Supplementary Materials

Small-molecule inhibitor of AF9/ENL-DOT1L/AF4/AFF4 interactions suppresses malignant gene expression and tumor growth

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Figure S1. Interactions between the AHD domain of AF9/ENL and AF4/AFF4/DOT1L. (A) Sequence alignment of the AHD domains of AF9 and ENL, showing 82% identity and 89% similarity; (B) Sequence alignment of AF4, AFF4 and DOT1L peptide with a consensus sequence of LxVxIxLxxL/V, which bind to AF9/ENL AHD; (C) NMR structure (PDB: 2MV7) of the AF9 AHD-DOT1L complex, with AF9 AHD shown as an electrostatic surface and the consensus interacting residues of DOT1L as ball and stick models.
Figure S2. Dose-responsive curves of FP assays from which the $K_d$ values between AF9/ENL and (A) DOT1L peptide; (B) AF4 peptide; and (C) AFF4 peptide were determined.
Figure S3. Compound 1 did not significantly inhibit the enzyme activities of DOT1L (the left two columns), LSD1, and p300 histone acetyltransferase at 30 or 100 μM, using our previous reported methods [Ref. 36, 37, and 44].
Figure S4. The cytoplasmic protein levels after treatment with Cpd-1 for 3 days. (A) In contrast to the protein levels in the nucleus, Cpd-1 did not significantly reduce the cytoplasmic levels of H3K79me1 and me2, ENL and AFF4 in Molm-13 cells; (B) Cpd-1 did not significantly reduce the cytoplasmic protein levels of H3K79me1 and me2, ENL and AFF4 in MV4;11 cells, except for ENL at 15 µM.
**Figure S5.** Treatment with Cpd-1 (5 μM for 4 days) did not reduce the H3K79-Me2 level in a non-transcribed DNA region (Ref. 32) in Molm-13 cells, presumably because SEC is not recruited there. In contrast, DOT1L inhibitor EPZ4777 decreased H3K79-Me2 in this DNA region.
Figure S6. Dose-responsive curves for the activities of compound 1 (7-day incubation) against proliferation of cancer cell lines.
Figure S7. Time-dependent antiproliferative activity of compound 1 against Molm-13 cells, showing at 10 μM (~2x EC₅₀) it did not significantly inhibit the cell proliferation on Day-2 or 3, but showed >90% inhibition on Day-5. At 15 μM (~3x EC₅₀) it had more potent antiproliferative activity.
Figure S8. Compound I induced significant apoptosis of Molm-13 leukemia cells at 10 and 15 µM (5-day incubation), as compared to the control. 5 µM of I did not cause significant apoptosis. The upper right (Q2) number in each figure refers to the proportion of propidium iodide-positive, apoptosed cells and the lower right (Q3) number refers to that of annexin-V-positive cells (early apoptosis).
**Figure S9.** MV4;11 tumor growth curves for individual mice for (A) the cohort-1 and (B) cohort-2 experiments, with control mice shown in black and treated mice in blue.
Figure S10. Treatment with Cpd-1 did not significantly affect the weights of experimental mice, showing no obvious toxicities.
Compound 1 is likely a non-competitive inhibitor of the PPIs between AF9/ENL and AF4/AFF4/DOT1L. All data are from Table 1. (A) Plots of IC$_{50}$ vs. 1/$K_d$ for non-biotinylated DOT1L peptide and Cpd-1 inhibiting AF9 AHD. DOT1L-peptide is a competitive inhibitor of AF9 AHD, with its IC$_{50}$ values against the AF9-DOT1L, -AF4 and -AFF4 interaction proportionally increase with the decreasing $K_d$ values of these PPIs, following the Cheng-Prusoff equation $IC_{50} = K_i + K_i \times [L]/K_d$, where $K_i$ is the inhibition constant of the inhibitor and [L] is the concentration of the biotinylated peptide (40 nM). The IC$_{50}$ values of compound 1 do not increase with the decreasing $K_d$ values of the PPIs, showing a non-competitive mode of inhibition; (B) Plots of IC$_{50}$ vs. 1/$K_d$ for non-biotinylated DOT1L peptide and Cpd-1 inhibiting ENL AHD. Similarly, competitive inhibitor DOT1L’s IC$_{50}$ values increase with the decreasing $K_d$ values of the ENL-AFF4 and -AF4 interactions, but not those of compound 1.
Table S1. Cytotoxicity EC_{50} (µM) of compounds 1, 3 (7-day incubation) and EPZ4777 (14-day).

