Electronic Supporting Information

Design, synthesis and biological evaluation of benzimidazole-rhodanine conjugates as potent topoisomerase II inhibitors

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$^1$H NMR and 2D NOESY (DMSO-$d_6$) Spectrum of Compound 3a

Fig. S1. $^1$H NMR (upper) and 2D NOESY analysis of 3a. The protons on the aromatic ring (6-H, 7-H, and 8-H) are easily assigned on the basis of 2D NOESY relations.
Fig. S2. $^1$H NMR and 2D NOESY analysis of 3b. The protons on the aromatic ring (4-H, 5-H, 7-H, and 8-H) are easily assigned on the basis of 2D NOESY relations.
Chemistry

General method for the synthesis of 1a–1d

The mixture of a substituted benzene-1,2-diamine (10 mmol) and glycolic acid (30 mmol) in HCl (4 N, 30 mL) was heated to reflux at 100 °C for 6 h and the reaction was quenched with saturated aqueous sodium bicarbonate. The white solid were collected by filtration. They were used directly without further purification.

General method for the synthesis of 2a–2s, 3a–3f, and 4a–4g

The solution of a 1a–1d (1 mmol) in DMF (2 mL) were added the appropriate benzyl bromide (2 mmol) and K₂CO₃ (5 mmol), and the reaction mixture was stirred at room temperature for 8 h. It was then diluted with DCM (8 mL) and H₂O (8 mL). The organic layer
was separated, and the aqueous layer was extracted with DCM (8 mL × 2). The combined organic layers were dried over MgSO₄ and concentrated in vacuo to provide a crude product, which was purified by PTLC (DCM/MeOH = 100/5, v/v) to yield the title compound.

**(1-(4-Bromobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2a)**

1-Bromo-4-(bromomethyl) benzene and 1a were used as reactants to give 2a. While solid, Yield: 76%. ¹H NMR (400 MHz, CDCl₃) δ 7.69 (d, J = 7.9 Hz, 1H), 7.39 (d, J = 8.3 Hz, 2H), 7.26 – 7.19 (m, 2H), 7.16 (d, J = 7.7 Hz, 1H), 6.97 (d, J = 8.2 Hz, 2H), 5.41 (s, 2H), 4.86 (s, 2H).

**(1-(4-Bromo-2-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2b)**

4-Bromo-1-(bromomethyl)-2-fluorobenzene and 1a were used as reactants to give 2b. While solid. Yield: 83%. ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 7.7 Hz, 1H), 7.30 (d, J = 9.7 Hz, 1H), 7.26 – 7.15 (m, 3H), 7.10 (d, J = 8.2 Hz, 1H), 7.03 – 6.95 (m, 1H), 7.03 (d, J = 8.2 Hz, 2H), 5.45 (s, 2H), 4.91 (s, 2H).

**4-((2-(Hydroxymethyl)-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (2c)**

4-(Bromomethyl)benzonitrile and 1a were used as reactants to give 2c. While solid. Yield: 71%. ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, J = 7.7 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 7.3 Hz, 1H), 7.22 (d, J = 7.4 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 7.8 Hz, 1H), 5.55 (s, 2H), 4.89 (s, 2H).

**(1-(4-Nitrobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2d)**

1-(Bromomethyl)-4-nitrobenzene and 1a were used as reactants to give 2d. While solid. Yield: 66%. ¹H NMR (400 MHz, CDCl₃) δ 8.12 (d, J = 8.5 Hz, 2H), 7.70 (d, J = 7.7 Hz, 1H), 7.29 (d, J = 7.1 Hz, 1H), 7.27 – 7.21 (m, 3H), 7.12 (d, J = 7.8 Hz, 1H), 5.60 (s, 2H), 4.91 (s, 2H).
(1-(4-Fluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2e)

1-(Bromomethyl)-4-fluorobenzene and 1a were used as reactants to give 2e. While solid.
Yield: 87%. 1H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 7.8 Hz, 1H), 7.25–7.19 (m, 3H), 7.12–7.06 (m, 2H), 7.00–6.92 (m, 2H), 5.42 (s, 2H), 4.87 (s, 2H).

(1-(Benzy1-1H-benzo[d]imidazol-2-yl)methanol (2f)

(Bromomethyl)benzene and 1a were used as reactants to give 2f. While solid. Yield: 69%. 1H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 7.6 Hz, 1H), 7.32–7.22 (m, 6H), 7.13–7.07 (m, 2H), 5.45 (s, 2H), 4.87 (s, 2H).

