13.401)	66.827 (60.219-73.434)	87.748 (71.546-103.949)
Et ₂ NH·HBr	154.05	1.00	38.833 (27.087-50.580)	42.133 (31.963-52.304)	>36 ^c
Et ₂ NH·HCl	109.60	1.00	>13 ^c	>95 ^c	80.518 (70.500-90.535)

^a 100% conversion is considered. For clarity, maximal possible amount of byproduct was used in calculations. ^b 95% confidence intervals are shown in parentheses. ^c The exact value could not be measured due to technical difficulties (insufficient solubility in the cultural media).

Table S3. bio-Factors and cytotoxicity potentials for synthesis of diphenylacetylene.

Reaction	Starting materials (SM2)	Catalyst (CT1) PdA ₂	Catalyst (CT2) CuX	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
							BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A-A	PhI	OAc	I	Et ₃ N	DMF	Et ₃ N·HI	0.78	1.17	0.92	0.82	0.75	1.14	0.85	0.8	0.89	0.93	0.82	0.78
A-A-A-A-B	PhI	OAc	I	Et ₃ N	NMP	Et ₃ N·HI	0.56	0.58	0.32	0.23	0.47	0.55	0.26	0.21	0.68	0.33	0.23	0.19
A-A-A-A-C	PhI	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.42	0.45	0.19	0.1	0.3	0.42	0.13	0.07	0.47	0.2	0.09	0.05
A-A-A-A-D	PhI	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.68	0.81	0.55	0.46	0.63	0.78	0.49	0.44	0.81	0.56	0.46	0.42
A-A-A-A-E	PhI	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.5	0.51	0.25	0.16	0.4	0.48	0.19	0.14	0.6	0.27	0.16	0.12
A-A-A-B-A	PhI	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.52	1.86	0.96	0.87	0.55	1.55	0.85	0.8	0.46	1.79	0.82	0.77
A-A-A-B-B	PhI	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.29	1.27	0.37	0.28	0.27	0.96	0.26	0.21	0.19	1.2	0.22	0.18
A-A-A-B-C	PhI	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.2	1.14	0.23	0.14	0.15	0.83	0.12	0.07	0.08	1.06	0.09	0.05
A-A-A-B-D	PhI	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.4	1.5	0.6	0.51	0.41	1.19	0.49	0.44	0.32	1.43	0.45	0.41
A-A-A-B-E	PhI	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.25	1.2	0.3	0.21	0.21	0.89	0.19	0.14	0.14	1.13	0.16	0.11
A-A-B-A-A	PhI	OAc	Br	Et ₃ N	DMF	Et ₃ N·HI	0.79	1.2	0.95	0.85	0.75	1.17	0.88	0.83	0.89	0.96	0.86	0.82
A-A-B-A-B	PhI	OAc	Br	Et ₃ N	NMP	Et ₃ N·HI	0.58	0.61	0.35	0.26	0.5	0.58	0.29	0.24	0.71	0.37	0.26	0.22
A-A-B-A-C	PhI	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.46	0.48	0.22	0.13	0.35	0.44	0.15	0.1	0.55	0.24	0.13	0.09
A-A-B-A-D	PhI	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.69	0.84	0.58	0.49	0.64	0.81	0.52	0.47	0.82	0.6	0.49	0.45
A-A-B-A-E	PhI	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.52	0.54	0.28	0.19	0.43	0.51	0.22	0.17	0.65	0.3	0.2	0.16
A-A-B-B-A	PhI	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.52	1.89	0.99	0.9	0.56	1.58	0.88	0.83	0.47	1.83	0.85	0.81
A-A-B-B-B	PhI	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.3	1.3	0.4	0.31	0.29	0.99	0.28	0.23	0.21	1.23	0.26	0.22
A-A-B-B-C	PhI	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.22	1.17	0.26	0.17	0.18	0.85	0.15	0.1	0.11	1.1	0.12	0.08
A-A-B-B-D	PhI	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.41	1.53	0.63	0.54	0.42	1.22	0.51	0.46	0.33	1.46	0.49	0.45
A-A-B-B-E	PhI	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.27	1.23	0.33	0.24	0.24	0.92	0.22	0.17	0.16	1.17	0.19	0.15
A-B-A-A-A	PhI	Cl	I	Et ₃ N	DMF	Et ₃ N·HI	0.78	1.18	0.92	0.83	0.75	1.16	0.87	0.81	0.89	0.93	0.83	0.79
A-B-A-A-B	PhI	Cl	I	Et ₃ N	NMP	Et ₃ N·HI	0.56	0.58	0.33	0.24	0.48	0.56	0.27	0.22	0.69	0.34	0.23	0.19
A-B-A-A-C	PhI	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.43	0.45	0.19	0.1	0.32	0.43	0.14	0.09	0.48	0.2	0.1	0.06
A-B-A-A-D	PhI	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.68	0.81	0.56	0.47	0.63	0.79	0.5	0.45	0.81	0.57	0.46	0.42
A-B-A-A-E	PhI	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.5	0.52	0.26	0.17	0.41	0.5	0.2	0.15	0.61	0.27	0.17	0.12
A-B-A-B-A	PhI	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.52	1.87	0.97	0.87	0.55	1.57	0.86	0.81	0.46	1.8	0.82	0.78
A-B-A-B-B	PhI	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.29	1.28	0.37	0.28	0.28	0.97	0.27	0.22	0.19	1.2	0.23	0.19
A-B-A-B-C	PhI	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.21	1.14	0.24	0.15	0.16	0.84	0.13	0.08	0.09	1.07	0.09	0.05
A-B-A-B-D	PhI	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.4	1.51	0.6	0.51	0.41	1.2	0.5	0.45	0.32	1.43	0.46	0.42
A-B-A-B-E	PhI	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.25	1.21	0.3	0.21	0.22	0.9	0.2	0.15	0.14	1.13	0.16	0.12
A-B-B-A-A	PhI	Cl	Br	Et ₃ N	DMF	Et ₃ N·HI	0.79	1.21	0.95	0.86	0.75	1.18	0.89	0.84	0.89	0.97	0.86	0.82
A-B-B-A-B	PhI	Cl	Br	Et ₃ N	NMP	Et ₃ N·HI	0.58	0.61	0.36	0.27	0.51	0.59	0.3	0.25	0.72	0.37	0.27	0.23
A-B-B-A-C	PhI	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.46	0.48	0.22	0.13	0.36	0.46	0.17	0.11	0.56	0.24	0.13	0.09
A-B-B-A-D	PhI	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.69	0.84	0.59	0.5	0.65	0.82	0.53	0.48	0.83	0.6	0.5	0.46
A-B-B-A-E	PhI	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.53	0.55	0.29	0.2	0.44	0.52	0.23	0.18	0.66	0.31	0.2	0.16
A-B-B-B-A	PhI	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.52	1.9	0.99	0.9	0.56	1.59	0.89	0.84	0.47	1.83	0.86	0.81
A-B-B-B-B	PhI	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.31	1.31	0.4	0.31	0.3	1	0.3	0.25	0.21	1.24	0.26	0.22
A-B-B-B-C	PhI	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.23	1.17	0.27	0.18	0.19	0.87	0.16	0.11	0.12	1.1	0.13	0.09
A-B-B-B-D	PhI	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.41	1.54	0.63	0.54	0.43	1.23	0.53	0.48	0.34	1.47	0.49	0.45
A-B-B-B-E	PhI	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.27	1.24	0.33	0.24	0.25	0.93	0.23	0.18	0.17	1.17	0.2	0.15
A-C-A-A-A	PhI	acac	I	Et ₃ N	DMF	Et ₃ N·HI	0.82	1.43	1.18	1.09	0.89	2.56	2.27	2.22	0.94	1.63	1.53	1.49

A-C-A-A-B	PhI	acac	I	Et ₃ N	NMP	Et ₃ N·HI	0.69	0.84	0.58	0.49	0.85	1.96	1.67	1.62	0.9	1.04	0.93	0.89
A-C-A-A-C	PhI	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.63	0.71	0.45	0.36	0.84	1.83	1.54	1.49	0.88	0.91	0.8	0.76
A-C-A-A-D	PhI	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.76	1.07	0.81	0.72	0.87	2.19	1.9	1.85	0.92	1.27	1.16	1.12
A-C-A-A-E	PhI	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.67	0.77	0.52	0.42	0.85	1.9	1.61	1.56	0.89	0.97	0.87	0.83
A-C-A-B-A	PhI	acac	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.57	2.13	1.22	1.13	0.76	2.97	2.26	2.21	0.61	2.5	1.52	1.48
A-C-A-B-B	PhI	acac	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.41	1.53	0.63	0.54	0.7	2.37	1.67	1.62	0.49	1.9	0.93	0.89
A-C-A-B-C	PhI	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.35	1.4	0.49	0.4	0.69	2.24	1.54	1.49	0.45	1.77	0.79	0.75
A-C-A-B-D	PhI	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.49	1.76	0.86	0.77	0.73	2.6	1.9	1.85	0.54	2.13	1.16	1.12
A-C-A-B-E	PhI	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.38	1.46	0.56	0.47	0.7	2.31	1.6	1.55	0.47	1.84	0.86	0.82
A-C-B-A-A	PhI	acac	Br	Et ₃ N	DMF	Et ₃ N·HI	0.82	1.46	1.21	1.12	0.89	2.59	2.3	2.25	0.94	1.67	1.56	1.52
A-C-B-A-B	PhI	acac	Br	Et ₃ N	NMP	Et ₃ N·HI	0.7	0.87	0.61	0.52	0.85	1.99	1.7	1.65	0.9	1.07	0.97	0.93
A-C-B-A-C	PhI	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.65	0.74	0.48	0.39	0.84	1.86	1.57	1.52	0.89	0.94	0.83	0.79
A-C-B-A-D	PhI	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.77	1.1	0.84	0.75	0.87	2.22	1.93	1.88	0.92	1.3	1.2	1.16
A-C-B-A-E	PhI	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.68	0.8	0.55	0.45	0.85	1.93	1.63	1.58	0.9	1.01	0.9	0.86
A-C-B-B-A	PhI	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.58	2.15	1.25	1.16	0.77	3	2.29	2.24	0.61	2.53	1.56	1.51
A-C-B-B-B	PhI	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.42	1.56	0.66	0.57	0.71	2.4	1.7	1.65	0.5	1.94	0.96	0.92
A-C-B-B-C	PhI	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.37	1.43	0.52	0.43	0.69	2.27	1.57	1.51	0.46	1.8	0.83	0.79
A-C-B-B-D	PhI	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.5	1.79	0.89	0.8	0.73	2.63	1.93	1.88	0.55	2.17	1.19	1.15
A-C-B-B-E	PhI	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.39	1.49	0.59	0.5	0.7	2.34	1.63	1.58	0.48	1.87	0.9	0.85
B-A-A-A-A	PhBr	OAc	I	Et ₃ N	DMF	Et ₃ N·HBr	0.85	1.05	0.9	0.81	0.81	1.05	0.85	0.8	0.93	0.88	0.82	0.78
B-A-A-A-B	PhBr	OAc	I	Et ₃ N	NMP	Et ₃ N·HBr	0.66	0.46	0.3	0.21	0.57	0.46	0.26	0.21	0.78	0.29	0.22	0.18
B-A-A-A-C	PhBr	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.51	0.33	0.17	0.08	0.39	0.32	0.13	0.08	0.6	0.15	0.09	0.05
B-A-A-A-D	PhBr	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.77	0.69	0.53	0.44	0.71	0.69	0.49	0.44	0.88	0.52	0.45	0.41
B-A-A-A-E	PhBr	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.6	0.39	0.24	0.14	0.49	0.39	0.19	0.14	0.72	0.22	0.16	0.12
B-A-A-B-A	PhBr	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.51	1.75	0.89	0.79	0.59	1.46	0.86	0.81	0.48	1.74	0.83	0.79
B-A-A-B-B	PhBr	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.25	1.15	0.29	0.2	0.31	0.87	0.27	0.21	0.21	1.15	0.24	0.2
B-A-A-B-C	PhBr	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.15	1.02	0.16	0.07	0.18	0.73	0.13	0.08	0.1	1.02	0.1	0.06
B-A-A-B-D	PhBr	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.38	1.38	0.52	0.43	0.45	1.1	0.5	0.44	0.34	1.38	0.47	0.43
B-A-A-B-E	PhBr	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.21	1.09	0.22	0.13	0.25	0.8	0.2	0.15	0.16	1.08	0.17	0.13
B-A-B-A-A	PhBr	OAc	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.85	1.08	0.93	0.84	0.82	1.08	0.88	0.83	0.93	0.92	0.85	0.81
B-A-B-A-B	PhBr	OAc	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.68	0.49	0.33	0.24	0.59	0.49	0.29	0.24	0.81	0.32	0.26	0.22
B-A-B-A-C	PhBr	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.55	0.36	0.2	0.11	0.44	0.35	0.15	0.1	0.67	0.19	0.13	0.08
B-A-B-A-D	PhBr	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.78	0.72	0.56	0.47	0.72	0.72	0.52	0.47	0.89	0.55	0.49	0.45
B-A-B-A-E	PhBr	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.63	0.42	0.27	0.17	0.53	0.42	0.22	0.17	0.76	0.25	0.19	0.15
B-A-B-B-A	PhBr	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.52	1.78	0.92	0.82	0.6	1.49	0.89	0.84	0.49	1.78	0.87	0.83
B-A-B-B-B	PhBr	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.27	1.18	0.32	0.23	0.33	0.9	0.29	0.24	0.23	1.18	0.27	0.23
B-A-B-B-C	PhBr	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.18	1.05	0.19	0.1	0.21	0.76	0.16	0.11	0.13	1.05	0.14	0.1
B-A-B-B-D	PhBr	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.39	1.41	0.55	0.46	0.46	1.13	0.52	0.47	0.36	1.41	0.5	0.46
B-A-B-B-E	PhBr	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.23	1.12	0.25	0.16	0.27	0.83	0.23	0.18	0.19	1.12	0.21	0.17
B-B-A-A-A	PhBr	Cl	I	Et ₃ N	DMF	Et ₃ N·HBr	0.85	1.06	0.9	0.81	0.81	1.06	0.87	0.82	0.93	0.89	0.82	0.78
B-B-A-A-B	PhBr	Cl	I	Et ₃ N	NMP	Et ₃ N·HBr	0.66	0.47	0.31	0.22	0.58	0.47	0.27	0.22	0.79	0.29	0.23	0.19
B-B-A-A-C	PhBr	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.52	0.33	0.17	0.08	0.41	0.34	0.14	0.09	0.61	0.16	0.1	0.05
B-B-A-A-D	PhBr	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.77	0.7	0.54	0.45	0.72	0.7	0.5	0.45	0.88	0.52	0.46	0.42
B-B-A-A-E	PhBr	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.6	0.4	0.24	0.15	0.51	0.4	0.2	0.15	0.72	0.22	0.16	0.12
B-B-A-B-A	PhBr	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.51	1.75	0.89	0.8	0.59	1.47	0.87	0.82	0.48	1.75	0.84	0.8

B-B-A-B-B	PhBr	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.26	1.16	0.3	0.2	0.31	0.88	0.28	0.23	0.21	1.15	0.24	0.2
B-B-A-B-C	PhBr	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.16	1.02	0.16	0.07	0.19	0.75	0.14	0.09	0.11	1.02	0.11	0.07
B-B-A-B-D	PhBr	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.38	1.39	0.53	0.44	0.46	1.11	0.51	0.46	0.34	1.38	0.47	0.43
B-B-A-B-E	PhBr	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.21	1.09	0.23	0.14	0.26	0.81	0.21	0.16	0.16	1.09	0.18	0.13
B-B-B-A-A	PhBr	Cl	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.85	1.09	0.93	0.84	0.82	1.09	0.89	0.84	0.93	0.92	0.86	0.82
B-B-B-A-B	PhBr	Cl	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.68	0.5	0.34	0.25	0.6	0.5	0.3	0.25	0.81	0.33	0.26	0.22
B-B-B-A-C	PhBr	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.56	0.36	0.2	0.11	0.46	0.36	0.17	0.12	0.68	0.19	0.13	0.09
B-B-B-A-D	PhBr	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.78	0.73	0.57	0.48	0.73	0.73	0.53	0.48	0.89	0.56	0.49	0.45
B-B-B-A-E	PhBr	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.63	0.43	0.27	0.18	0.54	0.43	0.23	0.18	0.76	0.26	0.2	0.16
B-B-B-B-A	PhBr	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.52	1.78	0.92	0.83	0.6	1.5	0.9	0.85	0.49	1.78	0.87	0.83
B-B-B-B-B	PhBr	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.27	1.19	0.33	0.23	0.34	0.91	0.31	0.25	0.23	1.19	0.28	0.24
B-B-B-B-C	PhBr	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.18	1.05	0.19	0.1	0.22	0.77	0.17	0.12	0.14	1.06	0.14	0.1
B-B-B-B-D	PhBr	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.39	1.42	0.56	0.46	0.47	1.14	0.54	0.48	0.36	1.42	0.51	0.47
B-B-B-B-E	PhBr	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.23	1.12	0.26	0.17	0.28	0.84	0.24	0.19	0.19	1.12	0.21	0.17
B-C-A-A-A	PhBr	acac	I	Et ₃ N	DMF	Et ₃ N·HBr	0.88	1.32	1.16	1.07	0.92	2.47	2.27	2.22	0.96	1.59	1.52	1.48
B-C-A-A-B	PhBr	acac	I	Et ₃ N	NMP	Et ₃ N·HBr	0.78	0.72	0.56	0.47	0.89	1.87	1.67	1.62	0.94	0.99	0.93	0.89
B-C-A-A-C	PhBr	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.73	0.59	0.43	0.34	0.89	1.74	1.54	1.49	0.93	0.86	0.8	0.75
B-C-A-A-D	PhBr	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.83	0.95	0.79	0.7	0.91	2.1	1.9	1.85	0.95	1.22	1.16	1.12
B-C-A-A-E	PhBr	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.76	0.65	0.5	0.4	0.89	1.81	1.61	1.56	0.93	0.92	0.86	0.82
B-C-A-B-A	PhBr	acac	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.57	2.01	1.15	1.05	0.79	2.88	2.27	2.22	0.63	2.45	1.54	1.5
B-C-A-B-B	PhBr	acac	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.39	1.41	0.55	0.46	0.74	2.28	1.68	1.63	0.51	1.85	0.94	0.9
B-C-A-B-C	PhBr	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.33	1.28	0.42	0.33	0.72	2.15	1.55	1.5	0.47	1.72	0.81	0.77
B-C-A-B-D	PhBr	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.48	1.64	0.78	0.69	0.76	2.51	1.91	1.86	0.56	2.08	1.17	1.13
B-C-A-B-E	PhBr	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.36	1.35	0.48	0.39	0.73	2.22	1.61	1.56	0.49	1.79	0.88	0.84
B-C-B-A-A	PhBr	acac	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.88	1.35	1.19	1.1	0.92	2.5	2.3	2.25	0.96	1.62	1.56	1.52
B-C-B-A-B	PhBr	acac	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.79	0.75	0.59	0.5	0.9	1.9	1.7	1.65	0.94	1.03	0.97	0.92
B-C-B-A-C	PhBr	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.74	0.62	0.46	0.37	0.89	1.77	1.57	1.52	0.93	0.89	0.83	0.79
B-C-B-A-D	PhBr	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.84	0.98	0.82	0.73	0.91	2.13	1.93	1.88	0.95	1.26	1.2	1.15
B-C-B-A-E	PhBr	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.77	0.68	0.53	0.43	0.89	1.83	1.64	1.59	0.94	0.96	0.9	0.86
B-C-B-B-A	PhBr	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.58	2.04	1.18	1.08	0.79	2.9	2.3	2.25	0.63	2.48	1.57	1.53
B-C-B-B-B	PhBr	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.4	1.44	0.58	0.49	0.74	2.31	1.71	1.66	0.52	1.89	0.98	0.94
B-C-B-B-C	PhBr	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.34	1.31	0.45	0.36	0.72	2.18	1.57	1.52	0.48	1.76	0.85	0.8
B-C-B-B-D	PhBr	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.49	1.67	0.81	0.72	0.76	2.54	1.94	1.89	0.57	2.12	1.21	1.17
B-C-B-B-E	PhBr	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.37	1.38	0.51	0.42	0.73	2.24	1.64	1.59	0.5	1.82	0.91	0.87
C-A-A-A-A	PhCl	OAc	I	Et ₃ N	DMF	Et ₃ N·HCl	0.92	1	0.91	0.82	0.84	1	0.85	0.8	0.98	0.85	0.83	0.79
C-A-A-A-B	PhCl	OAc	I	Et ₃ N	NMP	Et ₃ N·HCl	0.79	0.4	0.32	0.23	0.62	0.41	0.25	0.2	0.92	0.26	0.24	0.19
C-A-A-A-C	PhCl	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.69	0.27	0.18	0.09	0.43	0.28	0.12	0.07	0.83	0.12	0.1	0.06
C-A-A-A-D	PhCl	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.87	0.63	0.55	0.46	0.76	0.64	0.48	0.43	0.96	0.49	0.47	0.42
C-A-A-A-E	PhCl	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.75	0.33	0.25	0.16	0.54	0.34	0.19	0.14	0.89	0.19	0.17	0.13
C-A-A-B-A	PhCl	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.56	1.69	0.94	0.85	0.6	1.41	0.85	0.8	0.48	1.71	0.82	0.78
C-A-A-B-B	PhCl	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.31	1.09	0.34	0.25	0.31	0.82	0.25	0.2	0.2	1.12	0.22	0.18
C-A-A-B-C	PhCl	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.22	0.96	0.21	0.12	0.17	0.68	0.12	0.07	0.09	0.99	0.09	0.05
C-A-A-B-D	PhCl	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.43	1.32	0.57	0.48	0.46	1.05	0.48	0.43	0.34	1.35	0.45	0.41
C-A-A-B-E	PhCl	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.27	1.03	0.28	0.18	0.25	0.75	0.18	0.13	0.15	1.05	0.16	0.11
C-A-B-A-A	PhCl	OAc	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.92	1.03	0.94	0.85	0.85	1.03	0.88	0.82	0.98	0.89	0.87	0.82

C-A-B-A-B	PhCl	OAc	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.81	0.43	0.35	0.26	0.64	0.44	0.28	0.23	0.93	0.29	0.27	0.23
C-A-B-A-C	PhCl	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.72	0.3	0.21	0.12	0.49	0.3	0.15	0.1	0.87	0.16	0.14	0.1
C-A-B-A-D	PhCl	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.87	0.66	0.58	0.49	0.77	0.67	0.51	0.46	0.96	0.52	0.5	0.46
C-A-B-A-E	PhCl	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.77	0.36	0.28	0.19	0.58	0.37	0.21	0.16	0.91	0.23	0.2	0.16
C-A-B-B-A	PhCl	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.56	1.72	0.97	0.88	0.61	1.44	0.87	0.82	0.49	1.75	0.85	0.81
C-A-B-B-B	PhCl	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.33	1.12	0.37	0.28	0.33	0.85	0.28	0.23	0.22	1.16	0.26	0.22
C-A-B-B-C	PhCl	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.24	0.99	0.24	0.15	0.21	0.71	0.15	0.1	0.12	1.02	0.12	0.08
C-A-B-B-D	PhCl	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.45	1.35	0.6	0.51	0.47	1.08	0.51	0.46	0.35	1.39	0.49	0.45
C-A-B-B-E	PhCl	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.29	1.06	0.31	0.21	0.27	0.78	0.21	0.16	0.18	1.09	0.19	0.15
C-B-A-A-A	PhCl	Cl	I	Et ₃ N	DMF	Et ₃ N·HCl	0.92	1	0.92	0.83	0.85	1.02	0.86	0.81	0.98	0.86	0.84	0.79
C-B-A-A-B	PhCl	Cl	I	Et ₃ N	NMP	Et ₃ N·HCl	0.79	0.41	0.32	0.23	0.63	0.42	0.26	0.21	0.92	0.26	0.24	0.2
C-B-A-A-C	PhCl	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.69	0.27	0.19	0.1	0.46	0.29	0.13	0.08	0.84	0.13	0.11	0.07
C-B-A-A-D	PhCl	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.87	0.64	0.55	0.46	0.76	0.65	0.49	0.44	0.96	0.49	0.47	0.43
C-B-A-A-E	PhCl	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.75	0.34	0.26	0.16	0.56	0.35	0.2	0.15	0.89	0.19	0.17	0.13
C-B-A-B-A	PhCl	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.56	1.69	0.94	0.85	0.6	1.42	0.86	0.81	0.48	1.72	0.82	0.78
C-B-A-B-B	PhCl	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.32	1.1	0.35	0.26	0.32	0.83	0.26	0.21	0.2	1.12	0.23	0.19
C-B-A-B-C	PhCl	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.22	0.96	0.21	0.12	0.19	0.7	0.13	0.08	0.09	0.99	0.09	0.05
C-B-A-B-D	PhCl	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.43	1.33	0.58	0.49	0.47	1.06	0.49	0.44	0.34	1.35	0.46	0.42
C-B-A-B-E	PhCl	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.27	1.03	0.28	0.19	0.26	0.76	0.2	0.15	0.15	1.06	0.16	0.12
C-B-B-A-A	PhCl	Cl	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.92	1.03	0.95	0.86	0.85	1.04	0.89	0.84	0.98	0.89	0.87	0.83
C-B-B-A-B	PhCl	Cl	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.81	0.44	0.35	0.26	0.65	0.45	0.29	0.24	0.93	0.3	0.28	0.23
C-B-B-A-C	PhCl	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.72	0.3	0.22	0.13	0.5	0.32	0.16	0.11	0.87	0.16	0.14	0.1
C-B-B-A-D	PhCl	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.87	0.67	0.58	0.49	0.77	0.68	0.52	0.47	0.96	0.53	0.51	0.46
C-B-B-A-E	PhCl	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.77	0.37	0.29	0.19	0.59	0.38	0.23	0.18	0.91	0.23	0.21	0.17
C-B-B-B-A	PhCl	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.56	1.72	0.97	0.88	0.61	1.45	0.89	0.84	0.49	1.75	0.86	0.82
C-B-B-B-B	PhCl	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.33	1.13	0.38	0.29	0.34	0.86	0.29	0.24	0.23	1.16	0.26	0.22
C-B-B-B-C	PhCl	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.24	0.99	0.24	0.15	0.22	0.72	0.16	0.11	0.13	1.03	0.13	0.09
C-B-B-B-D	PhCl	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.45	1.36	0.61	0.52	0.48	1.09	0.52	0.47	0.35	1.39	0.49	0.45
C-B-B-B-E	PhCl	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.29	1.06	0.31	0.22	0.28	0.79	0.23	0.17	0.18	1.09	0.2	0.15
C-C-A-A-A	PhCl	acac	I	Et ₃ N	DMF	Et ₃ N·HCl	0.93	1.26	1.17	1.08	0.94	2.42	2.26	2.21	0.99	1.56	1.54	1.49
C-C-A-A-B	PhCl	acac	I	Et ₃ N	NMP	Et ₃ N·HCl	0.87	0.66	0.58	0.49	0.91	1.82	1.67	1.62	0.98	0.96	0.94	0.9
C-C-A-A-C	PhCl	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.84	0.53	0.44	0.35	0.91	1.69	1.53	1.48	0.98	0.83	0.81	0.77
C-C-A-A-D	PhCl	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.91	0.89	0.81	0.72	0.92	2.05	1.9	1.85	0.98	1.19	1.17	1.13
C-C-A-A-E	PhCl	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.86	0.6	0.51	0.42	0.91	1.76	1.6	1.55	0.98	0.9	0.87	0.83
C-C-A-B-A	PhCl	acac	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.61	1.95	1.2	1.11	0.8	2.83	2.26	2.21	0.63	2.42	1.52	1.48
C-C-A-B-B	PhCl	acac	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.45	1.35	0.6	0.51	0.75	2.23	1.67	1.62	0.51	1.83	0.93	0.89
C-C-A-B-C	PhCl	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.38	1.22	0.47	0.38	0.73	2.1	1.53	1.48	0.47	1.69	0.79	0.75
C-C-A-B-D	PhCl	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.53	1.58	0.83	0.74	0.77	2.46	1.9	1.85	0.56	2.06	1.16	1.12
C-C-A-B-E	PhCl	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.42	1.29	0.54	0.45	0.74	2.17	1.6	1.55	0.49	1.76	0.86	0.82
C-C-B-A-A	PhCl	acac	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.94	1.29	1.2	1.11	0.94	2.45	2.29	2.24	0.99	1.59	1.57	1.53
C-C-B-A-B	PhCl	acac	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.88	0.69	0.61	0.52	0.92	1.85	1.7	1.65	0.98	1	0.98	0.94
C-C-B-A-C	PhCl	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.85	0.56	0.47	0.38	0.91	1.72	1.56	1.51	0.98	0.86	0.84	0.8
C-C-B-A-D	PhCl	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.91	0.92	0.84	0.75	0.92	2.08	1.93	1.88	0.98	1.23	1.21	1.17
C-C-B-A-E	PhCl	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.87	0.63	0.54	0.45	0.91	1.78	1.63	1.58	0.98	0.93	0.91	0.87
C-C-B-B-A	PhCl	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.62	1.98	1.23	1.14	0.8	2.85	2.29	2.24	0.63	2.45	1.56	1.52

C-C-B-B-B	PhCl	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.46	1.38	0.63	0.54	0.75	2.26	1.69	1.64	0.52	1.86	0.96	0.92
C-C-B-B-C	PhCl	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.4	1.25	0.5	0.41	0.73	2.13	1.56	1.51	0.48	1.73	0.83	0.79
C-C-B-B-D	PhCl	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.53	1.61	0.86	0.77	0.77	2.49	1.92	1.87	0.57	2.09	1.19	1.15
C-C-B-B-E	PhCl	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.43	1.32	0.57	0.47	0.74	2.19	1.63	1.58	0.5	1.79	0.9	0.86

Target product P (diphenylacetylene) and starting material SM1 (phenylacetylene) are not shown. PhI, iodobenzene; PhBr, bromobenzene; PhCl, chlorobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green. Organic solvents mixed with water at a 1:1 mass ratio are indicated as solvent/H₂O.

Table S4. bio-Factors and cytotoxicity potentials for synthesis of 1-nitro-4-(phenylethynyl)benzene.

