

## *Supplementary Data*

### **Degradation of HaloTag-fused nuclear proteins using bestatin-HaloTag ligand hybrid molecules**

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### **1. Experimental procedures**

#### **1.1. Organic synthesis**

##### **General.**

Proton nuclear magnetic resonance spectra (<sup>1</sup>H NMR) and carbon nuclear magnetic resonance spectra (<sup>13</sup>C NMR) were recorded on a JEOL JNM-ECA500 (500 MHz) spectrometer in the indicated solvent. Chemical shifts (δ) are reported in parts per million relative to the internal standard tetramethylsilane (<sup>1</sup>H NMR) or the centerline of

the triplet at 77.0 ppm of CDCl<sub>3</sub> (<sup>13</sup>C NMR). <sup>1</sup>H and <sup>13</sup>C NMR spectra of compounds **1a-d** are shown in Figures S4-S7. Electrospray ionization (ESI) and fast atom bombardment (FAB) mass spectra were recorded on a BRUKER micrOTOF II mass spectrometer and JEOL JMA-HX110 mass spectrometer, respectively. Routine thin layer chromatography (TLC) was performed on silica gel 60 F254 plates (Merck, Germany). Flash column chromatography was performed on Silica gel 60 (spherical, particle size 40–100 μm; Kanto Chemical, Japan)

**(*S*)-2-((2*S*,3*R*)-3-*tert*-Butoxycarbonylamino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (6a)**

To a mixture of **4a** (25.1 mg, 93.6 μmol), **5** (38.2 mg, 93.6 μmol), 1-hydroxybenzotriazole monohydrate (20.3 mg, 150 μmol) and DIEA (50 μL, 281 μmol) in DMF (0.5 mL) was added EDC (27.4 mg, 143 μmol) at 0 °C. The reaction mixture was stirred at room temperature for 24 h, diluted with AcOEt, washed with brine/water (1:1), and dried over MgSO<sub>4</sub>. Filtration, evaporation of the solvent *in vacuo*, and purification of the residue by flash column chromatography (CHCl<sub>3</sub>/MeOH = 100:1 to 30:1) gave 48.7 mg (79%) of compound **6a** as a colorless amorphous solid. <sup>1</sup>H NMR

(500 MHz, CDCl<sub>3</sub>)  $\delta$  7.32 – 7.19 (m, 5H), 6.79 (s, 1H), 5.59 (s, 1H), 5.09 (s, 1H), 4.48 (br s, 1H), 4.13 (d,  $J$  = 4.6 Hz, 1H), 3.64 – 3.44 (m, 16H), 3.02 (d,  $J$  = 28.6 Hz, 2H), 1.80 – 1.74 (m, 2H), 1.70 – 1.59 (m, 5H), 1.48 – 1.23 (m, 13H), 0.92 (dd,  $J$  = 14.6, 6.0 Hz, 6H). MS (ESI)  $m/z$  680 (M + Na)<sup>+</sup>.

**(*S*)-2-((2*S*,3*R*)-3-*tert*-Butoxycarbonylamino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (6b)**

The title compound was prepared from **4b** (21.9 mg, 70.2  $\mu$ mol) according to the procedure described for **6a**. Yield: 39.7 mg (81%). Colorless amorphous solid. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.31 – 7.20 (m, 5H), 6.89 (s, 1H), 5.61 (s, 1H), 5.12 (br s, 1H), 4.49 (br s, 1H), 4.13 (br s, 1H), 3.65 – 3.44 (m, 20H), 3.00 (br s, 2H), 1.79 – 1.74 (m, 2H), 1.70 – 1.56 (m, 5H), 1.47 – 1.26 (m, 13H), 0.92 (dd,  $J$  = 14.9, 6.3 Hz, 6H). MS (ESI)  $m/z$  724 (M + Na)<sup>+</sup>.

**(*S*)-2-((2*S*,3*R*)-3-*tert*-Butoxycarbonylamino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (6c)**

The title compound was prepared from **4c** (11.8 mg, 33.3  $\mu$ mol) according to the

procedure described for **6a**. Yield: 18.7 mg (75%). Colorless amorphous solid.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27 – 7.17 (m, 5H), 4.47 (dd,  $J = 9.5, 5.4$  Hz, 1H), 4.15 (dd,  $J = 7.7, 5.4$  Hz, 1H), 3.97 (s, 1H), 3.65 – 3.51 (m, 20H), 3.47 (t,  $J = 6.6$  Hz, 2H), 3.37 – 3.34 (m, 2H), 2.88 – 2.84 (m, 2H), 1.79 – 1.73 (m, 2H), 1.67 – 1.55 (m, 5H), 1.45 – 1.37 (m, 13H), 0.93 (dd,  $J = 20.0, 6.3$  Hz, 6H). MS (FAB)  $m/z$ : 747 ( $\text{M} + \text{H}$ ) $^+$ .