(1-(4-Methylbenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2g)

1-(Bromomethyl)-4-methylbenzene and 1a were used as reactants to give 2g. While solid.
Yield: 73%. 1H NMR (400 MHz, CDCl₃) δ 7.72 (d, J = 7.6 Hz, 1H), 7.32–7.22 (m, 6H), 7.09 (d, J = 7.7 Hz, 2H), 6.99 (d, J = 7.7 Hz, 2H), 5.40 (s, 2H), 4.87 (s, 2H), 2.30 (s, 3H).

(1-(4-Chlorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2h)

1-(Bromomethyl)-4-chlorobenzene and 1a were used as reactants to give 2h. While solid.
Yield: 84%. 1H NMR (400 MHz, CDCl₃) δ 7.70 (d, J = 7.6 Hz, 1H), 7.29–7.25 (d, J = 8.2 Hz, 3H), 7.21 (d, J = 7.4 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.03 (d, J = 8.1 Hz, 2H), 5.43 (s, 2H), 4.87 (s, 2H).

(1-(4-(Trifluoromethyl)benzyl)-1H-benzo[d]imidazol-2-yl)methanol (2i)

1-(Bromomethyl)-4-(trifluoromethyl)benzene and 1a were used as reactants to give 2i. While solid. Yield: 86%. 1H NMR (400 MHz, CDCl₃) δ 7.71 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 7.2 Hz, 1H), 7.23 (d, 1H), 7.20 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 7.7 Hz, 1H), 5.54 (s, 2H), 4.90 (s, 2H).

(1-(2-Fluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2j)
1-(Bromomethyl)-2-fluorobenzene and 1a were used as reactants to give 2j. While solid. Yield: 77\%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.71 (d, $J$ = 7.3 Hz, 1H), 7.30 – 7.22 (m, 3H), 7.10 (d, $J$ = 9.2 Hz, 1H), 6.98 (d, $J$ = 7.4 Hz, 1H), 6.84 (d, $J$ = 7.4 Hz, 1H), 5.50 (s, 2H), 4.92 (s, 2H).

(I-(2,4-Difluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2k)

1-(Bromomethyl)-2,4-difluorobenzene and 1a were used as reactants to give 2k. While solid. Yield: 71\%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.70 (d, $J$ = 7.6 Hz, 1H), 7.26 – 7.16 (m, 3H), 6.90 – 6.82 (m, 2H), 6.70 (d, $J$ = 8.3 Hz, 1H), 5.46 (s, 2H), 4.92 (s, 2H).

(I-(3-Fluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2l)

1-(Bromomethyl)-3-fluorobenzene and 1a were used as reactants to give 2l. While solid. Yield: 84\%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, $J$ = 7.5 Hz, 1H), 7.26–7.18 (m, 4H), 6.97 (d, $J$ = 8.3 Hz, 1H), 6.89 (d, $J$ = 7.6 Hz, 1H), 6.82 (d, $J$ = 9.3 Hz, 1H), 5.46 (s, 2H), 4.88 (s, 2H), 4.37 (s, 1H).

(I-(3,4-Difluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2m)

4-(Bromomethyl)-1,2-difluorobenzene and 1a were used as reactants to give 2m. While solid. Yield: 74\%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.70 (d, $J$ = 7.7 Hz, 1H), 7.26 – 7.20 (m, 2H), 7.16 (d, $J$ = 7.5 Hz, 1H), 7.11–7.05 (m, 1H), 7.01 – 6.93 (m, 1H), 6.86 (d, $J$ = 6.6 Hz, 1H), 5.42 (s, 2H), 4.88 (s, 2H).

(I-(3,5-Dimethoxybenzyl)-1H-benzo[d]imidazol-2-yl)methanol (2n)

1-(Bromomethyl)-3,5-dimethoxybenzene and 1a were used as reactants to give 2n. While solid. Yield: 85\%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.72 (d, $J$ = 7.8 Hz, 1H), 7.22 (d, $J$ = 14.1 Hz, 3H), 6.35 (s, 1H), 6.25 (s, 2H), 5.37 (s, 2H), 4.87 (s, 2H), 3.69 (s, 6H).

(I-Ethyl-1H-benzo[d]imidazol-2-yl)methanol (2o)
Bromoethane and 1a were used as reactants to give 2o. $^1$H NMR (400 MHz, CDCl$_3$-d$_6$) $\delta$ 7.68 (d, $J = 6.7, 2.2$ Hz, 1H), 7.32 (d, $J = 6.7, 2.1$ Hz, 1H), 7.28 – 7.21 (m, 2H), 4.88 (s, 2H), 4.29 (q, $J = 7.3$ Hz, 2H), 1.46 (t, $J = 7.3$ Hz, 3H).

