Supplementary Information

2D, 3D and Hybrid QSAR Studies of Nostoclide Analogues as Inhibitors of the Photosystem II

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Table S1. 2D QSAR molecular descriptors values

Molecule	CO+CM	wHOA02	QMafYY	QMbYY	QMbZZ	PI[a] / %
m01	–0.2372	0.0434	–5.302	1.1836	–1.9310	29.2
m02	–0.2357	0.0515	–6.841	1.1717	–1.9003	26.0
m03	–0.2285	0.0454	–4.770	1.1336	–1.8820	16.7
m04	–0.2308	0.0493	0.464	1.1426	–1.8755	8.0
m06	–0.2380	0.0340	–5.952	1.1813	–1.9521	NE[b]
m07	–0.2293	0.0352	–13.512	1.1482	–1.9109	NE[b]
m08	–0.2522	0.0343	6.895	1.2770	–2.0727	44.9
m09i	–0.2509	0.0367	–2.556	1.3161	–2.0353	49.9
m10	–0.2536	0.0350	–17.753	1.3277	–2.0411	55.5
m11	–0.2350	0.0488	–2.051	1.2002	–1.8847	NE[b]
m12	–0.2448	0.0275	–1.103	1.2464	–1.9634	38.6
m13	–0.2450	0.0677	2.440	1.2536	–1.9099	7.1
m14	–0.2323	0.0680	–1.100	1.2602	–1.9139	25.4
m15	–0.2329	0.0331	–9.840	1.2016	–1.9745	39.5
m16	–0.2480	0.0299	–21.710	1.2724	–2.0062	57.8
m17	–0.2265	0.0595	–14.258	1.1861	–1.8775	NE[b]
m18i	–0.2318	0.0366	–2.580	1.1789	–1.9047	6.9
m19	–0.2291	0.0581	8.060	1.1272	–1.8502	6.5
m20i	–0.2299	0.0489	2.269	1.1704	–1.8789	NE[b]
m21	–0.2485	0.0599	4.008	1.1834	–1.9322	15.0
m22	–0.2449	0.0427	–8.594	1.2050	–1.9475	43.5
m24	–0.2323	0.0555	9.378	1.1538	–1.8784	NE[b]
m26i	–0.2357	0.0383	–5.241	1.2240	–1.9481	28.8
m27	–0.2343	0.0473	–1.262	1.3055	–1.9736	25.6
m29	–0.2324	0.0441	–8.154	1.2305	–1.9815	30.8
m30	–0.2448	0.0387	–3.852	1.2052	–1.9778	20.3
m31	–0.2297	0.0465	0.026	1.1934	–1.9216	5.8
m32	–0.2407	0.0434	–6.710	1.1881	–1.9754	21.8
m33i	–0.2314	0.0372	–4.160	1.1565	–1.8681	22.6

[a]Percentage of photosynthesis inhibition; [b]non effective: PI < 5 %.

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Table S2. 3D QSAR molecular descriptors values