**(*S*)-2-((2*S*,3*R*)-3-*tert*-Butoxycarbonylamino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (6d)**

The title compound was prepared from **4b** (13.7 mg, 34.2  $\mu\text{mol}$ ) according to the procedure described for **6a**. Yield: 20.9 mg (77%). Colorless amorphous solid.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 – 7.20 (m, 5H), 5.56 (d,  $J = 9.2$  Hz, 1H), 4.46 (t,  $J = 7.4$  Hz, 1H), 4.13 (d,  $J = 7.4$  Hz, 1H), 4.02 (s, 1H), 3.67 – 3.53 (m, 24H), 3.48 (t,  $J = 6.9$  Hz, 2H), 3.39 (d,  $J = 5.2$  Hz, 2H), 2.94 – 2.84 (m, 2H), 1.81 – 1.75 (m, 2H), 1.64 – 1.59 (m, 5H), 1.50 – 1.44 (m, 2H), 1.41 – 1.35 (m, 11H), 0.94 (dd,  $J = 17.8$  and 6.3 Hz, 6H). MS (ESI)  $m/z$ : 812 ( $\text{M} + \text{Na}$ ) $^+$ .

**(*S*)-2-((2*S*,3*R*)-3-Amino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(6-chlorohexyl**



**oxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (1a)**

4 M HCl/1,4-dioxane (1.0 mL) was added to a solution of **6a** (48.7 mg, 74.0  $\mu$ mol) in DCM (1.0 mL) and the mixture was stirred at room temperature for 4 h. Evaporation of the solvent *in vacuo* and purification of the residue by flash column chromatography (CHCl<sub>3</sub>/MeOH = 100:1 to 30:1) gave 41.0 mg (99%) of compound **1a** as a colorless amorphous solid. <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD)  $\delta$  7.32 – 7.20 (m, 5H), 4.43 (dd, *J* = 8.9, 5.4 Hz, 1H), 3.93 (d, *J* = 2.9 Hz, 1H), 3.60 – 3.46 (m, 14H), 3.39 – 3.31 (m, 2H), 2.78 (dq, *J* = 118.4, 7.0 Hz, 2H), 1.79 – 1.73 (m, 2H), 1.68 – 1.56 (m, 5H), 1.48 – 1.37 (m, 4H), 0.95 (dd, *J* = 10.6 and 6.0 Hz, 6H). <sup>13</sup>C NMR (125 MHz, a mixture of CDCl<sub>3</sub>/CD<sub>3</sub>OD)  $\delta$  173.37, 172.60, 137.97, 129.06, 128.43, 126.41, 77.58, 72.05, 71.07, 70.23, 69.83, 69.69, 69.29, 54.66, 51.27, 44.76, 40.84, 39.02, 32.26, 29.09, 26.41, 25.09, 24.60, 22.60, 21.39. HRMS (ESI) *m/z*: calcd for C<sub>28</sub>H<sub>49</sub>ClN<sub>3</sub>O<sub>6</sub><sup>+</sup>, 558.3304; found 558.3321.

**(*S*)-2-((2*S*,3*R*)-3-Amino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (1b)**

The title compound was prepared from **6b** (39.7 mg, 56.5  $\mu$ mol) according to the procedure described for **1a**. Yield: 35.2 mg (100%). Colorless amorphous solid. <sup>1</sup>H

NMR (500 MHz, a mixture of CDCl<sub>3</sub>/CD<sub>3</sub>OD)  $\delta$  7.33 – 7.24 (m, 5H), 4.44 (s, 1H), 3.98 (s, 1H), 3.661 – 3.36 (m, 21H), 2.81 (dq,  $J$  = 134.6, 6.9 Hz, 2H), 1.78 (t,  $J$  = 7.4 Hz, 2H), 1.63 – 1.59 (m, 5H), 1.49 – 1.43 (m, 2H), 1.41 – 1.35 (m, 2H), 0.95 (dd,  $J$  = 10.0, 4.9 Hz, 6H). <sup>13</sup>C NMR (125 MHz, a mixture of CDCl<sub>3</sub>/CD<sub>3</sub>OD)  $\delta$  173.44, 172.62, 138.10, 128.99, 128.35, 126.29, 72.21, 70.99, 70.19, 70.16, 70.12, 69.77, 69.68, 69.24, 54.61, 51.17, 44.68, 40.81, 39.10, 38.98, 32.22, 29.04, 26.35, 25.05, 24.55, 22.53, 21.30. HRMS (ESI)  $m/z$ : calcd for C<sub>30</sub>H<sub>53</sub>ClN<sub>3</sub>O<sub>7</sub><sup>+</sup>, 602.3567; found 602.3554.

**(*S*)-2-((2*S*,3*R*)-3-Amino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide (1c)**

The title compound was prepared from **6c** (7.8 mg, 10.5  $\mu$ mol) according to the procedure described for **1a**. Yield: 3.7 mg (54%). Colorless amorphous solid. <sup>1</sup>H NMR (500 MHz, a mixture of CDCl<sub>3</sub>/CD<sub>3</sub>OD)  $\delta$  7.34 – 7.22 (m, 5H), 4.46 (t,  $J$  = 7.2 Hz, 1H), 3.97 (d,  $J$  = 2.9 Hz, 1H), 3.68 – 3.54 (m, 20H), 3.50 (t,  $J$  = 6.6 Hz, 2H), 3.42 – 3.36 (m, 3H), 2.81 (dq,  $J$  = 121.6, 6.9 Hz, 2H), 1.82 – 1.76 (m, 2H), 1.69 – 1.59 (m, 5H), 1.52 – 1.46 (m, 2H), 1.44 – 1.339 (m, 2H), 0.98 (dd,  $J$  = 10.6 and 6.0 Hz, 6H). <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD)  $\delta$  174.88, 172.62, 139.10, 130.45, 129.80, 127.86, 72.17, 71.58, 71.55, 71.53, 71.24, 71.18, 70.46, 56.55, 53.15, 45.71, 42.11, 40.46, 40.41, 39.53, 33.77, 30.55,

27.73, 26.51, 26.03, 23.37, 22.22. HRMS (ESI)  $m/z$ : calcd for  $C_{32}H_{57}ClN_3O_8^+$ , 646.3829; found 646.3850.