1-(4-Fluorophenyl)-2-(2-(hydroxymethyl)-1H-benzo[d]imidazol-1-yl)ethanone (2p)

2-Bromo-1-(4-fluorophenyl)ethanone and 1a were used as reactants to give 2p. While solid. Yield: 77%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12–8.02 (dd, $J = 8.6, 5.3$ Hz, 2H), 7.72 – 7.67 (m, 1H), 7.25 – 7.19 (m, 4H), 7.12 – 7.08 (m, 1H), 5.65 (s, 2H), 4.80 (s, 2H).

2-(2-(hydroxymethyl)-1H-benzo[d]imidazol-1-yl)-1-(4-methoxyphenyl)ethanone(2q)

2-Bromo-1-(4-methoxyphenyl)ethanone and 1a were used as reactants to give 2q. While solid. Yield: 88%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.01 (d, $J = 8.8$ Hz, 2H), 7.72 (dd, $J = 6.3, 2.2$ Hz, 1H), 7.26 – 7.20 (m, 2H), 7.12 (dd, $J = 6.4, 2.4$ Hz, 1H), 7.01 (d, $J = 8.9$ Hz, 2H), 5.64 (s, 2H), 4.83 (s, 2H), 3.91 (s, 3H).

1-(4-chlorophenyl)-2-(2-(hydroxymethyl)-1H-benzo[d]imidazol-1-yl)ethanone (2r)

2-Bromo-1-(4-chlorophenyl)ethanone and 1a were used as reactants to give 2r. While solid. Yield: 81%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 (d, $J = 8.5$ Hz, 2H), 7.70 (d, $J = 8.6$ Hz, 1H), 7.51 (s, 2H), 7.26 – 7.22 (m, 2H), 7.12 – 7.09 (m, 1H), 5.65 (s, 2H), 4.81 (s, 2H).

2-(2-(Hydroxymethyl)-1H-benzo[d]imidazol-1-yl)-1-(p-tolyl)ethanone (2s)

2-Bromo-1-(p-tolyl)ethanone and 1a were used as reactants to give 2s. While solid. Yield: 75%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.93 (d, $J = 8.1$ Hz, 2H), 7.71 (d, $J = 7.9$ Hz, 1H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.25 – 7.20 (m, 2H), 7.13 – 7.09 (m, 1H), 5.66 (s, 2H), 4.81 (s, 2H), 2.46 (s, 3H).

(5 or 6-Chloro-1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)methanol (3a and 3b)
1-(Bromomethyl)-4-methylbenzene and 1b were used as reactants to give 3a and 3b. For 3a: while solid. Yield: 36%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.67 (d, $J = 1.3$ Hz, 1H), 7.21–7.09 (m, 4H), 6.98 (d, $J = 8.0$ Hz, 2H), 5.40 (s, 2H), 4.88 (s, 2H), 2.31 (s, 3H). For 3b: while solid. Yield: 41%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.61 (d, $J = 9.3$ Hz, 1H), 7.23 – 7.19 (m, 2H), 7.10 (d, $J = 7.9$ Hz, 2H), 6.97 (d, $J = 8.0$ Hz, 2H), 5.35 (s, 2H), 4.85 (s, 2H), 2.32 (s, 3H).

**5 or 6-Fluoro-1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)methanol (3c and 3d)**

1-(Bromomethyl)-4-methylbenzene and 1c were used as reactants to give 3c and 3d. For 3c: while solid. Yield: 33%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.42 – 7.30 (m, 1H), 7.12 – 7.08 (m, 3H), 7.02 – 6.94(dd, $J = 8.0$, 3.7 Hz, 3H), 5.39 (s, 2H), 4.86 (s, 2H), 2.31 (s, 3H). For 3d: while solid. Yield: 27%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 – 7.60 (m, 1H), 7.10 (d, $J = 8.0$ Hz, 2H), 6.99 (d, $J = 8.2$ Hz, 3H), 6.92 – 6.84 (m, 1H), 5.36 (s, 2H), 4.86 (s, 2H), 2.31 (s, 3H).

**5 or 6-Methoxy-1-(4-methylbenzyl)-1H-benzo[d]imidazol-2-yl)methanol (3e and 3f)**

1-(Bromomethyl)-4-methylbenzene and 1d were used as reactants to give 3e and 3f. For 3e: while solid. Yield: 42%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.17 (d, $J = 2.1$ Hz, 1H), 7.12 – 7.04 (m, 3H), 6.98 (d, $J = 8.0$ Hz, 2H), 6.91 – 6.83 (m, 1H), 5.38 (s, 2H), 4.85 (s, 2H), 3.82 (s, 3H), 2.30 (s, 3H). For 3f: while solid. Yield: 38%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.58 (d, $J = 8.8$ Hz, 1H), 7.09 (d, $J = 7.9$ Hz, 2H), 6.99 (d, $J = 8.0$ Hz, 2H), 6.87 (dd, $J = 8.7$, 2.2 Hz, 1H), 6.65 (d, $J = 2.1$ Hz, 1H), 5.36 (s, 2H), 4.82 (s, 2H), 3.77 (s, 3H), 2.30 (s, 3H).