Reaction	Starting materials (SM2)	Catalyst (CT1) PdA ₂	Catalyst (CT2) CuX	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
							BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A-A	R-I	OAc	I	Et ₃ N	DMF	Et ₃ N·HI	1	0.92	0.92	0.82	1	0.89	0.89	0.8	1.03	0.85	0.88	0.78
A-A-A-A-B	R-I	OAc	I	Et ₃ N	NMP	Et ₃ N·HI	1	0.33	0.33	0.23	1	0.3	0.3	0.21	1.11	0.26	0.29	0.19
A-A-A-A-C	R-I	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HI	1	0.2	0.2	0.1	1	0.17	0.17	0.07	1.23	0.12	0.15	0.05
A-A-A-A-D	R-I	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	1	0.56	0.56	0.46	1	0.53	0.53	0.44	1.06	0.49	0.52	0.42
A-A-A-A-E	R-I	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	1	0.26	0.26	0.16	1	0.23	0.23	0.14	1.15	0.19	0.22	0.12
A-A-A-B-A	R-I	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.6	1.62	0.97	0.87	0.68	1.3	0.89	0.8	0.51	1.71	0.87	0.77
A-A-A-B-B	R-I	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.37	1.02	0.38	0.28	0.42	0.71	0.3	0.21	0.25	1.12	0.28	0.18
A-A-A-B-C	R-I	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.27	0.89	0.24	0.14	0.28	0.58	0.16	0.07	0.15	0.99	0.15	0.05
A-A-A-B-D	R-I	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.48	1.25	0.61	0.51	0.56	0.94	0.53	0.44	0.38	1.35	0.51	0.41
A-A-A-B-E	R-I	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.32	0.95	0.31	0.21	0.36	0.64	0.23	0.14	0.2	1.05	0.21	0.11
A-A-B-A-A	R-I	OAc	Br	Et ₃ N	DMF	Et ₃ N·HI	1	0.95	0.95	0.85	1	0.92	0.92	0.83	1.03	0.89	0.92	0.82
A-A-B-A-B	R-I	OAc	Br	Et ₃ N	NMP	Et ₃ N·HI	1	0.36	0.36	0.26	1	0.33	0.33	0.24	1.1	0.29	0.32	0.22
A-A-B-A-C	R-I	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	1	0.23	0.23	0.13	1	0.19	0.19	0.1	1.18	0.16	0.19	0.09
A-A-B-A-D	R-I	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	1	0.59	0.59	0.49	1	0.56	0.56	0.47	1.06	0.52	0.55	0.45
A-A-B-A-E	R-I	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	1	0.29	0.29	0.19	1	0.26	0.26	0.17	1.13	0.23	0.26	0.16
A-A-B-B-A	R-I	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.61	1.65	1	0.9	0.69	1.33	0.92	0.83	0.52	1.75	0.91	0.81
A-A-B-B-B	R-I	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.39	1.05	0.41	0.31	0.44	0.74	0.32	0.23	0.27	1.16	0.32	0.22
A-A-B-B-C	R-I	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.3	0.92	0.27	0.17	0.32	0.6	0.19	0.1	0.18	1.02	0.18	0.08
A-A-B-B-D	R-I	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.5	1.28	0.64	0.54	0.57	0.97	0.56	0.46	0.39	1.39	0.55	0.45
A-A-B-B-E	R-I	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.34	0.98	0.34	0.24	0.38	0.67	0.26	0.17	0.23	1.09	0.25	0.15
A-B-A-A-A	R-I	Cl	I	Et ₃ N	DMF	Et ₃ N·HI	1	0.93	0.93	0.83	1	0.91	0.91	0.81	1.03	0.86	0.89	0.79
A-B-A-A-B	R-I	Cl	I	Et ₃ N	NMP	Et ₃ N·HI	1	0.34	0.34	0.24	1	0.31	0.31	0.22	1.11	0.26	0.29	0.19
A-B-A-A-C	R-I	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HI	1	0.2	0.2	0.1	1	0.18	0.18	0.09	1.22	0.13	0.16	0.06
A-B-A-A-D	R-I	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	1	0.57	0.57	0.47	1	0.54	0.54	0.45	1.06	0.49	0.52	0.42
A-B-A-A-E	R-I	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	1	0.27	0.27	0.17	1	0.25	0.24	0.15	1.15	0.2	0.22	0.12
A-B-A-B-A	R-I	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.6	1.62	0.97	0.87	0.69	1.32	0.9	0.81	0.51	1.72	0.88	0.78
A-B-A-B-B	R-I	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.37	1.03	0.38	0.28	0.43	0.72	0.31	0.22	0.25	1.13	0.29	0.19
A-B-A-B-C	R-I	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.28	0.89	0.25	0.15	0.3	0.59	0.17	0.08	0.15	0.99	0.15	0.05
A-B-A-B-D	R-I	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.49	1.26	0.61	0.51	0.57	0.95	0.54	0.45	0.38	1.36	0.52	0.42
A-B-A-B-E	R-I	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.33	0.96	0.31	0.21	0.37	0.65	0.24	0.15	0.21	1.06	0.22	0.12
A-B-B-A-A	R-I	Cl	Br	Et ₃ N	DMF	Et ₃ N·HI	1	0.96	0.96	0.86	1	0.93	0.93	0.84	1.03	0.89	0.92	0.82
A-B-B-A-B	R-I	Cl	Br	Et ₃ N	NMP	Et ₃ N·HI	1	0.37	0.37	0.27	1	0.34	0.34	0.25	1.1	0.3	0.33	0.23
A-B-B-A-C	R-I	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	1	0.23	0.23	0.13	1	0.21	0.21	0.11	1.18	0.16	0.19	0.09
A-B-B-A-D	R-I	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	1	0.6	0.6	0.5	1	0.57	0.57	0.48	1.05	0.53	0.56	0.46
A-B-B-A-E	R-I	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	1	0.3	0.3	0.2	1	0.27	0.27	0.18	1.13	0.23	0.26	0.16
A-B-B-B-A	R-I	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.61	1.65	1	0.9	0.69	1.34	0.93	0.84	0.52	1.75	0.91	0.81
A-B-B-B-B	R-I	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.39	1.06	0.41	0.31	0.45	0.75	0.34	0.25	0.28	1.16	0.32	0.22
A-B-B-B-C	R-I	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.3	0.92	0.28	0.18	0.33	0.62	0.2	0.11	0.18	1.03	0.19	0.09
A-B-B-B-D	R-I	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.5	1.29	0.64	0.54	0.58	0.98	0.57	0.48	0.4	1.39	0.55	0.45
A-B-B-B-E	R-I	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.35	0.99	0.34	0.24	0.4	0.68	0.27	0.18	0.23	1.09	0.25	0.15
A-C-A-A-A	R-I	acac	I	Et ₃ N	DMF	Et ₃ N·HI	1	1.19	1.19	1.09	1	2.31	2.31	2.22	1.02	1.56	1.59	1.49

A-C-A-A-B	R-I	acac	I	Et ₃ N	NMP	Et ₃ N·HI	1	0.59	0.59	0.49	1	1.71	1.71	1.62	1.03	0.96	0.99	0.89
A-C-A-A-C	R-I	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HI	1	0.46	0.46	0.36	1	1.58	1.58	1.49	1.03	0.83	0.86	0.76
A-C-A-A-D	R-I	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	1	0.82	0.82	0.72	1	1.94	1.94	1.85	1.02	1.19	1.22	1.12
A-C-A-A-E	R-I	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	1	0.52	0.52	0.42	1	1.65	1.65	1.56	1.03	0.9	0.93	0.83
A-C-A-B-A	R-I	acac	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.66	1.88	1.23	1.13	0.85	2.72	2.31	2.21	0.65	2.42	1.58	1.48
A-C-A-B-B	R-I	acac	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.5	1.28	0.64	0.54	0.81	2.12	1.71	1.62	0.54	1.83	0.99	0.89
A-C-A-B-C	R-I	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.44	1.15	0.5	0.4	0.79	1.99	1.58	1.49	0.5	1.69	0.85	0.75
A-C-A-B-D	R-I	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.57	1.51	0.87	0.77	0.82	2.35	1.94	1.85	0.59	2.06	1.22	1.12
A-C-A-B-E	R-I	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.47	1.22	0.57	0.47	0.8	2.06	1.64	1.55	0.52	1.76	0.92	0.82
A-C-B-A-A	R-I	acac	Br	Et ₃ N	DMF	Et ₃ N·HI	1	1.22	1.22	1.12	1	2.34	2.34	2.25	1.02	1.59	1.62	1.52
A-C-B-A-B	R-I	acac	Br	Et ₃ N	NMP	Et ₃ N·HI	1	0.62	0.62	0.52	1	1.74	1.74	1.65	1.03	1	1.03	0.93
A-C-B-A-C	R-I	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	1	0.49	0.49	0.39	1	1.61	1.61	1.52	1.03	0.86	0.89	0.79
A-C-B-A-D	R-I	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	1	0.85	0.85	0.75	1	1.97	1.97	1.88	1.02	1.23	1.26	1.16
A-C-B-A-E	R-I	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	1	0.55	0.55	0.45	1	1.68	1.68	1.58	1.03	0.93	0.96	0.86
A-C-B-B-A	R-I	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.66	1.91	1.26	1.16	0.85	2.75	2.33	2.24	0.66	2.46	1.61	1.51
A-C-B-B-B	R-I	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.51	1.31	0.67	0.57	0.81	2.15	1.74	1.65	0.55	1.86	1.02	0.92
A-C-B-B-C	R-I	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.45	1.18	0.53	0.43	0.8	2.02	1.61	1.51	0.51	1.73	0.89	0.79
A-C-B-B-D	R-I	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.58	1.54	0.9	0.8	0.83	2.38	1.97	1.88	0.6	2.09	1.25	1.15
A-C-B-B-E	R-I	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.48	1.25	0.6	0.5	0.8	2.09	1.67	1.58	0.53	1.79	0.95	0.85
B-A-A-A-A	R-Br	OAc	I	Et ₃ N	DMF	Et ₃ N·HBr	0.66	1.37	0.91	0.81	0.95	0.94	0.89	0.8	0.82	1.07	0.88	0.78
B-A-A-A-B	R-Br	OAc	I	Et ₃ N	NMP	Et ₃ N·HBr	0.4	0.78	0.31	0.21	0.86	0.35	0.3	0.21	0.59	0.48	0.28	0.18
B-A-A-A-C	R-Br	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.27	0.65	0.18	0.08	0.77	0.22	0.17	0.08	0.43	0.35	0.15	0.05
B-A-A-A-D	R-Br	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.54	1.01	0.54	0.44	0.91	0.58	0.53	0.44	0.72	0.71	0.51	0.41
B-A-A-A-E	R-Br	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.34	0.71	0.24	0.14	0.82	0.28	0.23	0.14	0.52	0.41	0.22	0.12
B-A-A-B-A	R-Br	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.43	2.07	0.89	0.79	0.66	1.35	0.9	0.81	0.46	1.94	0.89	0.79
B-A-A-B-B	R-Br	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.2	1.47	0.3	0.2	0.4	0.76	0.31	0.21	0.22	1.34	0.3	0.2
B-A-A-B-C	R-Br	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.12	1.34	0.17	0.07	0.27	0.63	0.17	0.08	0.13	1.21	0.16	0.06
B-A-A-B-D	R-Br	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.31	1.7	0.53	0.43	0.54	0.99	0.54	0.44	0.34	1.57	0.53	0.43
B-A-A-B-E	R-Br	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.17	1.4	0.23	0.13	0.34	0.69	0.24	0.15	0.18	1.28	0.23	0.13
B-A-B-A-A	R-Br	OAc	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.67	1.4	0.94	0.84	0.95	0.97	0.92	0.83	0.82	1.11	0.91	0.81
B-A-B-A-B	R-Br	OAc	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.42	0.81	0.34	0.24	0.87	0.38	0.33	0.24	0.62	0.51	0.32	0.22
B-A-B-A-C	R-Br	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.31	0.68	0.21	0.11	0.8	0.24	0.19	0.1	0.48	0.38	0.18	0.08
B-A-B-A-D	R-Br	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.55	1.04	0.57	0.47	0.92	0.61	0.56	0.47	0.74	0.74	0.55	0.45
B-A-B-A-E	R-Br	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.37	0.74	0.27	0.17	0.84	0.31	0.26	0.17	0.56	0.45	0.25	0.15
B-A-B-B-A	R-Br	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.44	2.1	0.92	0.82	0.67	1.38	0.93	0.84	0.47	1.97	0.93	0.83
B-A-B-B-B	R-Br	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.22	1.5	0.33	0.23	0.42	0.79	0.33	0.24	0.24	1.38	0.33	0.23
B-A-B-B-C	R-Br	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.14	1.37	0.2	0.1	0.31	0.65	0.2	0.11	0.16	1.24	0.2	0.1
B-A-B-B-D	R-Br	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.32	1.73	0.56	0.46	0.55	1.02	0.56	0.47	0.35	1.61	0.56	0.46
B-A-B-B-E	R-Br	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.18	1.43	0.26	0.16	0.37	0.72	0.27	0.18	0.2	1.31	0.27	0.17
B-B-A-A-A	R-Br	Cl	I	Et ₃ N	DMF	Et ₃ N·HBr	0.66	1.38	0.91	0.81	0.95	0.96	0.91	0.82	0.82	1.08	0.88	0.78
B-B-A-A-B	R-Br	Cl	I	Et ₃ N	NMP	Et ₃ N·HBr	0.4	0.79	0.32	0.22	0.86	0.36	0.31	0.22	0.59	0.48	0.29	0.19
B-B-A-A-C	R-Br	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.28	0.65	0.18	0.08	0.78	0.23	0.18	0.09	0.44	0.35	0.15	0.05
B-B-A-A-D	R-Br	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.54	1.02	0.55	0.45	0.92	0.59	0.54	0.45	0.73	0.71	0.52	0.42
B-B-A-A-E	R-Br	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.35	0.72	0.25	0.15	0.83	0.3	0.25	0.15	0.53	0.42	0.22	0.12
B-B-A-B-A	R-Br	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.43	2.07	0.9	0.8	0.67	1.37	0.91	0.82	0.46	1.94	0.9	0.8

B-B-A-B-B	R-Br	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.21	1.48	0.3	0.2	0.41	0.77	0.32	0.23	0.22	1.35	0.3	0.2
B-B-A-B-C	R-Br	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.13	1.34	0.17	0.07	0.29	0.64	0.18	0.09	0.14	1.21	0.17	0.07
B-B-A-B-D	R-Br	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.31	1.71	0.54	0.44	0.55	1	0.55	0.46	0.34	1.58	0.53	0.43
B-B-A-B-E	R-Br	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.17	1.41	0.24	0.14	0.36	0.7	0.25	0.16	0.18	1.28	0.23	0.13
B-B-B-A-A	R-Br	Cl	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.67	1.41	0.94	0.84	0.95	0.98	0.93	0.84	0.82	1.11	0.92	0.82
B-B-B-A-B	R-Br	Cl	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.42	0.82	0.35	0.25	0.87	0.39	0.34	0.25	0.62	0.52	0.32	0.22
B-B-B-A-C	R-Br	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.31	0.68	0.21	0.11	0.81	0.26	0.21	0.12	0.49	0.39	0.19	0.09
B-B-B-A-D	R-Br	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.55	1.05	0.58	0.48	0.92	0.62	0.57	0.48	0.74	0.75	0.55	0.45
B-B-B-A-E	R-Br	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.37	0.75	0.28	0.18	0.85	0.32	0.27	0.18	0.57	0.45	0.26	0.16
B-B-B-B-A	R-Br	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.44	2.1	0.93	0.83	0.67	1.39	0.94	0.85	0.47	1.98	0.93	0.83
B-B-B-B-B	R-Br	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.22	1.51	0.33	0.23	0.43	0.8	0.35	0.25	0.24	1.38	0.34	0.24
B-B-B-B-C	R-Br	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.15	1.37	0.2	0.1	0.32	0.67	0.21	0.12	0.16	1.25	0.2	0.1
B-B-B-B-D	R-Br	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.33	1.74	0.56	0.46	0.56	1.03	0.58	0.48	0.35	1.61	0.57	0.47
B-B-B-B-E	R-Br	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.19	1.44	0.27	0.17	0.38	0.73	0.28	0.19	0.21	1.32	0.27	0.17
B-C-A-A-A	R-Br	acac	I	Et ₃ N	DMF	Et ₃ N·HBr	0.71	1.64	1.17	1.07	0.98	2.36	2.31	2.22	0.89	1.78	1.58	1.48
B-C-A-A-B	R-Br	acac	I	Et ₃ N	NMP	Et ₃ N·HBr	0.55	1.04	0.57	0.47	0.97	1.76	1.71	1.62	0.83	1.18	0.99	0.89
B-C-A-A-C	R-Br	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.48	0.91	0.44	0.34	0.97	1.63	1.58	1.49	0.81	1.05	0.85	0.75
B-C-A-A-D	R-Br	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.63	1.27	0.8	0.7	0.97	1.99	1.94	1.85	0.86	1.41	1.22	1.12
B-C-A-A-E	R-Br	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.52	0.97	0.5	0.4	0.97	1.7	1.65	1.56	0.82	1.12	0.92	0.82
B-C-A-B-A	R-Br	acac	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.5	2.33	1.15	1.05	0.84	2.77	2.31	2.22	0.6	2.64	1.6	1.5
B-C-A-B-B	R-Br	acac	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.32	1.73	0.56	0.46	0.79	2.17	1.72	1.63	0.49	2.05	1	0.9
B-C-A-B-C	R-Br	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.27	1.6	0.43	0.33	0.78	2.04	1.59	1.5	0.45	1.91	0.87	0.77
B-C-A-B-D	R-Br	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.4	1.96	0.79	0.69	0.81	2.4	1.95	1.86	0.54	2.28	1.23	1.13
B-C-A-B-E	R-Br	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.3	1.67	0.49	0.39	0.78	2.11	1.65	1.56	0.47	1.98	0.94	0.84
B-C-B-A-A	R-Br	acac	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.72	1.67	1.2	1.1	0.98	2.39	2.34	2.25	0.89	1.81	1.62	1.52
B-C-B-A-B	R-Br	acac	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.56	1.07	0.6	0.5	0.97	1.79	1.74	1.65	0.84	1.22	1.02	0.92
B-C-B-A-C	R-Br	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.5	0.94	0.47	0.37	0.97	1.66	1.61	1.52	0.82	1.09	0.89	0.79
B-C-B-A-D	R-Br	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.64	1.3	0.83	0.73	0.98	2.02	1.97	1.88	0.86	1.45	1.25	1.15
B-C-B-A-E	R-Br	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.53	1	0.53	0.43	0.97	1.73	1.68	1.59	0.83	1.15	0.96	0.86
B-C-B-B-A	R-Br	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.5	2.36	1.18	1.08	0.84	2.8	2.34	2.25	0.61	2.68	1.63	1.53
B-C-B-B-B	R-Br	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.34	1.76	0.59	0.49	0.79	2.2	1.75	1.66	0.5	2.08	1.04	0.94
B-C-B-B-C	R-Br	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.28	1.63	0.46	0.36	0.78	2.07	1.61	1.52	0.46	1.95	0.9	0.8
B-C-B-B-D	R-Br	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.41	1.99	0.82	0.72	0.81	2.43	1.98	1.89	0.55	2.31	1.27	1.17
B-C-B-B-E	R-Br	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.31	1.7	0.52	0.42	0.79	2.14	1.68	1.59	0.48	2.02	0.97	0.87
C-A-A-A-A	R-Cl	OAc	I	Et ₃ N	DMF	Et ₃ N·HCl	0.98	0.94	0.92	0.82	0.96	0.93	0.89	0.8	1.04	0.85	0.89	0.79
C-A-A-A-B	R-Cl	OAc	I	Et ₃ N	NMP	Et ₃ N·HCl	0.95	0.34	0.33	0.23	0.88	0.33	0.29	0.2	1.14	0.26	0.29	0.19
C-A-A-A-C	R-Cl	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.92	0.21	0.19	0.09	0.79	0.2	0.16	0.07	1.28	0.13	0.16	0.06
C-A-A-A-D	R-Cl	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.97	0.57	0.56	0.46	0.93	0.56	0.52	0.43	1.07	0.49	0.52	0.42
C-A-A-A-E	R-Cl	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.94	0.28	0.26	0.16	0.85	0.27	0.23	0.14	1.18	0.19	0.23	0.13
C-A-A-B-A	R-Cl	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.58	1.63	0.95	0.85	0.66	1.34	0.89	0.8	0.51	1.72	0.88	0.78
C-A-A-B-B	R-Cl	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.34	1.03	0.35	0.25	0.39	0.74	0.29	0.2	0.25	1.12	0.28	0.18
C-A-A-B-C	R-Cl	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.24	0.9	0.22	0.12	0.26	0.61	0.16	0.07	0.15	0.99	0.15	0.05
C-A-A-B-D	R-Cl	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.46	1.26	0.58	0.48	0.54	0.97	0.52	0.43	0.38	1.35	0.51	0.41
C-A-A-B-E	R-Cl	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.29	0.97	0.28	0.18	0.33	0.68	0.23	0.13	0.2	1.06	0.21	0.11
C-A-B-A-A	R-Cl	OAc	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.98	0.97	0.95	0.85	0.96	0.96	0.92	0.82	1.04	0.89	0.92	0.82

C-A-B-A-B	R-Cl	OAc	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.96	0.37	0.36	0.26	0.89	0.36	0.32	0.23	1.12	0.29	0.33	0.23
C-A-B-A-C	R-Cl	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.93	0.24	0.22	0.12	0.82	0.23	0.19	0.1	1.22	0.16	0.2	0.1
C-A-B-A-D	R-Cl	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.97	0.6	0.59	0.49	0.93	0.59	0.55	0.46	1.07	0.52	0.56	0.46
C-A-B-A-E	R-Cl	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.95	0.31	0.29	0.19	0.86	0.3	0.25	0.16	1.15	0.23	0.26	0.16
C-A-B-B-A	R-Cl	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.59	1.66	0.98	0.88	0.67	1.37	0.91	0.82	0.52	1.75	0.91	0.81
C-A-B-B-B	R-Cl	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.36	1.06	0.38	0.28	0.42	0.77	0.32	0.23	0.27	1.16	0.32	0.22
C-A-B-B-C	R-Cl	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.27	0.93	0.25	0.15	0.29	0.64	0.19	0.1	0.18	1.02	0.18	0.08
C-A-B-B-D	R-Cl	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.47	1.29	0.61	0.51	0.55	1	0.55	0.46	0.39	1.39	0.55	0.45
C-A-B-B-E	R-Cl	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.32	1	0.31	0.21	0.36	0.71	0.25	0.16	0.23	1.09	0.25	0.15
C-B-A-A-A	R-Cl	Cl	I	Et ₃ N	DMF	Et ₃ N·HCl	0.98	0.94	0.93	0.83	0.96	0.94	0.9	0.81	1.04	0.86	0.89	0.79
C-B-A-A-B	R-Cl	Cl	I	Et ₃ N	NMP	Et ₃ N·HCl	0.95	0.35	0.33	0.23	0.88	0.35	0.31	0.21	1.13	0.26	0.3	0.2
C-B-A-A-C	R-Cl	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.93	0.21	0.2	0.1	0.8	0.21	0.17	0.08	1.27	0.13	0.17	0.07
C-B-A-A-D	R-Cl	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.97	0.58	0.56	0.46	0.93	0.58	0.54	0.44	1.07	0.49	0.53	0.43
C-B-A-A-E	R-Cl	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.94	0.28	0.26	0.16	0.85	0.28	0.24	0.15	1.18	0.2	0.23	0.13
C-B-A-B-A	R-Cl	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.58	1.63	0.95	0.85	0.67	1.35	0.9	0.81	0.51	1.72	0.88	0.78
C-B-A-B-B	R-Cl	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.34	1.04	0.36	0.26	0.4	0.76	0.3	0.21	0.25	1.13	0.29	0.19
C-B-A-B-C	R-Cl	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.25	0.91	0.22	0.12	0.27	0.62	0.17	0.08	0.15	0.99	0.15	0.05
C-B-A-B-D	R-Cl	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.46	1.27	0.59	0.49	0.54	0.99	0.53	0.44	0.38	1.36	0.52	0.42
C-B-A-B-E	R-Cl	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.3	0.97	0.29	0.19	0.34	0.69	0.24	0.15	0.21	1.06	0.22	0.12
C-B-B-A-A	R-Cl	Cl	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.98	0.97	0.96	0.86	0.96	0.97	0.93	0.84	1.04	0.89	0.93	0.83
C-B-B-A-B	R-Cl	Cl	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.96	0.38	0.36	0.26	0.89	0.37	0.33	0.24	1.12	0.3	0.33	0.23
C-B-B-A-C	R-Cl	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.93	0.24	0.23	0.13	0.83	0.24	0.2	0.11	1.21	0.17	0.2	0.1
C-B-B-A-D	R-Cl	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.97	0.61	0.59	0.49	0.93	0.61	0.56	0.47	1.07	0.53	0.56	0.46
C-B-B-A-E	R-Cl	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.95	0.31	0.29	0.19	0.87	0.31	0.27	0.18	1.15	0.23	0.27	0.17
C-B-B-B-A	R-Cl	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.59	1.66	0.98	0.88	0.67	1.38	0.93	0.84	0.52	1.76	0.92	0.82
C-B-B-B-B	R-Cl	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.36	1.07	0.39	0.29	0.42	0.78	0.33	0.24	0.28	1.16	0.32	0.22
C-B-B-B-C	R-Cl	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.27	0.93	0.25	0.15	0.31	0.65	0.2	0.11	0.18	1.03	0.19	0.09
C-B-B-B-D	R-Cl	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.47	1.3	0.62	0.52	0.55	1.01	0.56	0.47	0.4	1.39	0.55	0.45
C-B-B-B-E	R-Cl	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.32	1	0.32	0.22	0.37	0.72	0.27	0.17	0.23	1.1	0.25	0.15
C-C-A-A-A	R-Cl	acac	I	Et ₃ N	DMF	Et ₃ N·HCl	0.99	1.2	1.18	1.08	0.98	2.34	2.3	2.21	1.02	1.56	1.59	1.49
C-C-A-A-B	R-Cl	acac	I	Et ₃ N	NMP	Et ₃ N·HCl	0.97	0.6	0.59	0.49	0.98	1.75	1.71	1.62	1.04	0.96	1	0.9
C-C-A-A-C	R-Cl	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.97	0.47	0.45	0.35	0.97	1.62	1.57	1.48	1.04	0.83	0.87	0.77
C-C-A-A-D	R-Cl	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.98	0.83	0.82	0.72	0.98	1.98	1.94	1.85	1.03	1.19	1.23	1.13
C-C-A-A-E	R-Cl	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.97	0.54	0.52	0.42	0.98	1.68	1.64	1.55	1.04	0.9	0.93	0.83
C-C-A-B-A	R-Cl	acac	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.64	1.89	1.21	1.11	0.84	2.75	2.3	2.21	0.65	2.42	1.58	1.48
C-C-A-B-B	R-Cl	acac	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.47	1.29	0.61	0.51	0.79	2.16	1.71	1.62	0.54	1.83	0.99	0.89
C-C-A-B-C	R-Cl	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.41	1.16	0.48	0.38	0.78	2.02	1.57	1.48	0.5	1.69	0.85	0.75
C-C-A-B-D	R-Cl	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.55	1.53	0.84	0.74	0.81	2.39	1.94	1.85	0.59	2.06	1.22	1.12
C-C-A-B-E	R-Cl	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.44	1.23	0.55	0.45	0.78	2.09	1.64	1.55	0.52	1.76	0.92	0.82
C-C-B-A-A	R-Cl	acac	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.99	1.23	1.21	1.11	0.98	2.37	2.33	2.24	1.02	1.59	1.63	1.53
C-C-B-A-B	R-Cl	acac	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.97	0.63	0.62	0.52	0.98	1.78	1.74	1.65	1.04	1	1.04	0.94
C-C-B-A-C	R-Cl	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.97	0.5	0.48	0.38	0.97	1.64	1.6	1.51	1.04	0.87	0.9	0.8
C-C-B-A-D	R-Cl	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.98	0.86	0.85	0.75	0.98	2.01	1.97	1.88	1.03	1.23	1.27	1.17
C-C-B-A-E	R-Cl	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.97	0.57	0.55	0.45	0.98	1.71	1.67	1.58	1.04	0.93	0.97	0.87
C-C-B-B-A	R-Cl	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.64	1.92	1.24	1.14	0.84	2.78	2.33	2.24	0.66	2.46	1.62	1.52

C-C-B-B-B	R-Cl	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.48	1.32	0.64	0.54	0.79	2.19	1.73	1.64	0.55	1.86	1.02	0.92
C-C-B-B-C	R-Cl	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.43	1.19	0.51	0.41	0.78	2.05	1.6	1.51	0.51	1.73	0.89	0.79
C-C-B-B-D	R-Cl	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.56	1.55	0.87	0.77	0.81	2.42	1.97	1.87	0.6	2.09	1.25	1.15
C-C-B-B-E	R-Cl	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.46	1.26	0.57	0.47	0.79	2.12	1.67	1.58	0.53	1.8	0.96	0.86

Target product P (1-nitro-4-phenylethynyl-benzene) and starting material SM1 (phenylacetylene) are not shown. R-I, 1-iodo-4-nitrobenzene; R-Br, 1-bromo-4-nitrobenzene; R-Cl, 1-chloro-4-nitrobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green. Organic solvents mixed with water at a 1:1 mass ratio are indicated as solvent/H₂O.

Table S5. bio-Factors and cytotoxicity potentials for synthesis of 1-nitro-3-((4-nitrophenyl)ethynyl)benzene.

Reaction	Starting materials (SM2)	Catalyst (CT1) PdA ₂	Catalyst (CT2) CuX	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
							BF	CP _i	CP _f	CP _{f_rel}	BF	CP _i	CP _f	CP _{f_rel}	BF	CP _i	CP _f	CP _{f_rel}
A-A-A-A-A	PhI	OAc	I	Et ₃ N	DMF	Et ₃ N·HI	0.74	1.25	0.92	0.82	2.61	1.02	2.67	0.8	0.83	1.04	0.87	0.78
A-A-A-A-B	PhI	OAc	I	Et ₃ N	NMP	Et ₃ N·HI	0.5	0.66	0.33	0.23	4.83	0.43	2.08	0.21	0.61	0.45	0.27	0.19
A-A-A-A-C	PhI	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.37	0.53	0.2	0.1	6.56	0.3	1.94	0.07	0.45	0.31	0.14	0.05
A-A-A-A-D	PhI	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.63	0.89	0.56	0.46	3.5	0.66	2.31	0.44	0.74	0.68	0.5	0.42
A-A-A-A-E	PhI	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.44	0.59	0.26	0.16	5.54	0.36	2.01	0.14	0.54	0.38	0.21	0.12
A-A-A-B-A	PhI	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.5	1.95	0.97	0.87	1.86	1.43	2.67	0.8	0.45	1.91	0.86	0.77
A-A-A-B-B	PhI	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.28	1.35	0.37	0.28	2.47	0.84	2.07	0.21	0.2	1.31	0.27	0.18
A-A-A-B-C	PhI	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.2	1.22	0.24	0.14	2.75	0.71	1.94	0.07	0.11	1.18	0.13	0.05
A-A-A-B-D	PhI	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.38	1.58	0.6	0.51	2.16	1.07	2.3	0.44	0.32	1.54	0.5	0.41
A-A-A-B-E	PhI	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.24	1.28	0.31	0.21	2.6	0.77	2.01	0.14	0.16	1.24	0.2	0.11
A-A-B-A-A	PhI	OAc	Br	Et ₃ N	DMF	Et ₃ N·HI	0.74	1.28	0.95	0.85	2.57	1.05	2.7	0.83	0.84	1.08	0.9	0.82
A-A-B-A-B	PhI	OAc	Br	Et ₃ N	NMP	Et ₃ N·HI	0.52	0.69	0.36	0.26	4.59	0.46	2.11	0.24	0.64	0.48	0.31	0.22
A-A-B-A-C	PhI	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.41	0.56	0.23	0.13	6.08	0.32	1.97	0.1	0.5	0.35	0.18	0.09
A-A-B-A-D	PhI	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.64	0.92	0.59	0.49	3.39	0.69	2.34	0.47	0.76	0.71	0.54	0.45
A-A-B-A-E	PhI	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.47	0.62	0.29	0.19	5.21	0.39	2.04	0.17	0.58	0.42	0.24	0.16
A-A-B-B-A	PhI	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.51	1.98	1	0.9	1.85	1.46	2.7	0.83	0.46	1.94	0.9	0.81
A-A-B-B-B	PhI	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.29	1.38	0.4	0.31	2.42	0.87	2.1	0.23	0.23	1.35	0.3	0.22
A-A-B-B-C	PhI	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.22	1.25	0.27	0.17	2.68	0.73	1.97	0.1	0.14	1.21	0.17	0.08
A-A-B-B-D	PhI	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.39	1.61	0.63	0.54	2.13	1.1	2.33	0.46	0.34	1.58	0.53	0.45
A-A-B-B-E	PhI	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.26	1.31	0.34	0.24	2.54	0.8	2.04	0.17	0.19	1.28	0.24	0.15
A-B-A-A-A	PhI	Cl	I	Et ₃ N	DMF	Et ₃ N·HI	0.74	1.26	0.93	0.83	2.59	1.04	2.68	0.81	0.83	1.05	0.87	0.79
A-B-A-A-B	PhI	Cl	I	Et ₃ N	NMP	Et ₃ N·HI	0.5	0.66	0.33	0.24	4.73	0.44	2.09	0.22	0.62	0.45	0.28	0.19
A-B-A-A-C	PhI	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.38	0.53	0.2	0.1	6.35	0.31	1.96	0.09	0.46	0.32	0.15	0.06
A-B-A-A-D	PhI	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.63	0.89	0.56	0.47	3.45	0.67	2.32	0.45	0.75	0.68	0.51	0.42
A-B-A-A-E	PhI	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.45	0.6	0.27	0.17	5.39	0.38	2.02	0.15	0.55	0.39	0.21	0.12
A-B-A-B-A	PhI	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.5	1.95	0.97	0.87	1.86	1.45	2.68	0.81	0.45	1.91	0.87	0.78
A-B-A-B-B	PhI	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.28	1.36	0.38	0.28	2.45	0.85	2.09	0.22	0.21	1.32	0.27	0.19
A-B-A-B-C	PhI	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.2	1.22	0.25	0.15	2.72	0.72	1.95	0.08	0.12	1.18	0.14	0.05
A-B-A-B-D	PhI	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.38	1.59	0.61	0.51	2.14	1.08	2.32	0.45	0.33	1.55	0.5	0.42
A-B-A-B-E	PhI	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.24	1.29	0.31	0.21	2.58	0.78	2.02	0.15	0.17	1.25	0.21	0.12
A-B-B-A-A	PhI	Cl	Br	Et ₃ N	DMF	Et ₃ N·HI	0.74	1.29	0.96	0.86	2.55	1.06	2.71	0.84	0.84	1.08	0.91	0.82
A-B-B-A-B	PhI	Cl	Br	Et ₃ N	NMP	Et ₃ N·HI	0.52	0.69	0.36	0.27	4.5	0.47	2.12	0.25	0.64	0.49	0.31	0.23
A-B-B-A-C	PhI	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.41	0.56	0.23	0.13	5.9	0.34	1.98	0.11	0.51	0.35	0.18	0.09
A-B-B-A-D	PhI	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.64	0.92	0.59	0.5	3.35	0.7	2.35	0.48	0.76	0.72	0.54	0.46
A-B-B-A-E	PhI	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.47	0.63	0.3	0.2	5.08	0.4	2.05	0.18	0.59	0.42	0.25	0.16
A-B-B-B-A	PhI	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.51	1.98	1	0.9	1.84	1.47	2.71	0.84	0.46	1.95	0.9	0.81
A-B-B-B-B	PhI	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.3	1.39	0.41	0.31	2.41	0.88	2.12	0.25	0.23	1.35	0.31	0.22
A-B-B-B-C	PhI	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.22	1.25	0.28	0.18	2.66	0.75	1.98	0.11	0.14	1.22	0.17	0.09
A-B-B-B-D	PhI	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.4	1.62	0.64	0.54	2.11	1.11	2.35	0.48	0.34	1.58	0.54	0.45
A-B-B-B-E	PhI	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.26	1.32	0.34	0.24	2.52	0.81	2.05	0.18	0.19	1.28	0.24	0.15
A-C-A-A-A	PhI	acac	I	Et ₃ N	DMF	Et ₃ N·HI	0.78	1.51	1.18	1.09	1.68	2.44	4.09	2.22	0.9	1.75	1.57	1.49