**(*S*)-2-((2*S*,3*R*)-3-Amino-2-hydroxy-4-phenylbutanamido)-*N*-(2-(2-(2-(2-(2-(6-chlorohexyloxy)ethoxy)ethoxy)ethoxy)ethoxy)ethyl)-4-methylpentanamide**  
**(1d)**

The title compound was prepared from **6b** (9.4 mg, 11.9  $\mu$ mol) according to the procedure described for **1a**. Yield: 5.3 mg (65%). Colorless amorphous solid.  $^1H$  NMR (500 MHz, a mixture of  $CDCl_3/CD_3OD$ )  $\delta$  7.33 – 7.21 (m, 5H), 4.45 (t,  $J$  = 7.2 Hz, 1H), 3.97 (d,  $J$  = 2.9 Hz, 1H), 3.71 – 3.53 (m, 24H), 3.49 (t,  $J$  = 6.6 Hz, 2H), 3.40 – 3.36 (m, 3H), 2.80 (dq,  $J$  = 125.9, 6.9 Hz, 2H), 1.81 – 1.75 (m, 2H), 1.65 – 1.58 (m, 5H), 1.49 – 1.44 (m, 2H), 1.42 – 1.37 (m, 2H), 0.96 (dd,  $J$  = 10.9 and 6.3 Hz, 6H).  $^{13}C$  NMR (125 MHz,  $CD_3OD$ )  $\delta$  175.18, 174.64, 139.62, 130.44, 129.72, 127.70, 73.11, 72.16, 71.56, 71.54, 71.25, 71.19, 70.48, 56.60, 53.07, 45.71, 42.14, 40.45, 40.42, 40.18, 33.77, 30.56, 27.74, 26.51, 26.04, 23.39, 22.20. HRMS (ESI)  $m/z$ : calcd for  $C_{34}H_{61}ClN_3O_9^+$ , 690.4091; found 690.4090.

## **1.2. Biological assay**

### **Cell culture condition and transfection.**

Human embryonic kidney HEK293 cells were cultured in D-MEM containing 5% heat-inactivated fetal bovine serum (FBS), and penicillin and streptomycin mixture at 37 °C in a humidified atmosphere of 5% CO<sub>2</sub> in air. Breast cancer cell line MCF-7 cells were cultured in D-MEM containing 10% heat-inactivated FBS, and penicillin and streptomycin mixture at 37 °C in a humidified atmosphere of 5% CO<sub>2</sub> in air.

HEK293 cells stably expressing HaloTag-CREB1 were established by co-transfection with HaloTag 7-CREB1 cDNA (Kazusa DNA Res. Inst.) and mRFP cDNA (OriGene Technologies, Inc.: for selection) using Lipofectamine LTX reagent and PLUS reagent (Invitrogen), and G418 (Nacalai tesque) selection. MCF-7 cells were transiently transfected with HaloTag 7-c-jun cDNA (Kazusa DNA Res. Inst.) using Lipofectamine LTX reagent and PLUS reagent according to the manufacturer's instructions. Four hours after transfection, indicated compounds were treated for 21 h.

### **Western blotting.**

Cells were washed with PBS, lysed in SDS lysis buffer (1% SDS, 10 mM EDTA and 50 mM Tris, pH 8.1) and boiled for 5 min. Protein concentrations were determined

using bicinchoninic acid (BCA) protein assay and normalized by total protein concentration in each lysate. After boiling for 5 min with Laemmli buffer, each lysate was resolved by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) with SuperSep<sup>TM</sup> Ace 10-20% (Wako Pure Chemical Industries) and transferred onto PVDF membrane. After blocking with TBS-T (20 mM Tris, 137 mM NaCl, 0.1% Tween 20, pH 7.5) containing 5% skim milk, the transblotted membrane was probed with anti-HaloTag rabbit polyclonal antibody (Promega, 1:1000), anti-lamin antibody (Santa Cruz Biotechnology, Inc., 1:500), anti- $\beta$ -tubulin antibody (Boehringer Mannheim, 1:200), anti- $\beta$ -actin antibody-horseradish peroxidase (HRP) conjugates (Santa Cruz Biotechnology, Inc., 1:1000), anti-mouse IgG-HRP conjugates (Millipore, 1:1000), and anti-rabbit IgG-HRP conjugates (Amerham, 1:2000) in Can-Get-Signal solution (Toyobo). After probing, the membrane was washed twice more with TBS-T. The immunoblots were visualized by enhanced chemiluminescence with Immobilon<sup>TM</sup> Western Chemiluminescent HRP Substrate (Millipore).