Molecule	E1	E2	E3	E4	E5	L1	L2	PI[a] / %
m01	2.383	–350.93	241.82	241.82	–525.24	–2.6546	21.972	29.2
m02	–0.197	–313.81	192.15	192.15	–529.55	–2.9578	22.186	26.0
m03	1.688	–358.80	195.90	195.90	–528.56	–2.8425	21.666	16.7
m04	9.971	–346.27	207.25	207.94	–549.33	–2.7719	21.327	8.0
m06	19.291	–316.73	197.83	197.83	–531.27	–2.8339	22.361	NE[b]
m07	–22.118	–304.81	236.75	236.75	–487.08	–2.7748	22.242	NE[b]
m08	16.503	–327.02	212.11	212.11	–603.95	–3.2189	21.813	44.9
m09i	–79.017	–294.76	211.38	209.99	–649.85	–2.8856	21.510	49.9
m10	–38.744	–308.60	250.53	249.99	–564.48	–2.9148	23.184	55.5
m11	31.522	–357.31	154.32	161.32	–583.47	–2.8917	21.286	NE[b]
m12	–3.822	–343.88	209.45	199.85	–561.25	–3.0701	22.543	38.6
m13	32.784	–373.04	162.71	152.29	–595.11	–2.8724	21.599	7.1
m14	44.581	–359.05	191.42	183.52	–629.13	–3.1642	21.000	25.4
m15	18.061	–310.47	239.26	239.26	–503.86	–2.9711	22.924	39.5
m16	–48.911	–288.91	246.85	246.85	–539.39	–2.8702	22.213	57.8
m17	2.739	–331.14	166.29	166.29	–559.83	–2.8732	21.648	NE[b]
m18i	33.747	–376.81	201.06	201.06	–575.32	–2.7609	20.792	6.9
m19	–22.370	–344.08	180.99	180.99	–493.29	–2.7471	21.912	6.5
m20i	10.106	–403.05	181.81	181.81	–520.55	–2.9224	21.929	NE[b]
m21	36.733	–364.99	226.98	226.98	–518.62	–2.8098	22.166	15.0
m22	24.575	–328.69	203.55	203.55	–606.03	–3.1715	21.847	43.5
m24	–3.529	–364.39	154.89	139.49	–569.09	–2.9271	21.457	NE[b]
m26i	–26.174	–338.89	229.08	229.08	–565.01	–2.7028	22.450	28.8
m27	–10.455	–340.07	272.30	272.30	–571.53	–2.7010	21.540	25.6
m29	10.490	–335.84	225.06	225.06	–576.69	–2.9369	22.054	30.8
m30	9.265	–332.29	192.70	192.70	–590.96	–2.8313	22.490	20.3
m31	–13.520	–340.01	212.32	212.32	–511.56	–2.7779	21.862	5.8
m32	10.507	–348.54	206.91	206.91	–587.01	–3.0669	22.318	21.8
m33i	–25.047	–291.83	183.00	183.00	–519.98	–2.8486	22.795	22.6

[a]Percentage of photosynthesis inhibition; [b]non effective: PI < 5 %.