|       | Cpd-1   | Cpd-3   | EPZ4777 |
|-------|---------|---------|---------|
| MV4;11| 4.7 ± 0.4| >50     | 1.1 ± 0.3|
| Molm-13 | 4.9 ± 0.1| >50     | 1.2 ± 0.2|
| THP-1 | 11.4 ± 0.6| >50     | 3.4 (Ref 25) |
| HL60  | 7.3 ± 0.1| >50     | >50 (Ref 25) |
| Kasumi-1 | 8.9 ± 0.3| >50     | 33 (Ref 25) |
| Jurkat | 9.7 ± 0.3| >50     | >50 (Ref 25) |
| RPMI-8226 | 3.3 ± 0.1| >50     | >50     |
| U266  | 7.9 ± 0.4| >50     | >50     |
| MCF-7 | 19.8 ± 0.3| >50     | >50     |
| MDA-MB-231 | 13.5 ± 0.2| >50     | >50     |
| Panc-1 | 15.1 ± 0.2| >50     | >50     |
| Panc-28 | 23.8 ± 0.2| >50     | >50     |
Synthesis of inhibitors

All chemicals for synthesis were purchased from Alfa Aesar (Ward Hill, MA), Aldrich (Milwaukee, WI) or Combi-Blocks (San Diego, CA). The identity of the synthesized compounds was characterized by \(^1\)H and \(^{13}\)C NMR on a Varian (Palo Alto, CA) 400-MR spectrometer and mass spectrometer (Shimadzu LCMS-2020). The identity of compound 1 was confirmed with high resolution mass spectra (HRMS) using an Agilent 6550 iFunnel quadrupole-time-of-flight (Q-TOF) mass spectrometer with electrospray ionization (ESI). The purities of the final compounds were determined to be >95% with a Shimadzu Prominance HPLC using a Zorbax C18 (or C8) column (4.6 x 250 mm) monitored by UV at 254 nm. The synthetic methods for compounds 1-9 are shown in Schemes 1, 2 and 3.

Scheme 1. General Methods for Synthesizing Compounds 1, 7, 8 and 9\(^a\).

\(^a\)Reagents and conditions: (i) Benzonitrile, NaH, DMSO, 0 °C to rt, 12 h, 76%; (ii) Ethyl bromopyruvate, CBr\(_4\), MeCN, 90 °C, 12 h, 50%; (iii) NaOH, THF-H\(_2\)O(v/v, 3/1), reflux, 5 h; (iv) R\(^1\)NH\(_2\), HATU, DIPEA, DMF, 12 h, 60-66% for 2 steps; (v) HCl (4 N in p-dioxane), CH\(_2\)Cl\(_2\), rt, 5 h, 90-95%.

To a solution of 4-tert-butylaniline (10, 7.5 g, 50 mmol) in DMSO (50 mL) was slowly added NaH (2.4 g, 60 mmol, 60% dispersion in mineral oil) at 0 °C. After stirring at 0 °C for 1 h, benzonitrile (5.69 g, 55 mmol) in DMSO (30 mL) was added. The resulting mixture was warmed to room temperature and stirred for another 12 h. The reaction was quenched with icy water and extracted with ethyl acetate (3 \(\times\) 100 mL) and the combined organic
layers were washed with water and brine and dried over Na₂SO₄. The volatiles were removed in vacuo to afford a brown solid, which was purified by recrystallization (hexanes/ethyl acetate) to afford N-(4-(tert-butyl)phenyl)benzimidamide (11, 9.62 g, 76%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, J = 7.0 Hz, 2H), 7.49 – 7.39 (m, 3H), 7.37 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.3 Hz, 2H), 4.91 (s, 2H), 1.34 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 155.1, 146.7, 145.8, 136.0, 130.5, 128.6, 126.9, 126.4, 121.2, 34.4, 31.6.