### **Nuclear and cytoplasmic protein extraction**

HEK293 cells were harvested with trypsin-EDTA and the cytoplasmic and nuclear fractions were extracted using NE-PER Nuclear and Cytoplasmic Extraction Reagent

kit (Thermo Scientific) according to the manufacturer's instructions.

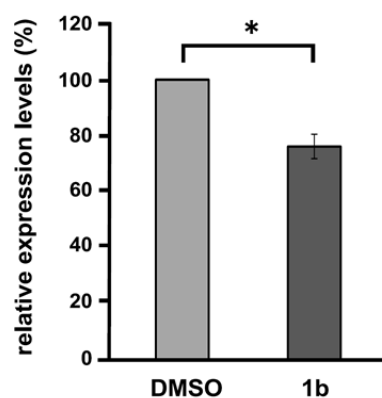
### **Fluorescence microscopic analysis**

HaloTag-fused proteins expressed in HEK293 cells or MCF-7 cells on glass-base dishes were labeled with HaloTag Oregon Green Ligand (Promega) according to the manufacturer's instructions, fixed with 10% formalin-PBS containing 0.4 µg/mL Hoechst 33342 (ICN Biomedicals) at room temperature for 30 min, and washed with PBS containing 0.05% Tween 20. Images were acquired using an IX70 inverted fluorescence microscope (Olympus).

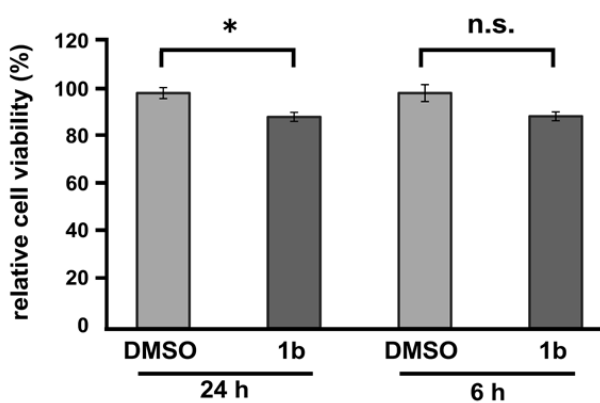
### **WST-1 cell viability assay**

Toxicity of compound **1b** was measured using Cell Counting Kit (Dojindo) according to the manufacturer's instructions.

## 2. Supplemental Figure

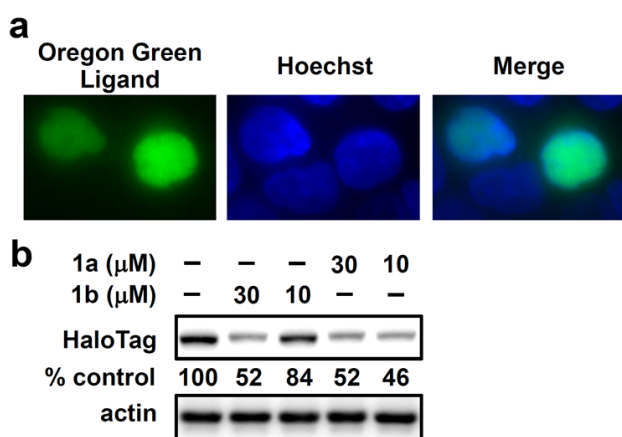


**Figure S1.** 6 h treatment of compound **1b** at 10  $\mu$ M reduced significantly HaloTag-CREB1 levels in HEK293 cells stably expressing HaloTag-CREB1. Signal intensities compared using an unpaired, two-sided Student's *t*-test. The *P*-value is indicated by an asterisk (\**P*<0.05). Error bars represent standard errors. Each assay was carried out individually seven times.



**Figure S2.** Compound **1b** showed low toxicity in HEK293 cells. WST-1 cell viability assay was performed after treatment for the indicated time with compound **1b** at 10  $\mu$ M.

Signal intensities were compared using an unpaired, two-sided Student's *t*-test. The *P*-value is indicated by an asterisk (\**P*<0.05). n.s. stands for not significant. Error bars represent standard errors. Each assay was carried out once in triplicate.

