

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

<sup>a</sup>Percentage of photosynthesis inhibition; <sup>b</sup>non effective: PI < 5 %.

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**Table S2.** 3D QSAR molecular descriptors values

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

<sup>a</sup>Percentage of photosynthesis inhibition; <sup>b</sup>non effective: PI < 5 %.

**Table S3.** Hybrid QSAR molecular descriptors values

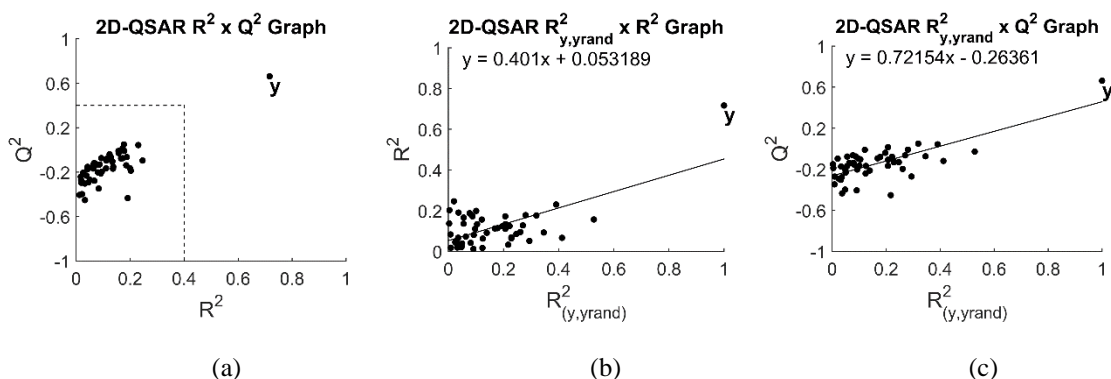
Molecule	CO+CM	wHO02	QMafYY	QMbYY	E1	E3	L1	PI <sup>a</sup> / %
<b>m01</b>	-0.2372	0.0434	-5.302	1.1836	2.383	241.82	-2.6546	29.2
<b>m02</b>	-0.2357	0.0515	-6.841	1.1717	-0.197	192.15	-2.9578	26.0
<b>m03</b>	-0.2285	0.0454	-4.770	1.1336	1.688	195.90	-2.8425	16.7
<b>m04</b>	-0.2308	0.0493	0.464	1.1426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

<sup>a</sup>Percentage of photosynthesis inhibition; <sup>b</sup>non effective: PI < 5 %.

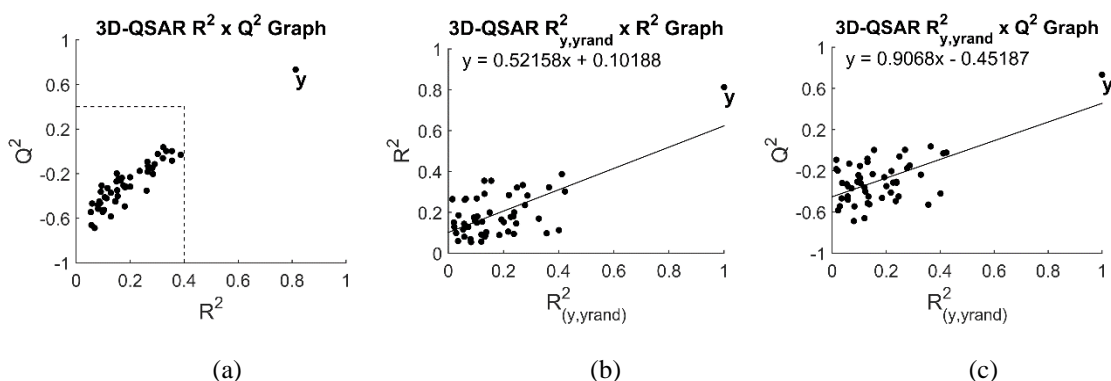
**Table S4.** Measured and predicted percentages of photosynthesis inhibition

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

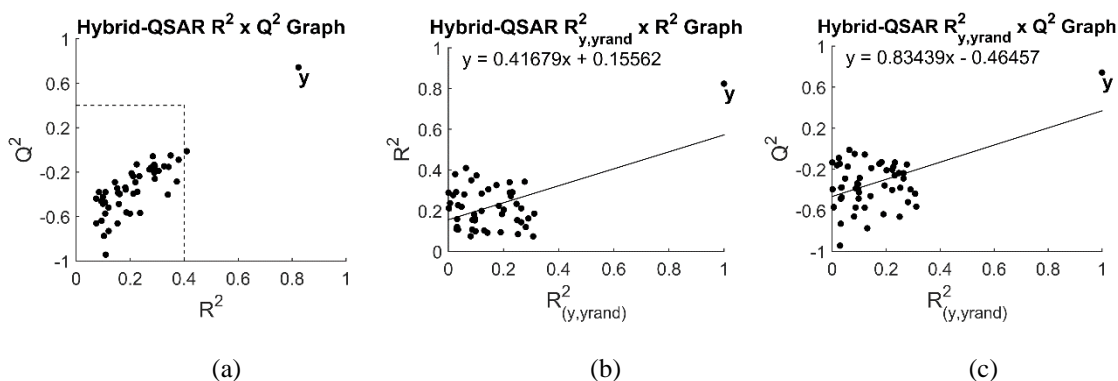
<sup>a</sup>Percentage of photosynthesis inhibition; <sup>b</sup>non effective: PI < 5 %.



**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.



**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.



**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.