A-C-A-A-B	PhI	acac	I	Et ₃ N	NMP	Et ₃ N·HI	0.64	0.92	0.59	0.49	1.89	1.84	3.49	1.62	0.85	1.15	0.98	0.89
A-C-A-A-C	PhI	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.58	0.79	0.46	0.36	1.96	1.71	3.36	1.49	0.83	1.02	0.85	0.76
A-C-A-A-D	PhI	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.71	1.15	0.82	0.72	1.79	2.07	3.72	1.85	0.87	1.38	1.21	1.12
A-C-A-A-E	PhI	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.61	0.85	0.52	0.42	1.93	1.78	3.43	1.56	0.84	1.09	0.91	0.83
A-C-A-B-A	PhI	acac	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.56	2.21	1.23	1.13	1.43	2.85	4.08	2.21	0.6	2.61	1.57	1.48
A-C-A-B-B	PhI	acac	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.39	1.61	0.64	0.54	1.55	2.25	3.49	1.62	0.48	2.02	0.97	0.89
A-C-A-B-C	PhI	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.34	1.48	0.5	0.4	1.58	2.12	3.36	1.49	0.45	1.88	0.84	0.75
A-C-A-B-D	PhI	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.47	1.84	0.87	0.77	1.5	2.48	3.72	1.85	0.54	2.25	1.2	1.12
A-C-A-B-E	PhI	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.37	1.54	0.57	0.47	1.57	2.19	3.42	1.55	0.47	1.95	0.91	0.82
A-C-B-A-A	PhI	acac	Br	Et ₃ N	DMF	Et ₃ N·HI	0.79	1.54	1.21	1.12	1.67	2.47	4.11	2.25	0.9	1.78	1.61	1.52
A-C-B-A-B	PhI	acac	Br	Et ₃ N	NMP	Et ₃ N·HI	0.65	0.95	0.62	0.52	1.88	1.87	3.52	1.65	0.85	1.19	1.02	0.93
A-C-B-A-C	PhI	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.6	0.82	0.49	0.39	1.95	1.74	3.39	1.52	0.84	1.06	0.88	0.79
A-C-B-A-D	PhI	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.72	1.18	0.85	0.75	1.78	2.1	3.75	1.88	0.88	1.42	1.25	1.16
A-C-B-A-E	PhI	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.63	0.88	0.55	0.45	1.91	1.81	3.45	1.58	0.85	1.12	0.95	0.86
A-C-B-B-A	PhI	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.56	2.24	1.26	1.16	1.43	2.88	4.11	2.24	0.61	2.65	1.6	1.51
A-C-B-B-B	PhI	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.41	1.64	0.66	0.57	1.54	2.28	3.52	1.65	0.49	2.05	1.01	0.92
A-C-B-B-C	PhI	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.35	1.51	0.53	0.43	1.58	2.15	3.38	1.51	0.46	1.92	0.88	0.79
A-C-B-B-D	PhI	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.48	1.87	0.9	0.8	1.49	2.51	3.75	1.88	0.54	2.28	1.24	1.15
A-C-B-B-E	PhI	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.38	1.57	0.6	0.5	1.56	2.21	3.45	1.58	0.47	1.98	0.94	0.85
B-A-A-A-A	PhBr	OAc	I	Et ₃ N	DMF	Et ₃ N·HBr	0.53	1.7	0.9	0.81	2.49	1.07	2.67	0.8	0.68	1.26	0.87	0.78
B-A-A-A-B	PhBr	OAc	I	Et ₃ N	NMP	Et ₃ N·HBr	0.28	1.11	0.31	0.21	4.33	0.48	2.08	0.21	0.4	0.67	0.27	0.18
B-A-A-A-C	PhBr	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.18	0.98	0.18	0.08	5.62	0.35	1.94	0.08	0.26	0.54	0.14	0.05
B-A-A-A-D	PhBr	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.4	1.34	0.54	0.44	3.25	0.71	2.31	0.44	0.56	0.9	0.5	0.41
B-A-A-A-E	PhBr	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.23	1.04	0.24	0.14	4.87	0.41	2.01	0.14	0.34	0.6	0.2	0.12
B-A-A-B-A	PhBr	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.37	2.4	0.89	0.79	1.81	1.48	2.68	0.81	0.41	2.13	0.88	0.79
B-A-A-B-B	PhBr	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.17	1.8	0.3	0.2	2.34	0.89	2.08	0.21	0.19	1.53	0.28	0.2
B-A-A-B-C	PhBr	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.1	1.67	0.17	0.07	2.58	0.76	1.95	0.08	0.11	1.4	0.15	0.06
B-A-A-B-D	PhBr	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.26	2.03	0.53	0.43	2.07	1.12	2.31	0.44	0.29	1.76	0.52	0.43
B-A-A-B-E	PhBr	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.13	1.73	0.23	0.13	2.45	0.82	2.02	0.15	0.15	1.47	0.22	0.13
B-A-B-A-A	PhBr	OAc	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.54	1.73	0.93	0.84	2.45	1.1	2.7	0.83	0.69	1.3	0.9	0.81
B-A-B-A-B	PhBr	OAc	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.3	1.14	0.34	0.24	4.14	0.51	2.11	0.24	0.43	0.71	0.31	0.22
B-A-B-A-C	PhBr	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.2	1.01	0.21	0.11	5.27	0.37	1.97	0.1	0.3	0.57	0.17	0.08
B-A-B-A-D	PhBr	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.42	1.37	0.57	0.47	3.16	0.74	2.34	0.47	0.57	0.94	0.54	0.45
B-A-B-A-E	PhBr	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.25	1.07	0.27	0.17	4.62	0.44	2.04	0.17	0.38	0.64	0.24	0.15
B-A-B-B-A	PhBr	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.38	2.43	0.92	0.82	1.79	1.51	2.71	0.84	0.42	2.16	0.91	0.83
B-A-B-B-B	PhBr	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.18	1.83	0.33	0.23	2.3	0.92	2.11	0.24	0.2	1.57	0.32	0.23
B-A-B-B-C	PhBr	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.12	1.7	0.2	0.1	2.52	0.78	1.98	0.11	0.13	1.43	0.19	0.1
B-A-B-B-D	PhBr	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.27	2.06	0.56	0.46	2.04	1.15	2.34	0.47	0.31	1.8	0.55	0.46
B-A-B-B-E	PhBr	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.15	1.76	0.26	0.16	2.4	0.85	2.05	0.18	0.17	1.5	0.25	0.17
B-B-A-A-A	PhBr	Cl	I	Et ₃ N	DMF	Et ₃ N·HBr	0.53	1.71	0.91	0.81	2.47	1.09	2.68	0.82	0.69	1.27	0.87	0.78
B-B-A-A-B	PhBr	Cl	I	Et ₃ N	NMP	Et ₃ N·HBr	0.28	1.11	0.31	0.22	4.25	0.49	2.09	0.22	0.41	0.67	0.28	0.19
B-B-A-A-C	PhBr	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.18	0.98	0.18	0.08	5.46	0.36	1.96	0.09	0.26	0.54	0.14	0.05
B-B-A-A-D	PhBr	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.41	1.34	0.54	0.45	3.21	0.72	2.32	0.45	0.56	0.9	0.51	0.42
B-B-A-A-E	PhBr	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.24	1.05	0.25	0.15	4.76	0.43	2.02	0.15	0.34	0.61	0.21	0.12
B-B-A-B-A	PhBr	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.37	2.4	0.9	0.8	1.8	1.5	2.69	0.82	0.41	2.13	0.88	0.8

B-B-A-B-B	PhBr	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.17	1.81	0.3	0.2	2.33	0.9	2.1	0.23	0.19	1.54	0.29	0.2
B-B-A-B-C	PhBr	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.1	1.67	0.17	0.07	2.56	0.77	1.96	0.09	0.11	1.4	0.16	0.07
B-B-A-B-D	PhBr	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.26	2.04	0.53	0.44	2.06	1.13	2.33	0.46	0.29	1.77	0.52	0.43
B-B-A-B-E	PhBr	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.14	1.74	0.24	0.14	2.43	0.83	2.03	0.16	0.15	1.47	0.22	0.13
B-B-B-A-A	PhBr	Cl	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.54	1.74	0.94	0.84	2.43	1.11	2.71	0.84	0.69	1.3	0.91	0.82
B-B-B-A-B	PhBr	Cl	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.3	1.14	0.34	0.25	4.07	0.52	2.12	0.25	0.44	0.71	0.31	0.22
B-B-B-A-C	PhBr	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.21	1.01	0.21	0.11	5.14	0.39	1.98	0.12	0.31	0.58	0.18	0.09
B-B-B-A-D	PhBr	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.42	1.37	0.57	0.48	3.13	0.75	2.35	0.48	0.58	0.94	0.54	0.45
B-B-B-A-E	PhBr	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.26	1.08	0.28	0.18	4.53	0.45	2.05	0.18	0.38	0.64	0.24	0.16
B-B-B-B-A	PhBr	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.38	2.43	0.93	0.83	1.78	1.52	2.72	0.85	0.42	2.17	0.92	0.83
B-B-B-B-B	PhBr	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.18	1.84	0.33	0.23	2.29	0.93	2.12	0.25	0.21	1.57	0.32	0.24
B-B-B-B-C	PhBr	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.12	1.7	0.2	0.1	2.5	0.8	1.99	0.12	0.13	1.44	0.19	0.1
B-B-B-B-D	PhBr	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.27	2.07	0.56	0.46	2.03	1.16	2.35	0.48	0.31	1.8	0.55	0.47
B-B-B-B-E	PhBr	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.15	1.77	0.27	0.17	2.39	0.86	2.06	0.19	0.17	1.51	0.26	0.17
B-C-A-A-A	PhBr	acac	I	Et ₃ N	DMF	Et ₃ N·HBr	0.59	1.96	1.16	1.07	1.64	2.49	4.09	2.22	0.8	1.97	1.57	1.48
B-C-A-A-B	PhBr	acac	I	Et ₃ N	NMP	Et ₃ N·HBr	0.42	1.37	0.57	0.47	1.84	1.89	3.49	1.62	0.71	1.38	0.98	0.89
B-C-A-A-C	PhBr	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.35	1.24	0.44	0.34	1.91	1.76	3.36	1.49	0.68	1.24	0.84	0.75
B-C-A-A-D	PhBr	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.5	1.6	0.8	0.7	1.75	2.12	3.72	1.85	0.75	1.61	1.21	1.12
B-C-A-A-E	PhBr	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.39	1.3	0.5	0.4	1.87	1.83	3.43	1.56	0.7	1.31	0.91	0.82
B-C-A-B-A	PhBr	acac	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.43	2.66	1.15	1.05	1.41	2.9	4.09	2.22	0.56	2.83	1.58	1.5
B-C-A-B-B	PhBr	acac	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.27	2.06	0.56	0.46	1.52	2.3	3.5	1.63	0.44	2.24	0.99	0.9
B-C-A-B-C	PhBr	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.22	1.93	0.43	0.33	1.55	2.17	3.36	1.5	0.41	2.1	0.86	0.77
B-C-A-B-D	PhBr	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.34	2.29	0.79	0.69	1.47	2.53	3.73	1.86	0.49	2.47	1.22	1.13
B-C-A-B-E	PhBr	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.25	1.99	0.49	0.39	1.53	2.24	3.43	1.56	0.43	2.17	0.92	0.84
B-C-B-A-A	PhBr	acac	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.6	1.99	1.19	1.1	1.64	2.52	4.12	2.25	0.8	2	1.61	1.52
B-C-B-A-B	PhBr	acac	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.43	1.4	0.6	0.5	1.83	1.92	3.52	1.65	0.72	1.41	1.01	0.92
B-C-B-A-C	PhBr	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.37	1.27	0.47	0.37	1.89	1.79	3.39	1.52	0.69	1.28	0.88	0.79
B-C-B-A-D	PhBr	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.51	1.63	0.83	0.73	1.74	2.15	3.75	1.88	0.76	1.64	1.24	1.15
B-C-B-A-E	PhBr	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.4	1.33	0.53	0.43	1.86	1.86	3.45	1.59	0.7	1.34	0.94	0.86
B-C-B-B-A	PhBr	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.44	2.69	1.18	1.08	1.41	2.93	4.12	2.25	0.56	2.87	1.62	1.53
B-C-B-B-B	PhBr	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.28	2.09	0.59	0.49	1.51	2.33	3.53	1.66	0.45	2.27	1.03	0.94
B-C-B-B-C	PhBr	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.23	1.96	0.46	0.36	1.54	2.2	3.39	1.52	0.42	2.14	0.89	0.8
B-C-B-B-D	PhBr	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.35	2.32	0.82	0.72	1.47	2.56	3.76	1.89	0.5	2.5	1.26	1.17
B-C-B-B-E	PhBr	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.26	2.02	0.52	0.42	1.53	2.26	3.46	1.59	0.43	2.21	0.96	0.87
C-A-A-A-A	PhCl	OAc	I	Et ₃ N	DMF	Et ₃ N·HCl	0.73	1.27	0.92	0.82	2.52	1.06	2.67	0.8	0.84	1.04	0.88	0.79
C-A-A-A-B	PhCl	OAc	I	Et ₃ N	NMP	Et ₃ N·HCl	0.49	0.67	0.33	0.23	4.46	0.46	2.07	0.2	0.63	0.45	0.28	0.19
C-A-A-A-C	PhCl	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.36	0.54	0.19	0.09	5.86	0.33	1.94	0.07	0.47	0.32	0.15	0.06
C-A-A-A-D	PhCl	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.62	0.9	0.56	0.46	3.31	0.69	2.3	0.43	0.75	0.68	0.51	0.42
C-A-A-A-E	PhCl	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.43	0.61	0.26	0.16	5.04	0.4	2	0.14	0.56	0.38	0.22	0.13
C-A-A-B-A	PhCl	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.48	1.96	0.94	0.85	1.82	1.47	2.66	0.8	0.45	1.91	0.86	0.78
C-A-A-B-B	PhCl	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.26	1.36	0.35	0.25	2.37	0.87	2.07	0.2	0.21	1.31	0.27	0.18
C-A-A-B-C	PhCl	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.18	1.23	0.22	0.12	2.62	0.74	1.94	0.07	0.12	1.18	0.14	0.05
C-A-A-B-D	PhCl	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.36	1.59	0.58	0.48	2.08	1.1	2.3	0.43	0.32	1.54	0.5	0.41
C-A-A-B-E	PhCl	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.22	1.3	0.28	0.18	2.48	0.81	2	0.13	0.16	1.25	0.2	0.11
C-A-B-A-A	PhCl	OAc	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.73	1.3	0.95	0.85	2.48	1.09	2.69	0.82	0.84	1.08	0.91	0.82

C-A-B-A-B	PhCl	OAc	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.51	0.7	0.36	0.26	4.26	0.49	2.1	0.23	0.66	0.49	0.32	0.23
C-A-B-A-C	PhCl	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.39	0.57	0.22	0.12	5.48	0.36	1.97	0.1	0.52	0.35	0.18	0.1
C-A-B-A-D	PhCl	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.63	0.93	0.59	0.49	3.22	0.72	2.33	0.46	0.77	0.72	0.55	0.46
C-A-B-A-E	PhCl	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.45	0.64	0.29	0.19	4.77	0.43	2.03	0.16	0.6	0.42	0.25	0.16
C-A-B-B-A	PhCl	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.49	1.99	0.97	0.88	1.8	1.5	2.69	0.82	0.46	1.94	0.9	0.81
C-A-B-B-B	PhCl	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.27	1.39	0.38	0.28	2.33	0.9	2.1	0.23	0.23	1.35	0.3	0.22
C-A-B-B-C	PhCl	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.2	1.26	0.25	0.15	2.56	0.77	1.96	0.1	0.14	1.21	0.17	0.08
C-A-B-B-D	PhCl	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.38	1.62	0.61	0.51	2.06	1.13	2.33	0.46	0.34	1.58	0.53	0.45
C-A-B-B-E	PhCl	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.24	1.33	0.31	0.21	2.43	0.83	2.03	0.16	0.19	1.28	0.24	0.15
C-B-A-A-A	PhCl	Cl	I	Et ₃ N	DMF	Et ₃ N·HCl	0.73	1.27	0.92	0.83	2.5	1.07	2.68	0.81	0.84	1.05	0.88	0.79
C-B-A-A-B	PhCl	Cl	I	Et ₃ N	NMP	Et ₃ N·HCl	0.49	0.68	0.33	0.23	4.37	0.48	2.08	0.21	0.63	0.45	0.29	0.2
C-B-A-A-C	PhCl	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.36	0.54	0.2	0.1	5.69	0.34	1.95	0.08	0.48	0.32	0.15	0.07
C-B-A-A-D	PhCl	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.62	0.91	0.56	0.46	3.27	0.71	2.31	0.44	0.76	0.69	0.52	0.43
C-B-A-A-E	PhCl	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.43	0.61	0.26	0.16	4.92	0.41	2.02	0.15	0.57	0.39	0.22	0.13
C-B-A-B-A	PhCl	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.48	1.96	0.95	0.85	1.81	1.48	2.68	0.81	0.45	1.91	0.87	0.78
C-B-A-B-B	PhCl	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.26	1.37	0.36	0.26	2.35	0.89	2.08	0.21	0.21	1.32	0.27	0.19
C-B-A-B-C	PhCl	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.18	1.23	0.22	0.12	2.59	0.75	1.95	0.08	0.12	1.18	0.14	0.05
C-B-A-B-D	PhCl	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.37	1.6	0.59	0.49	2.07	1.12	2.31	0.44	0.33	1.55	0.5	0.42
C-B-A-B-E	PhCl	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.22	1.3	0.29	0.19	2.46	0.82	2.02	0.15	0.17	1.25	0.21	0.12
C-B-B-A-A	PhCl	Cl	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.73	1.3	0.95	0.86	2.46	1.1	2.71	0.84	0.85	1.08	0.92	0.83
C-B-B-A-B	PhCl	Cl	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.51	0.71	0.36	0.26	4.18	0.5	2.11	0.24	0.66	0.49	0.32	0.23
C-B-B-A-C	PhCl	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.4	0.57	0.23	0.13	5.33	0.37	1.98	0.11	0.53	0.36	0.19	0.1
C-B-B-A-D	PhCl	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.63	0.94	0.59	0.49	3.19	0.73	2.34	0.47	0.77	0.72	0.55	0.46
C-B-B-A-E	PhCl	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.46	0.64	0.29	0.19	4.67	0.44	2.04	0.18	0.6	0.42	0.26	0.17
C-B-B-B-A	PhCl	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.49	1.99	0.98	0.88	1.79	1.51	2.7	0.84	0.46	1.95	0.9	0.82
C-B-B-B-B	PhCl	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.28	1.4	0.39	0.29	2.31	0.91	2.11	0.24	0.23	1.35	0.31	0.22
C-B-B-B-C	PhCl	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.2	1.26	0.25	0.15	2.53	0.78	1.98	0.11	0.14	1.22	0.18	0.09
C-B-B-B-D	PhCl	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.38	1.63	0.62	0.52	2.05	1.14	2.34	0.47	0.34	1.58	0.54	0.45
C-B-B-B-E	PhCl	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.24	1.33	0.32	0.22	2.41	0.85	2.04	0.17	0.19	1.29	0.24	0.15
C-C-A-A-A	PhCl	acac	I	Et ₃ N	DMF	Et ₃ N·HCl	0.77	1.53	1.18	1.08	1.65	2.47	4.08	2.21	0.9	1.75	1.58	1.49
C-C-A-A-B	PhCl	acac	I	Et ₃ N	NMP	Et ₃ N·HCl	0.63	0.93	0.59	0.49	1.86	1.88	3.49	1.62	0.86	1.16	0.99	0.9
C-C-A-A-C	PhCl	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.57	0.8	0.45	0.35	1.92	1.75	3.35	1.48	0.84	1.02	0.85	0.77
C-C-A-A-D	PhCl	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.7	1.16	0.82	0.72	1.76	2.11	3.72	1.85	0.88	1.39	1.22	1.13
C-C-A-A-E	PhCl	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.6	0.87	0.52	0.42	1.89	1.81	3.42	1.55	0.85	1.09	0.92	0.83
C-C-A-B-A	PhCl	acac	I	Et ₂ NH	DMF	Et ₂ NH·HCl	0.54	2.22	1.21	1.11	1.42	2.88	4.08	2.21	0.6	2.61	1.57	1.48
C-C-A-B-B	PhCl	acac	I	Et ₂ NH	NMP	Et ₂ NH·HCl	0.38	1.62	0.61	0.51	1.52	2.29	3.48	1.62	0.48	2.02	0.97	0.89
C-C-A-B-C	PhCl	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.32	1.49	0.48	0.38	1.56	2.15	3.35	1.48	0.45	1.88	0.84	0.75
C-C-A-B-D	PhCl	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.45	1.85	0.84	0.74	1.48	2.52	3.71	1.85	0.54	2.25	1.2	1.12
C-C-A-B-E	PhCl	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.35	1.56	0.54	0.45	1.54	2.22	3.42	1.55	0.47	1.95	0.91	0.82
C-C-B-A-A	PhCl	acac	Br	Et ₃ N	DMF	Et ₃ N·HCl	0.78	1.56	1.21	1.11	1.64	2.5	4.11	2.24	0.91	1.78	1.62	1.53
C-C-B-A-B	PhCl	acac	Br	Et ₃ N	NMP	Et ₃ N·HCl	0.64	0.96	0.62	0.52	1.84	1.91	3.51	1.65	0.86	1.19	1.02	0.94
C-C-B-A-C	PhCl	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HCl	0.58	0.83	0.48	0.38	1.91	1.77	3.38	1.51	0.84	1.06	0.89	0.8
C-C-B-A-D	PhCl	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HCl	0.71	1.19	0.85	0.75	1.75	2.14	3.74	1.88	0.88	1.42	1.25	1.17
C-C-B-A-E	PhCl	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HCl	0.61	0.9	0.55	0.45	1.87	1.84	3.45	1.58	0.85	1.12	0.96	0.87
C-C-B-B-A	PhCl	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HCl	0.55	2.25	1.23	1.14	1.41	2.91	4.11	2.24	0.61	2.65	1.6	1.52

C-C-B-B-B	PhCl	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HCl	0.39	1.65	0.64	0.54	1.52	2.32	3.51	1.64	0.49	2.05	1.01	0.92
C-C-B-B-C	PhCl	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HCl	0.33	1.52	0.51	0.41	1.55	2.18	3.38	1.51	0.46	1.92	0.88	0.79
C-C-B-B-D	PhCl	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HCl	0.46	1.88	0.87	0.77	1.47	2.55	3.74	1.87	0.54	2.28	1.24	1.15
C-C-B-B-E	PhCl	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HCl	0.36	1.59	0.57	0.47	1.53	2.25	3.45	1.58	0.47	1.99	0.94	0.86

Target product P (1-nitro-3-((4-nitrophenyl)ethynyl)benzene) and starting material SM1 (1-ethynyl-3-nitrobenzene) are not shown. R-I, 1-iodo-4-nitrobenzene; R-Br, 1-bromo-4-nitrobenzene; R-Cl, 1-chloro-4-nitrobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green. Organic solvents mixed with water at a 1:1 mass ratio are indicated as solvent/H₂O.

Table S6. bio-Factors and cytotoxicity potentials for synthesis of 1-((4-methoxyphenyl)ethynyl)-3-nitrobenzene.

Reaction	Starting materials (SM2)	Catalyst (CT1) PdA ₂	Catalyst (CT2) CuX	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
							BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A-A	R-I	OAc	I	Et ₃ N	DMF	Et ₃ N·HI	0.82	1.25	1.02	0.82	0.86	1.06	0.91	0.8	1.16	1.04	1.21	0.78
A-A-A-A-B	R-I	OAc	I	Et ₃ N	NMP	Et ₃ N·HI	0.65	0.65	0.42	0.23	0.68	0.46	0.31	0.21	1.38	0.45	0.62	0.19
A-A-A-A-C	R-I	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.56	0.52	0.29	0.1	0.54	0.33	0.18	0.07	1.54	0.32	0.48	0.05
A-A-A-A-D	R-I	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.74	0.88	0.65	0.46	0.78	0.7	0.54	0.44	1.25	0.68	0.85	0.42
A-A-A-A-E	R-I	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.61	0.59	0.36	0.16	0.62	0.4	0.25	0.14	1.44	0.38	0.55	0.12
A-A-A-B-A	R-I	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.55	1.94	1.06	0.87	0.62	1.47	0.91	0.8	0.63	1.91	1.21	0.77
A-A-A-B-B	R-I	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.35	1.34	0.47	0.28	0.36	0.87	0.31	0.21	0.47	1.31	0.61	0.18
A-A-A-B-C	R-I	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.28	1.21	0.34	0.14	0.24	0.74	0.18	0.07	0.41	1.18	0.48	0.05
A-A-A-B-D	R-I	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.44	1.57	0.7	0.51	0.49	1.1	0.54	0.44	0.55	1.54	0.84	0.41
A-A-A-B-E	R-I	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.32	1.28	0.4	0.21	0.3	0.81	0.24	0.14	0.44	1.25	0.55	0.11
A-A-B-A-A	R-I	OAc	Br	Et ₃ N	DMF	Et ₃ N·HI	0.82	1.28	1.05	0.85	0.86	1.09	0.94	0.83	1.16	1.08	1.25	0.82
A-A-B-A-B	R-I	OAc	Br	Et ₃ N	NMP	Et ₃ N·HI	0.67	0.68	0.45	0.26	0.69	0.49	0.34	0.24	1.35	0.48	0.65	0.22
A-A-B-A-C	R-I	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.58	0.55	0.32	0.13	0.58	0.36	0.21	0.1	1.48	0.35	0.52	0.09
A-A-B-A-D	R-I	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.75	0.91	0.68	0.49	0.79	0.72	0.57	0.47	1.24	0.71	0.88	0.45
A-A-B-A-E	R-I	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.63	0.62	0.39	0.19	0.65	0.43	0.28	0.17	1.41	0.42	0.59	0.16
A-A-B-B-A	R-I	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.56	1.97	1.09	0.9	0.62	1.5	0.93	0.83	0.64	1.94	1.24	0.81
A-A-B-B-B	R-I	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.36	1.37	0.5	0.31	0.38	0.9	0.34	0.23	0.48	1.35	0.65	0.22
A-A-B-B-C	R-I	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.29	1.24	0.37	0.17	0.27	0.77	0.21	0.1	0.42	1.21	0.51	0.08
A-A-B-B-D	R-I	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.45	1.6	0.73	0.54	0.5	1.13	0.57	0.46	0.56	1.58	0.88	0.45
A-A-B-B-E	R-I	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.33	1.31	0.43	0.24	0.33	0.84	0.27	0.17	0.45	1.28	0.58	0.15
A-B-A-A-A	R-I	Cl	I	Et ₃ N	DMF	Et ₃ N·HI	0.82	1.25	1.02	0.83	0.86	1.07	0.92	0.81	1.16	1.05	1.22	0.79
A-B-A-A-B	R-I	Cl	I	Et ₃ N	NMP	Et ₃ N·HI	0.65	0.66	0.43	0.24	0.68	0.48	0.33	0.22	1.37	0.45	0.62	0.19
A-B-A-A-C	R-I	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.56	0.52	0.3	0.1	0.56	0.34	0.19	0.09	1.53	0.32	0.49	0.06
A-B-A-A-D	R-I	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.74	0.89	0.66	0.47	0.79	0.71	0.56	0.45	1.25	0.68	0.85	0.42
A-B-A-A-E	R-I	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.61	0.59	0.36	0.17	0.63	0.41	0.26	0.15	1.44	0.39	0.56	0.12
A-B-A-B-A	R-I	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.55	1.94	1.07	0.87	0.62	1.48	0.92	0.81	0.63	1.91	1.21	0.78
A-B-A-B-B	R-I	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.35	1.35	0.47	0.28	0.36	0.89	0.32	0.22	0.47	1.32	0.62	0.19
A-B-A-B-C	R-I	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.28	1.21	0.34	0.15	0.25	0.75	0.19	0.08	0.41	1.18	0.48	0.05
A-B-A-B-D	R-I	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.45	1.58	0.7	0.51	0.5	1.12	0.55	0.45	0.55	1.55	0.85	0.42
A-B-A-B-E	R-I	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.32	1.28	0.41	0.21	0.31	0.82	0.26	0.15	0.44	1.25	0.55	0.12
A-B-B-A-A	R-I	Cl	Br	Et ₃ N	DMF	Et ₃ N·HI	0.82	1.28	1.05	0.86	0.86	1.1	0.95	0.84	1.16	1.08	1.25	0.82
A-B-B-A-B	R-I	Cl	Br	Et ₃ N	NMP	Et ₃ N·HI	0.67	0.69	0.46	0.27	0.7	0.51	0.35	0.25	1.35	0.49	0.66	0.23
A-B-B-A-C	R-I	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.59	0.55	0.33	0.13	0.59	0.37	0.22	0.11	1.48	0.36	0.52	0.09
A-B-B-A-D	R-I	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.75	0.92	0.69	0.5	0.79	0.74	0.58	0.48	1.24	0.72	0.89	0.46
A-B-B-A-E	R-I	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.63	0.62	0.39	0.2	0.66	0.44	0.29	0.18	1.4	0.42	0.59	0.16
A-B-B-B-A	R-I	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.56	1.97	1.1	0.9	0.63	1.51	0.95	0.84	0.64	1.95	1.25	0.81
A-B-B-B-B	R-I	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.37	1.38	0.5	0.31	0.38	0.91	0.35	0.25	0.48	1.35	0.65	0.22
A-B-B-B-C	R-I	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.3	1.24	0.37	0.18	0.28	0.78	0.22	0.11	0.43	1.22	0.52	0.09
A-B-B-B-D	R-I	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.46	1.61	0.73	0.54	0.51	1.14	0.58	0.48	0.56	1.58	0.88	0.45
A-B-B-B-E	R-I	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.33	1.31	0.44	0.24	0.34	0.85	0.28	0.18	0.46	1.28	0.59	0.15
A-C-A-A-A	R-I	acac	I	Et ₃ N	DMF	Et ₃ N·HI	0.85	1.51	1.28	1.09	0.94	2.47	2.32	2.22	1.1	1.75	1.92	1.49

