Supporting Information

Isoquinoline-1,3-diones as Selective Inhibitors of Tyrosyl DNA Phosphodiesterase II (TDP2)

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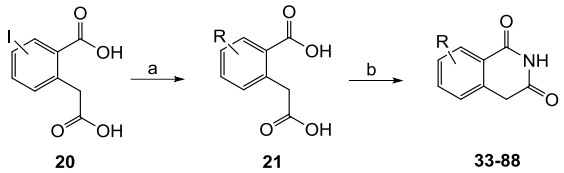
Supporting Information

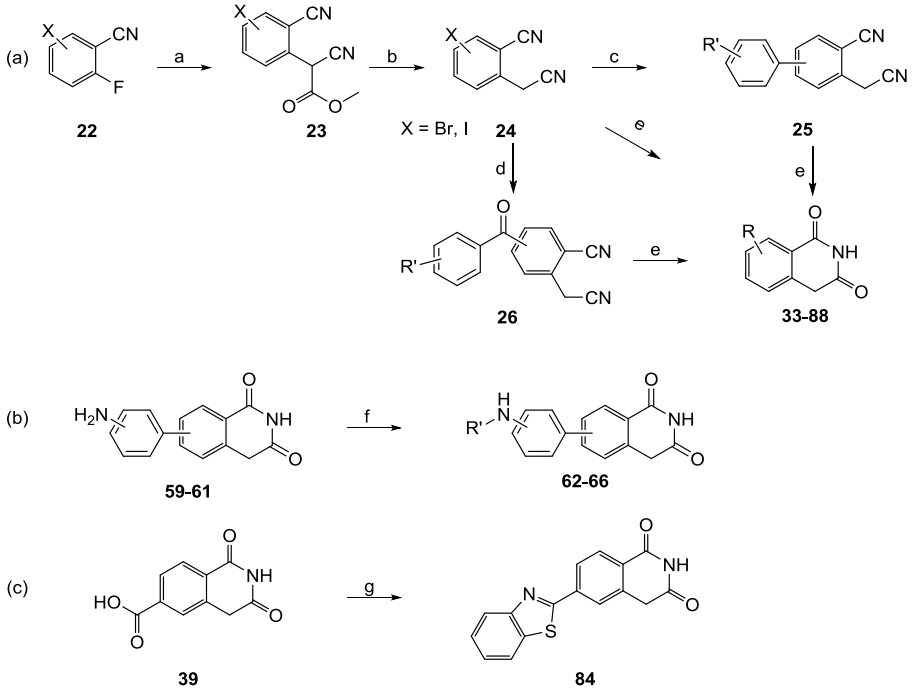
1. Synthetic Scheme.

Scheme 1[a].



[a] Reagents and conditions: a) arylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, EtOH/H_2O (1:1), 150 °C, 30 min, MW, 60-85%; b) urea, 1,2-dichlorobenzene, 170 °C, 45 min, MW, 55-80%.

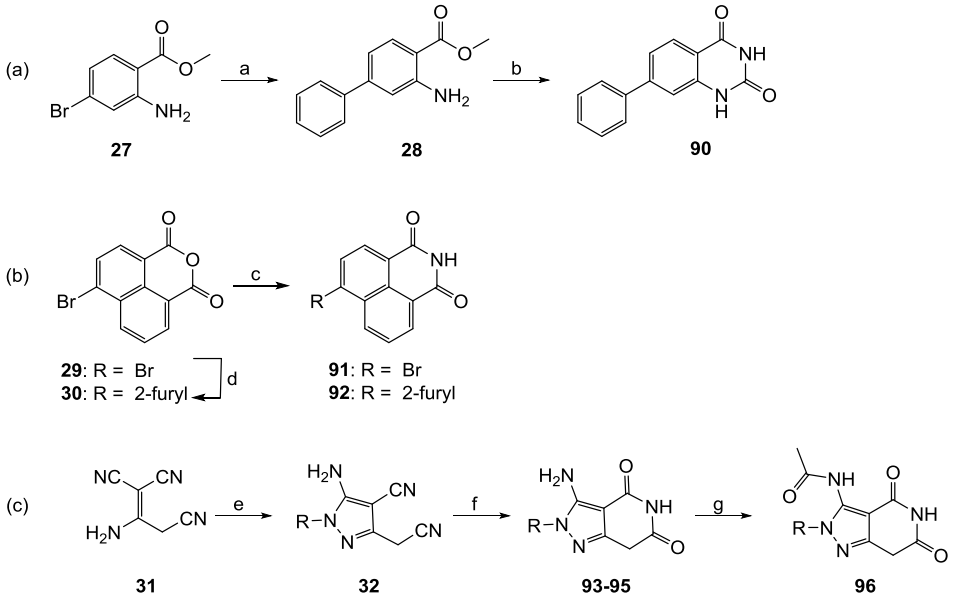
Scheme 2[a].