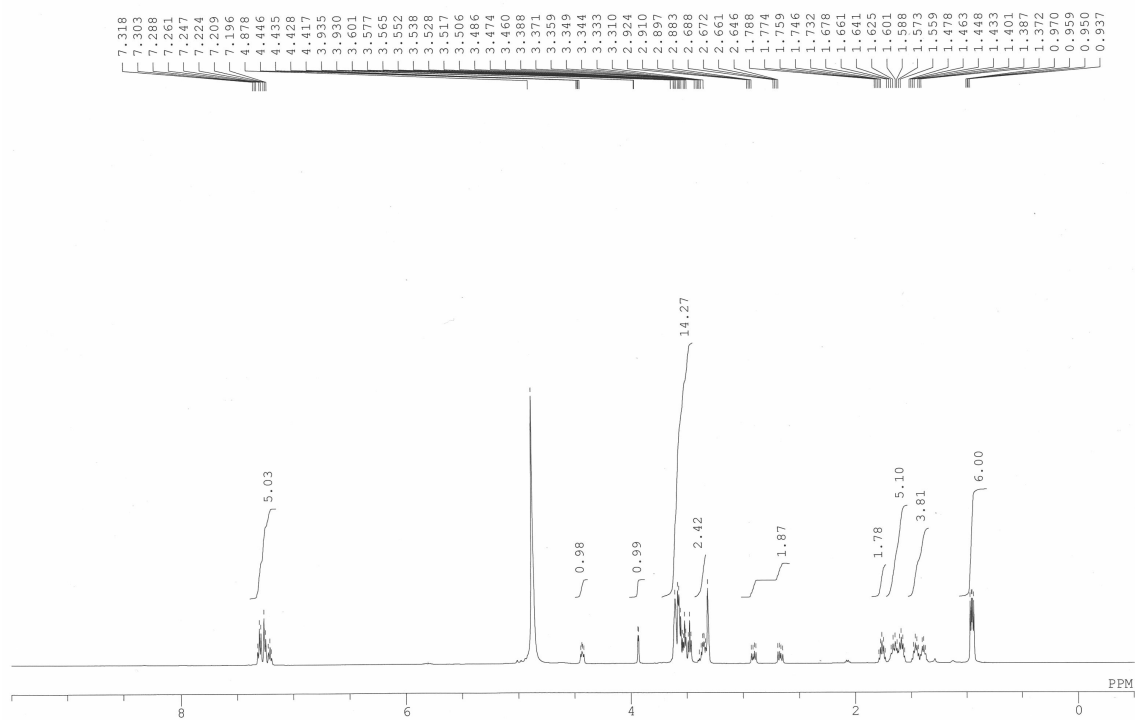


**Figure S3.** HaloTag-c-jun localized in the nucleus was degraded upon addition of compound **1a** or **1b** to MCF-7 cells transiently expressing HaloTag-c-jun. (a) Fluorescence-microscopic analysis of cellular localization of HaloTag-c-jun in MCF-7 cells transiently expressing HaloTag-c-jun. Left picture: HaloTag-c-jun stained with HaloTag Oregon Green Ligand. Middle picture: cell nuclei stained with Hoechst. Right picture: merged image. (b) Western blot analysis was performed after treatment for 21 h with the indicated concentration of compound **1a** or **1b**.

