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Aggregation-Induced Emission Enhancement Characteristics of Naphthalimide Derivatives and their Applications in Cell Imaging

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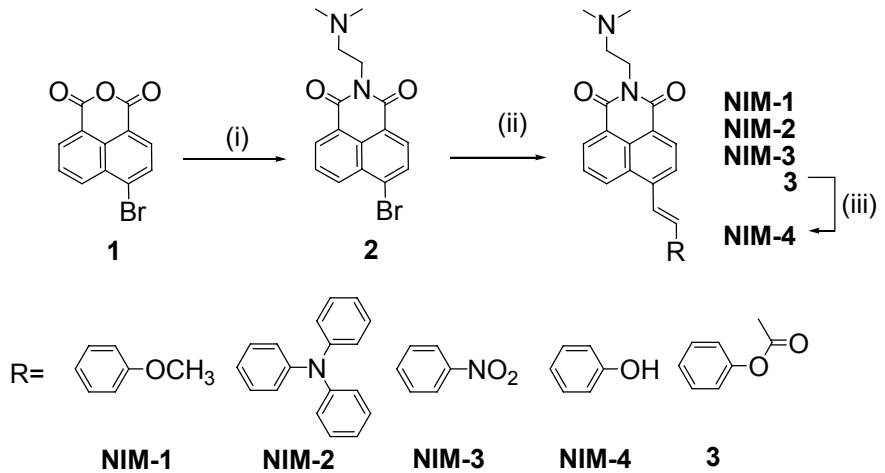
General procedure for the synthesis of naphthalimide derivatives (Scheme 1).

Synthesis of the naphthalimide derivatives is shown in Scheme 1. The first stage of the reaction, in which commercial starting material 4-bromo-1,8-naphthalic anhydride was reacted with the RNH_2, was performed conveniently in ethanol under room temperature. Next, the samples were subjected to the Heck coupling reaction with 4-methoxystyrene, 4-N, N-diphenylaminostyrene, 4-nitrostyrene or 4-acetoxystyrene under catalyst Pd $(OAc)_2$.



Scheme 1. Reagents and conditions: (i) N, N-dimethylethane-1, 2-diamine, EtOH, r.t. 24hr; (ii) $Pd(OAc)_2$ /(*o*-tol)$_3$P, 4-methoxystyrene (NIM-1), 4-(N, N-diphenylamino)styrene (NIM-2), 4-nitrostyrene (NIM-3) or 4-acetoxystyrene (compound 3), Et_3N/MeCN, N_2, reflux, 48hr. (iii) KOH/MeOH, reflux, 2hr; then HCl.

*4.6.1. 2-(6-bromo-1, 3-dioxo-1H-benzo[de] isoquinolin-2(3H)-yl)-N, N-dimethyl ethanamine (**compound 2**):*

4-Bromo-1, 8-naphthalic anhydride (10 mmole) and N, N-dimethylethane-1, 2-diamine (12 mmole) was stirred in ethanol solution (20 mL) under room temperature for 12h. The system was filtered to remove the excess N, N-dimethylethane-1, 2-diamine and the collected precipitate was crystallized from acetone/ethanol to get white solid (yield: 60%). Data for **2**: ^{1}HNMR (400Hz, $CDCl_3$, δ): δ(ppm)= 8.647 (d, *J*=8Hz, 1H), 8.560(d, *J*=8Hz, 1H), 8.405 (d, *J*=8Hz, 1H), 8.033 (d, *J*=8Hz, 1H), 7.839 (t, *J*=8Hz, 1H), 4.315 (t, *J*=8Hz, 2H), 2.647 (t, *J*=8Hz, 2H), 8.647 (s, 6H).

*4.6.2. 2-(6-(4-methoxystyryl)-1,3-dioxo-1H-benzo[de] isoquinolin-2(3H)-yl)-N, N-dimethyl ethanamine (**NIM-1**):*

Compound **2** (5 mmole) was added into to a high pressure bottle containing the a mixture of palladium (II) acetate (8 mg, Strem) and tri-*o*-tolyl phosphine (80 mg, Aldrich), then to which was added the solvent pair (triethylamine 5 ml / acetonitrile 15 ml) and 4-methoxystyrene (7 mmole, Acros). The bottle was then sealed after bubbling with nitrogen for 10 min. After keeping the system under ~105℃ for two days, the system was cooled to room temperature and then extracted with CH_2Cl_2 / H_2O twice. The organic layer was then dried by with $MgSO_4$ and evaporated in vacuum. The residue was subjected to chromatography on a silica gel by using Acetone / Hexane (1/1, Rf = 0.4). The deep-yellow solid was then obtained by recrystallizing with Acetone / Hexane (yield: 50%). Data for **NIM-1**: ^{1}HNMR(400Hz, $CDCl_3$, δ): δ=8.609(m, 3H; naphthalene H), 7.966 (d, *J*= 7.6 Hz, 1H; naphthalene H), 7.769 (t, *J*=7.6Hz, 1H; naphthalene H), 7.741 (d, *J*=16.2 Hz, 1H; vinyl H), 7.582 (d, *J*=8.4 Hz, 2H; Ar H), 7.301 (d, *J*=16.2 Hz, 1H; vinyl H), 6.964 (d, *J*=8.4 Hz, 2H; Ar H), 4.389 (t, *J*=6.8 Hz, 2H; ethylene H), 3.870 (s, 3H; OCH_3 H), 2.827 (d, *J*=6.8Hz, 2H; ethylene H), 2.492 (s, 6H; dimethylamine H). HRMS (ESI, *m/z*): $[M+H]^+$ 400.1786; found, 400.2878. Anal. calcd for For $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00; found, C, 74.31; H, 6.09; N, 6.91.