[a] Reagents and conditions: a) Methyl cyanoacetate, NaH, DMSO, 90 °C; b) DMSO/H_2O (9:1), 120 °C, 16 h, 70-85%; c) arylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, DME/H_2O (4:1), 110 °C, 40 min, MW, 55-87%; d) $Pd(OAc)_2$, $Mo(CO)_6$, K_2CO_3, anisole (0.2M), 140 °C, 30 min, MW, 50-62%; e) Con HCl, 70 °C, 4 h, 60-

90%; f) sulfonyl or acryloyl chloride , pyridine, dioxane, r.t; 65-79%; g) 2-aminothiophenol, T3P (50% in EtOAc), DIPEA, 100 °C, 30 min, MW, 69%.

Scheme 3[a].



[a] Reagents and conditions: a) phenylboronic acid, K_2CO_3, $Pd(PPh_3)_4$, DME/H_2O (4:1), 110 °C, 45 min, MW, 50%; b) i) KOCN, toluene, r.t; ii) NaOH, EtOH, reflux, 68%; c) NH_4OH, 40 °C, 4 h, 70-90%; d) 2-(tributylstannyl)furan, $Pd(PPh_3)_4$, toluene, 150 °C, 30 min, 72%; e) R-$NHNH_2$, EtOH, reflux, 70-95%; f) Con HCl, 70 °C, 4 h, 65-85%; g) acetyl chloride, AcOH, 70 °C, 62%.

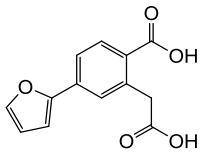
2. General Procedures.

General Procedure for Suzuki Coupling (21, 25). The mixture of compound **20 or 24** (1.0 eq), aryl boronic acid (1.6 eq), $Pd(PPh_3)_4$ (0.065 eq), K_2CO_3 (3.6 eq) in EtOH/H_2O (1:1) was irradiated at 150 °C for 30 min under microwave conditions. The black residue formed was filtered through celite and the solvent was concentrated *in vacuo*. The resulting aqueous solution was acidified (pH = 3) using 2N HCl. A white precipitate was obtained *via* filtration, which was washed with water and dried under vacuum to furnish desired compounds **(21, 25)** as colorless solid.

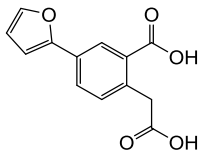
General Procedure for the Synthesis of Dinitriles (24). A solution of compound **23** in DMSO/H_2O (9:1) mixture was stirred at 120 °C for 16 h before quenched with water. The aqueous solution was extracted using EtOAc (2 x 30 mL). The combined organics were washed with water (2 x 20 mL), brine (30 mL), dried over Na_2SO_4, and concentrated *in vacuo*. The crude mixture was purified using CombiFlash with 0-20% EtOAc in hexane as an eluent to yield the desired products (**24**) as yellow solid. Yield: 70-85% over 2 steps.

General Procedure for the Synthesis of 32. To a suspension of 2-amino-1-propene-1,1,3-tricarbonitrile (**31**, 7.6 mmol, 1.0 eq) in EtOH (10 mL) was added arylhydrazine (8.4 mmol, 1.1 eq) slowly and the solution was heated at reflux for 30 min before it was cooled. The solvent was removed *in vacuo* to leave pale brown solid. Recrystallization of the crude mixture from EtOH furnished intermediates **32** as brown needles. Yield: 70-95%.

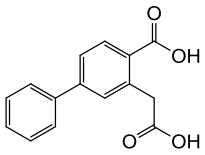
3. Spectral Characterization of Data.



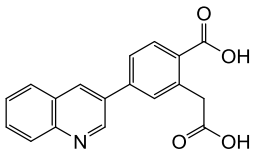
2-(Carboxymethyl)-4-(furan-2-yl)benzoic acid (21a). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.81 (s, 1H), 12.35 (s, 1H), 8.17 (d, *J* = 2.0 Hz, 1H), 7.81 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.77 (d, *J* = 1.8 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.02 (d, *J* = 3.4 Hz, 1H), 6.61 (dd, *J* = 3.4, 1.8 Hz, 1H), 3.94 (s, 2H).