To a solution of compound 11 (8 g, 62 mmol) in acetonitrile (60 mL) was added ethyl bromopyruvate (4.2 g, 68 mmol) and tetrabromomethane (8.29 g, 25.0 mmol). After stirring at room temperature for 12 h, the solvent was removed under vacuum. The mixture was extracted with ethyl acetate (3 × 100 mL) and the combined organic layers were washed with water and brine and dried over Na₂SO₄. The volatiles were removed in vacuo to afford a crude oil, which was purified by column chromatography (silica gel, hexanes: ethyl acetate from 5:1 to 3:1) to afford ethyl 1-(4-(tert-butyl)phenyl)-2-phenyl-1H-imidazole-4-carboxylate 12 (2.92 g, 50%) as colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.72 (s, 1H), 7.32 (t, J = 8.3 Hz, 4H), 7.19 – 7.10 (m, 3H), 7.03 (d, J = 8.4 Hz, 2H), 4.31 (dd, J = 14.2, 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H), 1.23 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 162.8, 151.9, 147.5, 134.8, 133.1, 129.1, 128.84, 128.79, 128.4, 127.9, 126.4, 125.0, 60.4, 34.6, 31.1, 14.3.

To a solution of compound 12 (2.2 g, 6.3 mmol) in THF/H₂O (9/3 mL) was added sodium hydroxide (632 mg, 15.8 mmol). The resulting mixture was refluxed for 5 h. The solvent was removed under vacuum and acidified with 3N HCl, extracted with ethyl acetate (3 × 50 mL) and the combined organic layers were washed with water and brine and dried over Na₂SO₄. The volatiles were removed in vacuo to afford a crude product, which was used for the next step without further purification.

To a solution of the crude acid and 4-amino-1-Boc-piperidine (1.51 g, 7.56 mmol) in DMF (30 mL) was added N, N-diisopropylethylamine (2.19 mL, 12.6 mmol) and 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU, 3.59 g, 9.45 mmol). The mixture was stirred for 12 h before it was quenched with H₂O. The mixture was extracted with ethyl acetate (3 × 80 mL) and the combined organic layers were washed with water and brine and dried over Na₂SO₄. The volatiles were removed in vacuo to
afford a crude oil, which was purified by column chromatography (silica gel, hexanes: ethyl acetate from 2:1 to 1:1) to afford 13 (2.1 g, 66% for 2 steps) as colorless oil. 13a (Intermediate of compound 1): 1H NMR (400 MHz, CDCl₃) δ 7.78 (s, 1H), 7.45 – 7.38 (m, 4H), 7.35 – 7.28 (m, 3H), 7.19 (d, J = 8.3 Hz, 1H), 7.13 (d, J = 8.5 Hz, 2H), 4.21 – 4.06 (m, 3H), 2.99 – 2.89 (m, 2H), 2.06 – 1.99 (m, 2H), 1.54 – 1.44 (m, 11H), 1.36 (s, 9H); 13C NMR (100 MHz, CDCl₃) δ 161.7, 154.5, 152.0, 146.3, 136.6, 135.2, 129.7, 128.7, 128.6, 128.1, 126.3, 125.2, 125.01, 124.98, 79.2, 46.2, 42.7, 34.6, 32.0, 31.1, 28.3.

Compound 7: 1-(4-((Tert-butyl)phenyl)-2-phenyl-N-(pyridin-4-yl)-1H-imidazole-4-carboxamide

1H NMR (400 MHz, DMSO-d₆) δ 11.75 (s, 1H), 8.76 (d, J = 7.0 Hz, 2H), 8.70 (s, 1H), 8.53 (d, J = 7.1 Hz, 2H), 7.51 (d, J = 8.6 Hz, 2H), 7.46 – 7.35 (m, 5H), 7.31 (d, J = 8.5 Hz, 2H), 1.29 (s, 9H); 13C NMR (100 MHz, DMSO-d₆) δ 161.5, 153.4, 151.8, 146.8, 141.8, 134.3, 133.8, 129.6, 129.3, 129.0, 128.5, 126.4, 125.6, 115.1, 34.6, 31.0; MS (ESI) [M+H]+ 397.2.