**5 or 6-Chloro-1-(2-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (4a and 4b)**

1-(Bromomethyl)-2-fluorobenzene and 1b were used as reactants to give 4a and 4b. For 4a: while solid. Yield: 37%. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.66 (s, 1H), 7.32 – 7.27 (m, 1H), 7.21 – 7.15 (m, 1H), 7.18 – 7.06 (m, 2H), 7.02 (t, $J = 7.5$ Hz, 1H), 6.87 (t, $J = 7.1$ Hz, 1H), 5.49 (s,
2H), 4.92 (s, 2H). For 4b: while solid. Yield: 29%. 1H NMR (400 MHz, CDCl$_3$) δ 7.61 (d, $J = 8.3$ Hz, 1H), 7.33 – 7.27 (m, 1H), 7.25 – 7.20 (m, 2H), 7.14 – 7.09 (m, 1H), 7.03 (t, $J = 7.5$ Hz, 1H), 6.85 (t, $J = 7.2$ Hz, 1H), 5.46 (s, 2H), 4.90 (s, 2H).

(5 or 6-fluoro-1-(2-fluorobenzyl)-1H-benzo[d]imidazol-2-yl)methanol (4c and 4d)

1-(Bromomethyl)-2-fluorobenzene and 1c were used as reactants to give 4c and 4d. For 4c: while solid. Yield: 42%. 1H NMR (400 MHz, CDCl$_3$) δ 7.41 – 7.33 (m, 1H), 7.32 – 7.27 (m, 1H), 7.04 – 6.94 (m, 2H), 6.87 (t, $J = 7.6$ Hz, 1H), 5.49 (s, 2H), 4.92 (s, 2H). For 4d: while solid. Yield: 38%. 1H NMR (400 MHz, CDCl$_3$) δ 7.63 (d, $J = 8.7$, 4.7 Hz, 1H), 7.35 – 7.29 (m, 1H), 7.14 – 7.08 (m, 1H), 7.03 (t, $J = 5.1$ Hz, 1H), 7.01 – 6.95 (m, 1H), 6.94 – 6.86 (m, 2H), 5.46 (s, 2H), 4.91 (s, 2H).

(1-(2-Fluorobenzyl)-5 or 6-methoxy-1H-benzo[d]imidazol-2-yl)methanol (4e and 4f)

1-(Bromomethyl)-2-fluorobenzene and 1d were used as reactants to give 4e and 4f. For 4e: while solid. Yield: 34%. 1H NMR (400 MHz, CDCl$_3$) δ 7.26 – 7.22 (m, 1H), 7.18 (d, $J = 2.3$ Hz, 1H), 7.12 – 7.07 (m, 2H), 6.97 (t, $J = 7.5$ Hz, 1H), 6.86 – 6.80 (m, 2H), 5.47 (s, 2H), 4.89 (s, 2H), 3.83 (s, 3H). For 4f: while solid. Yield: 40%. 1H NMR (400 MHz, CDCl$_3$) δ 7.58 (d, $J = 8.8$ Hz, 1H), 7.30 – 7.26 (m, 1H), 7.13 – 7.08 (m, 1H), 7.00 (t, $J = 7.5$ Hz, 1H), 6.89 – 6.83 (m, 2H), 6.65 (d, $J = 2.2$ Hz, 1H), 5.46 (s, 2H), 4.88 (s, 2H), 3.78 (s, 3H).

**General method for the synthesis of 5a–5s, 6a–6f, and 7a–7g**

To a solution of 2a–2s, 3a–3f, or 4a–4f (1 mmol) in DCM (10 mL) was added Dess-Martin reagent (1.1 mmol), and the reaction was stirred at 4 °C for 1 h. The reaction was quenched with a saturated aqueous sodium thiosulfate solution (3 mL) and subsequent mixture was extracted with DCM (10 mL × 3). The combined organic extracts were dried over MgSO$_4$.
and concentrated. The crude product obtained was purified by PTLC (DCM/MeOH = 100/5, v/v) to yield the title products.