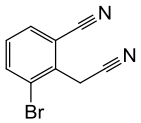
2-(Carboxymethyl)-5-(furan-2-yl)benzoic acid (21b). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.64 (br s, 2H), 8.17 (d, *J* = 2.0 Hz, 1H), 7.79 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.75 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 6.99 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.59 (dd, *J* = 3.4, 1.8 Hz, 1H), 3.93 (s, 2H).



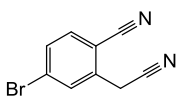
3-(Carboxymethyl)-[1,1'-biphenyl]-4-carboxylic acid (21c). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.68 (s, 1H), 12.36 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 2H), 7.70-7.65 (m, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 4.03 (s, 2H).



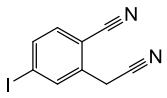
2-(Carboxymethyl)-4-(quinolin-3-yl)benzoic acid (21d). ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.93 (s, 1H), 12.27 (s, 1H), 9.32 (d, *J* = 2.2 Hz, 1H), 8.76 (d, *J* = 2.2 Hz, 1H), 8.11-8.06 (m, 2H), 7.96 – 7.91 (m, 2H), 7.82 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.68 (dd, *J* = 11.4, 4.6 Hz, 1H), 7.65-7.60 (m, 1H), 4.08 (s, 2H).



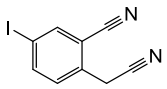
3-Bromo-2-(cyanomethyl)benzonitrile (24a). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.10 (dd, *J* = 8.2, 1.0 Hz, 1H), 8.00 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 4.25 (s, 2H).



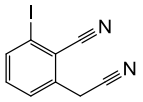
4-Bromo-2-(cyanomethyl)benzonitrile (24b). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.91-7.87 (m, 2H), 7.82 (d, *J* = 8.3 Hz, 1H), 4.28 (s, 2H).



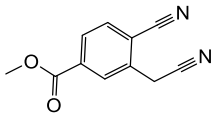
2-(Cyanomethyl)-4-iodobenzonitrile (24c). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.06 (s, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 7.68 (d, *J* = 8.1 Hz, 1H), 4.24 (s, 2H).



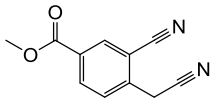
2-(Cyanomethyl)-5-iodobenzonitrile (24d). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.32 (d, *J* = 1.8 Hz, 1H), 8.13 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 4.24 (s, 2H).



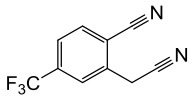
2-(Cyanomethyl)-6-iodobenzonitrile (24e). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.04 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.9 Hz, 1H), 4.31 (s, 2H).



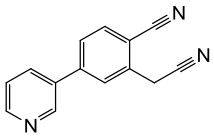
Methyl-4-cyano-3-(cyanomethyl)benzoate (24f). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 (d, *J* = 1.5 Hz, 1H), 7.85 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 4.21 (s, 2H), 3.98 (s, 3H).



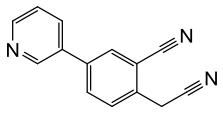
Methyl-3-cyano-4-(cyanomethyl)benzoate (24g). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.39 (s, 1H), 8.29 (d, *J* = 8.1 Hz, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 4.41 (s, 2H), 3.90 (s, 3H).



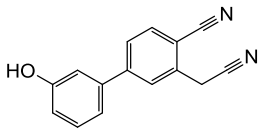
2-(Cyanomethyl)-4-(trifluoromethyl)benzonitrile (24h). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.19 (d, J = 8.1 Hz, 1H), 8.02 (s, 1H), 7.97 (d, J = 8.1 Hz, 1H), 4.38 (s, 2H).



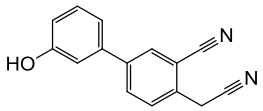
2-(Cyanomethyl)-4-(pyridin-3-yl)benzonitrile (25a) ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.98 (s, 1H), 8.67 (d, J = 3.9 Hz, 1H), 8.18 (d, J = 7.9 Hz, 1H), 8.06 (d, J = 8.0 Hz, 1H), 8.03 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.57 (dd, J = 7.7, 4.8 Hz, 1H), 4.33 (s, 2H).