*4.6.3. 2-(6-(N, N-diphenyl-4-aminostyryl)-1,3-dioxo-1H-benzo[de] isoquinolin-2 (3H)-yl)-N, N-dimethyl ethanamine (**NIM-2**):*

Similar procedure as NIM-1 with compound 2 (5mmole) and N, N-diphenyl-4-vinylbenzenamine (7mmole) were added. The impurity residue was purified with chromatographing on silica gel by Hexane / Acetone (2/1). The orange compound was obtained by recrystallizing with acetone / Hexane (yield: 35%). Data for **NIM-2** : ^{1}HNMR (400Hz, $CDCl_3$, δ): δ 8.622 (d, *J*= 7.2 Hz, 1H; naphthalene H), 8.570 (m, 2H; naphthalene H), 7.972 (d, *J*= 7.6 Hz, 1H; naphthalene H), 7.764 (t, *J*=7.6 Hz, 1H; naphthalene H), 7.758 (d, *J*=16.0Hz, 1H; vinyl H), 7.501 (d, *J*=8.4 Hz, 2H; triphenylamine H), 7.296 (m, 6H; triphenylamine H), 7.149 (d, *J*=8.4 Hz, 4H; triphenylamine H), 7.085 (m, 3H:

vinyl+triphenylamine H), 4.372 (t, *J*=7.6 Hz, 2H; ethylene H), 2.759 (t, *J*=7.6 Hz, 2H; ethylene H), 2.422 (s, 6H; dimethylamine H). HRMS (ESI, *m/z*): $[M+H]^+$ 537.2416; found, 537.8551. Anal. Calcd for $C_{36}H_{31}N_3O_2$ (**NIM-2•1H$_2$O**: $C_{36}H_{33}N_3O_3$): C, 80.42 (77.81); H, 5.81 (5.99); N, 7.82 (7.56); found, C, 77.74; H, 6.00; N, 7.55

*4.6.4. 2-(6-(4-nitrostyryl)-1,3-dioxo-1H-benzo[de] isoquinolin-2(3H)-yl)-N, N-dimethyl ethanamine (**NIM-3**):*

A procedure similar to that used to prepare the **NIM-1** was employed; however, 1-nitro-4-vinylbenzene (7 mmole, Merck) was added and the residue was chromatographed on silica gel by Hexane /Acetone 2:1. This compound was recrystallized by using acetone / Hexane (Yield: 40%) with deep-yellow powder. Data for this compound: ^{1}HNMR (400Hz, $CDCl_3$, δ): δ=8.661 (d, *J*=7.6 Hz, 1H; naphthalene H), 8.622 (d, *J*= 8.0 Hz, 1H; naphthalene H), 8.561 (d, *J*= 8.4 Hz, 1H; naphthalene H), 8.305 (d, *J*=8.4 Hz, 2H; Ar H), 8.054 (d, *J*=16.0 Hz, 1H; vinyl H), 8.030 (d, *J*=7.6 Hz, 1H; naphthalene H), 7.831 (t, *J*=7.6 Hz, 1H; naphthalene H), 7.783 (d, *J*=8.4 Hz, 2H; Ar H), 7.382 (d, *J*=16.0 Hz, 1H; vinyl H), 4.349 (t, *J*=7.4 Hz, 2H; ethylene H), 2.680 (d, *J*=7.4 Hz, 2H; ethylene H), 2.368 (s, 6H; dimethylamine H). HRMS (ESI, *m/z*): $[M+H]^+$ 415.1532; found, 415.1690. Anal. Calcd for $C_{24}H_{21}N_3O_4$: C, 69.39, H, 5.10; N, 10.11; found: C, 69.29; H, 5.09; N, 10.09

*4.6.5. 2-(6-(4-hydroxystyryl)-1,3-dioxo-1H-benzo[de] isoquinolin-2(3H)-yl)-N, N-dimethyl ethanamine (**NIM-4**):*