![Chemical structures](image)

- **Compound 2a**: 1-(4-Bromobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5a)
  - 5a: R₁ = H, R₂ = p-Br;
  - 5b: R₁ = H, R₂ = o-F, p-Br;
  - 5c: R₁ = H, R₂ = p-CN;
  - 5d: R₁ = H, R₂ = p-NO₂;
  - 5e: R₁ = H, R₂ = p-F;
  - 5f: R₁ = H, R₂ = H;
  - 5g: R₁ = H, R₂ = p-CH₃;
  - 5h: R₁ = H, R₂ = p-Cl;
  - 5i: R₁ = H, R₂ = p-CF₃;
  - 5j: R₁ = H, R₂ = o-F;
  - 5k: R₁ = H, R₂ = o-F; p-F;
  - 5l: R₁ = H, R₂ = m-F;
  - 5m: R₁ = H, R₂ = m-F; p-F;
  - 5n: R₁ = H, R₂ = m-OCH₃; m-OCH₃;
  
  **1-(4-Bromobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5a)**

  While solid. Yield: 48%. ¹H NMR (400 MHz, CDCl₃) δ 10.14 (s, 1H), 7.97 (d, J = 7.7 Hz, 1H), 7.49 – 7.39 (m, 5H), 7.04 (d, J = 8.1 Hz, 2H), 5.80 (s, 2H).

- **Compound 2b**: 1-(4-Bromo-2-fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5b)
  - 5b: R₁ = H, R₂ = o-F, p-Br;
  - 5c: R₁ = H, R₂ = p-CN;
  - 5d: R₁ = H, R₂ = p-NO₂;
  - 5e: R₁ = H, R₂ = p-F;
  - 5f: R₁ = H, R₂ = H;
  - 5g: R₁ = H, R₂ = p-CH₃;
  - 5h: R₁ = H, R₂ = p-Cl;
  - 5i: R₁ = H, R₂ = p-CF₃;
  - 5j: R₁ = H, R₂ = o-F;
  - 5k: R₁ = H, R₂ = o-F; p-F;
  - 5l: R₁ = H, R₂ = m-F;
  - 5m: R₁ = H, R₂ = m-F; p-F;
  - 5n: R₁ = H, R₂ = m-OCH₃; m-OCH₃;

  **1-(4-Bromo-2-fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5b)**

  While solid. Yield: 53%. ¹H NMR (400 MHz, CDCl₃) δ 10.15 (s, 1H), 7.96 (d, J = 7.9 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.31 – 7.27 (m, 1H), 7.22 – 7.16 (m, 1H), 6.80 (t, J = 8.1 Hz, 1H), 5.87 (s, 2H).

- **Compound 2c**: 4-((2-Formyl-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (5c)
  - 5c: R₁ = 5-Cl, R₂ = p-CH₃; 6a: R₁ = 5-Cl, R₂ = p-CH₃;
  - 5d: R₁ = 6-Cl, R₂ = p-CH₃;
  - 6b: R₁ = 6-Cl, R₂ = p-CH₃;
  - 6c: R₁ = 5-F, R₂ = p-CH₃;
  - 6d: R₁ = 6-F, R₂ = p-CH₃;
  - 6e: R₁ = 5-OCH₃, R₂ = p-CH₃;
  - 6f: R₁ = 6-OCH₃, R₂ = p-CH₃;
  - 5p: R₁ = p-F;
  - 5q: R₁ = p-OCH₃;
  - 5r: R₁ = p-Cl;
  - 5s: R₁ = p-CH₃;

  **4-((2-Formyl-1H-benzo[d]imidazol-1-yl)methyl)benzonitrile (5c)**

  While solid. Yield: 52%. ¹H NMR (400 MHz,
CDCl$_3$ $\delta$ 10.12 (s, 1H), 7.99 (d, $J$ = 8.0 Hz, 1H), 7.60 (d, $J$ = 8.1 Hz, 2H), 7.51 – 7.42 (m, 2H), 7.40 (d, $J$ = 7.9 Hz, 1H), 7.24 (d, $J$ = 8.0 Hz, 2H), 5.90 (s, 2H).

**1-(4-Nitrobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5d)**

Compound 2d was used as reactant to give 5d. While solid. Yield: 47%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.13 (s, 1H), 8.16 (d, $J$ = 8.4 Hz, 2H), 8.00 (d, $J$ = 7.9 Hz, 1H), 7.52 – 7.39 (m, 3H), 7.30 (d, $J$ = 8.3 Hz, 2H), 5.95 (s, 2H).

**1-(4-Fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5e)**

Compound 2e was used as reactant to give 5e. While solid. Yield: 57%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.14 (s, 1H), 7.96 (d, $J$ = 8.0 Hz, 1H), 7.50 – 7.38 (m, 3H), 7.21 – 7.13 (m, 2H), 6.98 (t, $J$ = 8.5 Hz, 2H), 5.82 (s, 2H).