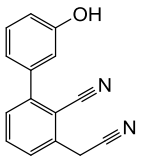
2-(Cyanomethyl)-5-(pyridin-3-yl)benzonitrile (25b). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.00 (d, J = 2.3 Hz, 1H), 8.65 (dd, J = 4.8, 1.4 Hz, 1H), 8.37 (d, J = 2.0 Hz, 1H), 8.30-8.19 (m, 1H), 8.16 (dd, J = 8.1, 2.0 Hz, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.56 (dd, J = 7.9, 4.8 Hz, 1H), 4.35 (s, 2H).



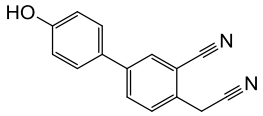
3-(Cyanomethyl)-3'-hydroxy-[1,1'-biphenyl]-4-carbonitrile (25c). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.72 (s, 1H), 7.98 (d, J = 8.1 Hz, 1H), 7.89 (s, 1H), 7.80 (dd, J = 8.1, 1.6 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 7.16 (d, J = 7.9 Hz, 1H), 7.10 (t, J = 2.1 Hz, 1H), 6.88 (dd, J = 8.1, 2.1Hz, 1H), 4.33 (s, 2H).



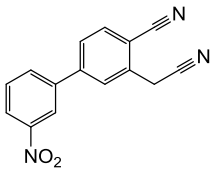
4-(Cyanomethyl)-3'-hydroxy-[1,1'-biphenyl]-3-carbonitrile (25d). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.64 (s, 1H), 8.15 (d, *J* = 1.8 Hz, 1H), 8.00 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.08 (s, 1H), 6.84 (dd, *J* = 8.1, 2.1 Hz, 1H), 4.31 (s, 2H).



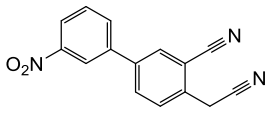
3-(Cyanomethyl)-3'-hydroxy-[1,1'-biphenyl]-2-carbonitrile (25e). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.75 (s, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 6.96 (dd, *J* = 4.5, 3.6 Hz, 1H), 6.94 (t, *J* = 1.9 Hz, 1H), 6.90 (ddd, *J* = 8.0, 2.3, 0.6 Hz, 1H), 4.34 (s, 2H).



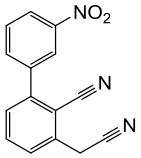
4-(Cyanomethyl)-4'-hydroxy-[1,1'-biphenyl]-3-carbonitrile (25f). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.73 (s, 1H), 8.13 (d, *J* = 2.0 Hz, 1H), 7.97 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.62-7.57 (m, 2H), 6.95-6.78 (m, 2H), 4.27 (s, 2H).



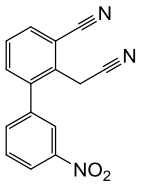
3-(Cyanomethyl)-3'-nitro-[1,1'-biphenyl]-4-carbonitrile (25g). ^{1}H NMR (600 MHz, DMSO-d_6) δ 11.37 (s, 1H), 8.53 (t, *J* = 1.5 Hz, 1H), 8.29 (dd, *J* = 8.2, 1.5 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.86 (s, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 4.12 (s, 2H).



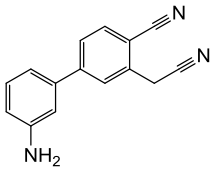
4-(Cyanomethyl)-3'-nitro-[1,1'-biphenyl]-3-carbonitrile (25h). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.58 (s, 1H), 8.43 (s, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 7.7 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 4.36 (s, 2H).



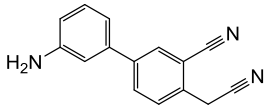
3-(Cyanomethyl)-3'-nitro-[1,1'-biphenyl]-2-carbonitrile (25i). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.42 (t, *J* = 2.1 Hz, 1H), 8.37 (ddd, *J* = 8.2, 2.1, 0.9 Hz, 1H), 8.07 (ddd, *J* = 7.7, 1.6, 0.9 Hz, 1H), 7.91-7.87 (m, 2H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 4.37 (s, 2H).