Compound 9: 1-(4-((Tert-butyl)phenyl)-N-(4-chloro-3-fluorophenyl)-2-phenyl-1H-imidazole-4-carboxamide

1H NMR (400 MHz, CDCl₃) δ 9.13 (s, 1H), 7.95 (dd, J = 6.5, 2.5 Hz, 1H), 7.84 (s, 1H), 7.56 – 7.50 (m, 1H), 7.45 – 7.38 (m, 4H), 7.36 – 7.27 (m, 3H), 7.17 – 7.08 (m, 3H), 1.35 (s, 9H); 13C NMR (100 MHz, DMSO-d₆) δ 161.1, 154.8, 152.4, 151.8, 146.6, 136.6, 136.1, 135.2, 129.9, 129.5, 129.2, 128.7, 127.3, 126.8, 126.0, 122.0, 120.9, 120.9, 119.4, 119.2, 117.2, 117.0, 35.0, 31.4; MS (ESI) [M+H]+ 448.2.

To a solution of compound 13a (1.5 g, 2.98 mmol) in dichloromethane (20 mL) was added dropwise HCl (2.2 mL, 4 N in p-dioxane) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 5 h. The volatiles were removed in vacuo to afford an oil, which was triturated in diether ether and solidified to give the final product as a hydrochloric salt (1, 1.18 g, 90%) as a white powder.

Compound 1: 1-(4-((Tert-butyl)phenyl)-2-phenyl-N-(piperidin-4-yl)-1H-imidazole-4-carboxamide hydrochloride

1H NMR (400 MHz, DMSO-d₆) δ 9.43 (d, J = 8.9 Hz, 1H), 9.23 (d, J = 6.3 Hz, 1H), 9.10 (d, J = 8.7 Hz, 1H), 8.71 (s, 1H), 7.55 – 7.50 (m, 2H), 7.50 – 7.38 (m, 5H), 7.38 – 7.32 (m, 2H), 4.11 (s, 1H), 3.33 (d, J = 11.6 Hz,
Compound 8: 1-(4-(Tert-butyl)phenyl)-2-phenyl-N-(piperidin-4-ylmethyl)-1H-imidazole-4-carboxamide hydrochloride

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 9.01 (s, 1H), 8.70 (s, 2H), 8.21 (s, 1H), 7.50 (dd, $J = 8.5, 3.0$ Hz, 2H), 7.43 – 7.34 (m, 5H), 7.30 (dd, $J = 8.5, 2.7$ Hz, 2H), 3.27 – 3.18 (m, 4H), 2.81 (q, $J = 11.5$ Hz, 2H), 1.89 – 1.76 (m, 3H), 1.39 (dd, $J = 24.2, 12.5$ Hz, 2H), 1.29 (s, 9H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 160.5, 151.8, 145.6, 134.2, 133.7, 129.8, 129.1, 128.4, 127.4, 126.4, 125.6, 43.2, 42.7, 34.6, 33.8, 31.0, 26.2; MS (ESI) [M+H]$^+$ 417.3.

Scheme 2. Synthesis of compounds 2 and 3$^a$.

\[ \begin{align*}
\text{Scheme 2: Synthesis of compounds 2 and 3.} & \\
\text{Reagents and conditions: (i) Benzonitrile, NaH, DMSO, 0 °C to rt, 12 h, 77%; (ii) Ethyl bromopyruvate, CBr$_4$, MeCN, 90 °C, 12 h, 48%; (iii) NaOH, THF-H$_2$O(v/v, 3/1), reflux, 5 h; (iv) 4-Amino-1-Boc-piperidine, HATU, DIPEA, DMF, 5 h, 62%; (v) Arylboronic acid, Pd(PPh$_3$)$_4$, Na$_2$CO$_3$, p-dioxane-H$_2$O, 110 °C, 24 h, 82% and 76% for 18a and 18b, respectively; (vi) HCl (4 N in p-dioxane), CH$_2$Cl$_2$, rt, 3 h, 95% and 92% for 2 and 3, respectively.} \\
\end{align*} \]