**1-Benzyl-1H-benzo[d]imidazole-2-carbaldehyde (5f)**

Compound 2f was used as reactant to give 5f. While solid. Yield: 64%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.15 (s, 1H), 7.96 (d, $J$ = 7.9 Hz, 1H), 7.48 – 7.38 (m, 3H), 7.30 – 7.25 (m, 3H), 7.17 (d, $J$ = 7.1 Hz, 2H), 5.87 (s, 2H).

**1-(4-Methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5g)**

Compound 2g was used as reactant to give 5g. While solid. Yield: 58%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.15 (s, 1H), 7.95 (d, $J$ = 7.9 Hz, 1H), 7.49 – 7.37 (m, 3H), 7.12 – 7.05 (m, 4H), 5.82 (s, 2H), 2.29 (s, 3H).

**1-(4-Chlorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5h)**

Compound 2h was used as reactant to give 5h. While solid. Yield: 64%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.14 (s, 1H), 7.96 (d, $J$ = 7.8 Hz, 1H), 7.49 – 7.39 (m, 3H), 7.27 (d, $J$ = 5.9 Hz, 2H), 7.11 (d, $J$ = 8.0 Hz, 2H), 5.82 (s, 2H).
1-(4-(Trifluoromethyl)benzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5i)

Compound 2i was used as reactant to give 5i. While solid. Yield: 55%. 1H NMR (400 MHz, CDCl₃) δ 10.14 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.48 – 7.44 (m, 3H), 7.26 (s, 2H), 5.92 (s, 2H).

1-(2-Fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5j)

Compound 2j was used as reactant to give 5j. While solid. Yield: 49%. 1H NMR (400 MHz, CDCl₃) δ 10.17 (s, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.50 – 7.38 (m, 3H), 7.25 (d, J = 10.5 Hz, 1H), 7.09 (t, J = 9.2 Hz, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 5.94 (s, 2H).

1-(2,4-Difluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5k)

Compound 2k was used as reactant to give 5k. While solid. Yield: 67%. 1H NMR (400 MHz, CDCl₃) δ 10.16 (s, 1H), 7.96 (d, J = 7.5 Hz, 1H), 7.51 – 7.39 (m, 3H), 6.99 – 6.95 (m, 1H), 6.85 (t, J = 8.0 Hz, 1H), 6.76 (t, J = 7.1 Hz, 1H), 5.88 (s, 2H).

1-(3-Fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5l)

Compound 2l was used as reactant to give 5l. While solid. Yield: 55%. 1H NMR (400 MHz, CDCl₃) δ 10.16 (s, 1H), 7.98 (d, J = 7.5 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.29 – 7.26 (m, 1H), 6.96 (t, J = 8.8 Hz, 2H), 6.85 (d, J = 9.4 Hz, 1H), 5.85 (s, 2H).

1-(3,4-Difluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5m)

Compound 2m was used as reactant to give 5m. While solid. Yield: 46%. 1H NMR (400 MHz, CDCl₃) δ 10.14 (s, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.51 – 7.41 (m, 3H), 7.13 – 7.05 (m, 1H), 7.03 – 6.97 (m, 1H), 6.93 (m, 1H), 5.80 (s, 2H).

1-(3,5-Dimethoxybenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (5n)
Compound **2n** was used as reactant to give **5n**. While solid. Yield: 49%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.07 (s, 1H), 7.91 (d, $J = 8.1$ Hz, 1H), 7.75 (d, $J = 8.3$ Hz, 1H), 7.48 (t, $J = 7.6$ Hz, 1H), 7.40 (t, $J = 7.6$ Hz, 1H), 6.40 (s, 1H), 6.32 (s, 2H), 5.81 (s, 2H), 3.67 (s, 6H).

**1-Ethyl-1H-benzo[d]imidazole-2-carbaldehyde (5o)**

Compound **2o** was used as reactant to give **5o**. While solid. Yield: 42%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.13 (s, 1H), 7.94 (d, $J = 8.3$ Hz, 1H), 7.55 – 7.45 (m, 2H), 7.46 – 7.34 (m, 1H), 4.67 (q, $J = 7.2$ Hz, 2H), 1.46 (t, $J = 7.2$ Hz, 3H).

**1-(2-(4-Fluorophenyl)-2-oxoethyl)-1H-benzo[d]imidazole-2-carbaldehyde (5p)**

Compound **2p** was used as reactant to give **5p**. While solid. Yield: 55%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.09 (s, 1H), 8.14 – 8.06 (m, $J = 7.0$, 5.0, 2.4 Hz, 2H), 8.00 (d, $J = 7.6$ Hz, 1H), 7.50 – 7.40 (m, 2H), 7.32 (d, $J = 7.9$ Hz, 1H), 7.26 – 7.21 (m, 2H), 6.03 (s, 2H).