A-C-A-A-B	R-I	acac	I	Et ₃ N	NMP	Et ₃ N·HI	0.75	0.91	0.69	0.49	0.92	1.88	1.73	1.62	1.15	1.15	1.32	0.89
A-C-A-A-C	R-I	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HI	0.71	0.78	0.55	0.36	0.91	1.75	1.59	1.49	1.17	1.02	1.19	0.76
A-C-A-A-D	R-I	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.8	1.14	0.92	0.72	0.93	2.11	1.96	1.85	1.12	1.38	1.55	1.12
A-C-A-A-E	R-I	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.73	0.85	0.62	0.42	0.92	1.81	1.66	1.56	1.16	1.09	1.26	0.83
A-C-A-B-A	R-I	acac	I	Et ₂ NH	DMF	Et ₂ NH·HI	0.6	2.2	1.32	1.13	0.8	2.88	2.32	2.21	0.73	2.61	1.91	1.48
A-C-A-B-B	R-I	acac	I	Et ₂ NH	NMP	Et ₂ NH·HI	0.46	1.6	0.73	0.54	0.75	2.29	1.73	1.62	0.65	2.02	1.32	0.89
A-C-A-B-C	R-I	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.41	1.47	0.6	0.4	0.74	2.15	1.59	1.49	0.63	1.88	1.18	0.75
A-C-A-B-D	R-I	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.52	1.83	0.96	0.77	0.78	2.52	1.96	1.85	0.69	2.25	1.55	1.12
A-C-A-B-E	R-I	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.43	1.54	0.66	0.47	0.75	2.22	1.66	1.55	0.64	1.95	1.25	0.82
A-C-B-A-A	R-I	acac	Br	Et ₃ N	DMF	Et ₃ N·HI	0.85	1.54	1.31	1.12	0.94	2.5	2.35	2.25	1.09	1.78	1.95	1.52
A-C-B-A-B	R-I	acac	Br	Et ₃ N	NMP	Et ₃ N·HI	0.76	0.94	0.72	0.52	0.92	1.91	1.76	1.65	1.14	1.19	1.36	0.93
A-C-B-A-C	R-I	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HI	0.72	0.81	0.58	0.39	0.91	1.77	1.62	1.52	1.16	1.06	1.22	0.79
A-C-B-A-D	R-I	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HI	0.81	1.17	0.95	0.75	0.93	2.14	1.99	1.88	1.12	1.42	1.59	1.16
A-C-B-A-E	R-I	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HI	0.74	0.88	0.65	0.45	0.92	1.84	1.69	1.58	1.15	1.12	1.29	0.86
A-C-B-B-A	R-I	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HI	0.61	2.23	1.35	1.16	0.81	2.91	2.35	2.24	0.74	2.65	1.95	1.51
A-C-B-B-B	R-I	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HI	0.47	1.63	0.76	0.57	0.76	2.32	1.75	1.65	0.66	2.05	1.35	0.92
A-C-B-B-C	R-I	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HI	0.42	1.5	0.63	0.43	0.74	2.18	1.62	1.51	0.64	1.92	1.22	0.79
A-C-B-B-D	R-I	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HI	0.53	1.86	0.99	0.8	0.78	2.55	1.98	1.88	0.69	2.28	1.58	1.15
A-C-B-B-E	R-I	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HI	0.44	1.57	0.69	0.5	0.75	2.25	1.69	1.58	0.65	1.99	1.29	0.85
B-A-A-A-A	R-Br	OAc	I	Et ₃ N	DMF	Et ₃ N·HBr	0.75	1.33	1	0.81	0.81	1.13	0.91	0.8	1.15	1.06	1.21	0.78
B-A-A-A-B	R-Br	OAc	I	Et ₃ N	NMP	Et ₃ N·HBr	0.55	0.74	0.41	0.21	0.59	0.53	0.31	0.21	1.33	0.46	0.61	0.18
B-A-A-A-C	R-Br	OAc	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.45	0.6	0.27	0.08	0.45	0.4	0.18	0.08	1.47	0.33	0.48	0.05
B-A-A-A-D	R-Br	OAc	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.66	0.97	0.64	0.44	0.71	0.76	0.54	0.44	1.22	0.69	0.84	0.41
B-A-A-A-E	R-Br	OAc	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.51	0.67	0.34	0.14	0.53	0.47	0.25	0.14	1.39	0.39	0.55	0.12
B-A-A-B-A	R-Br	OAc	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.49	2.02	0.99	0.79	0.59	1.54	0.91	0.81	0.64	1.92	1.22	0.79
B-A-A-B-B	R-Br	OAc	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.28	1.43	0.39	0.2	0.34	0.94	0.32	0.21	0.47	1.32	0.63	0.2
B-A-A-B-C	R-Br	OAc	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.2	1.29	0.26	0.07	0.23	0.81	0.19	0.08	0.42	1.19	0.49	0.06
B-A-A-B-D	R-Br	OAc	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.38	1.66	0.62	0.43	0.47	1.17	0.55	0.44	0.55	1.55	0.86	0.43
B-A-A-B-E	R-Br	OAc	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.24	1.36	0.33	0.13	0.29	0.88	0.25	0.15	0.45	1.26	0.56	0.13
B-A-B-A-A	R-Br	OAc	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.76	1.36	1.03	0.84	0.81	1.16	0.94	0.83	1.14	1.09	1.24	0.81
B-A-B-A-B	R-Br	OAc	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.57	0.77	0.44	0.24	0.61	0.56	0.34	0.24	1.31	0.5	0.65	0.22
B-A-B-A-C	R-Br	OAc	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.48	0.63	0.3	0.11	0.49	0.43	0.21	0.1	1.42	0.36	0.52	0.08
B-A-B-A-D	R-Br	OAc	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.67	1	0.67	0.47	0.72	0.79	0.57	0.47	1.21	0.73	0.88	0.45
B-A-B-A-E	R-Br	OAc	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.53	0.7	0.37	0.17	0.56	0.5	0.28	0.17	1.36	0.43	0.58	0.15
B-A-B-B-A	R-Br	OAc	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.5	2.05	1.02	0.82	0.6	1.57	0.94	0.84	0.64	1.95	1.26	0.83
B-A-B-B-B	R-Br	OAc	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.29	1.46	0.42	0.23	0.36	0.97	0.35	0.24	0.49	1.36	0.66	0.23
B-A-B-B-C	R-Br	OAc	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.22	1.32	0.29	0.1	0.26	0.84	0.21	0.11	0.43	1.23	0.53	0.1
B-A-B-B-D	R-Br	OAc	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.39	1.69	0.65	0.46	0.48	1.2	0.58	0.47	0.56	1.59	0.89	0.46
B-A-B-B-E	R-Br	OAc	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.26	1.39	0.36	0.16	0.31	0.9	0.28	0.18	0.46	1.29	0.6	0.17
B-B-A-A-A	R-Br	Cl	I	Et ₃ N	DMF	Et ₃ N·HBr	0.75	1.34	1	0.81	0.81	1.14	0.92	0.82	1.14	1.06	1.21	0.78
B-B-A-A-B	R-Br	Cl	I	Et ₃ N	NMP	Et ₃ N·HBr	0.55	0.74	0.41	0.22	0.6	0.55	0.33	0.22	1.33	0.47	0.62	0.19
B-B-A-A-C	R-Br	Cl	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.45	0.61	0.28	0.08	0.47	0.41	0.19	0.09	1.46	0.33	0.49	0.05
B-B-A-A-D	R-Br	Cl	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.66	0.97	0.64	0.45	0.72	0.78	0.56	0.45	1.22	0.7	0.85	0.42
B-B-A-A-E	R-Br	Cl	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.51	0.67	0.34	0.15	0.54	0.48	0.26	0.15	1.38	0.4	0.55	0.12
B-B-A-B-A	R-Br	Cl	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.49	2.03	0.99	0.8	0.6	1.55	0.93	0.82	0.64	1.92	1.23	0.8

B-B-A-B-B	R-Br	Cl	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.28	1.43	0.4	0.2	0.35	0.95	0.33	0.23	0.48	1.33	0.63	0.2
B-B-A-B-C	R-Br	Cl	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.2	1.3	0.27	0.07	0.24	0.82	0.2	0.09	0.42	1.19	0.5	0.07
B-B-A-B-D	R-Br	Cl	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.38	1.66	0.63	0.44	0.47	1.18	0.56	0.46	0.55	1.56	0.86	0.43
B-B-A-B-E	R-Br	Cl	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.24	1.37	0.33	0.14	0.3	0.89	0.26	0.16	0.45	1.26	0.57	0.13
B-B-B-A-A	R-Br	Cl	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.76	1.36	1.03	0.84	0.81	1.17	0.95	0.84	1.14	1.1	1.25	0.82
B-B-B-A-B	R-Br	Cl	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.57	0.77	0.44	0.25	0.62	0.57	0.36	0.25	1.31	0.5	0.65	0.22
B-B-B-A-C	R-Br	Cl	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.48	0.64	0.31	0.11	0.5	0.44	0.22	0.12	1.42	0.37	0.52	0.09
B-B-B-A-D	R-Br	Cl	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.67	1	0.67	0.48	0.73	0.8	0.59	0.48	1.21	0.73	0.88	0.45
B-B-B-A-E	R-Br	Cl	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.53	0.7	0.37	0.18	0.57	0.51	0.29	0.18	1.35	0.43	0.59	0.16
B-B-B-B-A	R-Br	Cl	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.5	2.06	1.02	0.83	0.6	1.58	0.95	0.85	0.64	1.96	1.26	0.83
B-B-B-B-B	R-Br	Cl	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.29	1.46	0.43	0.23	0.37	0.98	0.36	0.25	0.49	1.36	0.67	0.24
B-B-B-B-C	R-Br	Cl	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.22	1.33	0.3	0.1	0.27	0.85	0.23	0.12	0.43	1.23	0.53	0.1
B-B-B-B-D	R-Br	Cl	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.39	1.69	0.66	0.46	0.49	1.21	0.59	0.48	0.56	1.59	0.9	0.47
B-B-B-B-E	R-Br	Cl	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.26	1.4	0.36	0.17	0.32	0.92	0.29	0.19	0.46	1.3	0.6	0.17
B-C-A-A-A	R-Br	acac	I	Et ₃ N	DMF	Et ₃ N·HBr	0.79	1.59	1.26	1.07	0.91	2.54	2.32	2.22	1.09	1.76	1.91	1.48
B-C-A-A-B	R-Br	acac	I	Et ₃ N	NMP	Et ₃ N·HBr	0.67	1	0.67	0.47	0.89	1.95	1.73	1.62	1.13	1.17	1.32	0.89
B-C-A-A-C	R-Br	acac	I	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.62	0.86	0.53	0.34	0.88	1.81	1.6	1.49	1.15	1.03	1.19	0.75
B-C-A-A-D	R-Br	acac	I	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.73	1.23	0.9	0.7	0.9	2.18	1.96	1.85	1.11	1.4	1.55	1.12
B-C-A-A-E	R-Br	acac	I	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.64	0.93	0.6	0.4	0.88	1.88	1.66	1.56	1.14	1.1	1.25	0.82
B-C-A-B-A	R-Br	acac	I	Et ₂ NH	DMF	Et ₂ NH·HBr	0.55	2.28	1.25	1.05	0.79	2.95	2.33	2.22	0.73	2.62	1.93	1.5
B-C-A-B-B	R-Br	acac	I	Et ₂ NH	NMP	Et ₂ NH·HBr	0.39	1.69	0.66	0.46	0.74	2.36	1.73	1.63	0.66	2.03	1.33	0.9
B-C-A-B-C	R-Br	acac	I	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.34	1.55	0.52	0.33	0.72	2.22	1.6	1.5	0.63	1.9	1.2	0.77
B-C-A-B-D	R-Br	acac	I	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.46	1.92	0.89	0.69	0.76	2.59	1.96	1.86	0.69	2.26	1.56	1.13
B-C-A-B-E	R-Br	acac	I	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.36	1.62	0.59	0.39	0.73	2.29	1.67	1.56	0.65	1.96	1.27	0.84
B-C-B-A-A	R-Br	acac	Br	Et ₃ N	DMF	Et ₃ N·HBr	0.8	1.62	1.29	1.1	0.91	2.57	2.35	2.25	1.09	1.8	1.95	1.52
B-C-B-A-B	R-Br	acac	Br	Et ₃ N	NMP	Et ₃ N·HBr	0.68	1.03	0.7	0.5	0.89	1.98	1.76	1.65	1.13	1.2	1.36	0.92
B-C-B-A-C	R-Br	acac	Br	Et ₃ N	H ₂ O	Et ₃ N·HBr	0.63	0.89	0.56	0.37	0.88	1.84	1.62	1.52	1.14	1.07	1.22	0.79
B-C-B-A-D	R-Br	acac	Br	Et ₃ N	DMF/H ₂ O	Et ₃ N·HBr	0.74	1.26	0.93	0.73	0.9	2.21	1.99	1.88	1.11	1.43	1.59	1.15
B-C-B-A-E	R-Br	acac	Br	Et ₃ N	NMP/H ₂ O	Et ₃ N·HBr	0.66	0.96	0.63	0.43	0.89	1.91	1.69	1.59	1.14	1.13	1.29	0.86
B-C-B-B-A	R-Br	acac	Br	Et ₂ NH	DMF	Et ₂ NH·HBr	0.55	2.31	1.28	1.08	0.79	2.98	2.36	2.25	0.74	2.66	1.96	1.53
B-C-B-B-B	R-Br	acac	Br	Et ₂ NH	NMP	Et ₂ NH·HBr	0.4	1.72	0.68	0.49	0.74	2.39	1.76	1.66	0.66	2.06	1.37	0.94
B-C-B-B-C	R-Br	acac	Br	Et ₂ NH	H ₂ O	Et ₂ NH·HBr	0.35	1.58	0.55	0.36	0.72	2.25	1.63	1.52	0.64	1.93	1.24	0.8
B-C-B-B-D	R-Br	acac	Br	Et ₂ NH	DMF/H ₂ O	Et ₂ NH·HBr	0.47	1.95	0.92	0.72	0.76	2.62	1.99	1.89	0.7	2.29	1.6	1.17
B-C-B-B-E	R-Br	acac	Br	Et ₂ NH	NMP/H ₂ O	Et ₂ NH·HBr	0.37	1.65	0.62	0.42	0.73	2.32	1.7	1.59	0.65	2	1.3	0.87

Target product P (1-((4-methoxyphenyl)ethynyl)-3-nitrobenzene) and starting material SM1 (1-ethynyl-3-nitrobenzene) are not shown. R-I, 1-iodo-4-methoxybenzene; R-Br, 1-bromo-4-methoxybenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green. Organic solvents mixed with water at a 1:1 mass ratio are indicated as solvent/H₂O.

Table S7. bio-Factors and cytotoxicity potentials for synthesis of (*E*)-stilbene.

Reaction	Starting materials (SM2)	Catalyst (CT) PdA ₂	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
						BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A	PhI	OAc	Et ₃ N	DMF	Et ₃ N·HI	0.7	1.18	0.82	0.8	0.71	1.16	0.82	0.79	0.66	0.35	0.23	0.21
A-A-A-B	PhI	OAc	Et ₃ N	NMP	Et ₃ N·HI	0.39	0.58	0.23	0.21	0.41	0.58	0.24	0.21	0.57	0.27	0.15	0.13
A-A-B-A	PhI	OAc	Et ₂ NH	DMF	Et ₂ NH·HI	0.46	1.87	0.87	0.85	0.52	1.57	0.82	0.79	0.18	1.21	0.22	0.21
A-A-B-B	PhI	OAc	Et ₂ NH	NMP	Et ₂ NH·HI	0.21	1.27	0.27	0.25	0.24	0.99	0.24	0.2	0.13	1.13	0.15	0.13
A-B-A-A	PhI	Cl	Et ₃ N	DMF	Et ₃ N·HI	0.7	1.18	0.83	0.81	0.71	1.17	0.83	0.8	0.67	0.35	0.23	0.22
A-B-A-B	PhI	Cl	Et ₃ N	NMP	Et ₃ N·HI	0.39	0.59	0.23	0.21	0.42	0.59	0.25	0.22	0.57	0.27	0.16	0.14
A-B-B-A	PhI	Cl	Et ₂ NH	DMF	Et ₂ NH·HI	0.46	1.87	0.87	0.85	0.53	1.58	0.83	0.8	0.19	1.21	0.23	0.21
A-B-B-B	PhI	Cl	Et ₂ NH	NMP	Et ₂ NH·HI	0.22	1.28	0.28	0.26	0.25	1	0.25	0.22	0.13	1.14	0.15	0.13
A-C-A-A	PhI	acac	Et ₃ N	DMF	Et ₃ N·HI	0.75	1.44	1.08	1.06	0.87	2.57	2.24	2.21	0.89	1.05	0.94	0.92
A-C-A-B	PhI	acac	Et ₃ N	NMP	Et ₃ N·HI	0.58	0.84	0.49	0.47	0.83	1.99	1.65	1.62	0.88	0.97	0.86	0.84
A-C-B-A	PhI	acac	Et ₂ NH	DMF	Et ₂ NH·HI	0.53	2.13	1.13	1.11	0.75	2.98	2.23	2.2	0.49	1.91	0.93	0.91
A-C-B-B	PhI	acac	Et ₂ NH	NMP	Et ₂ NH·HI	0.35	1.53	0.53	0.52	0.69	2.4	1.65	1.62	0.46	1.84	0.85	0.83
B-A-A-A	PhBr	OAc	Et ₃ N	DMF	Et ₃ N·HBr	0.76	1.06	0.8	0.78	0.77	1.07	0.82	0.79	0.76	0.3	0.23	0.21
B-A-A-B	PhBr	OAc	Et ₃ N	NMP	Et ₃ N·HBr	0.45	0.46	0.21	0.19	0.49	0.48	0.24	0.21	0.67	0.22	0.15	0.13
B-A-B-A	PhBr	OAc	Et ₂ NH	DMF	Et ₂ NH·HBr	0.45	1.75	0.79	0.77	0.56	1.48	0.83	0.8	0.21	1.16	0.24	0.22
B-A-B-B	PhBr	OAc	Et ₂ NH	NMP	Et ₂ NH·HBr	0.17	1.16	0.2	0.18	0.27	0.89	0.24	0.21	0.15	1.08	0.16	0.14
B-B-A-A	PhBr	Cl	Et ₃ N	DMF	Et ₃ N·HBr	0.76	1.06	0.81	0.79	0.77	1.08	0.83	0.8	0.76	0.3	0.23	0.21
B-B-A-B	PhBr	Cl	Et ₃ N	NMP	Et ₃ N·HBr	0.45	0.47	0.21	0.19	0.51	0.5	0.25	0.22	0.68	0.23	0.15	0.14
B-B-B-A	PhBr	Cl	Et ₂ NH	DMF	Et ₂ NH·HBr	0.45	1.75	0.8	0.78	0.56	1.49	0.84	0.81	0.21	1.17	0.24	0.23
B-B-B-B	PhBr	Cl	Et ₂ NH	NMP	Et ₂ NH·HBr	0.17	1.16	0.2	0.18	0.28	0.91	0.26	0.23	0.15	1.09	0.17	0.15
B-C-A-A	PhBr	acac	Et ₃ N	DMF	Et ₃ N·HBr	0.81	1.32	1.06	1.04	0.9	2.48	2.24	2.21	0.93	1	0.93	0.91
B-C-A-B	PhBr	acac	Et ₃ N	NMP	Et ₃ N·HBr	0.65	0.72	0.47	0.45	0.87	1.9	1.65	1.62	0.92	0.93	0.85	0.84
B-C-B-A	PhBr	acac	Et ₂ NH	DMF	Et ₂ NH·HBr	0.52	2.01	1.05	1.03	0.78	2.89	2.24	2.21	0.51	1.87	0.95	0.93
B-C-B-B	PhBr	acac	Et ₂ NH	NMP	Et ₂ NH·HBr	0.32	1.42	0.46	0.44	0.72	2.31	1.66	1.63	0.48	1.79	0.87	0.85
C-A-A-A	PhCl	OAc	Et ₃ N	DMF	Et ₃ N·HCl	0.82	1	0.82	0.8	0.8	1.02	0.82	0.79	0.88	0.27	0.24	0.22
C-A-A-B	PhCl	OAc	Et ₃ N	NMP	Et ₃ N·HCl	0.55	0.4	0.22	0.21	0.53	0.44	0.23	0.2	0.83	0.19	0.16	0.14
C-A-B-A	PhCl	OAc	Et ₂ NH	DMF	Et ₂ NH·HCl	0.5	1.69	0.84	0.82	0.57	1.43	0.81	0.78	0.2	1.13	0.22	0.21
C-A-B-B	PhCl	OAc	Et ₂ NH	NMP	Et ₂ NH·HCl	0.23	1.1	0.25	0.23	0.27	0.84	0.23	0.2	0.14	1.05	0.15	0.13
C-B-A-A	PhCl	Cl	Et ₃ N	DMF	Et ₃ N·HCl	0.82	1	0.82	0.8	0.8	1.03	0.83	0.8	0.88	0.27	0.24	0.23
C-B-A-B	PhCl	Cl	Et ₃ N	NMP	Et ₃ N·HCl	0.56	0.41	0.23	0.21	0.55	0.45	0.24	0.21	0.84	0.2	0.16	0.15
C-B-B-A	PhCl	Cl	Et ₂ NH	DMF	Et ₂ NH·HCl	0.5	1.69	0.85	0.83	0.57	1.44	0.83	0.8	0.2	1.14	0.23	0.21
C-B-B-B	PhCl	Cl	Et ₂ NH	NMP	Et ₂ NH·HCl	0.23	1.1	0.25	0.24	0.28	0.86	0.24	0.21	0.14	1.06	0.15	0.13
C-C-A-A	PhCl	acac	Et ₃ N	DMF	Et ₃ N·HCl	0.86	1.26	1.08	1.06	0.92	2.43	2.23	2.2	0.97	0.97	0.94	0.93
C-C-A-B	PhCl	acac	Et ₃ N	NMP	Et ₃ N·HCl	0.73	0.67	0.48	0.47	0.89	1.85	1.65	1.62	0.96	0.9	0.87	0.85
C-C-B-A	PhCl	acac	Et ₂ NH	DMF	Et ₂ NH·HCl	0.57	1.95	1.1	1.09	0.78	2.84	2.23	2.2	0.51	1.84	0.93	0.91
C-C-B-B	PhCl	acac	Et ₂ NH	NMP	Et ₂ NH·HCl	0.37	1.36	0.51	0.49	0.73	2.26	1.65	1.61	0.48	1.76	0.85	0.83

Target product P(*E*-stilbene) and starting material SM1 (styrene) are not shown. PhI, iodobenzene; PhBr, bromobenzene; PhCl, chlorobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green.

Table S8. bio-Factors and cytotoxicity potentials for synthesis of (*E*)-4-nitrostilbene.

Reaction	Starting materials (SM2)	Catalyst (CT) PdA ₂	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
						BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A	R-I	OAc	Et ₃ N	DMF	Et ₃ N·HI	0.97	0.93	0.9	0.8	0.92	0.91	0.84	0.79	1.2	0.27	0.32	0.21
A-A-A-B	R-I	OAc	Et ₃ N	NMP	Et ₃ N·HI	0.93	0.33	0.31	0.21	0.77	0.33	0.25	0.21	1.28	0.19	0.25	0.13
A-A-B-A	R-I	OAc	Et ₂ NH	DMF	Et ₂ NH·HI	0.59	1.62	0.95	0.85	0.63	1.32	0.83	0.79	0.28	1.13	0.32	0.21
A-A-B-B	R-I	OAc	Et ₂ NH	NMP	Et ₂ NH·HI	0.35	1.03	0.35	0.25	0.34	0.74	0.25	0.2	0.23	1.06	0.24	0.13
A-B-A-A	R-I	Cl	Et ₃ N	DMF	Et ₃ N·HI	0.97	0.93	0.91	0.81	0.92	0.92	0.85	0.8	1.19	0.28	0.33	0.22
A-B-A-B	R-I	Cl	Et ₃ N	NMP	Et ₃ N·HI	0.93	0.34	0.31	0.21	0.78	0.34	0.26	0.22	1.27	0.2	0.25	0.14
A-B-B-A	R-I	Cl	Et ₂ NH	DMF	Et ₂ NH·HI	0.59	1.62	0.95	0.85	0.64	1.33	0.85	0.8	0.28	1.14	0.32	0.21
A-B-B-B	R-I	Cl	Et ₂ NH	NMP	Et ₂ NH·HI	0.35	1.03	0.36	0.26	0.35	0.75	0.26	0.22	0.23	1.06	0.24	0.13
A-C-A-A	R-I	acac	Et ₃ N	DMF	Et ₃ N·HI	0.98	1.19	1.16	1.06	0.97	2.32	2.25	2.21	1.05	0.98	1.03	0.92
A-C-A-B	R-I	acac	Et ₃ N	NMP	Et ₃ N·HI	0.96	0.59	0.57	0.47	0.96	1.74	1.67	1.62	1.06	0.9	0.95	0.84
A-C-B-A	R-I	acac	Et ₂ NH	DMF	Et ₂ NH·HI	0.64	1.88	1.21	1.11	0.82	2.73	2.25	2.2	0.56	1.84	1.02	0.91
A-C-B-B	R-I	acac	Et ₂ NH	NMP	Et ₂ NH·HI	0.48	1.28	0.61	0.51	0.77	2.15	1.66	1.62	0.54	1.76	0.94	0.83
B-A-A-A	R-Br	OAc	Et ₃ N	DMF	Et ₃ N·HBr	0.64	1.38	0.88	0.78	0.87	0.96	0.84	0.79	0.65	0.49	0.32	0.21
B-A-A-B	R-Br	OAc	Et ₃ N	NMP	Et ₃ N·HBr	0.37	0.78	0.29	0.19	0.67	0.38	0.25	0.21	0.58	0.41	0.24	0.13
B-A-B-A	R-Br	OAc	Et ₂ NH	DMF	Et ₂ NH·HBr	0.42	2.07	0.87	0.77	0.62	1.37	0.84	0.8	0.25	1.35	0.33	0.22
B-A-B-B	R-Br	OAc	Et ₂ NH	NMP	Et ₂ NH·HBr	0.19	1.48	0.28	0.18	0.33	0.79	0.26	0.21	0.2	1.28	0.26	0.14
B-B-A-A	R-Br	Cl	Et ₃ N	DMF	Et ₃ N·HBr	0.64	1.38	0.89	0.79	0.87	0.97	0.85	0.8	0.65	0.5	0.32	0.21
B-B-A-B	R-Br	Cl	Et ₃ N	NMP	Et ₃ N·HBr	0.37	0.79	0.29	0.19	0.68	0.39	0.27	0.22	0.59	0.42	0.25	0.14
B-B-B-A	R-Br	Cl	Et ₂ NH	DMF	Et ₂ NH·HBr	0.42	2.07	0.88	0.78	0.62	1.38	0.85	0.81	0.25	1.36	0.34	0.23
B-B-B-B	R-Br	Cl	Et ₂ NH	NMP	Et ₂ NH·HBr	0.19	1.48	0.28	0.18	0.34	0.8	0.27	0.23	0.2	1.28	0.26	0.15
B-C-A-A	R-Br	acac	Et ₃ N	DMF	Et ₃ N·HBr	0.7	1.64	1.14	1.04	0.95	2.37	2.25	2.21	0.86	1.2	1.03	0.91
B-C-A-B	R-Br	acac	Et ₃ N	NMP	Et ₃ N·HBr	0.53	1.04	0.55	0.45	0.93	1.79	1.67	1.62	0.85	1.12	0.95	0.84
B-C-B-A	R-Br	acac	Et ₂ NH	DMF	Et ₂ NH·HBr	0.49	2.33	1.13	1.03	0.81	2.78	2.26	2.21	0.5	2.06	1.04	0.93
B-C-B-B	R-Br	acac	Et ₂ NH	NMP	Et ₂ NH·HBr	0.31	1.73	0.54	0.44	0.76	2.2	1.67	1.63	0.48	1.98	0.96	0.85
C-A-A-A	R-Cl	OAc	Et ₃ N	DMF	Et ₃ N·HCl	0.96	0.94	0.9	0.8	0.88	0.94	0.83	0.79	1.22	0.27	0.33	0.22
C-A-A-B	R-Cl	OAc	Et ₃ N	NMP	Et ₃ N·HCl	0.88	0.35	0.31	0.21	0.68	0.36	0.25	0.2	1.31	0.19	0.25	0.14
C-A-B-A	R-Cl	OAc	Et ₂ NH	DMF	Et ₂ NH·HCl	0.57	1.63	0.92	0.82	0.61	1.35	0.83	0.78	0.28	1.14	0.32	0.21
C-A-B-B	R-Cl	OAc	Et ₂ NH	NMP	Et ₂ NH·HCl	0.32	1.04	0.33	0.23	0.32	0.77	0.25	0.2	0.23	1.06	0.24	0.13
C-B-A-A	R-Cl	Cl	Et ₃ N	DMF	Et ₃ N·HCl	0.96	0.94	0.9	0.8	0.88	0.96	0.84	0.8	1.21	0.28	0.34	0.23
C-B-A-B	R-Cl	Cl	Et ₃ N	NMP	Et ₃ N·HCl	0.89	0.35	0.31	0.21	0.69	0.37	0.26	0.21	1.3	0.2	0.26	0.15
C-B-B-A	R-Cl	Cl	Et ₂ NH	DMF	Et ₂ NH·HCl	0.57	1.64	0.93	0.83	0.62	1.37	0.84	0.8	0.28	1.14	0.32	0.21
C-B-B-B	R-Cl	Cl	Et ₂ NH	NMP	Et ₂ NH·HCl	0.32	1.04	0.34	0.24	0.33	0.78	0.26	0.21	0.23	1.06	0.25	0.13
C-C-A-A	R-Cl	acac	Et ₃ N	DMF	Et ₃ N·HCl	0.97	1.2	1.16	1.06	0.95	2.36	2.24	2.2	1.06	0.98	1.04	0.93
C-C-A-B	R-Cl	acac	Et ₃ N	NMP	Et ₃ N·HCl	0.93	0.61	0.57	0.47	0.94	1.78	1.66	1.62	1.07	0.9	0.96	0.85
C-C-B-A	R-Cl	acac	Et ₂ NH	DMF	Et ₂ NH·HCl	0.63	1.89	1.18	1.08	0.81	2.77	2.24	2.2	0.56	1.84	1.02	0.91
C-C-B-B	R-Cl	acac	Et ₂ NH	NMP	Et ₂ NH·HCl	0.45	1.3	0.59	0.49	0.76	2.18	1.66	1.61	0.54	1.76	0.95	0.83

Target product P ((*E*)-4-nitrostilbene) and starting material SM1 (styrene) are not shown. R-I, 1-iodo-4-nitrobenzene; R-Br, 1-bromo-4-nitrobenzene; R-Cl, 1-chloro-4-nitrobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green.

Table S9. bio-Factors and cytotoxicity potentials for synthesis of (*E*)-4-chlorostilbene.

Reaction	Starting materials (SM2)	Catalyst (CT) PdA ₂	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
						BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A	PhI	OAc	Et ₃ N	DMF	Et ₃ N·HI	0.73	1.34	0.98	0.8	0.77	1.58	1.22	0.79	0.81	0.41	0.33	0.21
A-A-A-B	PhI	OAc	Et ₃ N	NMP	Et ₃ N·HI	0.52	0.74	0.39	0.21	0.64	1	0.64	0.21	0.77	0.33	0.25	0.13
A-A-B-A	PhI	OAc	Et ₂ NH	DMF	Et ₂ NH·HI	0.51	2.03	1.03	0.85	0.61	1.99	1.22	0.79	0.26	1.27	0.33	0.21
A-A-B-B	PhI	OAc	Et ₂ NH	NMP	Et ₂ NH·HI	0.3	1.44	0.43	0.25	0.45	1.41	0.63	0.2	0.21	1.19	0.25	0.13
A-B-A-A	PhI	Cl	Et ₃ N	DMF	Et ₃ N·HI	0.73	1.34	0.99	0.81	0.77	1.59	1.23	0.8	0.81	0.41	0.34	0.22
A-B-A-B	PhI	Cl	Et ₃ N	NMP	Et ₃ N·HI	0.52	0.75	0.39	0.21	0.64	1.01	0.65	0.22	0.77	0.34	0.26	0.14
A-B-B-A	PhI	Cl	Et ₂ NH	DMF	Et ₂ NH·HI	0.51	2.03	1.03	0.85	0.61	2	1.23	0.8	0.26	1.28	0.33	0.21
A-B-B-B	PhI	Cl	Et ₂ NH	NMP	Et ₂ NH·HI	0.3	1.44	0.44	0.26	0.45	1.42	0.64	0.22	0.21	1.2	0.25	0.13
A-C-A-A	PhI	acac	Et ₃ N	DMF	Et ₃ N·HI	0.78	1.6	1.24	1.06	0.88	2.99	2.63	2.21	0.93	1.11	1.04	0.92
A-C-A-B	PhI	acac	Et ₃ N	NMP	Et ₃ N·HI	0.64	1	0.65	0.47	0.85	2.41	2.05	1.62	0.93	1.04	0.96	0.84
A-C-B-A	PhI	acac	Et ₂ NH	DMF	Et ₂ NH·HI	0.56	2.29	1.29	1.11	0.77	3.4	2.63	2.2	0.52	1.98	1.03	0.91
A-C-B-B	PhI	acac	Et ₂ NH	NMP	Et ₂ NH·HI	0.41	1.7	0.69	0.52	0.73	2.82	2.05	1.62	0.5	1.9	0.95	0.83
B-A-A-A	PhBr	OAc	Et ₃ N	DMF	Et ₃ N·HBr	0.79	1.22	0.96	0.78	0.82	1.49	1.22	0.79	0.91	0.36	0.33	0.21
B-A-A-B	PhBr	OAc	Et ₃ N	NMP	Et ₃ N·HBr	0.59	0.63	0.37	0.19	0.7	0.9	0.64	0.21	0.88	0.28	0.25	0.13
B-A-B-A	PhBr	OAc	Et ₂ NH	DMF	Et ₂ NH·HBr	0.5	1.91	0.95	0.77	0.65	1.9	1.23	0.8	0.28	1.22	0.34	0.22
B-A-B-B	PhBr	OAc	Et ₂ NH	NMP	Et ₂ NH·HBr	0.27	1.32	0.36	0.18	0.49	1.31	0.64	0.21	0.23	1.15	0.26	0.14
B-B-A-A	PhBr	Cl	Et ₃ N	DMF	Et ₃ N·HBr	0.79	1.22	0.97	0.79	0.82	1.5	1.23	0.8	0.91	0.37	0.33	0.21
B-B-A-B	PhBr	Cl	Et ₃ N	NMP	Et ₃ N·HBr	0.59	0.63	0.37	0.19	0.71	0.92	0.65	0.22	0.89	0.29	0.25	0.14
B-B-B-A	PhBr	Cl	Et ₂ NH	DMF	Et ₂ NH·HBr	0.5	1.92	0.96	0.78	0.65	1.91	1.24	0.81	0.28	1.23	0.35	0.23
B-B-B-B	PhBr	Cl	Et ₂ NH	NMP	Et ₂ NH·HBr	0.27	1.32	0.36	0.18	0.49	1.33	0.65	0.23	0.23	1.15	0.27	0.15
B-C-A-A	PhBr	acac	Et ₃ N	DMF	Et ₃ N·HBr	0.83	1.48	1.22	1.04	0.91	2.9	2.64	2.21	0.97	1.07	1.03	0.91
B-C-A-B	PhBr	acac	Et ₃ N	NMP	Et ₃ N·HBr	0.71	0.89	0.63	0.45	0.88	2.32	2.05	1.62	0.97	0.99	0.96	0.84
B-C-B-A	PhBr	acac	Et ₂ NH	DMF	Et ₂ NH·HBr	0.56	2.17	1.21	1.03	0.8	3.31	2.64	2.21	0.54	1.93	1.05	0.93
B-C-B-B	PhBr	acac	Et ₂ NH	NMP	Et ₂ NH·HBr	0.39	1.58	0.62	0.44	0.75	2.73	2.06	1.63	0.52	1.85	0.97	0.85
C-A-A-A	PhCl	OAc	Et ₃ N	DMF	Et ₃ N·HCl	0.84	1.16	0.98	0.8	0.84	1.44	1.21	0.79	1.03	0.33	0.34	0.22
C-A-A-B	PhCl	OAc	Et ₃ N	NMP	Et ₃ N·HCl	0.68	0.57	0.38	0.21	0.74	0.86	0.63	0.2	1.03	0.25	0.26	0.14
C-A-B-A	PhCl	OAc	Et ₂ NH	DMF	Et ₂ NH·HCl	0.54	1.85	1	0.82	0.66	1.85	1.21	0.78	0.27	1.19	0.33	0.21
C-A-B-B	PhCl	OAc	Et ₂ NH	NMP	Et ₂ NH·HCl	0.32	1.26	0.41	0.23	0.5	1.26	0.63	0.2	0.22	1.12	0.25	0.13
C-B-A-A	PhCl	Cl	Et ₃ N	DMF	Et ₃ N·HCl	0.84	1.16	0.98	0.8	0.84	1.45	1.23	0.8	1.02	0.34	0.34	0.23
C-B-A-B	PhCl	Cl	Et ₃ N	NMP	Et ₃ N·HCl	0.68	0.57	0.39	0.21	0.74	0.87	0.64	0.21	1.03	0.26	0.27	0.15
C-B-B-A	PhCl	Cl	Et ₂ NH	DMF	Et ₂ NH·HCl	0.54	1.86	1.01	0.83	0.66	1.86	1.22	0.8	0.28	1.2	0.33	0.21
C-B-B-B	PhCl	Cl	Et ₂ NH	NMP	Et ₂ NH·HCl	0.33	1.26	0.41	0.24	0.5	1.28	0.64	0.21	0.23	1.12	0.25	0.13
C-C-A-A	PhCl	acac	Et ₃ N	DMF	Et ₃ N·HCl	0.87	1.42	1.24	1.06	0.92	2.85	2.63	2.2	1.01	1.04	1.04	0.93
C-C-A-B	PhCl	acac	Et ₃ N	NMP	Et ₃ N·HCl	0.78	0.83	0.64	0.47	0.9	2.27	2.04	1.62	1.01	0.96	0.97	0.85
C-C-B-A	PhCl	acac	Et ₂ NH	DMF	Et ₂ NH·HCl	0.6	2.11	1.26	1.09	0.81	3.26	2.63	2.2	0.54	1.9	1.03	0.91
C-C-B-B	PhCl	acac	Et ₂ NH	NMP	Et ₂ NH·HCl	0.44	1.52	0.67	0.49	0.76	2.68	2.04	1.61	0.52	1.82	0.95	0.83

Target product P(*E*)-4-chlorostilbene) and starting material SM1 (4-chlorostyrene) are not shown. PhI, iodobenzene; PhBr, bromobenzene; PhCl, chlorobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green.