Compounds 15, 16, and 17 were synthesized following the same procedure as that of compounds 11-13. Compound 17 (102 mg, 0.19 mmol), 4-tert-butylphenylboronic acid (42 mg, 0.24 mmol), tetrakis(triphenylphosphine)palladium (15 mg, 0.013 mmol), and sodium carbonate (40 mg, 0.38 mmol) in p-dioxane/H$_2$O (5/1, 6 mL) were placed in a sealed tube. The mixture was degassed and heated to 110 °C for 24 h.
The reaction was then cooled and quenched with brine (10 mL). The product was extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were washed with water and brine and dried over Na₂SO₄. The volatiles were removed in vacuo to give a crude oil, which was purified by column chromatography (silica gel, hexanes: ethyl acetate from 2:1 to 1:1) to afford the product 18a (90 mg, 82%) as a white foam.

To a solution of compound 18a (90 mg, 0.16 mmol) in dichloromethane (6 mL) was added dropwise HCl (0.2 mL, 4 N in p-dioxane) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 3 h. The volatiles were removed in vacuo to afford an oil, which was triturated in diether ether and solidified to give the final product 2 as a hydrochloric salt (white powder, 78 mg, 95%).

**Compound 2**: 1-(4′-(Tert-butyl)-[1,1′-biphenyl]-4-yl)-2-phenyl-N-(piperidin-4-yl)-1H-imidazole-4-carboxamide hydrochloride

^1H NMR (400 MHz, DMSO-d₆) δ 9.21 (d, J = 9.5 Hz, 1H), 8.98 (d, J = 8.5 Hz, 1H), 8.82 (d, J = 7.1 Hz, 1H), 8.46 (s, 1H), 7.78 (d, J = 8.1 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.52 – 7.42 (m, 7H), 7.40 (d, J = 7.2 Hz, 2H), 4.11 (s, 1H), 3.32 (d, J = 11.9 Hz, 2H), 3.01 (dd, J = 21.5, 11.4 Hz, 2H), 1.99 (d, J = 11.9 Hz, 2H), 1.89 (dd, J = 22.7, 11.2 Hz, 2H), 1.30 (s, 9H); ^13C NMR (100 MHz, DMSO-d₆) δ 159.2, 150.7, 145.7, 140.8, 135.6, 135.3, 132.4, 130.3, 129.4, 128.5, 127.5, 126.6, 126.6, 126.4, 126.1, 125.9, 44.0, 42.1, 34.3, 31.1, 28.1; MS (ESI) [M+H]^+ 479.3.

**Compound 3**: 1-(4-(1H-pyrazol-4-yl)phenyl)-2-phenyl-N-(piperidin-4-yl)-1H-imidazole-4-carboxamide hydrochloride

^1H NMR (400 MHz, DMSO-d₆) δ 9.12 (s, 1H), 8.94 (d, J = 8.6 Hz, 1H), 8.85 (s, 1H), 8.45 (s, 1H), 8.17 (s, 2H), 7.74 (d, J = 8.2 Hz, 2H), 7.48 – 7.35 (m, 7H), 4.16 – 4.03 (m, 1H), 3.32 (d, J = 11.9 Hz, 2H), 3.01 (dd, J = 21.1, 10.6 Hz, 2H), 1.98 (d, J = 11.7 Hz, 2H), 1.87 (dd, J = 21.3, 10.5 Hz, 2H); ^13C NMR (100 MHz, DMSO-d₆) δ 158.9, 145.6, 134.1, 133.7, 132.0, 131.4, 131.3, 131.3, 130.4, 129.4, 128.5, 126.5, 126.1, 125.9, 119.9, 44.0, 42.1, 28.1; MS (ESI) [M+H]^+ 413.2.
Scheme 3. General methods for synthesizing compounds 4, 5 and 6.

**Reagents and conditions:** (i) Alkyl-nitrile, AlCl₃, 120 °C, 2 h, 65-81%; (ii) Ethyl bromopyruvate, CBr₄, MeCN, 90 °C, 12 h, 35-57%; (iii) NaOH, THF-H₂O(v/v, 3/1), reflux, 5 h; (iv) 4-Amino-1-Boc-piperidine, HATU, DIPEA, DMF, 5 h, 62-69% for 2 steps; (v) HCl (4 N in p-dioxane), CH₂Cl₂, rt, 3h, 92-95%.