Table S3. Hybrid QSAR molecular descriptors values

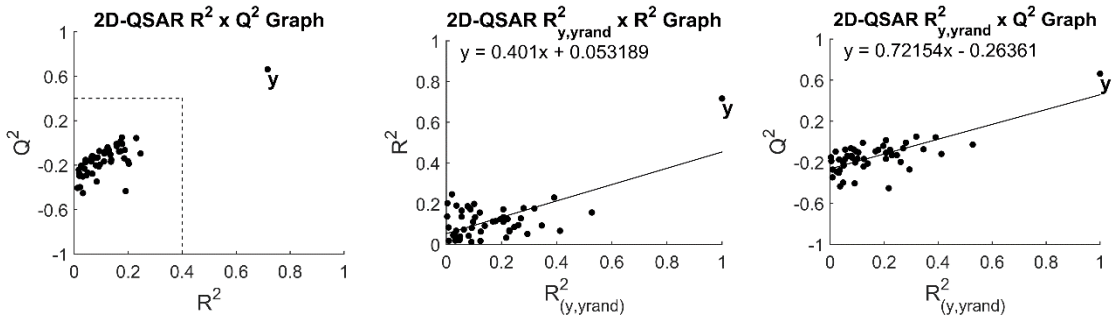
Molecule	CO+CM	wHO02	QMafYY	QMbYY	E1	E3	L1	PI[a] / %
m01	–0.2372	0.0434	–5.302	1.1836	2.383	241.82	–2.6546	29.2
m02	–0.2357	0.0515	–6.841	1.1717	–0.197	192.15	–2.9578	26.0
m03	–0.2285	0.0454	–4.770	1.1336	1.688	195.90	–2.8425	16.7
m04	–0.2308	0.0493	0.464	1.1426	9.971	207.25	–2.7719	8.0
m06	–0.2380	0.0340	–5.952	1.1813	19.291	197.83	–2.8339	NE[b]
m07	–0.2293	0.0352	–13.512	1.1482	–22.118	236.75	–2.7748	NE[b]
m08	–0.2522	0.0343	6.895	1.2770	16.503	212.11	–3.2189	44.9
m09i	–0.2509	0.0367	–2.556	1.3161	–79.017	211.38	–2.8856	49.9
m10	–0.2536	0.0350	–17.753	1.3277	–38.744	250.53	–2.9148	55.5
m11	–0.2350	0.0488	–2.051	1.2002	31.522	154.32	–2.8917	NE[b]
m12	–0.2448	0.0275	–1.103	1.2464	–3.822	209.45	–3.0701	38.6
m13	–0.2450	0.0677	2.440	1.2536	32.784	162.71	–2.8724	7.1
m14	–0.2323	0.0680	–1.100	1.2602	44.581	191.42	–3.1642	25.4
m15	–0.2329	0.0331	–9.840	1.2016	18.061	239.26	–2.9711	39.5
m16	–0.2480	0.0299	–21.710	1.2724	–48.911	246.85	–2.8702	57.8
m17	–0.2265	0.0595	–14.258	1.1861	2.739	166.29	–2.8732	NE[b]
m18i	–0.2318	0.0366	–2.580	1.1789	33.747	201.06	–2.7609	6.9
m19	–0.2291	0.0581	8.060	1.1272	–22.370	180.99	–2.7471	6.5
m20i	–0.2299	0.0489	2.269	1.1704	10.106	181.81	–2.9224	NE[b]
m21	–0.2485	0.0599	4.008	1.1834	36.733	226.98	–2.8098	15.0
m22	–0.2449	0.0427	–8.594	1.2050	24.575	203.55	–3.1715	43.5
m24	–0.2323	0.0555	9.378	1.1538	–3.529	154.89	–2.9271	NE[b]
m26i	–0.2357	0.0383	–5.241	1.2240	–26.174	229.08	–2.7028	28.8
m27	–0.2343	0.0473	–1.262	1.3055	–10.455	272.30	–2.7010	25.6
m29	–0.2324	0.0441	–8.154	1.2305	10.490	225.06	–2.9369	30.8
m30	–0.2448	0.0387	–3.852	1.2052	9.265	192.70	–2.8313	20.3
m31	–0.2297	0.0465	0.026	1.1934	–13.520	212.32	–2.7779	5.8
m32	–0.2407	0.0434	–6.710	1.1881	10.507	206.91	–3.0669	21.8
m33i	–0.2314	0.0372	–4.160	1.1565	–25.047	183.00	–2.8486	22.6

[a]Percentage of photosynthesis inhibition; [b]non effective: PI < 5 %.