Table S10. bio-Factors and cytotoxicity potentials for synthesis of (*E*)-4-chloro-4'-nitrostilbene.

Reaction	Starting materials (SM2)	Catalyst (CT) PdA ₂	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
						BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A	R-I	OAc	Et ₃ N	DMF	Et ₃ N·HI	0.89	1.09	0.97	0.8	0.65	1.33	0.87	0.79	0.87	0.33	0.29	0.21
A-A-A-B	R-I	OAc	Et ₃ N	NMP	Et ₃ N·HI	0.76	0.5	0.38	0.21	0.38	0.75	0.28	0.21	0.83	0.25	0.21	0.13
A-A-B-A	R-I	OAc	Et ₂ NH	DMF	Et ₂ NH·HI	0.57	1.78	1.02	0.85	0.5	1.74	0.87	0.79	0.24	1.19	0.28	0.21
A-A-B-B	R-I	OAc	Et ₂ NH	NMP	Et ₂ NH·HI	0.36	1.19	0.42	0.25	0.24	1.16	0.28	0.2	0.18	1.12	0.21	0.13
A-B-A-A	R-I	Cl	Et ₃ N	DMF	Et ₃ N·HI	0.89	1.09	0.98	0.81	0.66	1.34	0.88	0.8	0.87	0.34	0.29	0.22
A-B-A-B	R-I	Cl	Et ₃ N	NMP	Et ₃ N·HI	0.76	0.5	0.38	0.21	0.39	0.76	0.3	0.22	0.84	0.26	0.22	0.14
A-B-B-A	R-I	Cl	Et ₂ NH	DMF	Et ₂ NH·HI	0.57	1.79	1.02	0.85	0.5	1.75	0.88	0.8	0.24	1.2	0.29	0.21
A-B-B-B	R-I	Cl	Et ₂ NH	NMP	Et ₂ NH·HI	0.36	1.19	0.43	0.26	0.25	1.17	0.29	0.22	0.19	1.12	0.21	0.13
A-C-A-A	R-I	acac	Et ₃ N	DMF	Et ₃ N·HI	0.91	1.35	1.23	1.06	0.83	2.74	2.28	2.21	0.96	1.04	0.99	0.92
A-C-A-B	R-I	acac	Et ₃ N	NMP	Et ₃ N·HI	0.84	0.75	0.64	0.47	0.79	2.16	1.7	1.62	0.96	0.96	0.92	0.84
A-C-B-A	R-I	acac	Et ₂ NH	DMF	Et ₂ NH·HI	0.62	2.04	1.27	1.11	0.72	3.15	2.28	2.2	0.52	1.9	0.99	0.91
A-C-B-B	R-I	acac	Et ₂ NH	NMP	Et ₂ NH·HI	0.47	1.45	0.68	0.51	0.66	2.57	1.7	1.62	0.5	1.82	0.91	0.83
B-A-A-A	R-Br	OAc	Et ₃ N	DMF	Et ₃ N·HBr	0.62	1.54	0.95	0.78	0.63	1.38	0.87	0.79	0.52	0.55	0.29	0.21
B-A-A-B	R-Br	OAc	Et ₃ N	NMP	Et ₃ N·HBr	0.38	0.95	0.36	0.19	0.36	0.8	0.29	0.21	0.44	0.48	0.21	0.13
B-A-B-A	R-Br	OAc	Et ₂ NH	DMF	Et ₂ NH·HBr	0.42	2.23	0.94	0.77	0.49	1.79	0.87	0.8	0.21	1.42	0.3	0.22
B-A-B-B	R-Br	OAc	Et ₂ NH	NMP	Et ₂ NH·HBr	0.21	1.64	0.35	0.18	0.24	1.21	0.29	0.21	0.17	1.34	0.22	0.14
B-B-A-A	R-Br	Cl	Et ₃ N	DMF	Et ₃ N·HBr	0.62	1.54	0.96	0.79	0.63	1.39	0.88	0.8	0.52	0.56	0.29	0.21
B-B-A-B	R-Br	Cl	Et ₃ N	NMP	Et ₃ N·HBr	0.38	0.95	0.36	0.19	0.37	0.81	0.3	0.22	0.44	0.48	0.21	0.14
B-B-B-A	R-Br	Cl	Et ₂ NH	DMF	Et ₂ NH·HBr	0.42	2.24	0.94	0.78	0.49	1.8	0.89	0.81	0.21	1.42	0.3	0.23
B-B-B-B	R-Br	Cl	Et ₂ NH	NMP	Et ₂ NH·HBr	0.21	1.64	0.35	0.18	0.25	1.22	0.3	0.23	0.17	1.34	0.23	0.15
B-C-A-A	R-Br	acac	Et ₃ N	DMF	Et ₃ N·HBr	0.67	1.8	1.21	1.04	0.82	2.79	2.28	2.21	0.79	1.26	0.99	0.91
B-C-A-B	R-Br	acac	Et ₃ N	NMP	Et ₃ N·HBr	0.51	1.2	0.62	0.45	0.77	2.21	1.7	1.62	0.77	1.18	0.91	0.84
B-C-B-A	R-Br	acac	Et ₂ NH	DMF	Et ₂ NH·HBr	0.48	2.49	1.2	1.03	0.71	3.2	2.29	2.21	0.47	2.12	1	0.93
B-C-B-B	R-Br	acac	Et ₂ NH	NMP	Et ₂ NH·HBr	0.32	1.9	0.6	0.44	0.65	2.62	1.71	1.63	0.45	2.04	0.93	0.85
C-A-A-A	R-Cl	OAc	Et ₃ N	DMF	Et ₃ N·HCl	0.88	1.1	0.97	0.8	0.63	1.36	0.86	0.79	0.89	0.33	0.3	0.22
C-A-A-B	R-Cl	OAc	Et ₃ N	NMP	Et ₃ N·HCl	0.73	0.51	0.37	0.21	0.36	0.78	0.28	0.2	0.86	0.26	0.22	0.14
C-A-B-A	R-Cl	OAc	Et ₂ NH	DMF	Et ₂ NH·HCl	0.55	1.79	0.99	0.82	0.49	1.77	0.86	0.78	0.24	1.2	0.28	0.21
C-A-B-B	R-Cl	OAc	Et ₂ NH	NMP	Et ₂ NH·HCl	0.33	1.2	0.4	0.23	0.23	1.19	0.28	0.2	0.18	1.12	0.21	0.13
C-B-A-A	R-Cl	Cl	Et ₃ N	DMF	Et ₃ N·HCl	0.88	1.11	0.97	0.8	0.64	1.38	0.87	0.8	0.89	0.34	0.3	0.23
C-B-A-B	R-Cl	Cl	Et ₃ N	NMP	Et ₃ N·HCl	0.74	0.51	0.38	0.21	0.37	0.79	0.29	0.21	0.86	0.26	0.22	0.15
C-B-B-A	R-Cl	Cl	Et ₂ NH	DMF	Et ₂ NH·HCl	0.55	1.8	1	0.83	0.49	1.79	0.87	0.8	0.24	1.2	0.29	0.21
C-B-B-B	R-Cl	Cl	Et ₂ NH	NMP	Et ₂ NH·HCl	0.33	1.2	0.4	0.24	0.24	1.2	0.29	0.21	0.19	1.12	0.21	0.13
C-C-A-A	R-Cl	acac	Et ₃ N	DMF	Et ₃ N·HCl	0.9	1.36	1.23	1.06	0.82	2.78	2.28	2.2	0.97	1.04	1	0.93
C-C-A-B	R-Cl	acac	Et ₃ N	NMP	Et ₃ N·HCl	0.82	0.77	0.63	0.47	0.77	2.2	1.69	1.62	0.96	0.96	0.92	0.85
C-C-B-A	R-Cl	acac	Et ₂ NH	DMF	Et ₂ NH·HCl	0.61	2.05	1.25	1.08	0.71	3.19	2.28	2.2	0.52	1.9	0.99	0.91
C-C-B-B	R-Cl	acac	Et ₂ NH	NMP	Et ₂ NH·HCl	0.45	1.46	0.66	0.49	0.65	2.6	1.69	1.61	0.5	1.82	0.91	0.83

Target product P ((*E*)-4-chloro-4'-nitrostilbene) and starting material SM1 (4-chlorostyrene) are not shown. R-I, 1-iodo-4-nitrobenzene; R-Br, 1-bromo-4-nitrobenzene; R-Cl, 1-chloro-4-nitrobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green.

Table S11. bio-Factors and cytotoxicity potentials for synthesis of (*E*)-4-fluoro-4'-nitrostilbene.

Reaction	Starting materials (SM2)	Catalyst (CT) PdA ₂	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
						BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A	R-I	OAc	Et ₃ N	DMF	Et ₃ N·HI	1.26	1.03	1.3	0.8	0.78	1.08	0.85	0.79	0.92	0.3	0.28	0.21
A-A-A-B	R-I	OAc	Et ₃ N	NMP	Et ₃ N·HI	1.62	0.44	0.71	0.21	0.52	0.5	0.26	0.21	0.9	0.22	0.2	0.13
A-A-B-A	R-I	OAc	Et ₂ NH	DMF	Et ₂ NH·HI	0.78	1.72	1.35	0.85	0.56	1.49	0.84	0.79	0.23	1.17	0.27	0.21
A-A-B-B	R-I	OAc	Et ₂ NH	NMP	Et ₂ NH·HI	0.67	1.13	0.75	0.25	0.29	0.91	0.26	0.2	0.18	1.09	0.2	0.13
A-B-A-A	R-I	Cl	Et ₃ N	DMF	Et ₃ N·HI	1.26	1.04	1.31	0.81	0.78	1.1	0.86	0.8	0.92	0.31	0.28	0.22
A-B-A-B	R-I	Cl	Et ₃ N	NMP	Et ₃ N·HI	1.61	0.44	0.71	0.21	0.54	0.51	0.27	0.22	0.9	0.23	0.21	0.14
A-B-B-A	R-I	Cl	Et ₂ NH	DMF	Et ₂ NH·HI	0.78	1.73	1.35	0.85	0.57	1.51	0.86	0.8	0.24	1.17	0.28	0.21
A-B-B-B	R-I	Cl	Et ₂ NH	NMP	Et ₂ NH·HI	0.67	1.14	0.76	0.26	0.29	0.92	0.27	0.22	0.18	1.09	0.2	0.13
A-C-A-A	R-I	acac	Et ₃ N	DMF	Et ₃ N·HI	1.21	1.29	1.56	1.06	0.9	2.5	2.26	2.21	0.98	1.01	0.98	0.92
A-C-A-B	R-I	acac	Et ₃ N	NMP	Et ₃ N·HI	1.39	0.7	0.97	0.47	0.88	1.92	1.68	1.62	0.97	0.93	0.91	0.84
A-C-B-A	R-I	acac	Et ₂ NH	DMF	Et ₂ NH·HI	0.81	1.98	1.61	1.11	0.78	2.91	2.26	2.2	0.52	1.87	0.98	0.91
A-C-B-B	R-I	acac	Et ₂ NH	NMP	Et ₂ NH·HI	0.73	1.39	1.01	0.51	0.72	2.32	1.67	1.62	0.5	1.79	0.9	0.83
B-A-A-A	R-Br	OAc	Et ₃ N	DMF	Et ₃ N·HBr	0.87	1.48	1.28	0.78	0.75	1.13	0.85	0.79	0.53	0.52	0.28	0.21
B-A-A-B	R-Br	OAc	Et ₃ N	NMP	Et ₃ N·HBr	0.78	0.89	0.69	0.19	0.48	0.55	0.26	0.21	0.44	0.45	0.2	0.13
B-A-B-A	R-Br	OAc	Et ₂ NH	DMF	Et ₂ NH·HBr	0.59	2.17	1.27	0.77	0.55	1.54	0.85	0.8	0.21	1.39	0.29	0.22
B-A-B-B	R-Br	OAc	Et ₂ NH	NMP	Et ₂ NH·HBr	0.43	1.58	0.68	0.18	0.28	0.96	0.27	0.21	0.16	1.31	0.21	0.14
B-B-A-A	R-Br	Cl	Et ₃ N	DMF	Et ₃ N·HBr	0.87	1.49	1.29	0.79	0.75	1.15	0.86	0.8	0.53	0.53	0.28	0.21
B-B-A-B	R-Br	Cl	Et ₃ N	NMP	Et ₃ N·HBr	0.78	0.89	0.69	0.19	0.49	0.56	0.28	0.22	0.45	0.45	0.2	0.14
B-B-B-A	R-Br	Cl	Et ₂ NH	DMF	Et ₂ NH·HBr	0.59	2.18	1.28	0.78	0.56	1.56	0.86	0.81	0.21	1.39	0.29	0.23
B-B-B-B	R-Br	Cl	Et ₂ NH	NMP	Et ₂ NH·HBr	0.43	1.59	0.68	0.18	0.29	0.97	0.28	0.23	0.16	1.31	0.22	0.15
B-C-A-A	R-Br	acac	Et ₃ N	DMF	Et ₃ N·HBr	0.89	1.74	1.54	1.04	0.89	2.55	2.26	2.21	0.8	1.23	0.98	0.91
B-C-A-B	R-Br	acac	Et ₃ N	NMP	Et ₃ N·HBr	0.83	1.15	0.95	0.45	0.85	1.97	1.68	1.62	0.78	1.15	0.9	0.84
B-C-B-A	R-Br	acac	Et ₂ NH	DMF	Et ₂ NH·HBr	0.63	2.43	1.53	1.03	0.77	2.96	2.27	2.21	0.48	2.09	0.99	0.93
B-C-B-B	R-Br	acac	Et ₂ NH	NMP	Et ₂ NH·HBr	0.51	1.84	0.94	0.44	0.71	2.37	1.68	1.63	0.46	2.01	0.92	0.85
C-A-A-A	R-Cl	OAc	Et ₃ N	DMF	Et ₃ N·HCl	1.24	1.05	1.3	0.8	0.75	1.12	0.84	0.79	0.94	0.3	0.29	0.22
C-A-A-B	R-Cl	OAc	Et ₃ N	NMP	Et ₃ N·HCl	1.56	0.45	0.71	0.21	0.48	0.54	0.26	0.2	0.92	0.23	0.21	0.14
C-A-B-A	R-Cl	OAc	Et ₂ NH	DMF	Et ₂ NH·HCl	0.76	1.74	1.32	0.82	0.55	1.53	0.84	0.78	0.23	1.17	0.27	0.21
C-A-B-B	R-Cl	OAc	Et ₂ NH	NMP	Et ₂ NH·HCl	0.64	1.14	0.73	0.23	0.27	0.94	0.26	0.2	0.18	1.09	0.2	0.13
C-B-A-A	R-Cl	Cl	Et ₃ N	DMF	Et ₃ N·HCl	1.24	1.05	1.3	0.8	0.75	1.13	0.85	0.8	0.94	0.31	0.29	0.23
C-B-A-B	R-Cl	Cl	Et ₃ N	NMP	Et ₃ N·HCl	1.56	0.46	0.71	0.21	0.49	0.55	0.27	0.21	0.93	0.23	0.21	0.15
C-B-B-A	R-Cl	Cl	Et ₂ NH	DMF	Et ₂ NH·HCl	0.76	1.74	1.33	0.83	0.55	1.54	0.85	0.8	0.24	1.17	0.28	0.21
C-B-B-B	R-Cl	Cl	Et ₂ NH	NMP	Et ₂ NH·HCl	0.64	1.15	0.74	0.24	0.28	0.96	0.27	0.21	0.18	1.09	0.2	0.13
C-C-A-A	R-Cl	acac	Et ₃ N	DMF	Et ₃ N·HCl	1.19	1.3	1.56	1.06	0.89	2.53	2.25	2.2	0.98	1.01	0.99	0.93
C-C-A-B	R-Cl	acac	Et ₃ N	NMP	Et ₃ N·HCl	1.36	0.71	0.97	0.47	0.86	1.95	1.67	1.62	0.98	0.93	0.91	0.85
C-C-B-A	R-Cl	acac	Et ₂ NH	DMF	Et ₂ NH·HCl	0.79	2	1.58	1.08	0.77	2.94	2.25	2.2	0.52	1.87	0.98	0.91
C-C-B-B	R-Cl	acac	Et ₂ NH	NMP	Et ₂ NH·HCl	0.71	1.4	0.99	0.49	0.71	2.36	1.67	1.61	0.5	1.79	0.9	0.83

Target product P ((*E*)-4-fluoro-4'-nitrostilbene) and starting material SM1 (4-fluorostyrene) are not shown. R-I, 1-iodo-4-nitrobenzene; R-Br, 1-bromo-4-nitrobenzene; R-Cl, 1-chloro-4-nitrobenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential. The reactions with the five lowest CPs are highlighted with green.

Table S12. bio-Factors and cytotoxicity potentials for synthesis of (*E*)-4-methoxystilbene.

Reaction	Starting materials (SM2)	Catalyst (CT) PdA ₂	Reagent (R)	Solvent (S)	Byproduct (BP)	CaCo-2				FRSN				HEK293T			
						BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}	BF	CP _i	CP _f	CP _{f,rel}
A-A-A-A	R-I	OAc	Et ₃ N	DMF	Et ₃ N·HI	0.91	0.92	0.83	0.8	0.87	0.95	0.82	0.79	1.24	0.27	0.34	0.21
A-A-A-B	R-I	OAc	Et ₃ N	NMP	Et ₃ N·HI	0.73	0.33	0.24	0.21	0.66	0.36	0.24	0.21	1.34	0.19	0.26	0.13
A-A-B-A	R-I	OAc	Et ₂ NH	DMF	Et ₂ NH·HI	0.54	1.61	0.88	0.85	0.6	1.35	0.82	0.79	0.29	1.13	0.33	0.21
A-A-B-B	R-I	OAc	Et ₂ NH	NMP	Et ₂ NH·HI	0.28	1.02	0.28	0.25	0.3	0.77	0.23	0.2	0.24	1.06	0.25	0.13
A-B-A-A	R-I	Cl	Et ₃ N	DMF	Et ₃ N·HI	0.91	0.93	0.84	0.81	0.87	0.96	0.83	0.8	1.24	0.28	0.34	0.22
A-B-A-B	R-I	Cl	Et ₃ N	NMP	Et ₃ N·HI	0.74	0.33	0.24	0.21	0.67	0.37	0.25	0.22	1.34	0.2	0.26	0.14
A-B-B-A	R-I	Cl	Et ₂ NH	DMF	Et ₂ NH·HI	0.55	1.62	0.88	0.85	0.61	1.37	0.83	0.8	0.3	1.14	0.34	0.21
A-B-B-B	R-I	Cl	Et ₂ NH	NMP	Et ₂ NH·HI	0.28	1.02	0.29	0.26	0.32	0.78	0.25	0.22	0.24	1.06	0.26	0.13
A-C-A-A	R-I	acac	Et ₃ N	DMF	Et ₃ N·HI	0.93	1.18	1.09	1.06	0.95	2.36	2.24	2.21	1.07	0.98	1.04	0.92
A-C-A-B	R-I	acac	Et ₃ N	NMP	Et ₃ N·HI	0.85	0.59	0.5	0.47	0.93	1.78	1.65	1.62	1.07	0.9	0.96	0.84
A-C-B-A	R-I	acac	Et ₂ NH	DMF	Et ₂ NH·HI	0.61	1.87	1.14	1.11	0.81	2.77	2.23	2.2	0.56	1.84	1.04	0.91
A-C-B-B	R-I	acac	Et ₂ NH	NMP	Et ₂ NH·HI	0.43	1.28	0.54	0.52	0.75	2.18	1.65	1.62	0.54	1.76	0.96	0.83
B-A-A-A	R-Br	OAc	Et ₃ N	DMF	Et ₃ N·HBr	0.81	1	0.81	0.78	0.81	1.01	0.82	0.79	1.18	0.28	0.33	0.21
B-A-A-B	R-Br	OAc	Et ₃ N	NMP	Et ₃ N·HBr	0.54	0.41	0.22	0.19	0.55	0.43	0.24	0.21	1.25	0.21	0.26	0.13
B-A-B-A	R-Br	OAc	Et ₂ NH	DMF	Et ₂ NH·HBr	0.47	1.7	0.8	0.77	0.58	1.42	0.83	0.8	0.3	1.15	0.35	0.22
B-A-B-B	R-Br	OAc	Et ₂ NH	NMP	Et ₂ NH·HBr	0.19	1.1	0.21	0.18	0.29	0.84	0.24	0.21	0.25	1.07	0.27	0.14
B-B-A-A	R-Br	Cl	Et ₃ N	DMF	Et ₃ N·HBr	0.81	1.01	0.82	0.79	0.81	1.03	0.83	0.8	1.18	0.29	0.34	0.21
B-B-A-B	R-Br	Cl	Et ₃ N	NMP	Et ₃ N·HBr	0.54	0.41	0.22	0.19	0.57	0.44	0.25	0.22	1.24	0.21	0.26	0.14
B-B-B-A	R-Br	Cl	Et ₂ NH	DMF	Et ₂ NH·HBr	0.47	1.7	0.81	0.78	0.58	1.44	0.84	0.81	0.31	1.15	0.35	0.23
B-B-B-B	R-Br	Cl	Et ₂ NH	NMP	Et ₂ NH·HBr	0.19	1.11	0.21	0.18	0.3	0.85	0.26	0.23	0.26	1.07	0.27	0.15
B-C-A-A	R-Br	acac	Et ₃ N	DMF	Et ₃ N·HBr	0.85	1.26	1.07	1.04	0.92	2.43	2.24	2.21	1.05	0.99	1.04	0.91
B-C-A-B	R-Br	acac	Et ₃ N	NMP	Et ₃ N·HBr	0.72	0.67	0.48	0.45	0.9	1.84	1.65	1.62	1.06	0.91	0.96	0.84
B-C-B-A	R-Br	acac	Et ₂ NH	DMF	Et ₂ NH·HBr	0.54	1.96	1.06	1.03	0.79	2.84	2.24	2.21	0.57	1.85	1.05	0.93
B-C-B-B	R-Br	acac	Et ₂ NH	NMP	Et ₂ NH·HBr	0.34	1.36	0.47	0.44	0.74	2.25	1.66	1.63	0.55	1.77	0.98	0.85

Target product P (*E*)-4-methoxystilbene) and starting material SM1 (styrene) are not shown. R-I, 1-iodo-4-methoxybenzene; R-Br, 1-bromo-4-methoxybenzene; DMF, dimethylformamide; NMP, *N*-methylpyrrolidone; BF, bio-Factor; CP_i, initial cytotoxicity potential; CP_f, final cytotoxicity potential; CP_{f,rel}, relative final cytotoxicity potential.

The reactions with the five lowest CPs are highlighted with green.

Table S13. Dependence of CP_f and CP_{f_rel} on the Pd : Cu ratio during the reaction period by example of synthesis of diphenylacetylene measured in CaCo-2 cells.^a

CP_f									
Pd, n (mmol)^b	0	0.0025	0.005	0.0075	0.01	0.0125	0.015	0.0175	0.02
Conversion, %									
100	0.907306	0.904502	0.901699	0.898895	0.896091	0.893287	0.890484	0.88768	0.88488
90	0.923189	0.920385	0.917582	0.914778	0.911974	0.90917	0.906367	0.903563	0.90076
80	0.939072	0.936268	0.933464	0.930661	0.927857	0.925053	0.922249	0.919446	0.91664
70	0.954955	0.952151	0.949347	0.946544	0.94374	0.940936	0.938132	0.935329	0.93252
60	0.970838	0.968034	0.96523	0.962426	0.959623	0.956819	0.954015	0.951211	0.94841
50	0.98672	0.983917	0.981113	0.978309	0.975505	0.972702	0.969898	0.967094	0.96429
40	1.002603	0.9998	0.996996	0.994192	0.991388	0.988585	0.985781	0.982977	0.98017
30	1.018486	1.015682	1.012879	1.010075	1.007271	1.004467	1.001664	0.99886	0.99606
20	1.034369	1.031565	1.028762	1.025958	1.023154	1.02035	1.017547	1.014743	1.01194
10	1.050252	1.047448	1.044644	1.041841	1.039037	1.036233	1.033429	1.030626	1.02782
0^c	1.066135	1.063331	1.060527	1.057723	1.05492	1.052116	1.049312	1.046508	1.04370
CP_{f_rel}									
Pd, n (mmol)^b	0	0.0025	0.005	0.0075	0.01	0.0125	0.015	0.0175	0.02
Conversion, %									
100	0.816397	0.813593	0.81079	0.807986	0.805182	0.802378	0.799575	0.796771	0.79397
90	0.841371	0.838567	0.835763	0.83296	0.830156	0.827352	0.824548	0.821745	0.81894
80	0.866345	0.863541	0.860737	0.857933	0.85513	0.852326	0.849522	0.846718	0.84391
70	0.891318	0.888515	0.885711	0.882907	0.880103	0.8773	0.874496	0.871692	0.86889
60	0.916292	0.913488	0.910685	0.907881	0.905077	0.902273	0.89947	0.896666	0.89386
50	0.941266	0.938462	0.935658	0.932855	0.930051	0.927247	0.924443	0.92164	0.91884
40	0.96624	0.963436	0.960632	0.957828	0.955025	0.952221	0.949417	0.946613	0.94381
30	0.991213	0.98841	0.985606	0.982802	0.979998	0.977195	0.974391	0.971587	0.96878
20	1.016187	1.013383	1.01058	1.007776	1.004972	1.002168	0.999365	0.996561	0.99376
10	1.041161	1.038357	1.035553	1.03275	1.029946	1.027142	1.024338	1.021535	1.01873
0^c	1.066135	1.063331	1.060527	1.057723	1.05492	1.052116	1.049312	1.046508	1.04370

^a Synthesis from phenylacetylene and bromobenzene using Pd(OAc)₂ and CuI as catalysts and Et₃N as a base in DMF is considered. ^b The summarized content of Pd and Cu in the reaction equals 0.02 mmol. ^c Final CPs at 0% conversion equals the initial CPs of the reaction.

Table S14. Dependence of CP_f and CP_{f_rel} on the Pd : Cu ratio during the reaction period by example of synthesis of diphenylacetylene measured in FRSN cells.^a

CP_f									
Pd, n (mmol)^b	0	0.0025	0.005	0.0075	0.01	0.0125	0.015	0.0175	0.02
Conversion, %									
100	0.894355	0.889707	0.885059	0.880411	0.875763	0.871115	0.866467	0.861819	0.857171
90	0.914211	0.909563	0.904915	0.900267	0.895619	0.890971	0.886323	0.881675	0.877027
80	0.934066	0.929418	0.92477	0.920122	0.915474	0.910826	0.906178	0.90153	0.896882
70	0.953922	0.949274	0.944626	0.939978	0.93533	0.930682	0.926034	0.921386	0.916738
60	0.973777	0.969129	0.964481	0.959833	0.955185	0.950537	0.945889	0.941241	0.936593
50	0.993633	0.988985	0.984337	0.979689	0.975041	0.970393	0.965745	0.961097	0.956449
40	1.013489	1.008841	1.004193	0.999545	0.994896	0.990248	0.9856	0.980952	0.976304
30	1.033344	1.028696	1.024048	1.0194	1.014752	1.010104	1.005456	1.000808	0.99616
20	1.0532	1.048552	1.043904	1.039256	1.034608	1.02996	1.025312	1.020664	1.016016
10	1.073055	1.068407	1.063759	1.059111	1.054463	1.049815	1.045167	1.040519	1.035871
0^c	1.092911	1.088263	1.083615	1.078967	1.074319	1.069671	1.065023	1.060375	1.055727
CP_{f_rel}									
Pd, n (mmol)^b	0	0.0025	0.005	0.0075	0.01	0.0125	0.015	0.0175	0.02
Conversion, %									
100	0.843825	0.839177	0.834529	0.829881	0.825233	0.820585	0.815937	0.811289	0.806641
90	0.868733	0.864085	0.859437	0.854789	0.850141	0.845493	0.840845	0.836197	0.831549
80	0.893642	0.888994	0.884346	0.879698	0.87505	0.870402	0.865754	0.861106	0.856458
70	0.918551	0.913902	0.909254	0.904606	0.899958	0.89531	0.890662	0.886014	0.881366
60	0.943459	0.938811	0.934163	0.929515	0.924867	0.920219	0.915571	0.910923	0.906275
50	0.968368	0.96372	0.959072	0.954424	0.949776	0.945128	0.94048	0.935832	0.931184
40	0.993276	0.988628	0.98398	0.979332	0.974684	0.970036	0.965388	0.96074	0.956092
30	1.018185	1.013537	1.008889	1.004241	0.999593	0.994945	0.990297	0.985649	0.981001
20	1.043094	1.038446	1.033798	1.02915	1.024501	1.019853	1.015205	1.010557	1.005909
10	1.068002	1.063354	1.058706	1.054058	1.04941	1.044762	1.040114	1.035466	1.030818
0^c	1.092911	1.088263	1.083615	1.078967	1.074319	1.069671	1.065023	1.060375	1.055727

^a Synthesis from phenylacetylene and bromobenzene using $Pd(OAc)_2$ and CuI as catalysts and Et_3N as a base in DMF is considered. ^b The summarized content of Pd and Cu in the reaction equals 0.02 mmol. ^c Final CPs at 0% conversion equals the initial CPs of the reaction.

Table S15. Dependence of CP_f and CP_{f_rel} on the Pd : Cu ratio during the reaction period by example of synthesis of diphenylacetylene measured in HEK293T cells.^a

CP_f									
Pd, n (mmol)^b	0	0.0025	0.005	0.0075	0.01	0.0125	0.015	0.0175	0.02
Conversion, %									
100	0.273452	0.271722	0.269992	0.268262	0.266532	0.264802	0.263072	0.261342	0.259612
90	0.279631	0.277901	0.276171	0.274441	0.272711	0.270981	0.269251	0.267521	0.265791
80	0.285809	0.284079	0.282349	0.280619	0.278889	0.277159	0.275429	0.273699	0.271969
70	0.291987	0.290257	0.288527	0.286797	0.285067	0.283337	0.281607	0.279877	0.278147
60	0.298165	0.296435	0.294705	0.292976	0.291246	0.289516	0.287786	0.286056	0.284326
50	0.304344	0.302614	0.300884	0.299154	0.297424	0.295694	0.293964	0.292234	0.290504
40	0.310522	0.308792	0.307062	0.305332	0.303602	0.301872	0.300142	0.298412	0.296682
30	0.3167	0.31497	0.31324	0.31151	0.30978	0.30805	0.30632	0.30459	0.30286
20	0.322879	0.321149	0.319419	0.317689	0.315959	0.314229	0.312499	0.310769	0.309039
10	0.329057	0.327327	0.325597	0.323867	0.322137	0.320407	0.318677	0.316947	0.315217
0^c	0.335235	0.333505	0.331775	0.330045	0.328315	0.326585	0.324855	0.323125	0.321395
CP_{f_rel}									
Pd, n (mmol)^b	0	0.0025	0.005	0.0075	0.01	0.0125	0.015	0.0175	0.02
Conversion, %									
100	0.231786	0.230056	0.228326	0.226596	0.224866	0.223136	0.221406	0.219676	0.217946
90	0.242131	0.240401	0.238671	0.236941	0.235211	0.233481	0.231751	0.230021	0.228291
80	0.252476	0.250746	0.249016	0.247286	0.245556	0.243826	0.242096	0.240366	0.238636
70	0.262821	0.261091	0.259361	0.257631	0.255901	0.254171	0.252441	0.250711	0.248981
60	0.273165	0.271435	0.269705	0.267976	0.266246	0.264516	0.262786	0.261056	0.259326
50	0.28351	0.28178	0.28005	0.27832	0.27659	0.27486	0.27313	0.271401	0.269671
40	0.293855	0.292125	0.290395	0.288665	0.286935	0.285205	0.283475	0.281745	0.280015
30	0.3042	0.30247	0.30074	0.29901	0.29728	0.29555	0.29382	0.29209	0.29036
20	0.314545	0.312815	0.311085	0.309355	0.307625	0.305895	0.304165	0.302435	0.300705
10	0.32489	0.32316	0.32143	0.3197	0.31797	0.31624	0.31451	0.31278	0.31105
0^c	0.335235	0.333505	0.331775	0.330045	0.328315	0.326585	0.324855	0.323125	0.321395

^a Synthesis from phenylacetylene and bromobenzene using $Pd(OAc)_2$ and CuI as catalysts and Et_3N as a base in DMF is considered. ^b The summarized content of Pd and Cu in the reaction equals 0.02 mmol. ^c Final CPs at 0% conversion equals the initial CPs of the reaction.