**1-(2-(4-methoxyphenyl)-2-oxoethyl)-1H-benzo[d]imidazole-2-carbaldehyde (5q)**

Compound **2q** was used as reactant to give **5q**. While solid. Yield: 59%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.09 (s, 1H), 8.03 (d, $J = 8.8$ Hz, 2H), 7.98 (d, $J = 7.8$ Hz, 1H), 7.48 – 7.39 (m, 2H), 7.32 (d, $J = 8.1$ Hz, 1H), 7.03 (d, $J = 8.8$ Hz, 2H), 6.03 (s, 2H), 3.92 (s, 3H).

**1-(2-(4-Chlorophenyl)-2-oxoethyl)-1H-benzo[d]imidazole-2-carbaldehyde (5r)**

Compound **2r** was used as reactant to give **5r**. While solid. Yield: 63%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.08 (s, 1H), 7.99 (d, $J = 8.6$ Hz, 3H), 7.54 (d, $J = 8.5$ Hz, 2H), 7.49 – 7.41 (m, 2H), 7.32 (d, $J = 7.9$ Hz, 1H), 6.02 (s, 2H).

**1-(2-Oxo-2-(p-tolyl)ethyl)-1H-benzo[d]imidazole-2-carbaldehyde (5s)**
Compound 2s was used as reactant to give 5s. While solid. Yield: 49%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.10 (s, 1H), 7.99 – 7.95 (m, 3H), 7.50 – 7.38 (m, 3H), 7.38 – 7.30 (m, 3H), 6.05 (s, 2H), 2.47 (s, 3H).

5-Chloro-1-(4-methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (6a)

Compound 3a was used as reactant to give 6a. While solid. Yield: 57%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.13 (s, 1H), 7.92 (s, 1H), 7.38 (s, 2H), 7.10 (d, $J$ = 8.0 Hz, 2H), 7.04 (d, $J$ = 8.1 Hz, 2H), 5.80 (s, 2H), 2.30 (s, 3H).

6-Chloro-1-(4-methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (6b)

Compound 3b was used as reactant to give 6b. While solid. Yield: 39%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.12 (s, 1H), 7.86 (d, $J$ = 8.8 Hz, 1H), 7.45 (d, $J$ = 1.6 Hz, 1H), 7.39 – 7.31 (m, 1H), 7.11 (d, $J$ = 8.0 Hz, 2H), 7.05 (d, $J$ = 8.0 Hz, 2H), 5.77 (s, 2H), 2.31 (s, 3H).

5-Fluoro-1-(4-methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (6c)

Compound 3c was used as reactant to give 6c. While solid. Yield: 45%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.13 (s, 1H), 7.61 – 7.67 (m, 1H), 7.41 – 7.35 (m, 1H), 7.26 – 7.18 (m, 1H), 7.10 (d, $J$ = 8.0 Hz, 2H), 7.05 (d, $J$ = 8.1 Hz, 2H), 5.81 (s, 2H), 2.30 (s, 3H).

6-Fluoro-1-(4-methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (6d)

Compound 3d was used as reactant to give 6d. While solid. Yield: 36%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.09 (s, 1H), 7.91 – 7.87 (m, 1H), 7.17 – 7.09 (m, 4H), 7.06 (d, $J$ = 8.1 Hz, 2H), 5.77 (s, 2H), 2.30 (s, 3H).

5-Methoxy-1-(4-methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (6e)

Compound 3e was used as reactant to give 6e. While solid. Yield: 61%. $^1$H NMR (400 MHz, CDCl$_3$) δ 10.10 (s, 1H), 7.36 – 7.28 (m, 2H), 7.10 (d, $J$ = 2.2 Hz, 1H), 7.09 – 7.04 (m, 4H), 5.77 (s, 2H), 2.30 (s, 3H).
5.79 (s, 2H), 3.88 (s, 3H), 2.29 (s, 3H).

6-Methoxy-1-(4-methylbenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (6f)

Compound 3f was used as reactant to give 6f. While solid. Yield: 63%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.05 (s, 1H), 7.81 (d, $J = 9.0$ Hz, 1H), 7.10 (d, $J = 8.2$ Hz, 2H), 7.08 – 7.01 (m, 3H), 6.77 (d, $J = 2.3$ Hz, 1H), 5.78 (s, 2H), 3.84 (s, 3H), 2.30 (s, 3H).