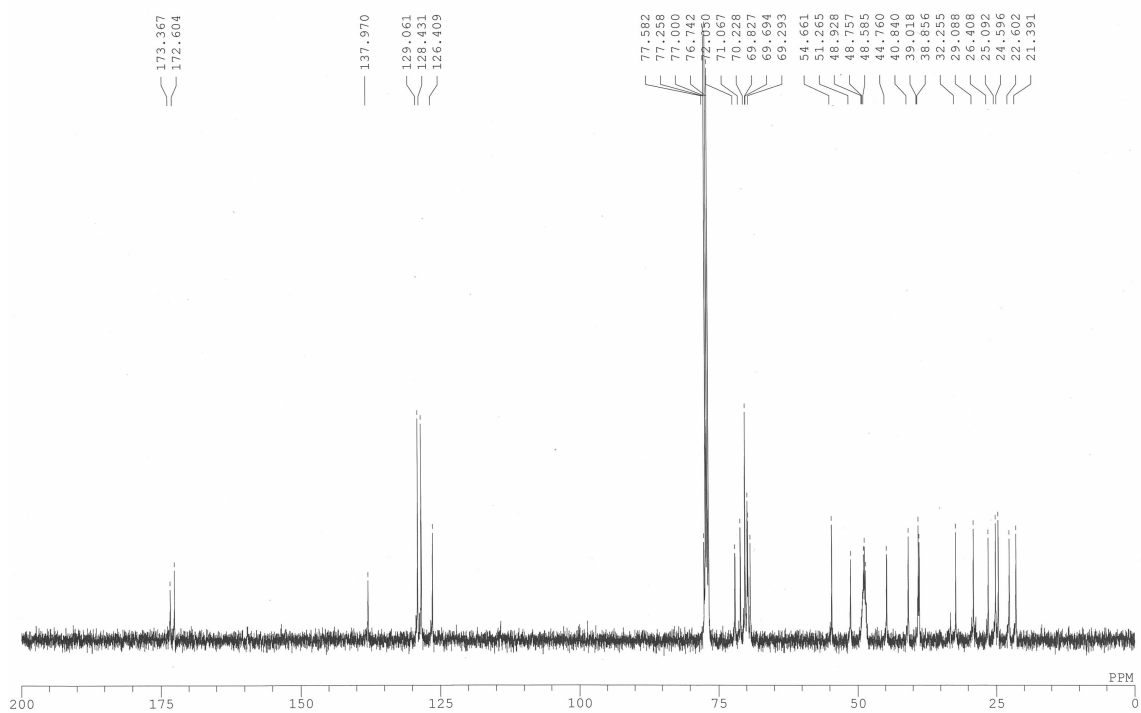


### 3. NMR Spectra

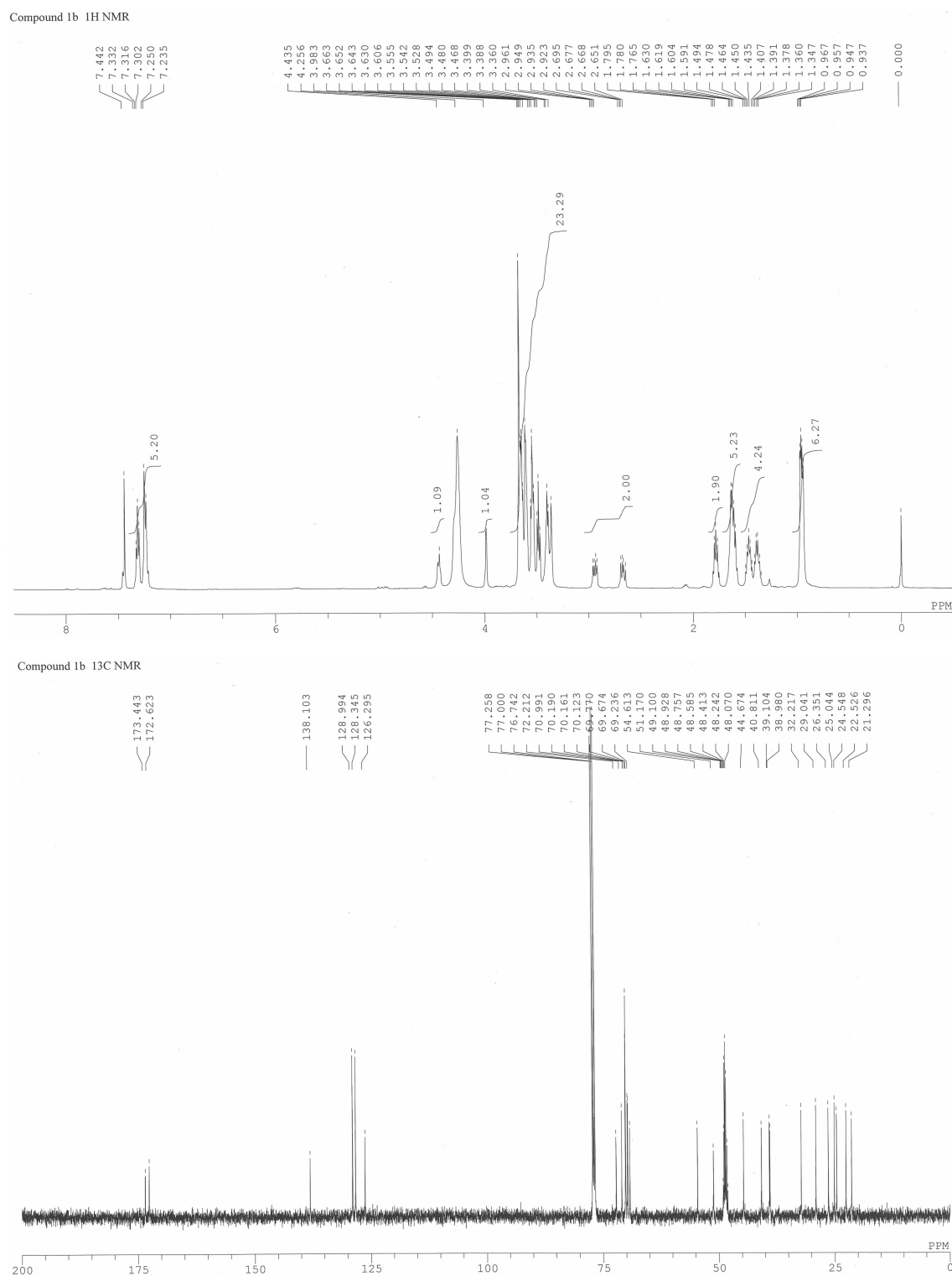
Compound 1a <sup>1</sup>H NMR



Compound 1a <sup>13</sup>C NMR

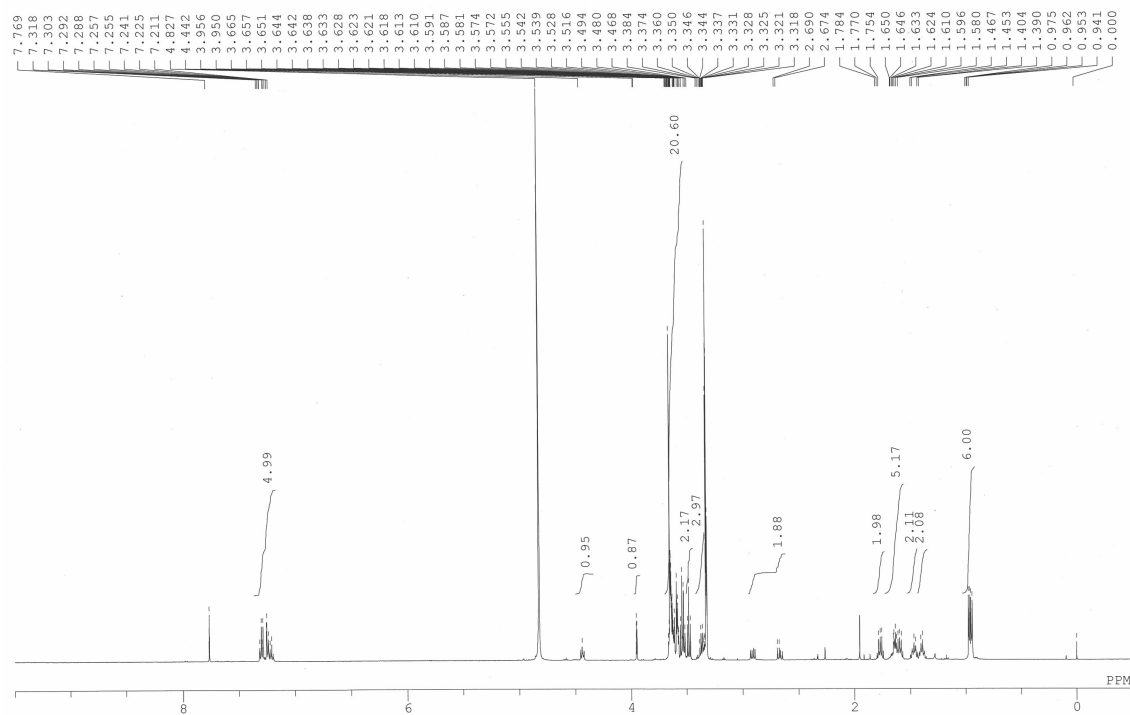


**Figure S4.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **1a**.