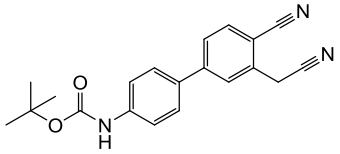
2-(Cyanomethyl)-3'-nitro-[1,1'-biphenyl]-3-carbonitrile (25j). ^{1}H NMR (600 MHz, CD_3OD) δ 8.36 (dt, *J* = 6.8, 2.3 Hz, 1H), 8.29-8.25 (m, 1H), 7.92 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.79 (dd, *J* = 9.5, 5.0 Hz, 2H), 7.72-7.66 (m, 2H), 3.97 (s, 2H).



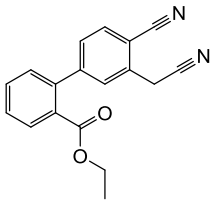
3'-Amino-3-(cyanomethyl)-[1,1'-biphenyl]-4-carbonitrile (25k). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.96 (d, J = 8.0 Hz, 1H), 7.83 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 6.89 (s, 1H), 6.84 (d, J = 7.8 Hz, 1H), 6.68-6.62 (m, 1H), 5.30 (s, 2H), 4.32 (s, 2H).



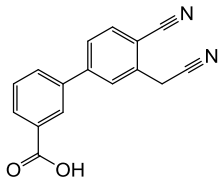
3'-Amino-4-(cyanomethyl)-[1,1'-biphenyl]-3-carbonitrile (25l). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.07 (d, J = 1.8 Hz, 1H), 7.94 (dd, J = 8.2, 1.8 Hz, 1H), 7.70 (d, J = 8.2 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 6.88 (s, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.62 (dd, J = 7.8, 1.8 Hz, 1H), 5.22 (s, 2H), 4.30 (s, 2H).



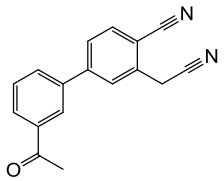
Tert-butyl(4'-cyano-3'-(cyanomethyl)-[1,1'-biphenyl]-4-yl)carbamate (25m). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.59 (s, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 1.7 Hz, 1H), 7.83 (dd, J = 8.1, 1.7 Hz, 1H), 7.68 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 4.30 (s, 2H), 1.50 (s, 9H).



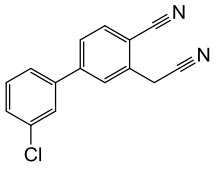
Ethyl-4'-cyano-3'-(cyanomethyl)-[1,1'-biphenyl]-2-carboxylate (25n). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.9 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.59 (dd, *J* = 11.2, 3.8 Hz, 2H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 4.04 (s, 2H), 1.16 (t, *J* = 7.1 Hz, 3H).



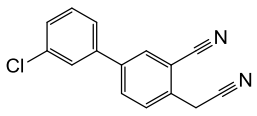
4'-Cyano-3'-(cyanomethyl)-[1,1'-biphenyl]-3-carboxylic acid (25o). 1H NMR (600 MHz, DMSO-d_6) δ 8.27 (s, 1H), 8.03-7.92 (m, 2H), 7.67-7.55 (m, 4H) 4.35 (s, 2H).



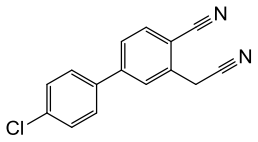
3'-Acetyl-3-(cyanomethyl)-[1,1'-biphenyl]-4-carbonitrile (25p). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.27 (s, 1H), 8.07-8.04 (m, 3H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 4.34 (s, 2H), 2.67 (s, 3H).



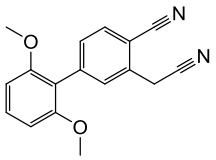
3'-Chloro-3-(cyanomethyl)-[1,1'-biphenyl]-4-carbonitrile (25q). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.04-8.01 (m, 2H), 7.96-7.69 (m, 3H), 7.59-7.56 (s, 2H), 4.31 (s, 2H).



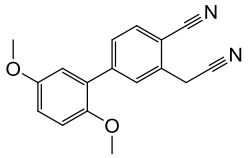
3'-Chloro-4-(cyanomethyl)-[1,1'-biphenyl]-3-carbonitrile (25r). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.32 (d, *J* = 1.8 Hz, 1H), 8.12 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.88 (s, 1H), 7.74 (t, *J* = 7.3 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 4.33 (s, 2H).