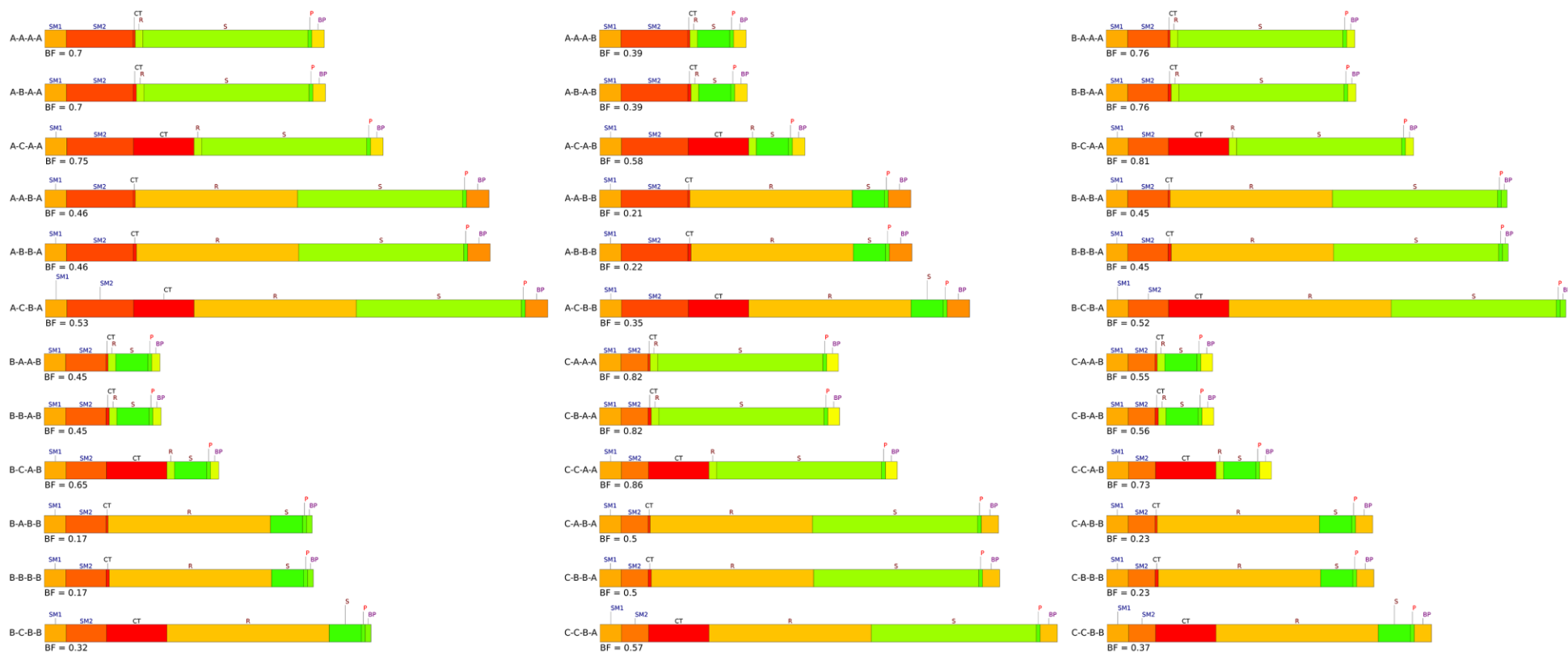
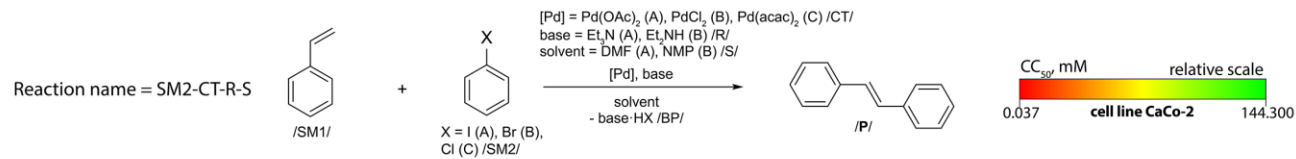


Fig. S1. bio-Strips of 36 synthetic routes for (*E*)-stilbene (based on 24-h CC_{50} values measured in CaCo-2 cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: iodobenzene (A), bromobenzene (B), or chlorobenzene (C)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in CaCo-2 cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

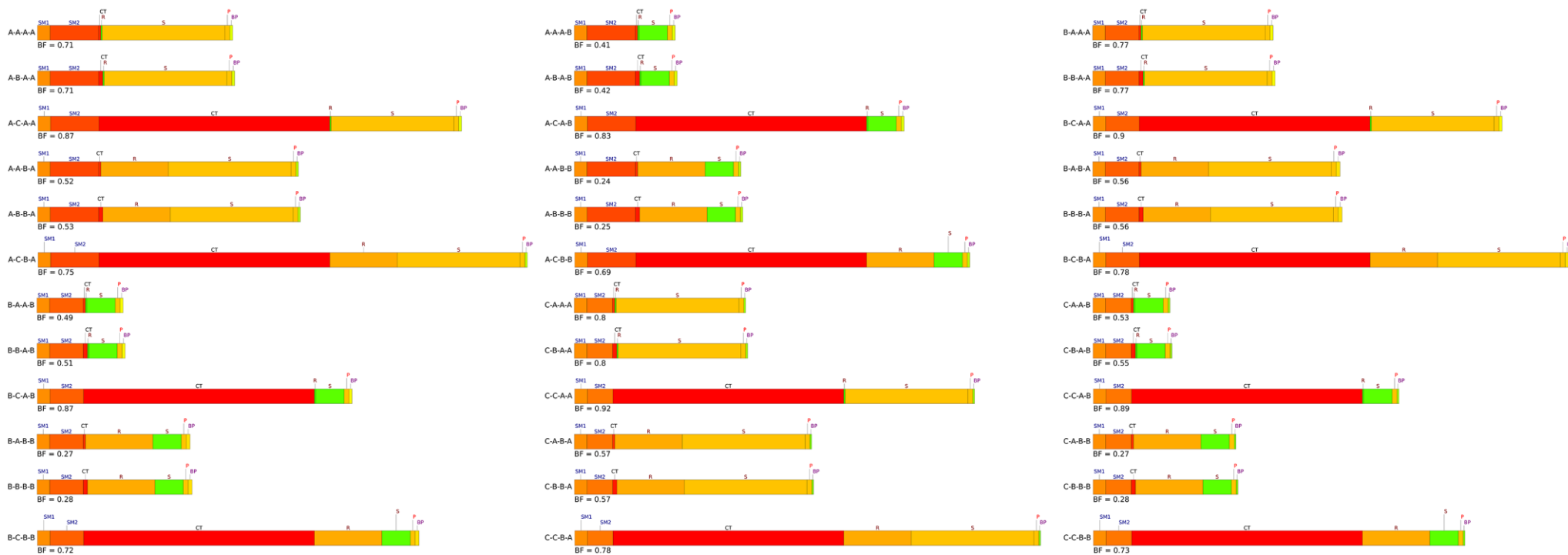
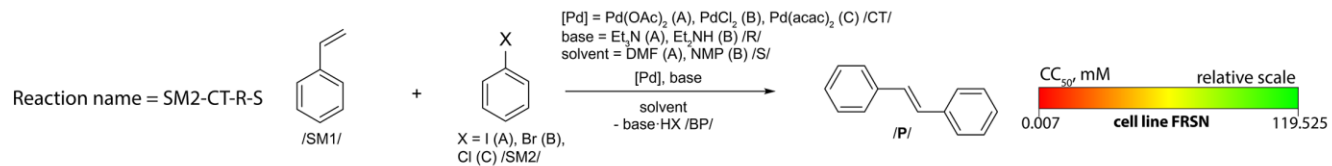


Fig. S2. bio-Strips of 36 synthetic routes for (*E*)-stilbene (based on 24-h CC₅₀ values measured in FR5N cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: iodobenzene (A), bromobenzene (B), or chlorobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in FR5N cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

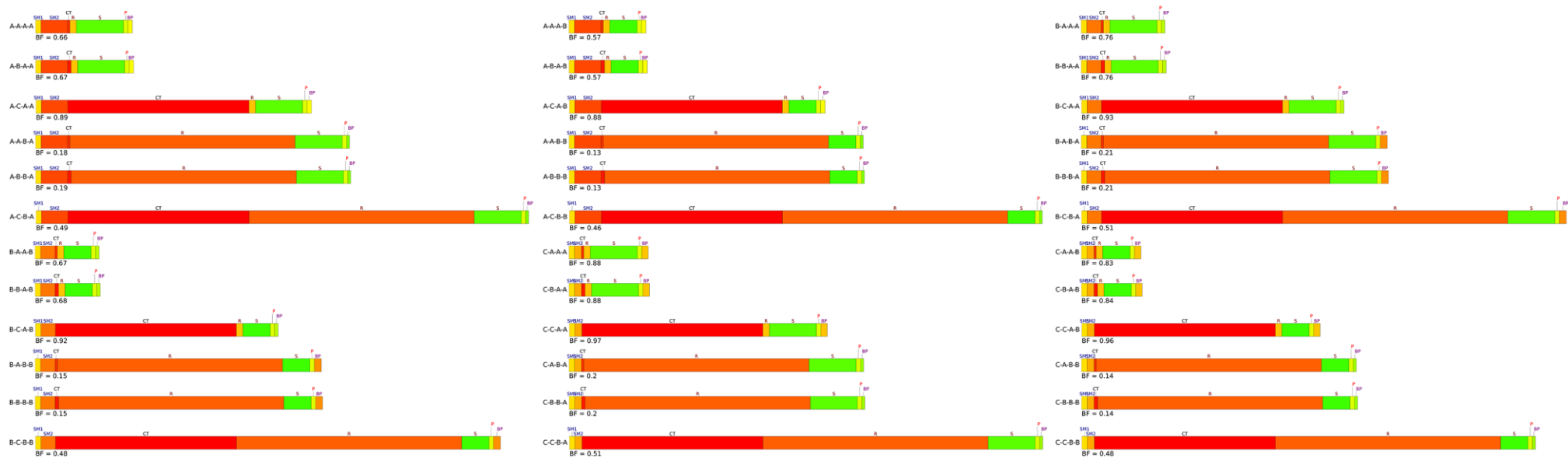
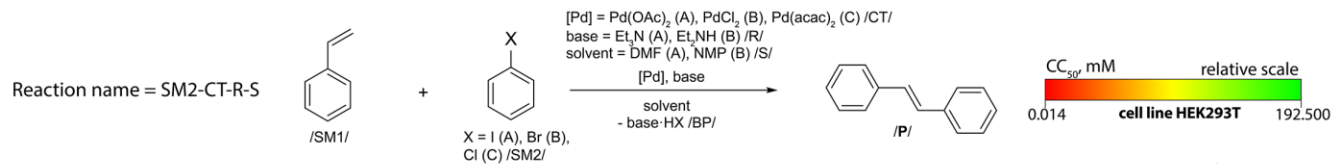


Fig. S3. bio-Strips of 36 synthetic routes for (*E*)-stilbene (based on 24-h CC₅₀ values measured in HEK293T cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: iodobenzene (A), bromobenzene (B), or chlorobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in HEK293T cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

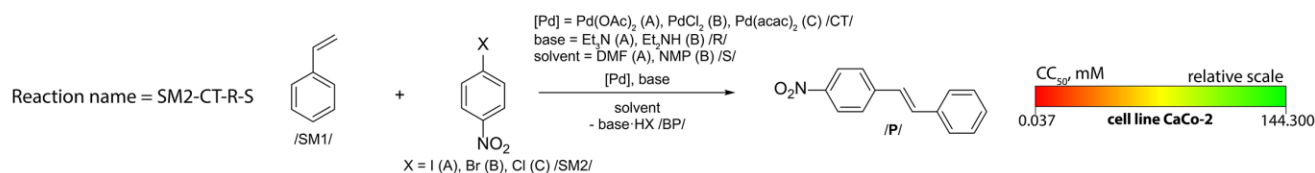


Fig. S4. bio-Strips of 36 synthetic routes for (*E*)-4-nitrostilbene (based on 24-h CC₅₀ values measured in CaCo-2 cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in CaCo-2 cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

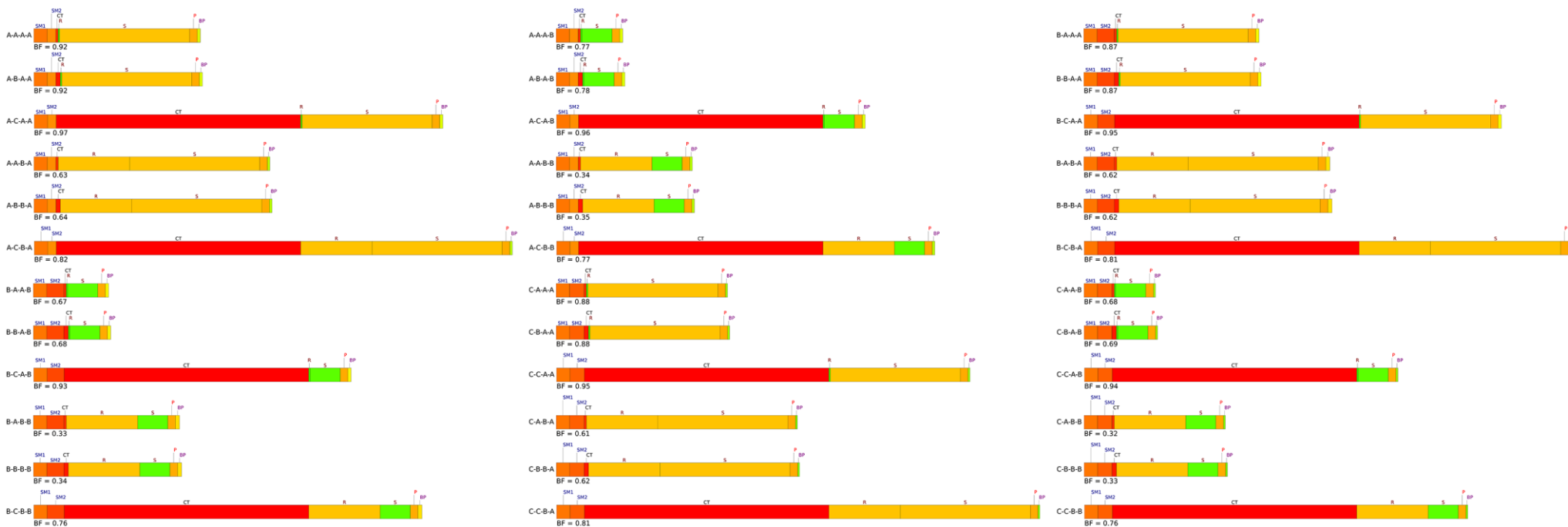
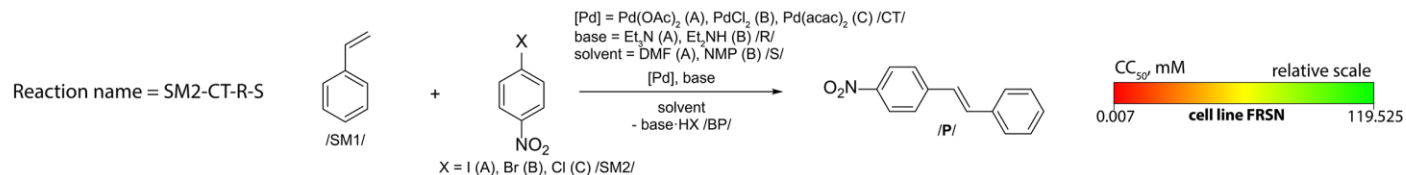
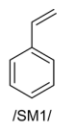


Fig. S5. bio-Strips of 36 synthetic routes for (E)-4-nitrostilbene (based on 24-h CC₅₀ values measured in FRSN cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in FRSN cells (see the cytotoxicity scale above the bio-Strips). Bio-Factors are shown below the strips.

Reaction name = SM2-CT-R-S



X = I (A), Br (B), Cl (C) /SM2/

[Pd] = Pd(OAc)₂ (A), PdCl₂ (B), Pd(acac)₂ (C) /CT/
 base = Et₃N (A), Et₂NH (B) /R/
 solvent = DMF (A), NMP (B) /S/

[Pd], base
 solvent
 - base·HX /BP/

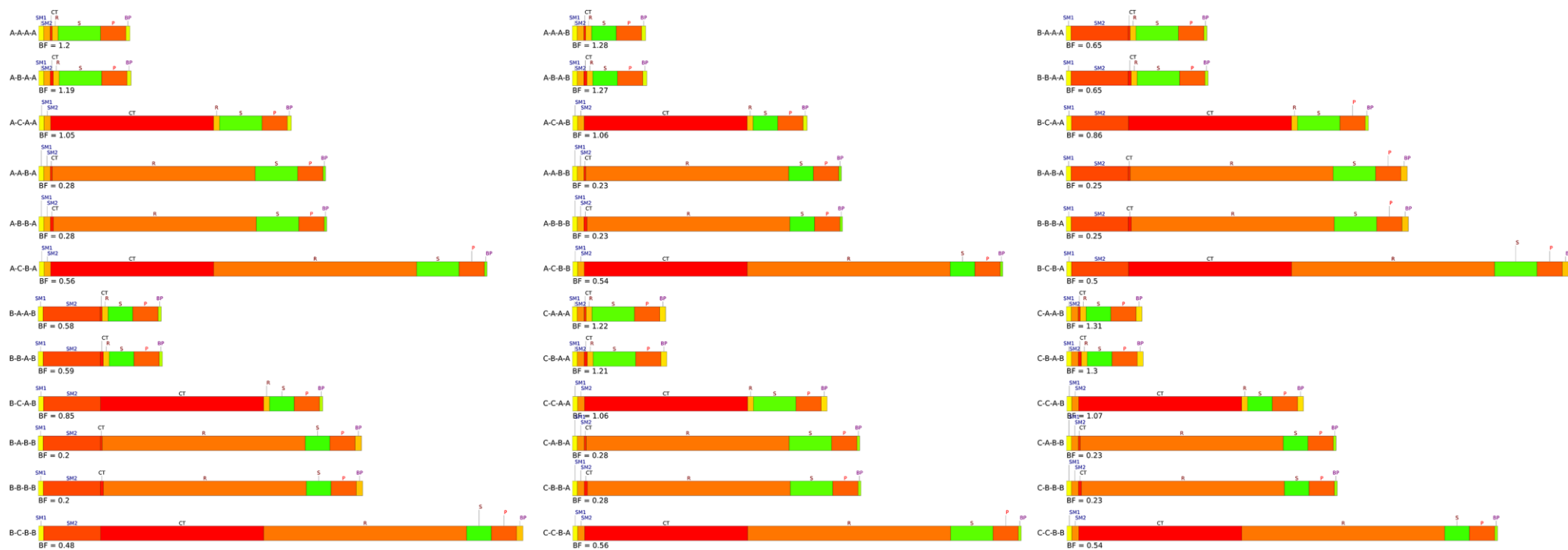
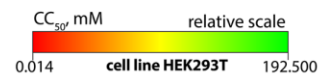
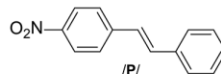


Fig. S6. bio-Strips of 36 synthetic routes for (*E*)-4-nitrostilbene (based on 24-h CC₅₀ values measured in HEK293T cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in HEK293T cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

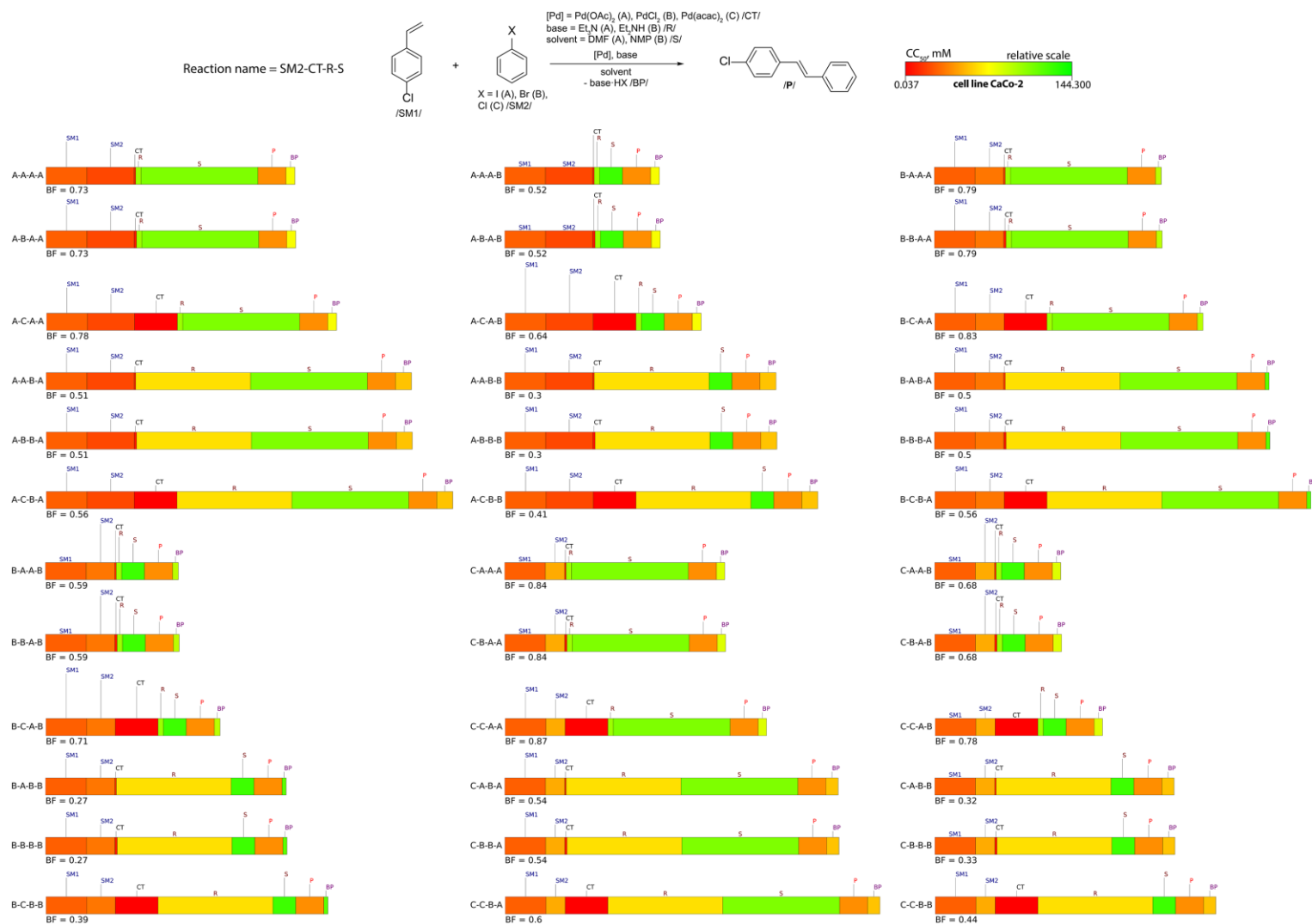


Fig. S7. bio-Strips of 36 synthetic routes for (*E*)-4-chlorostilbene (based on 24-h CC_{50} values measured in CaCo-2 cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: iodobenzene (A), bromobenzene (B), or chlorobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in CaCo-2 cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

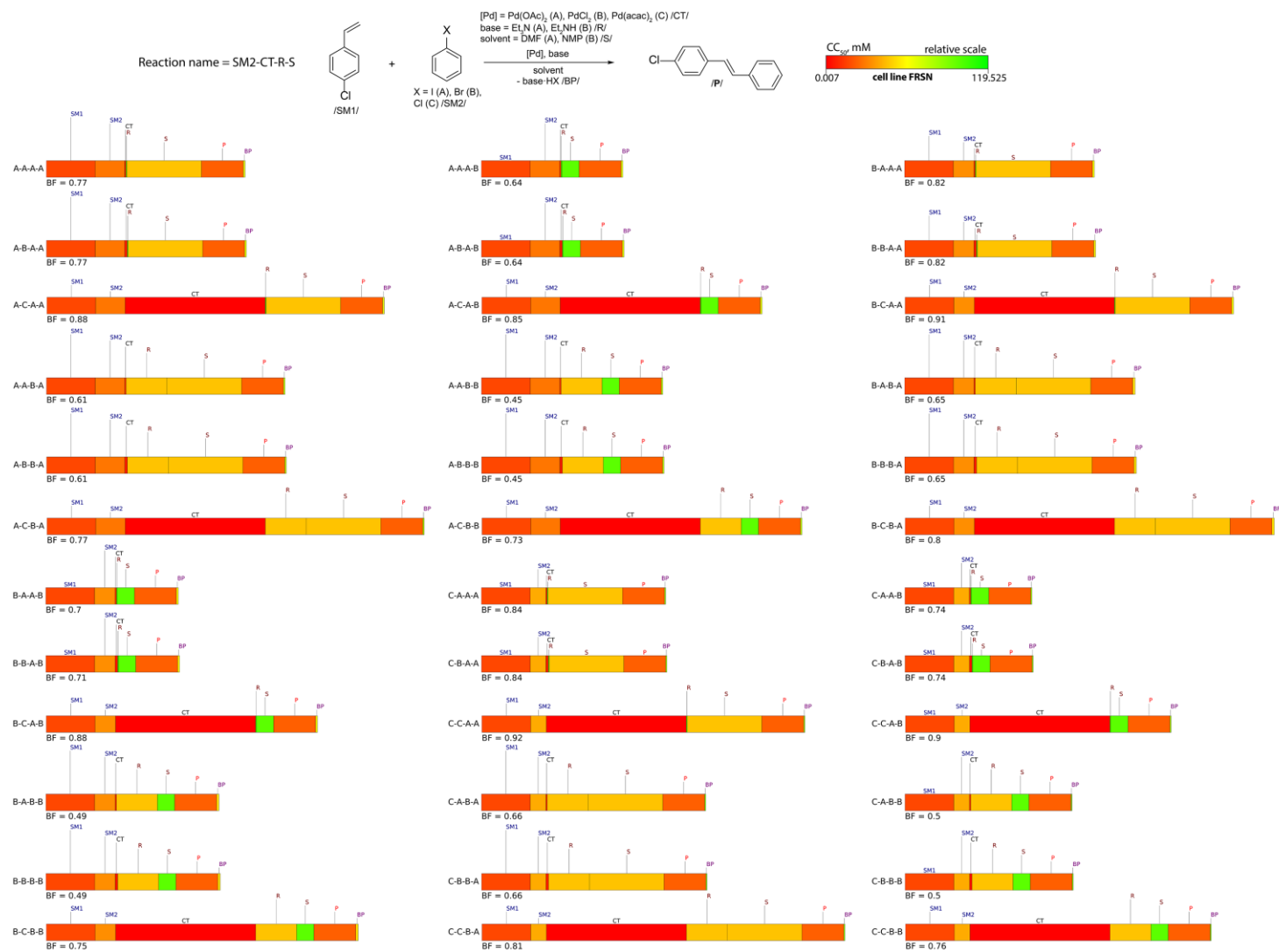


Fig. S8. bio-Strips of 36 synthetic routes for (*E*)-4-chlorostilbene (based on 24-h CC_{50} values measured in FRSN cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: iodobenzene (A), bromobenzene (B), or chlorobenzene (C)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in FRSN cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

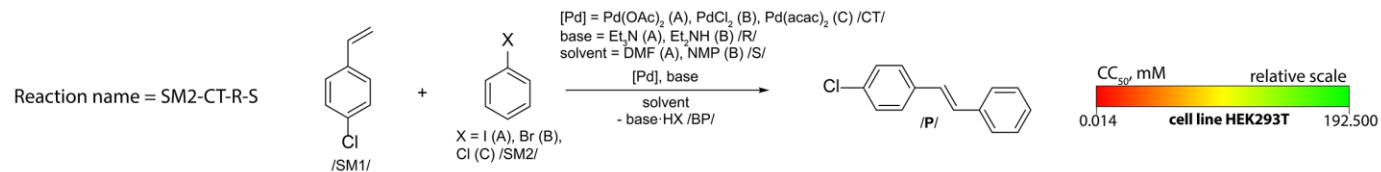


Fig. S9. bio-Strips of 36 synthetic routes for (*E*)-4-chlorostilbene (based on 24-h CC₅₀ values measured in HEK293T cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: iodobenzene (A), bromobenzene (B), or chlorobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in HEK293T cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

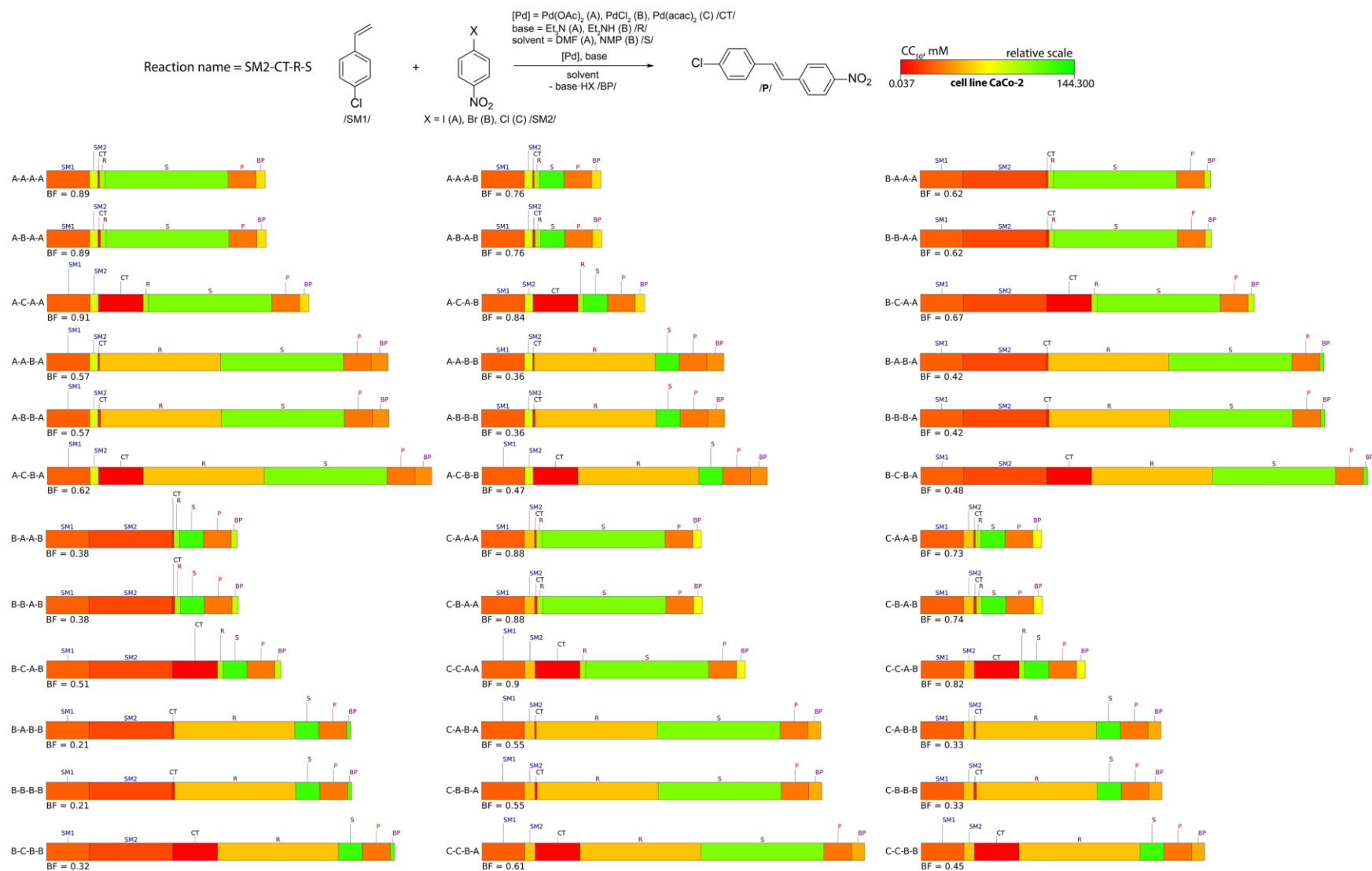


Fig. S10. bio-Strips of 36 synthetic routes for (*E*)-4-chloro-4'-nitrostilbene (based on 24-h CC_{50} values measured in CaCo-2 cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in CaCo-2 cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