**Figure S5.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of **1b**.

Compound 1c <sup>1</sup>H NMR



Compound 1c <sup>13</sup>C NMR

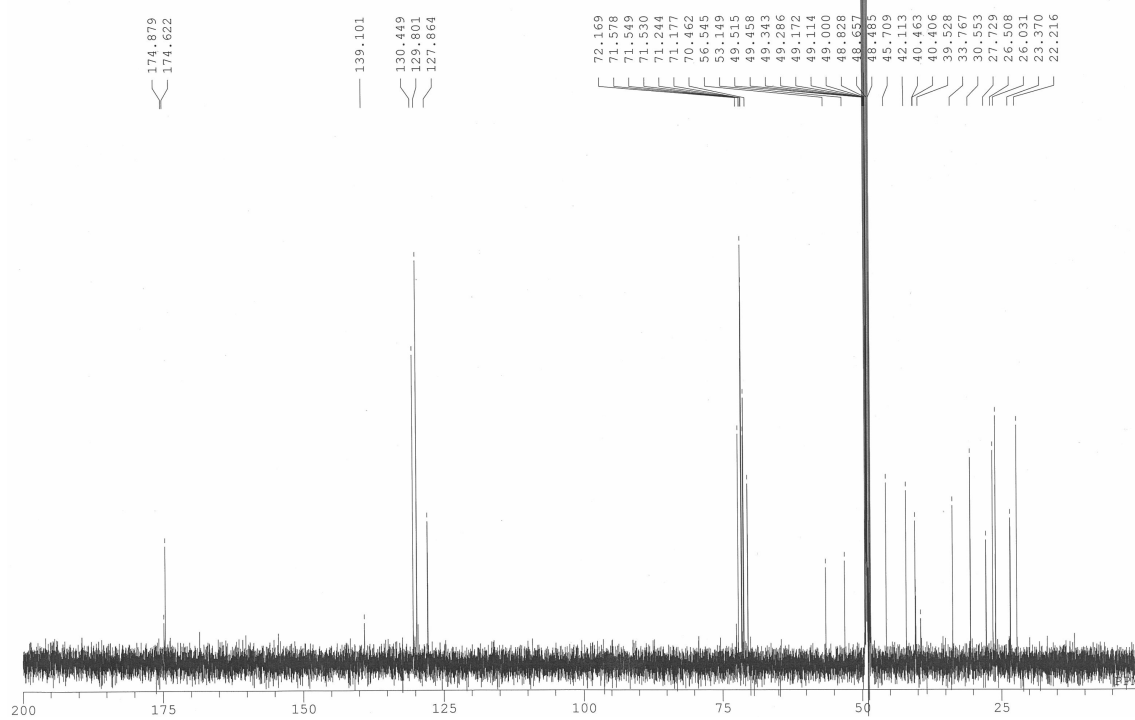


Figure S6. <sup>1</sup>H and <sup>13</sup>C NMR spectra of 1c.