Similar synthesis and purify procedure as **NIM-1** while 4-acetoxystyrene (7mmole) were added. The precursor *2-(6-(4-acetoxystyryl)-1, 3-dioxo-1H-benzo[de] isoquinolin-2(3H)-yl)-N, N-dimethyl ethanamine (**compound 3**)* was collected. Then the mixture was reflux under alkali solution and system was chromatographed on silica gel by Hexane / Acetone (1/1). The orange compound was obtained by recrystallizing with acetone / Hexane (yield: 40%). Data for **NIM-4**: ^{1}HNMR (400Hz, DMSO-d_6, δ): 9.840 (s, 1H; Ar OH), 8.954 (d, *J*= 7.2 Hz, 1H; naphthalene H), 8.510 (d, *J*=7.2Hz, 1H; naphthalene H), 8.432 (d, *J*= 8.0 Hz, 1H; naphthalene H), 8.176 (d, *J*=8.0 Hz, 1H; naphthalene H), 7.971 (d, J=16.0 Hz,

1H; vinyl H), 7.868 (t, *J*=8.0 Hz, 1H; naphthalene H), 7.790 (d, *J*=8.4 Hz, 2H; Ar H), 7.509 (d, *J*=16.0 Hz, 1H; vinyl H), 6.832 (d, *J*=8.4 Hz, 2H; Ar H), 4.145 (t, *J*=7.2 Hz, 2H; ethylene H), 2.510 (t, *J*=7.2 Hz, 2H; ethylene H), 2.203 (s, 6H; dimethylamine H). HRMS (ESI, *m/z*): $[M+H]^+$ 386.1630; found, 387.1264. Anal. calcd for $C_{24}H_{22}N_2O_3$ (**NIM-4•0.5H_2O**: $C_{24}H_{23}N_2O_{3.5}$): C, 74.59 (72.89); H, 5.74 (5.86); N, 7.25 (7.08); found: C, 72.64; H, 5.89; N, 7.05.

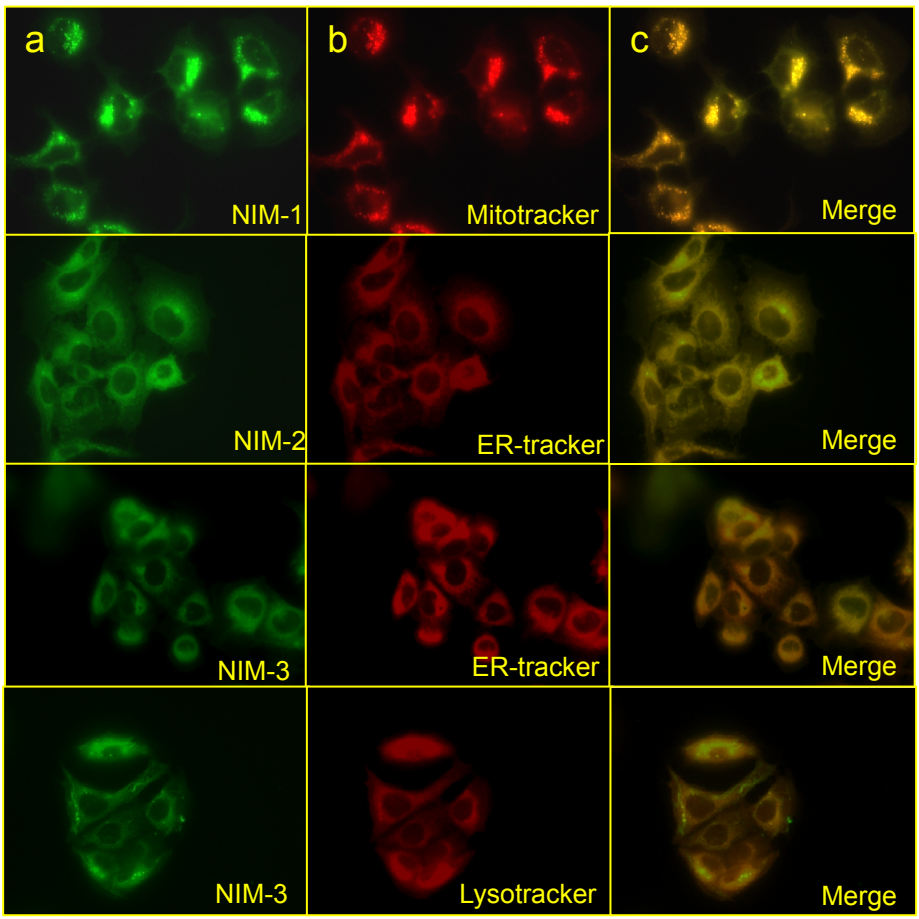


Fig. S Immunofluorescence staining: The intracellular localization images of 10 μM NIM compounds under MCF-7 breast cancer cell. Cells were incubated first with compound for 4 hours, followed by 1 μM organelle probes (MitoTracker® Red CMH2XRos, LysoTracker® Red DND-99, ER-Tracker™ Red BODIPY® TR for 30 min at 37 °C). The excitation source and detection were (a) for compound: light path through a 380/10 nm bp filter and emission was collected and filtered through a 450-nm lp filter. (b) For tracker red: light path through a 550/10 nm bp filter and emission was collected and filtered through a 590 nm lp filter. (c) Merge photos.