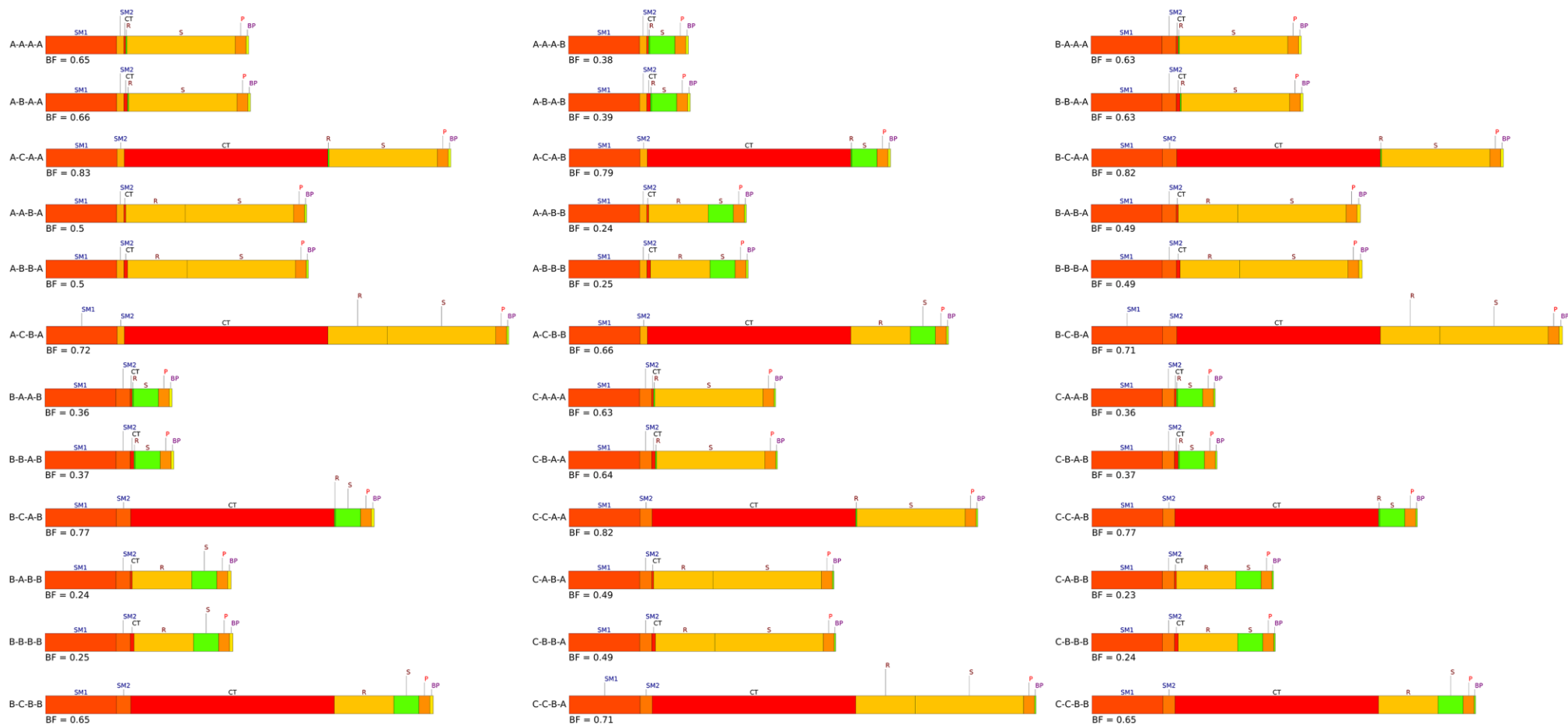
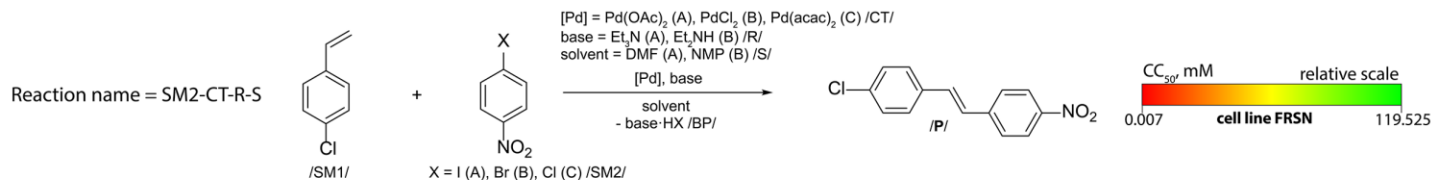


Fig. S11. bio-Strips of 36 synthetic routes for (*E*)-4-chloro-4'-nitrostilbene (based on 24-h CC_{50} values measured in FRSN cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in FRSN cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

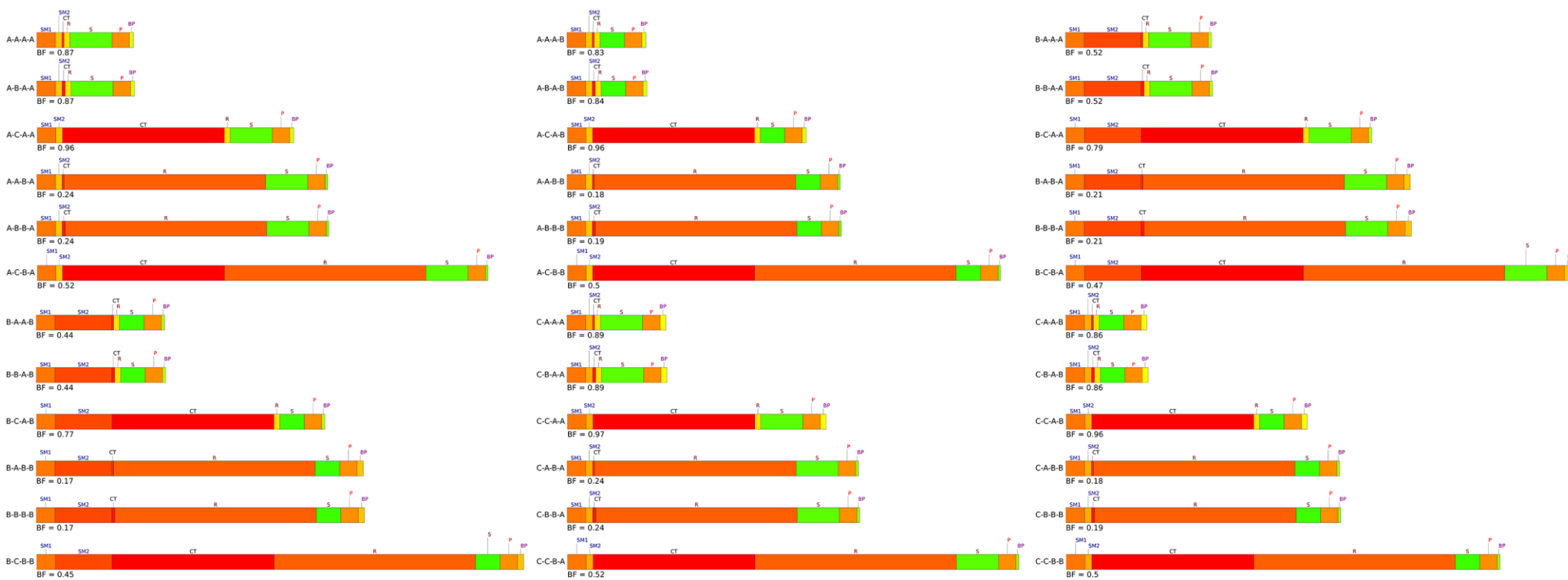
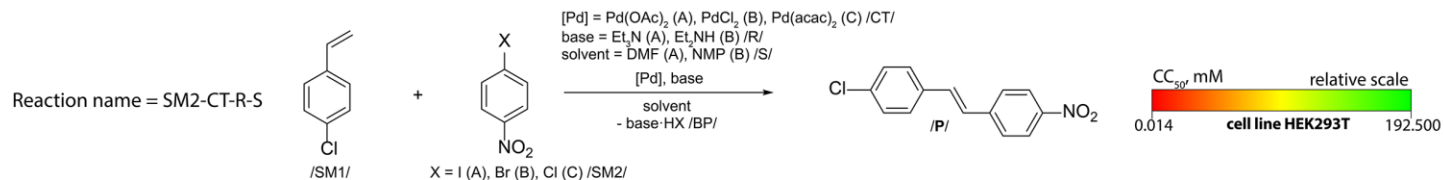


Fig. S12. bio-Strips of 36 synthetic routes for (E)-4-chloro-4'-nitrostilbene (based on 24-h CC_{50} values measured in HEK293T cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in HEK293T cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

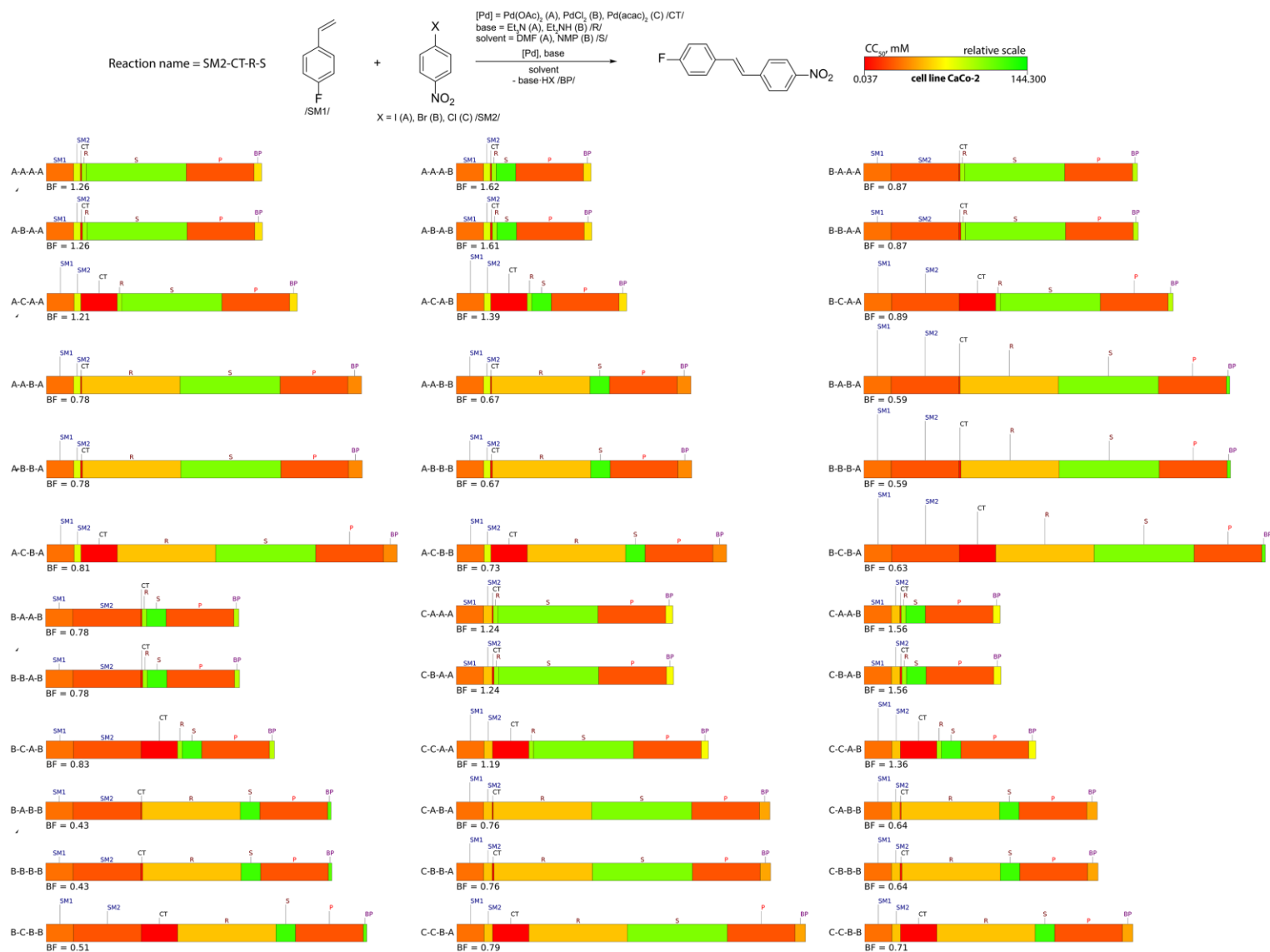
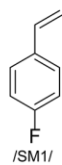
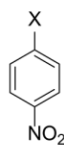


Fig. S13. bio-Strips of 36 synthetic routes for (*E*)-4-fluoro-4'-nitrostilbene (based on 24-h CC₅₀ values measured in CaCo-2 cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in CaCo-2 cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

Reaction name = SM2-CT-R-S



+



X = I (A), Br (B), Cl (C) /SM2/

[Pd] = Pd(OAc)₂ (A), PdCl₂ (B), Pd(acac)₂ (C) /CT/

base = Et₃N (A), Et₂NH (B) /R/

solvent = DMF (A), NMP (B) /S/

[Pd], base

solvent

- base-HX /BP/

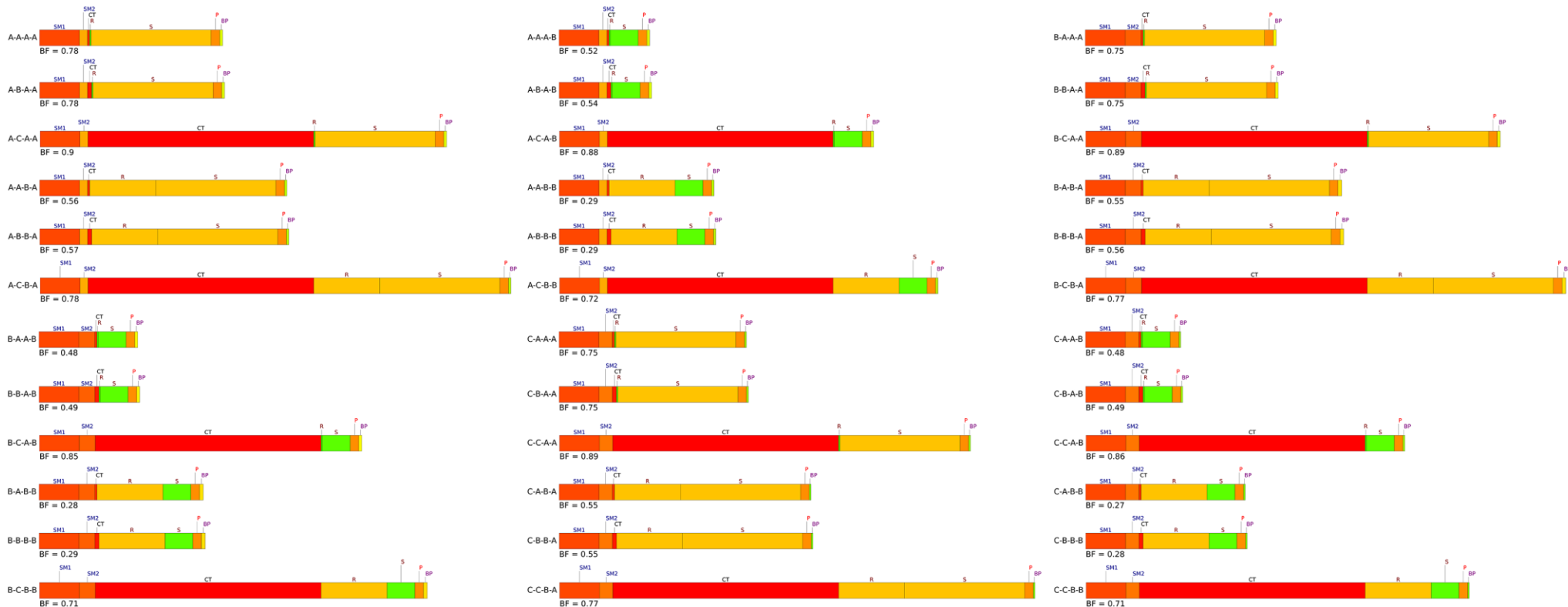
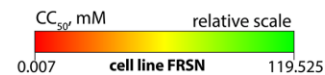
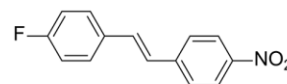


Fig. S14. bio-Strips of 36 synthetic routes for (*E*)-4-fluoro-4'-nitrostilbene (based on 24-h CC₅₀ values measured in FRSN cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in FRSN cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

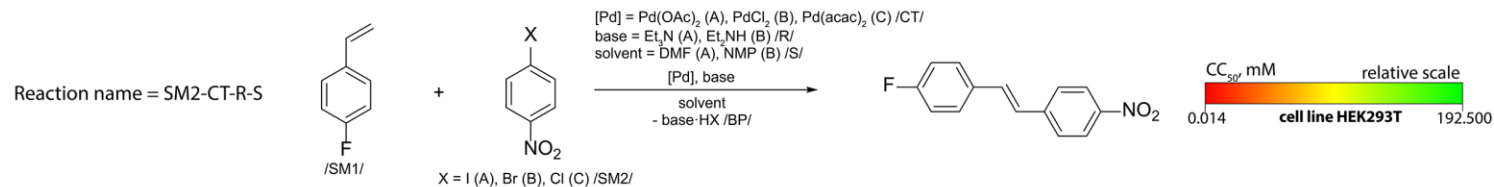


Fig. S15. bio-Strips of 36 synthetic routes for (*E*)-4-fluoro-4'-nitrostilbene (based on 24-h CC_{50} values measured in HEK293T cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-nitrobenzene (A), 1-bromo-4-nitrobenzene (B), or 1-chloro-4-nitrobenzene (C)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC_{50} of a particular substance in HEK293T cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

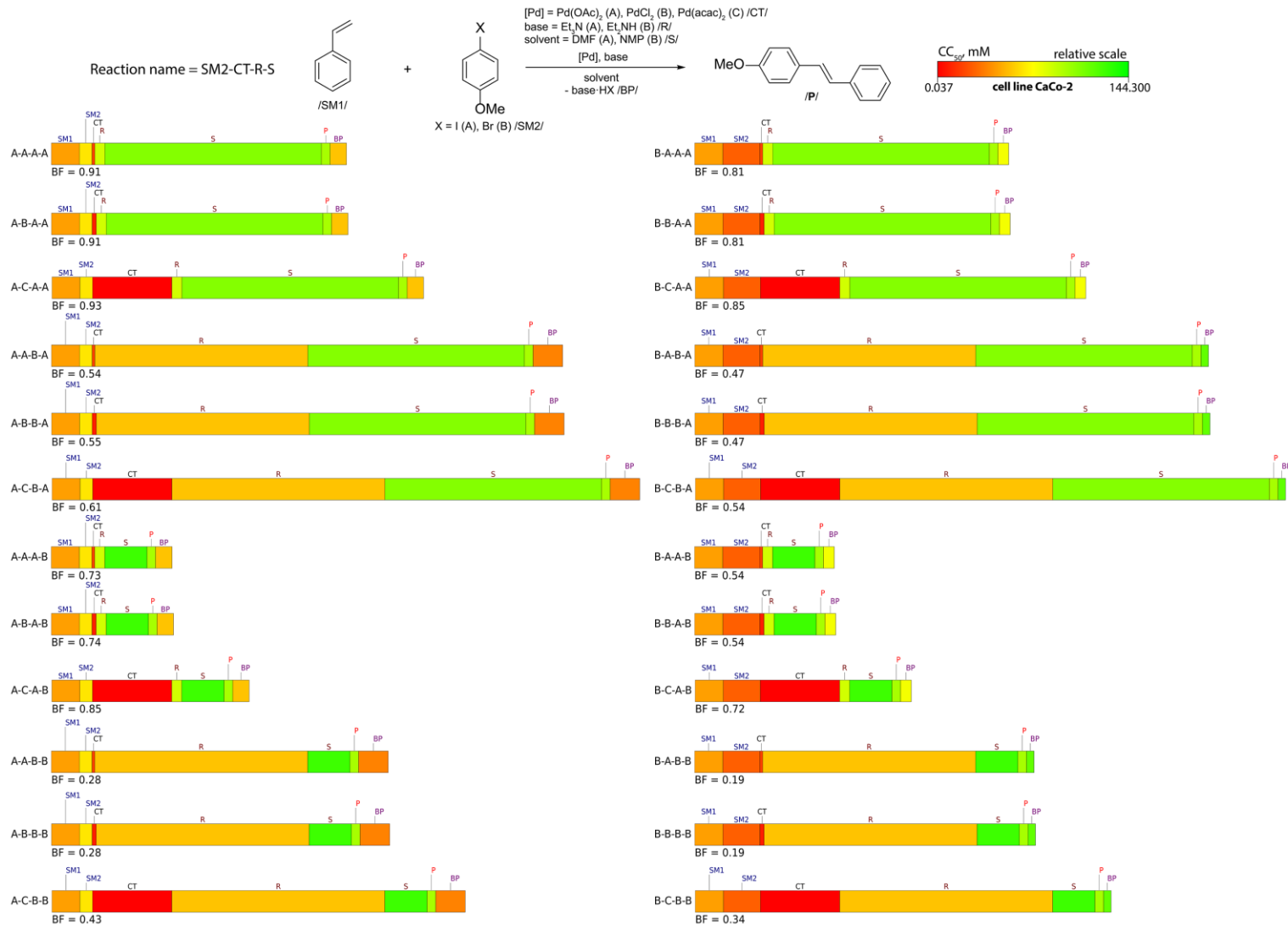


Fig. S16. bio-Strips of 24 synthetic routes for (*E*)-4-methoxystilbene (based on 24-h CC_{50} values measured in CaCo-2 cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-methoxybenzene (A) or 1-bromo-4-methoxybenzene (B)), catalyst (CT: $Pd(OAc)_2$ (A), $PdCl_2$ (B), or $Pd(acac)_2$ (C)), base (R: Et_3N (A) or Et_2NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively). The color of the strip sections corresponds to the CC_{50} of a particular substance in CaCo-2 cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

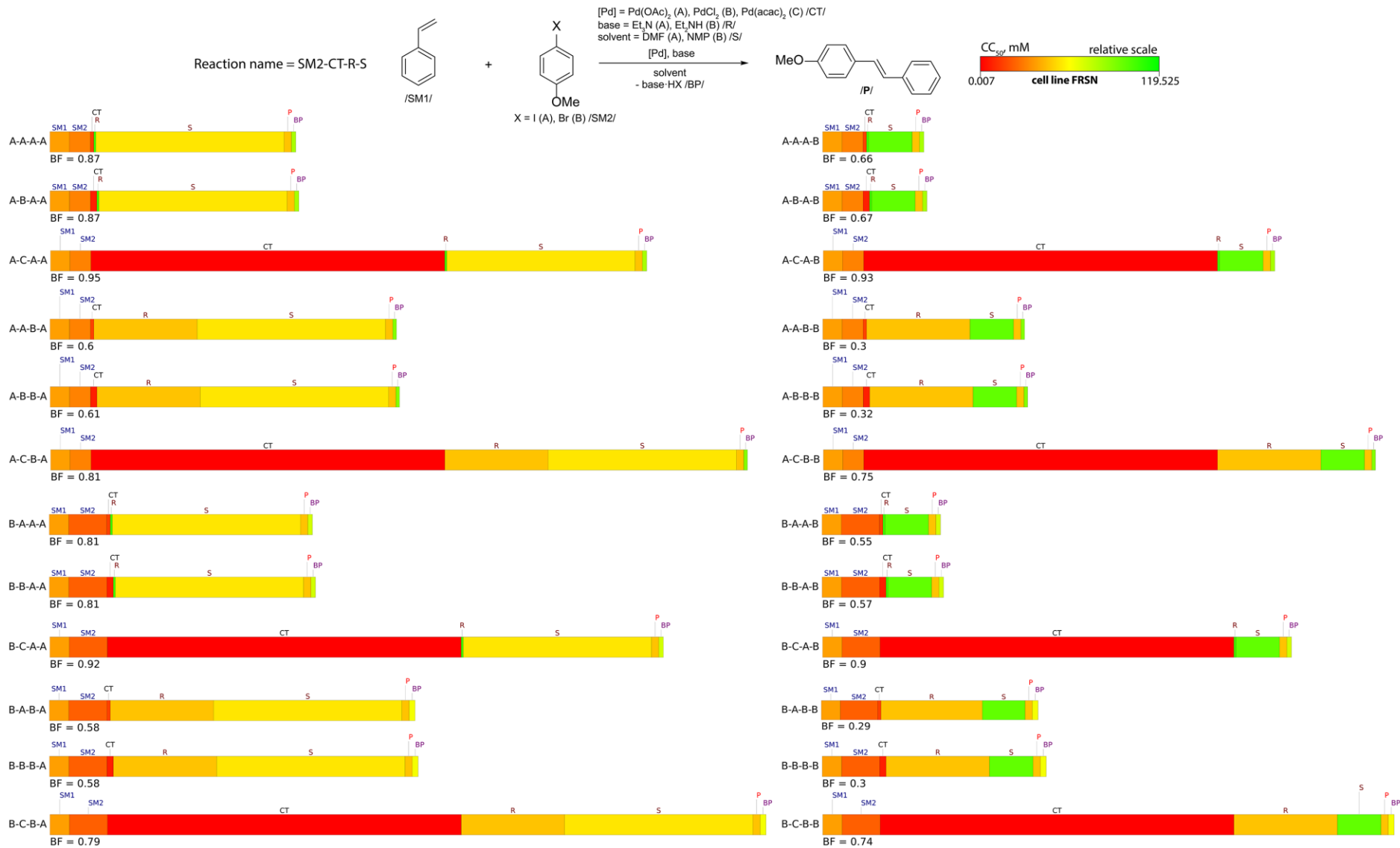


Fig. S17. bio-Strips of 24 synthetic routes for (E)-4-methoxystilbene (based on 24-h CC₅₀ values measured in FRSN cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-methoxybenzene (A) or 1-bromo-4-methoxybenzene (B)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₂NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in FRSN cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

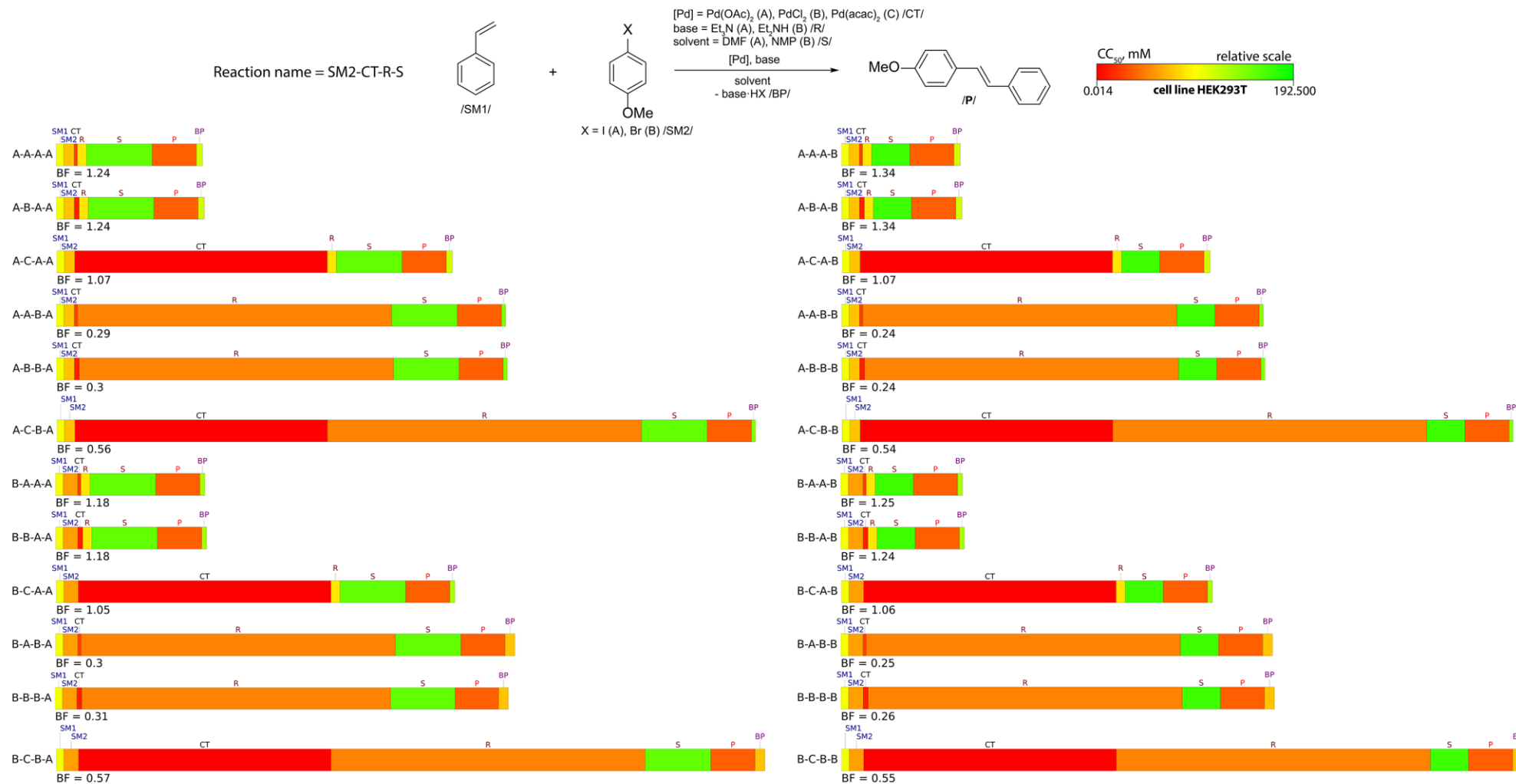


Fig. S18. bio-Strips of 24 synthetic routes for (*E*)-4-methoxystilbene (based on 24-h CC₅₀ values measured in HEK293T cells). The 1st, 2nd, 3rd, and 4th letters in the reaction names correspond to the types of starting material (SM2: 1-iodo-4-methoxybenzene (A) or 1-bromo-4-methoxybenzene (B)), catalyst (CT: Pd(OAc)₂ (A), PdCl₂ (B), or Pd(acac)₂ (C)), base (R: Et₃N (A) or Et₃NH (B)), and solvent (S: DMF (A) or NMP (B)), respectively. The color of the strip sections corresponds to the CC₅₀ of a particular substance in HEK293T cells (see the cytotoxicity scale above the bio-Strips). bio-Factors are shown below the strips.

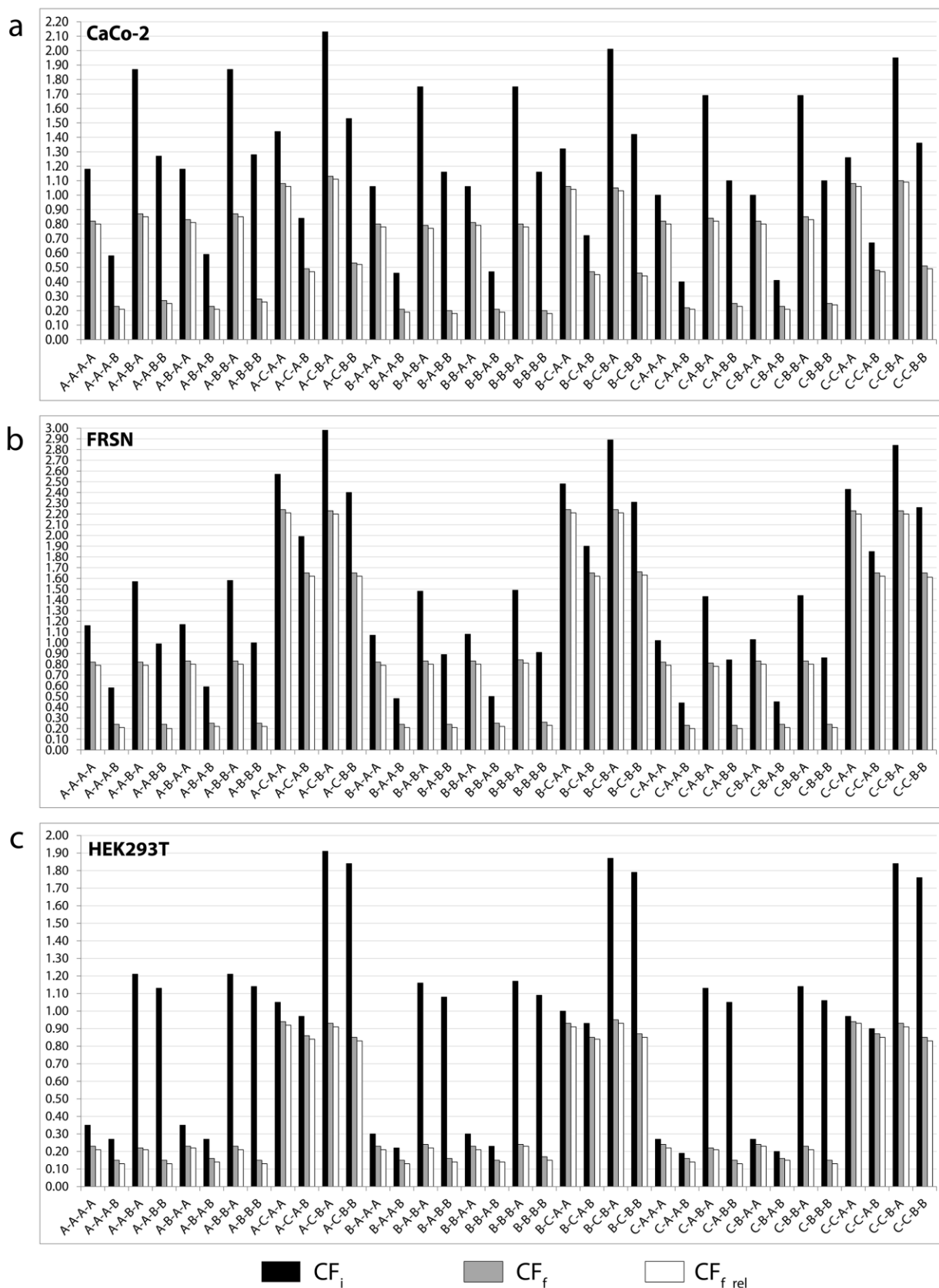


Fig. S19. Cytotoxicity potentials (CPs) of 32 routes of synthesis of (*E*)-stilbene on the basis of CC₅₀ values measured in (a) CaCo-2, (b) FRSN, and (c) HEK293T cells. Exact values are provided in Table S7.