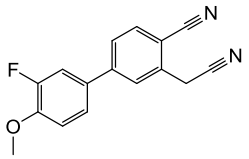
4'-Chloro-3-(cyanomethyl)-[1,1'-biphenyl]-4-carbonitrile (25s). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.15 (s, H), 7.97 (d, *J* = 8.6 Hz, 2H), 7.89 (d, *J* = 8.6 Hz, 2H), 7.61-7.58 (m, 2H), 4.32 (s, 2H).



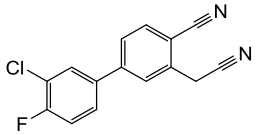
3-(Cyanomethyl)-2',6'-dimethoxy-[1,1'-biphenyl]-4-carbonitrile (25t). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.89 (d, *J* = 7.9 Hz, 1H), 7.49 (d, *J* = 1.5 Hz, 1H), 7.40 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.37 (t, *J* = 8.4 Hz, 1H), 6.79-6.76 (m, 2H), 4.30 (s, 2H), 3.68 (s, 6H).



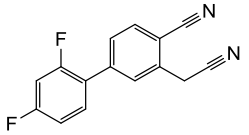
3-(Cyanomethyl)-2',5'-dimethoxy-[1,1'-biphenyl]-4-carbonitrile (25u). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 1.6 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.11 (d, *J* = 9.0 Hz, 1H), 7.00 (dd, *J* = 9.0, 3.1 Hz, 1H), 6.93 (d, *J* = 3.1 Hz, 1H), 4.31 (s, 2H), 3.76 (s, 3H), 3.73 (s, 3H).



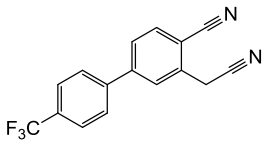
3-(Cyanomethyl)-3'-fluoro-4'-methoxy-[1,1'-biphenyl]-4-carbonitrile (25v). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.96-7.93 (m, 2H), 7.86 (dd, J = 8.1, 1.8 Hz, 1H), 7.70 (dd, J = 12.8, 2.3 Hz, 1H), 7.61-7.57 (m, 1H), 7.32 (t, J = 8.8 Hz, 1H), 4.28 (s, 2H), 3.90 (s, 3H).



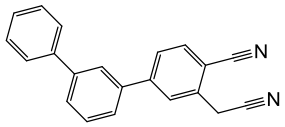
3'-Chloro-3-(cyanomethyl)-4'-fluoro-[1,1'-biphenyl]-4-carbonitrile (25w). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.07-7.96 (m, 3H), 7.96-7.89 (m, 1H), 7.86 – 7.77 (m, 1H), 7.58-7.55 (m, 1H), 4.30 (s, 2H).



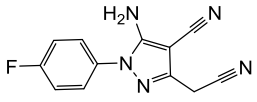
3-(Cyanomethyl)-2', 4'-difluoro-[1,1'-biphenyl]-4-carbonitrile (25x). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.03 (d, J = 8.1 Hz, 1H), 7.81 (s, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.68 (td, J = 8.9, 6.6 Hz, 1H), 7.46 (ddd, J = 11.5, 9.3, 2.5 Hz, 1H), 7.28 (td, J = 8.4, 2.3 Hz, 1H), 4.34 (s, 2H).



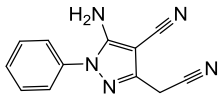
3-(Cyanomethyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carbonitrile (25y). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.07 (d, J = 8.1 Hz, 1H), 8.03 (d, J = 1.8 Hz, 1H), 7.98 (d, J = 8.3 Hz, 2H), 7.95 (dd, J = 8.1, 1.8 Hz, 1H), 7.91 (d, J = 8.3 Hz, 2H), 4.35 (s, 2H).



3-(Cyanomethyl)-[1,1':3',1''-terphenyl]-4-carbonitrile (25z). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.79 (d, *J* = 5.3 Hz, 2H), 7.73 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 3.0 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 4.5 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.3 Hz, 1H), 4.07 (s, 2H).



5-Amino-3-(cyanomethyl)-1-(4-fluorophenyl)-1H-pyrazole-4-carbonitrile (32a). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.60-7.44 (m, 1H), 7.43-7.30 (m, 1H), 6.86 (s, 1H), 4.07 (s, 1H).



5-Amino-3-(cyanomethyl)-1-phenyl-1H-pyrazole-4-carbonitrile (32b). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.56-7.51 (m, 2H), 7.50-7.47 (m, 2H), 7.44 (dt, *J* = 8.4, 1.2 Hz, 1H), 6.85 (s, 2H), 4.07 (s, 2H).