Table S4. Measured and predicted percentages of photosynthesis inhibition

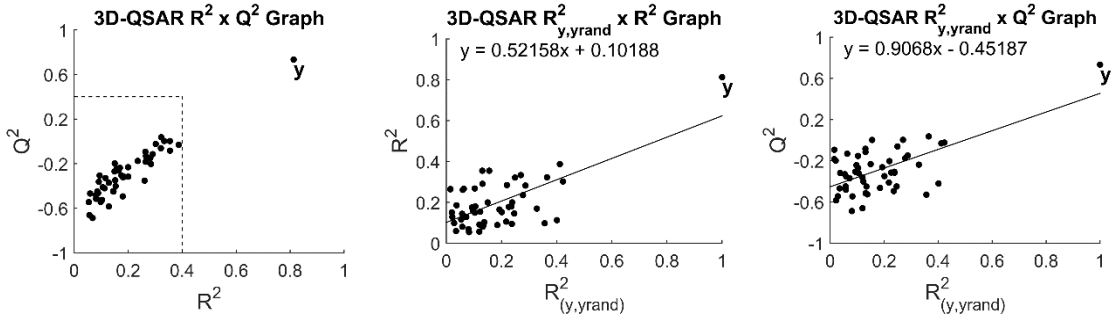
Molecule	Predicted PI (2D QSAR)	Predicted PI (3D QSAR)	Predicted PI (hybrid QSAR)	Measured PI[a] / %
m01	20.709	12.861	14.750	29.2
m02	14.602	22.628	18.026	26.0
m03	7.366	8.622	7.351	16.7
m04	6.335	12.062	5.705	8.0
m06	27.100	19.221	21.262	NE[b]
m07	19.795	28.444	23.457	NE[b]
m08	44.184	44.693	45.929	44.9
m09i	46.849	44.790	47.659	49.9
m10	55.668	49.366	59.558	55.5
m11	15.181	4.047	10.914	NE[b]
m12	34.929	32.402	40.500	38.6
m13	19.853	3.633	17.459	7.1
m14	12.814	27.708	18.398	25.4
m15	27.583	32.472	27.267	39.5
m16	46.283	40.906	49.411	57.8
m17	11.672	11.990	10.567	NE[b]
m18i	17.486	2.938	11.395	6.9
m19	–4.317	1.787	–3.540	6.5
m20i	8.111	0.757	9.897	NE[b]
m21	19.523	12.362	18.567	15.0
m22	28.477	38.709	34.021	43.5
m24	3.272	4.529	3.654	NE[b]
m26i	26.078	26.375	22.785	28.8
m27	30.565	36.282	32.857	25.6
m29	26.913	32.384	25.468	30.8
m30	31.770	24.320	24.300	20.3
m31	14.974	14.526	14.032	5.8
m32	27.532	35.448	30.296	21.8
m33i	11.593	24.405	13.955	22.6

[a]Percentage of photosynthesis inhibition; [b]non effective: PI < 5 %.



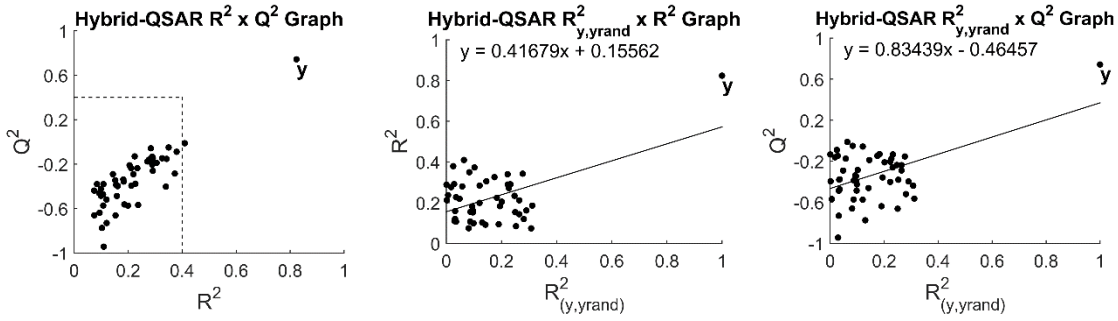
(a) (b) (c)

Figure S1. Graphs of (a) $R^2 \times Q^2$; (b) $R^2_{(y,yrand)} \times R^2$; and (c) $R^2_{(y,yrand)} \times Q^2$ of the y-randomization test for 2D-QSAR model.



(a) (b) (c)

Figure S2. Graphs of (a) $R^2 \times Q^2$; (b) $R^2_{(y,yrand)} \times R^2$; and (c) $R^2_{(y,yrand)} \times Q^2$ of the y-randomization test for 3D-QSAR model.



(a) (b) (c)

Figure S3. Graphs of (a) $R^2 \times Q^2$; (b) $R^2_{(y,yrand)} \times R^2$; and (c) $R^2_{(y,yrand)} \times Q^2$ of the y-randomization test for hybrid-QSAR model.