5-Chloro-1-(2-fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (7a)

Compound 4a was used as reactant to give 7a. While solid. Yield: 53%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.14 (s, 1H), 7.93 (d, $J = 0.8$ Hz, 1H), 7.44 – 7.37 (m, 2H), 7.36 – 7.28 (m, 1H), 7.12 – 7.06 (m, 1H), 7.06 – 7.00 (m, 1H), 6.98 – 6.90 (m, $J = 7.6, 1.4$ Hz, 1H), 5.92 (s, 2H).

6-Chloro-1-(2-fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (7b)

Compound 4b was used as reactant to give 7b. While solid. Yield: 56%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.13 (s, 1H), 7.86 (d, $J = 8.8$ Hz, 1H), 7.47 (d, $J = 1.6$ Hz, 1H), 7.40 – 7.32 (m, 1H), 7.32 – 7.27 (m, 1H), 7.14 – 7.08 (m, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 6.94 (t, $J = 7.5$ Hz, 1H), 5.89 (s, 2H).

5-Fluoro-1-(2-fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (7c)

Compound 4c was used as reactant to give 7c. While solid. Yield: 62%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.14 (s, 1H), 7.63 – 7.55 (m, 1H), 7.47 – 7.39 (m, 1H), 7.31 – 7.26 (m, 1H), 7.23 – 7.19 (m, 1H), 7.12 – 7.07 (m, 1H), 7.13 – 7.05 (m, 1H), 6.97 – 6.93 (m, 1H), 5.92 (s, 2H).

6-Fluoro-1-(2-fluorobenzyl)-1H-benzo[d]imidazole-2-carbaldehyde (7d)

Compound 4d was used as reactant to give 7d. While solid. Yield: 57%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.11 (s, 1H), 7.92 – 7.88 (m, 1H), 7.32 – 7.26 (m, 1H), 7.17 – 7.09 (m, 3H), 7.06 – 7.02 (m, 1H), 7.02 – 6.94 (m, 1H), 5.89 (s, 2H).

1-(2-Fluorobenzyl)-5-methoxy-1H-benzo[d]imidazole-2-carbaldehyde (7e)
Compound 4e was used as reactant to give 7e. While solid. Yield: 42%.\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 10.11 (s, 1H), 7.35 (d, \(J = 9.1\) Hz, 1H), 7.31 (d, \(J = 2.2\) Hz, 1H), 7.26 – 7.22 (m, 1H), 7.13 – 7.05 (m, 2H), 7.01 (t, \(J = 7.5\) Hz, 1H), 6.92 (t, \(J = 7.6\) Hz, 1H), 5.91 (s, 2H), 3.88 (s, 3H).

1-(2-Fluorobenzyl)-6-methoxy-1H-benzo[d]imidazole-2-carbaldehyde (7f)

Compound 4f was used as reactant to give 7f. While solid. Yield: 45%.\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 10.07 (s, 1H), 7.81 (d, \(J = 9.0\) Hz, 1H), 7.30 – 7.26 (m, 1H), 7.13 – 7.07 (m, 1H), 7.06 – 7.00 (m, 2H), 6.98 – 6.94 (m, 1H), 6.82 (d, \(J = 2.3\) Hz, 1H), 5.90 (s, 2H), 3.85 (s, 3H).
$^1$H NMR and $^{13}$C NMR Spectrum of Target Compounds

$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of $8a$

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of $8a$
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8b

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8b
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8c

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8c
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8d

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8d
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8e

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8e
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of $8f$

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of $8f$
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8g

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8g
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8h

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8h
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8i

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8i
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8j

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8j
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8k

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8k
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of $8l$

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of $8l$
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8m

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8m
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8n

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8n
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 8o

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 8o
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 9a

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 9a
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 9b

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 9b
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 9c

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 9c
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 9d

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 9d
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10a

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10a
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10b

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10b
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10c

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10c
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10d

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10d
$^{1}$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10e

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10e
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10f

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10f
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10g

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10g
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 10i

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 10i
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 11a

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 11a
\textsuperscript{1}H NMR (400 MHz, DMSO-\textit{d}\textsubscript{6}) spectrum of 11b

\textsuperscript{13}C NMR (400 MHz, DMSO-\textit{d}\textsubscript{6}) spectrum of 11b
$^{1}H$ NMR (400 MHz, DMSO-$d_6$) spectrum of 11c

$^{13}C$ NMR (400 MHz, DMSO-$d_6$) spectrum of 11c
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 11d

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 11d
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of $^{11}$e

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of $^{11}$e
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 11f

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 11f
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of $^{11}g$

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of $^{11}g$
$^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of 11h

$^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of 11h