Chemical shifts (ppm): 7.516, 7.515, 7.514, 7.513, 7.512, 7.511, 7.510, 7.509, 7.508, 7.507, 7.506, 7.505, 7.504, 7.503, 7.502, 7.501, 7.500, 7.499, 7.498, 7.497, 7.496, 7.495, 7.494, 7.493, 7.492, 7.491, 7.490, 7.489, 7.488, 7.487, 7.486, 7.485, 7.484, 7.483, 7.482, 7.481, 7.480, 7.479, 7.478, 7.477, 7.476, 7.475, 7.474, 7.473, 7.472, 7.471, 7.470, 7.469, 7.468, 7.467, 7.466, 7.465, 7.464, 7.463, 7.462, 7.461, 7.460, 7.459, 7.458, 7.457, 7.456, 7.455, 7.454, 7.453, 7.452, 7.451, 7.450, 7.449, 7.448, 7.447, 7.446, 7.445, 7.444, 7.443, 7.442, 7.441, 7.440, 7.439, 7.438, 7.437, 7.436, 7.435, 7.434, 7.433, 7.432, 7.431, 7.430, 7.429, 7.428, 7.427, 7.426, 7.425, 7.424, 7.423, 7.422, 7.421, 7.420, 7.419, 7.418, 7.417, 7.416, 7.415, 7.414, 7.413, 7.412, 7.411, 7.410, 7.409, 7.408, 7.407, 7.406, 7.405, 7.404, 7.403, 7.402, 7.401, 7.400, 7.399, 7.398, 7.397, 7.396, 7.395, 7.394, 7.393, 7.392, 7.391, 7.390, 7.389, 7.388, 7.387, 7.386, 7.385, 7.384, 7.383, 7.382, 7.381, 7.380, 7.379, 7.378, 7.377, 7.376, 7.375, 7.374, 7.373, 7.372, 7.371, 7.370, 7.369, 7.368, 7.367, 7.366, 7.365, 7.364, 7.363, 7.362, 7.361, 7.360, 7.359, 7.358, 7.357, 7.356, 7.355, 7.354, 7.353, 7.352, 7.351, 7.350, 7.349, 7.348, 7.347, 7.346, 7.345, 7.344, 7.343, 7.342, 7.341, 7.340, 7.339, 7.338, 7.337, 7.336, 7.335, 7.334, 7.333, 7.332, 7.331, 7.330, 7.329, 7.328, 7.327, 7.326, 7.325, 7.324, 7.323, 7.322, 7.321, 7.320, 7.319, 7.318, 7.317, 7.316, 7.315, 7.314, 7.313, 7.312, 7.311, 7.310, 7.309, 7.308, 7.307, 7.306, 7.305, 7.304, 7.303, 7.302, 7.301, 7.300, 7.299, 7.298, 7.297, 7.296, 7.295, 7.294, 7.293, 7.292, 7.291, 7.290, 7.289, 7.288, 7.287, 7.286, 7.285, 7.284, 7.283, 7.282, 7.281, 7.280, 7.279, 7.278, 7.277, 7.276, 7.275, 7.274, 7.273, 7.272, 7.271, 7.270, 7.269, 7.268, 7.267, 7.266, 7.265, 7.264, 7.263, 7.262, 7.261, 7.260, 7.259, 7.258, 7.257, 7.256, 7.255, 7.254, 7.253, 7.252, 7.251, 7.250, 7.249, 7.248, 7.247, 7.246, 7.245, 7.244, 7.243, 7.242, 7.241, 7.240, 7.239, 7.238, 7.237, 7.236, 7.235, 7.234, 7.233, 7.232, 7.231, 7.230, 7.229, 7.228, 7.227, 7.226, 7.225, 7.224, 7.223, 7.222, 7.221, 7.220, 7.219, 7.218, 7.217, 7.216, 7.215, 7.214, 7.213, 7.212, 7.211, 7.210, 7.209, 7.208, 7.207, 7.206, 7.205, 7.204, 7.203, 7.202, 7.201, 7.200, 7.199, 7.198, 7.197, 7.196, 7.195, 7.194, 7.193, 7.192, 7.191, 7.190, 7.189, 7.188, 7.187, 7.186, 7.185, 7.184, 7.183, 7.182, 7.181, 7.180, 7.179, 7.178, 7.177, 7.176, 7.175, 7.174, 7.173, 7.172, 7.171, 7.170, 7.169, 7.168, 7.167, 7.166, 7.165, 7.164, 7.163, 7.162, 7.161, 7.160, 7.159, 7.158, 7.157, 7.156, 7.155, 7.154, 7.153, 7.152, 7.151, 7.150, 7.149, 7.148, 7.147, 7.146, 7.145, 7.144, 7.143, 7.142, 7.141, 7.140, 7.139, 7.138, 7.137, 7.136, 7.135, 7.134, 7.133, 7.132, 7.131, 7.130, 7.129, 7.128, 7.127, 7.126, 7.125, 7.124, 7.123, 7.122, 7.121, 7.120, 7.119, 7.118, 7.117, 7.116, 7.115, 7.114, 7.113, 7.112, 7.111, 7.110, 7.109, 7.108, 7.107, 7.106, 7.105, 7.104, 7.103, 7.102, 7.101, 7.100, 7.099, 7.098, 7.097, 7.096, 7.095, 7.094, 7.093, 7.092, 7.091, 7.090, 7.089, 7.088, 7.087, 7.086, 7.085, 7.084, 7.083, 7.082, 7.081, 7.080, 7.079, 7.078, 7.077, 7.076, 7.075, 7.074, 7.073, 7.072, 7.071, 7.070, 7.069, 7.068, 7.067, 7.066, 7.065, 7.064, 7.063, 7.062, 7.061, 7.060, 7.059, 7.058, 7.057, 7.056, 7.055, 7.054, 7.053, 7.052, 7.051, 7.050, 7.049, 7.048, 7.047, 7.046, 7.045, 7.044, 7.043, 7.042, 7.041, 7.040, 7.039, 7.038, 7.037, 7.036, 7.035, 7.034, 7.033, 7.032, 7.031, 7.030, 7.029, 7.028, 7.027, 7.026, 7.025, 7.024, 7.023, 7.022, 7.021, 7.020, 7.019, 7.018, 7.017, 7.016, 7.015, 7.014, 7.013, 7.012, 7.011, 7.010, 7.009, 7.008, 7.007, 7.006, 7.005, 7.004, 7.003, 7.002, 7.001, 7.000.

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