To a mixture of 4-tert-butylaniline 10 (3.0 g, 20.13 mmol) and acetonitrile (1.05 mL, 20.13 mmol) was added AlCl₃ (2.68 g, 20.13 mmol) in portions. The resulting slurry was stirred vigorously and heated at 120 °C for 2 h. After cooling to room temperature, the reaction was quenched with icy water, basified with sodium hydroxide (4 M solution), and extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with water and brine and dried over Na₂SO₄. The volatiles were removed *in vacuo* to give a residue, which was purified by recrystallization (hexanes/ethyl acetate) to afford 19 (3.1g, 81%) as a white solid. 

**Compound 4:** 1-(4-(Tert-butyl)phenyl)-2-cyclohexyl-N-(piperidin-4-yl)-1H-imidazole-4-carboxamide hydrochloride

**1H NMR** (400 MHz, DMSO-d₆) δ 9.50 (s, 1H), 9.32 (s, 1H), 9.00 (d, J = 8.0 Hz, 1H), 8.62 (s, 1H), 7.67 (d, J = 8.5 Hz, 2H), 7.54 (d, J = 8.5 Hz, 2H), 4.13 – 4.08 (m, 1H), 3.33 (d, J = 11.6 Hz, 2H), 2.99 (dd, J = 21.4, 11.6 Hz, 2H), 2.65 (t, J = 11.4 Hz, 1H), 1.98 (d, J = 11.1 Hz, 2H), 1.91 – 1.79 (m, 6H), 1.72 (d, J = 11.1 Hz, 2H), 1.61 (d, 2H), 1.43 (t, J = 7.5 Hz, 3H), 1.13 (s, 9H), 0.89 (d, J = 6.8 Hz, 3H).
$J = 8.8 \text{ Hz, 2H}$, 1.34 (s, 9H), 1.18 – 1.08 (m, 2H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 156.5, 153.3, 152.1, 132.0, 127.3, 126.9, 125.8, 125.4, 44.1, 41.7, 34.8, 34.7, 31.0, 30.1, 27.8, 25.2, 24.7; MS (ESI) [M+H]$^+$ 409.3.

**Compound 5**: 1-((4-((Tert-butyl)phenyl)-2-isopropyl-N-(piperidin-4-yl)-1H-imidazole-4-carboxamide hydrochloride

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 9.17 (s, 1H), 9.02 (s, 1H), 8.86 (s, 1H), 8.43 (s, 1H), 7.62 (d, $J = 6.6$ Hz, 2H), 7.50 (d, $J = 6.7$ Hz, 2H), 4.07 (s, 1H), 3.32 (s, 2H), 2.96 (s, 3H), 1.95 (d, $J = 12.8$ Hz, 2H), 1.87 – 1.76 (m, 2H), 1.34 – 1.20 (m, 13H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 157.3, 153.7, 153.6, 132.3, 128.1, 127.2, 126.1, 124.8, 44.2, 42.1, 35.0, 31.2, 28.4, 28.0, 25.7, 20.7; MS (ESI) [M+H]$^+$ 369.3.

**Compound 6**: 1-((4-((Tert-butyl)phenyl)-2-methyl-N-(piperidin-4-yl)-1H-imidazole-4-carboxamide hydrochloride

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.17 (s, 1H), 7.62 (d, $J = 8.7$ Hz, 2H), 7.49 (d, $J = 8.6$ Hz, 2H), 4.09 – 4.00 (m, 1H), 3.31 (d, $J = 12.9$ Hz, 2H), 2.99 (t, $J = 11.3$ Hz, 2H), 2.43 (s, 3H), 1.97 (d, $J = 12.5$ Hz, 2H), 1.78 – 1.67 (m, 2H), 1.31 (s, 9H); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ 158.3, 153.2, 146.4, 132.9, 127.2, 125.5, 124.0, 110.0, 44.3, 42.5, 35.1, 31.4, 28.3, 12.3; MS (ESI) [M+H]$^+$ 341.2.