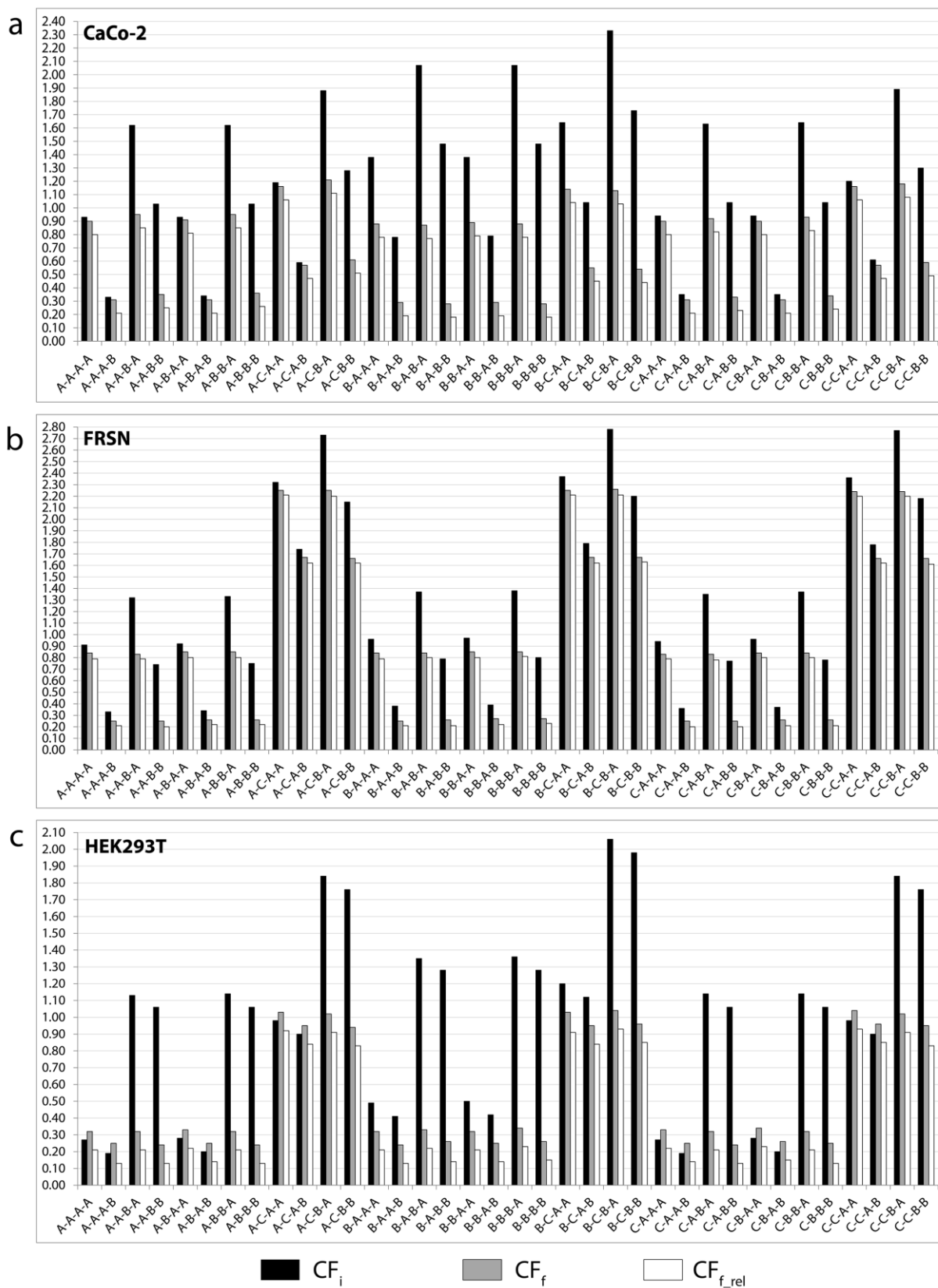


Fig. S20. Cytotoxicity potentials (CPs) of 32 routes of synthesis of (*E*)-4-nitrostilbene on the basis of CC_{50} values measured in (a) CaCo-2, (b) FRSN, and (c) HEK293T cells. Exact values are provided in Table S8.

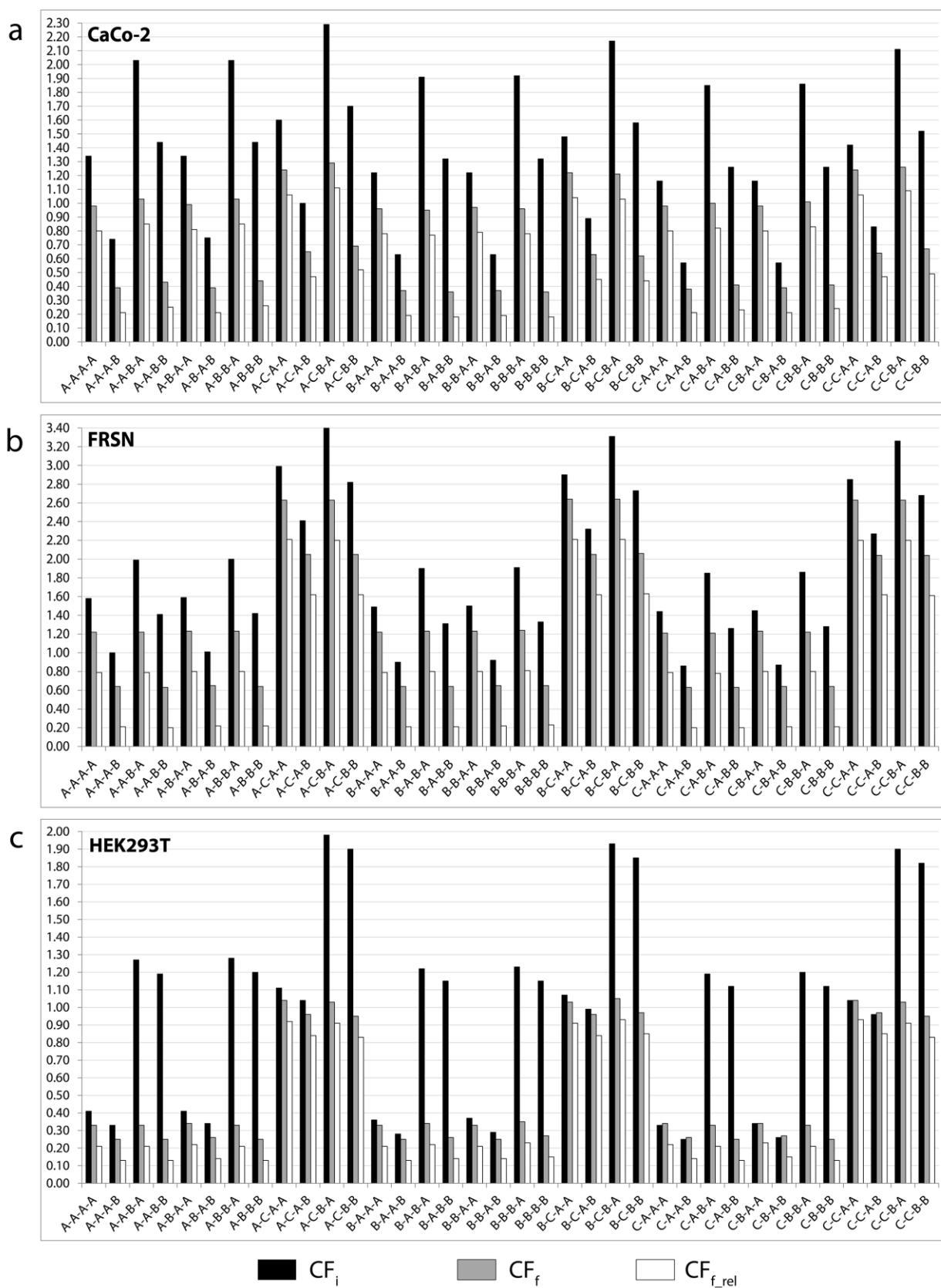


Fig. S21. Cytotoxicity potentials (CPs) of 32 routes of synthesis of (*E*)-4-chlorostilbene on the basis of CC_{50} values measured in (a) CaCo-2, (b) FRSN, and (c) HEK293T cells. Exact values are provided in Table S9.

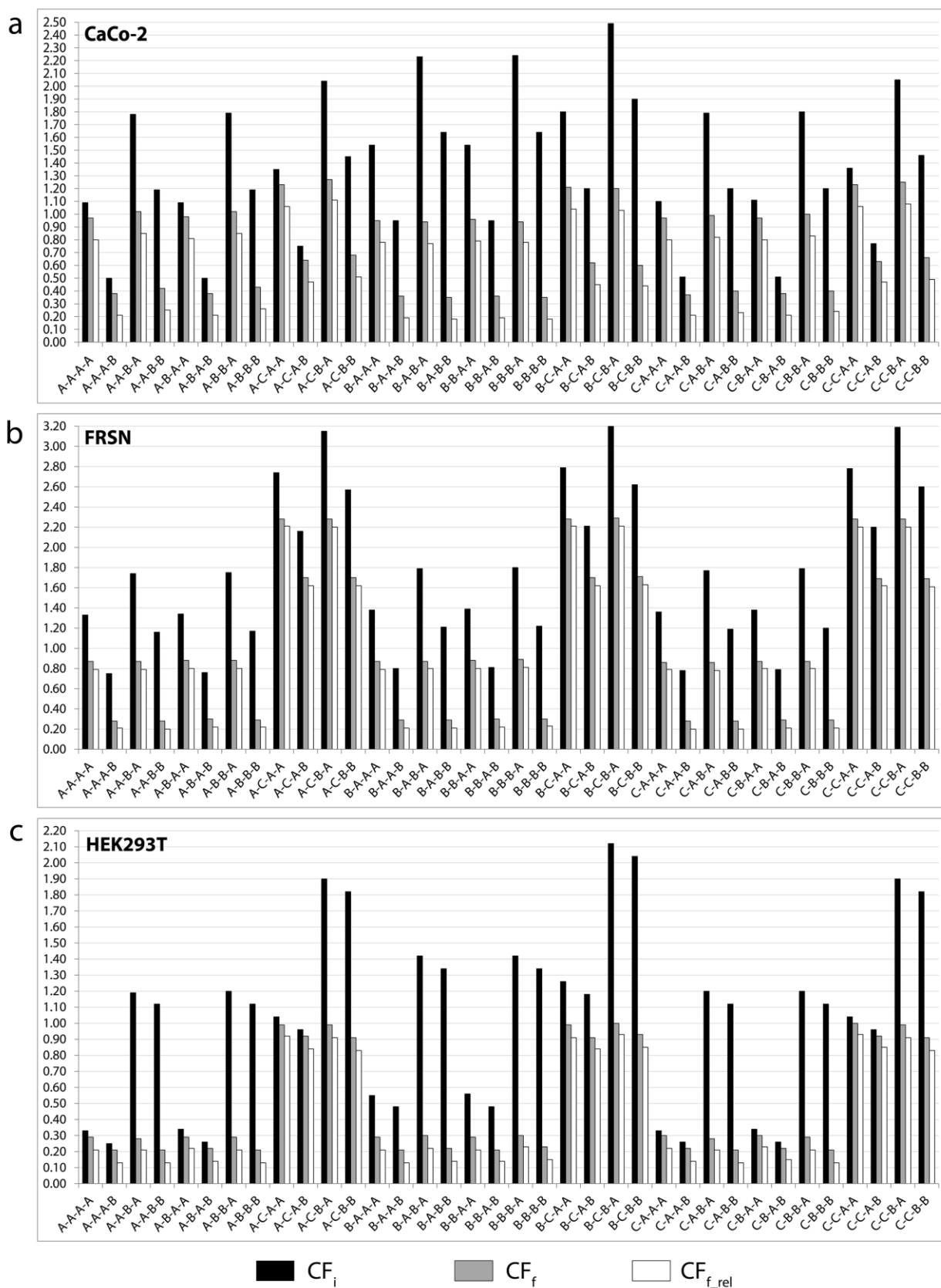


Fig. S22. Cytotoxicity potentials (CPs) of 32 routes of synthesis of (E)-4-chloro-4'-nitrostilbene on the basis of CC_{50} values measured in (a) CaCo-2, (b) FRSN, and (c) HEK293T cells. Exact values are provided in Table S10.

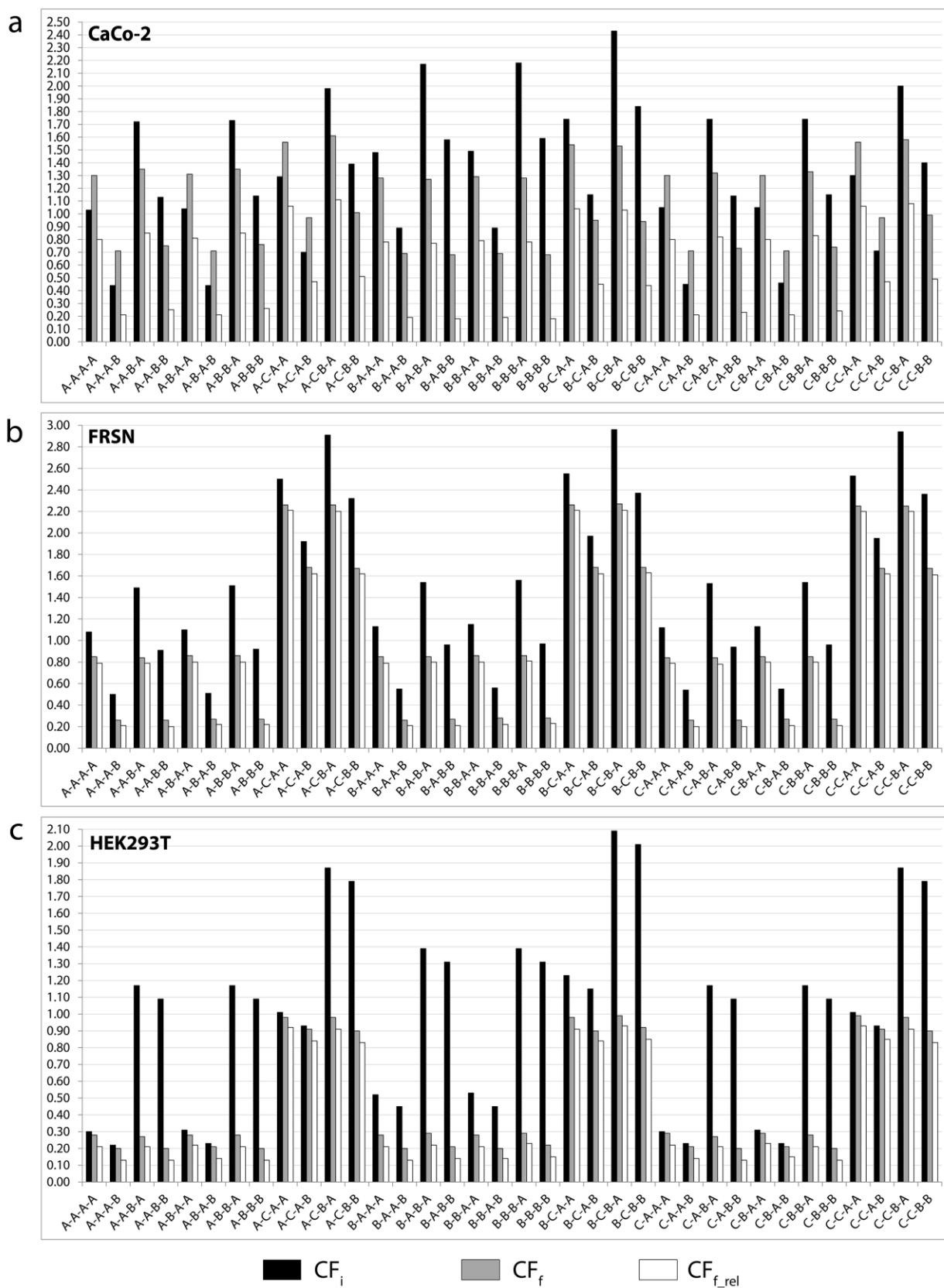


Fig. S23. Cytotoxicity potentials (CPs) of 32 routes of synthesis of (*E*)-4-fluoro-4'-nitrostilbene on the basis of CC_{50} values measured in (a) CaCo-2, (b) FRSN, and (c) HEK239T cells. Exact values are provided in Table S11.

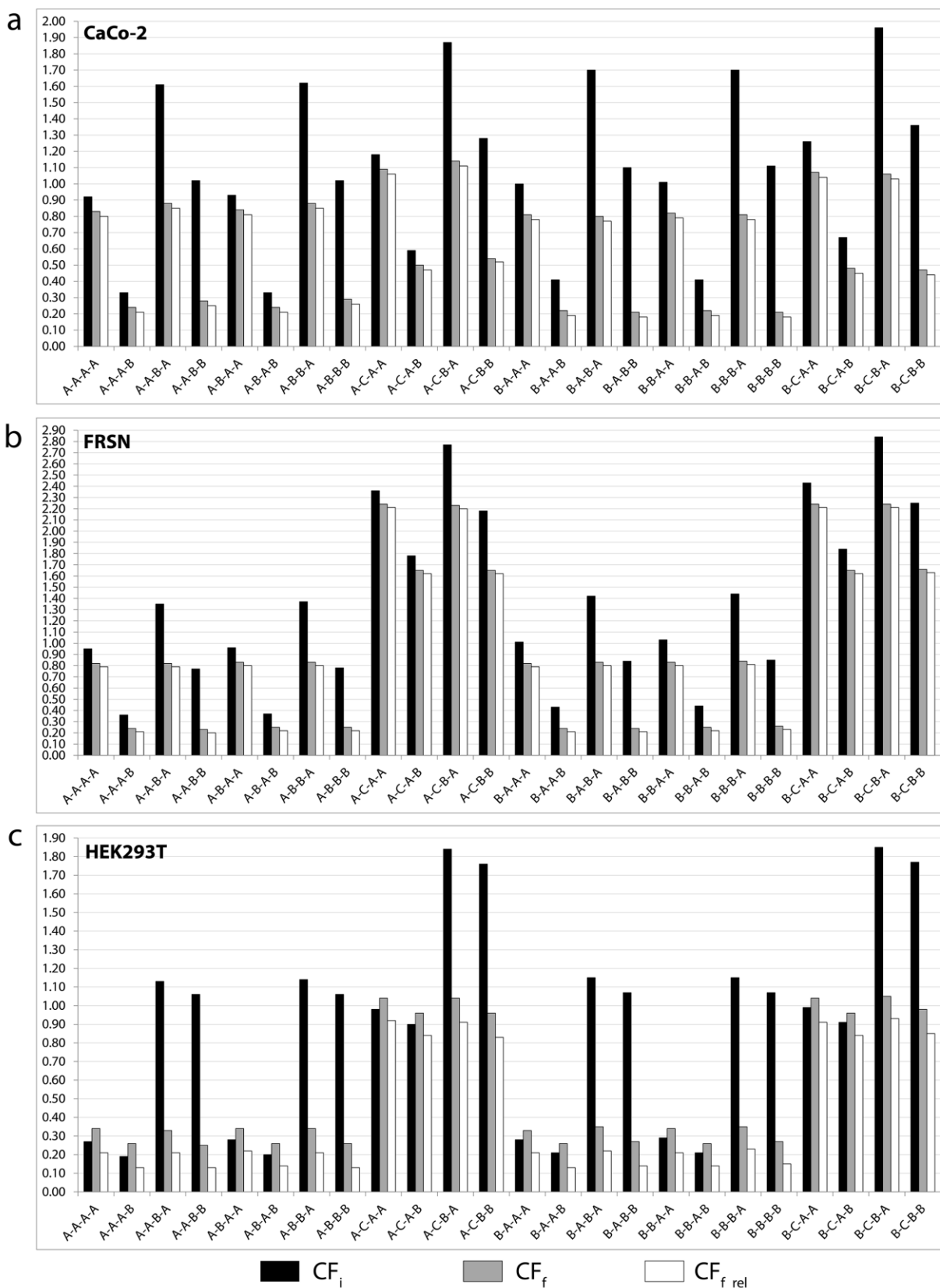


Fig. S24. Cytotoxicity potentials (CPs) of 24 routes of synthesis of (*E*)-4-methoxystilbene on the basis of CC_{50} values measured in (a) CaCo-2, (b) FRSN, and (c) HEK293T cells. Exact values are provided in Table S12.

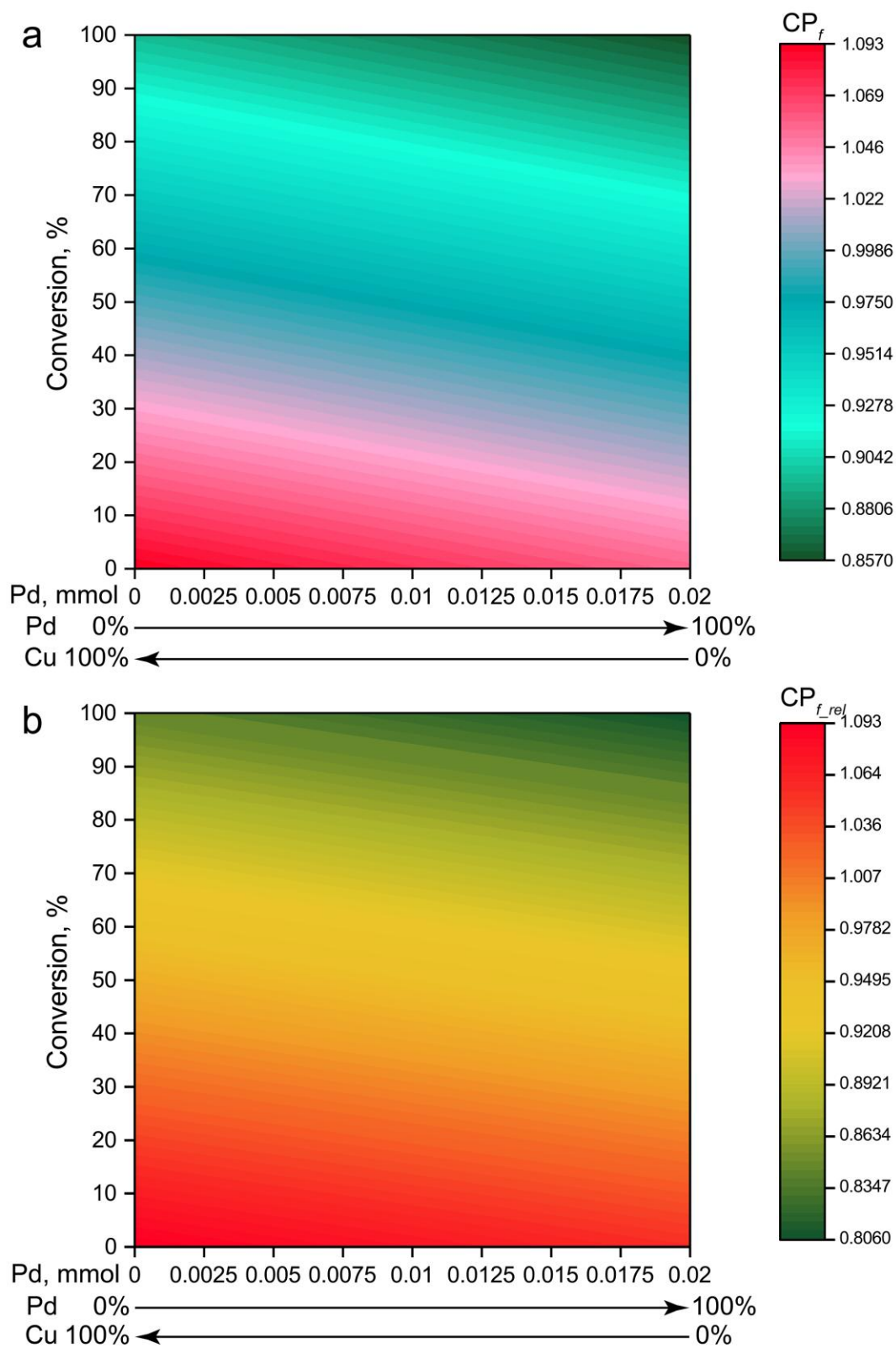


Fig. S25. Dependence of (a) CP_f and (b) $CP_{f,rel}$ on the Pd : Cu ratio during the reaction period by example of synthesis of diphenylacetylene from phenylacetylene and bromobenzene using $Pd(OAc)_2$ and CuI as catalysts and Et_3N as a base in DMF as measured in FRSN cells. The color legend is provided to the right. The data used in the plots are given in Table S14.

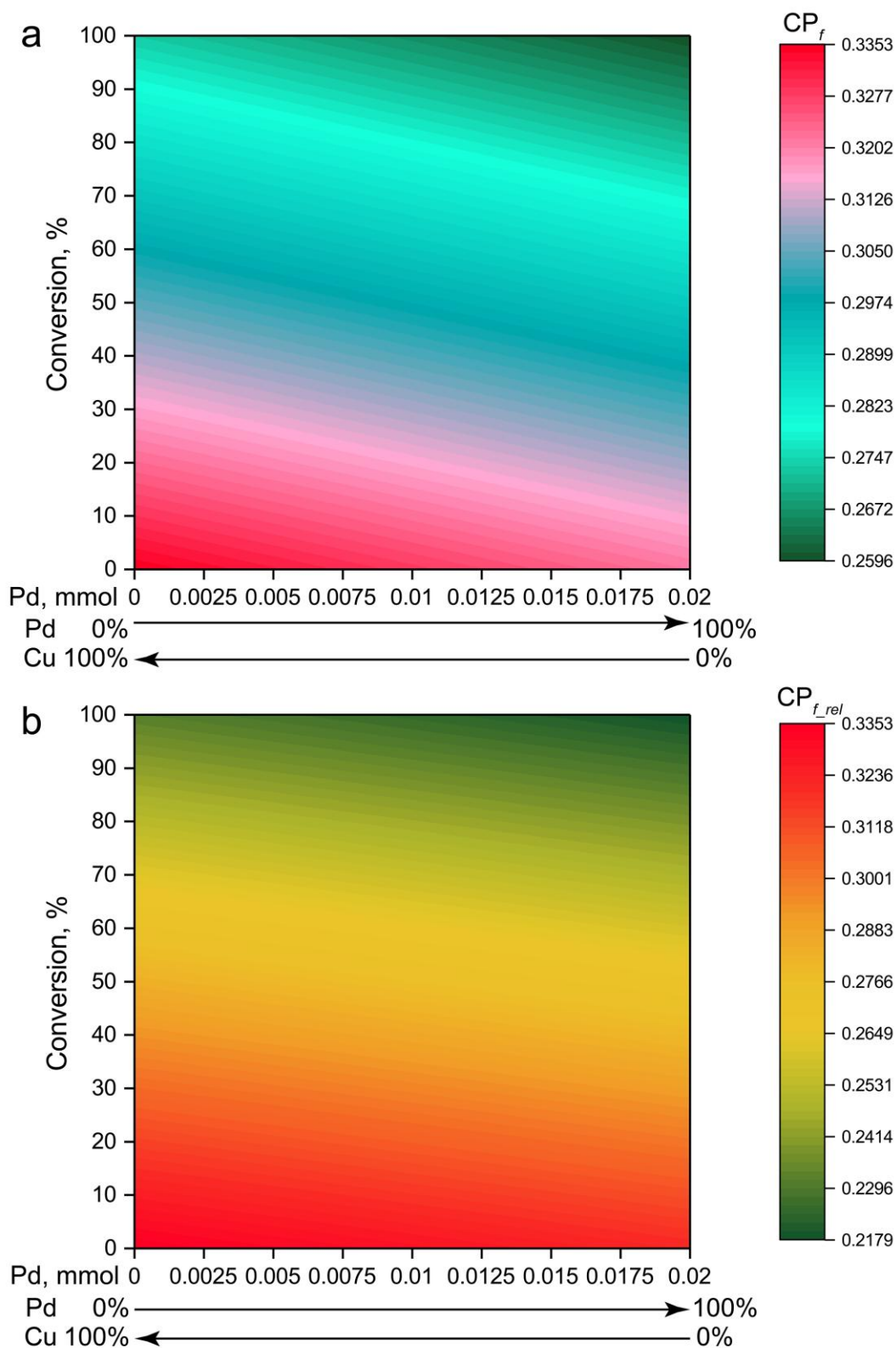


Fig. S26. Dependence of (a) CP_f and (b) CP_{f_rel} on the Pd : Cu ratio during the reaction period by example of synthesis of diphenylacetylene from phenylacetylene and bromobenzene using $Pd(OAc)_2$ and CuI as catalysts and Et_3N as a base in DMF as measured in HEK293T cells. The color legend is provided to the right. The data used in the plots are given in Table S15.

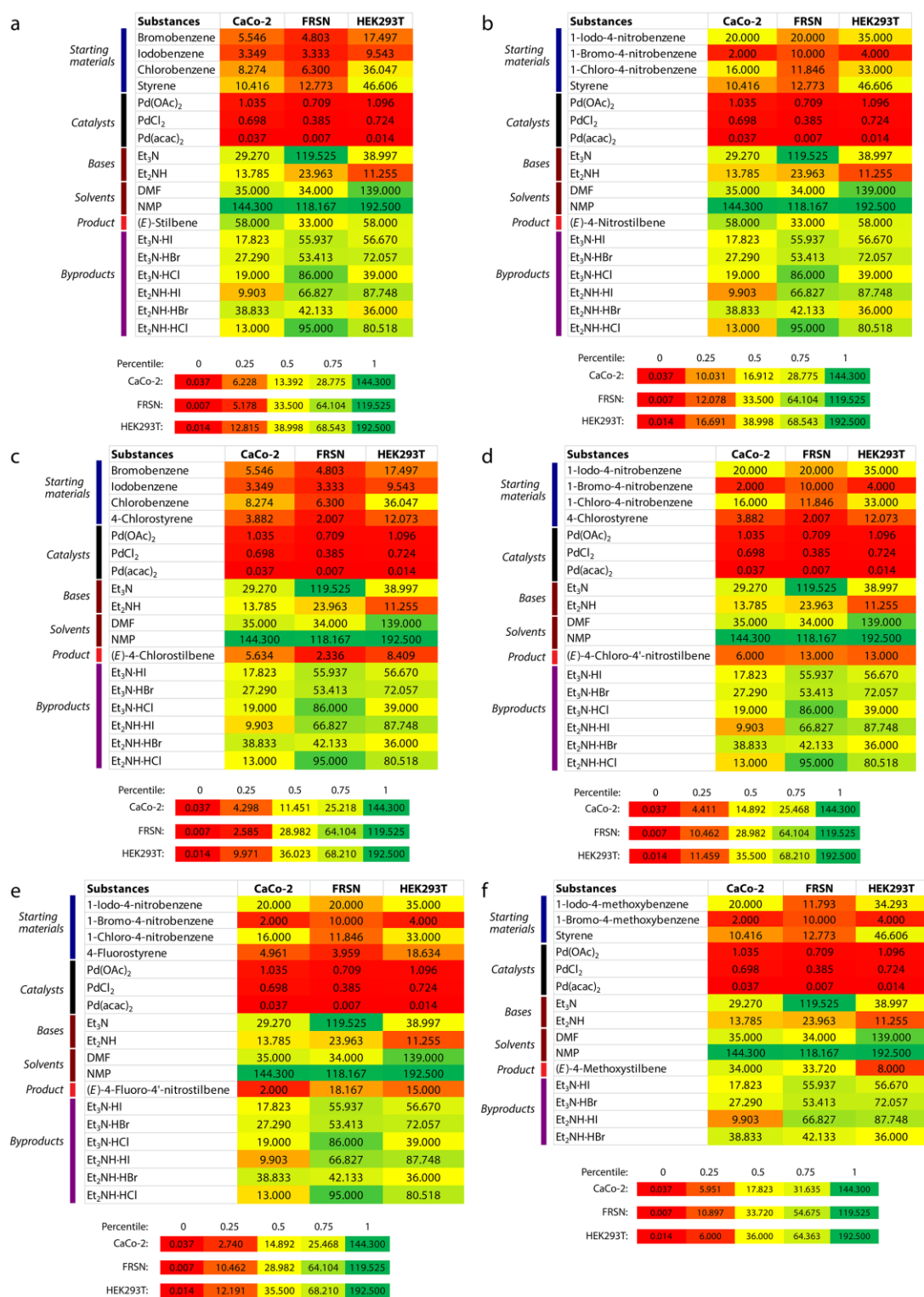


Fig. S27. Comparison of the cytotoxicity of the substances employed in the Mizoroki-Heck reactions in CaCo-2, HEK293T, and FRSN cell lines. The compounds involved in the synthesis of (a) (E)-stilbene, (b) (E)-4-nitrostilbene, (c) (E)-4-chlorostilbene, (d) (E)-4-chloro-4'-nitrostilbene, (e) (E)-4-fluoro-4'-nitrostilbene, and (f) (E)-4-methoxystilbene are shown. The colors of cells in the heatmaps reflect the 24-h CC₅₀ values of the corresponding substances in the corresponding cell line (see the legends below the heatmaps; the coloration is in accordance with the percentile distribution of the CC₅₀ values).