Supporting Information:

3,5-Dimethylisoxazoles act as acetyl-lysine mimetic bromodomain ligands

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Abbreviations used in Supporting Information:
BRD(1): First bromodomain of bromodomain-containing protein 4; CREBBP: c-AMP response element binding protein binding protein; DMAC: N,N-dimethylacetamide; DMEM: Dulbecco’s modified Eagle’s medium; LE: Ligand efficiency; MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; RuPhos: 2-dicyclohexylphosphino-2’,6’-diisoproxybiphenyl
Supporting Figure S1. Mass spectra of 1

1 is liable to oxidation under laboratory conditions. **A**: Mass spectrum of purchased 1 after storage in DMSO for one month; [M-H]^+ is likely to arise from oxidation at the benzylic position; **B**: Mass spectrum of freshly-prepared MeCN suspension of purchased 1; [M+H]^+ is observed, but [M-H]^+ is not; **C**: High-resolution LCMS of resynthesized 1 after stirring in DMSO for 5 days; [M-H]^+ present. For 1, calculated [M+H]^+: 258.1237, [M-H]^+: 256.1081. Details of MS experiments are given below (S11).
Supporting Figure S2. Cytotoxicity assay.

Cytotoxicity of lead compound 1, 4d and (+)-JQ1 in HeLa cells, as determined by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenylltetrazolium bromide) assay, indicating mitochondrial reductase activity. A reduction in viability indicates cytotoxicity in this cell line. Experiments were performed in triplicate. Error bars indicate standard deviation.
**Supporting Figure S3.** Overlays of crystal structure of 2, JQ1, and comparison with predicted binding mode of 4d.

A: Overlay of the crystal structure of lead 2 (yellow, PDB ID: 3SVF) and predicted binding mode of compound 4d (magenta) bound to BRD4(1); B: Comparison of the crystal structure of compound 4d (green, PDB ID: 3SVG) and its predicted binding mode; C: Comparison of the crystal structure of lead compound 2 (yellow) and the crystal structure of final compound 4d (green); D: Overlay of the crystal structures of compound 4d and JQ1 bound to BRD4(1) (PDB ID: 3MXF).
Supporting Figure S4. Selected dose-response curves

Dose-response curves for A: 4b and B: 4d in three bromodomains. Curves were constrained to 0% and 100% inhibition. Experiments were carried out in duplicate on the same plate; intra-experimental variation was too small to be visualized with error bars. Curves plotted in GraphPad Prism (GraphPad Software).
**Supporting Figure S5.** Calculation of minimum energy torsion angle.

Calculated energy as a function of torsion angle around C–C bond (indicated). 0° corresponds to planarity. Energy is in kcal/mol relative to the energy minimum. Calculations were performed in Macromodel (Schrödinger) using OPLS2005 force field.
Supporting Scheme S1. Synthesis of 4-aryl-3,5-dimethylisoxazoles 3a-b, 4a by direct arylation of 3,5-dimethylisoxazole.\(^a\)

\[
\begin{align*}
\text{Br} & \quad \text{Me} & \quad \text{N} & \quad \text{Me} \\
R^1 & \quad R^2 & \quad R^3 & \quad R^4 \\
\end{align*}
\]

\(^a\)Conditions: (a) \(R^1 = H, R^2 = H\): PdCl\(_2\), KOAc, DMAc, 130 °C, 27 h, 69%; \(R^1 = Ac, R^2 = H\): PdCl\(_2\), KOAc, DMAc, 130 °C, 20 h, 51%; \(R^1 = CO_2Et, R^2 = OEt\): PdCl\(_2\), KOAc, DMAc, 130 °C, 44 h, 44%.\(^1\)

Supporting Scheme S2. Synthesis of 3-bromoethoxybenzene 7.\(^a\)

\[
\begin{align*}
\text{Br} & \quad \text{EtO} \\
\text{HO} & \quad \text{Br} \\
\end{align*}
\]

\(^a\)Conditions: (a) EtBr, K\(_2\)CO\(_3\), MeOH, 120 °C (microwave), 20 min, 95%.\(^2\)

Supporting Scheme S3. Synthesis of 6-(3,5-dimethylisoxazol-4-yl)-3-methyl-3,4-dihydroquinazolin-2(1H)-one 1.\(^a\)

\[
\begin{align*}
\text{Br} & \quad \text{Me} & \quad \text{N} & \quad \text{Me} \\
\text{NO} & \quad \text{N} & \quad \text{Me} \\
\end{align*}
\]

\(^a\)Conditions: (a) \(N\)-Bromosuccinimide, DMF, rt, 2 h, 12%; (b) \(8, Na_2CO_3, Pd(OAc)_2, RuPhos, EtOH, 110 °C\) (microwave), 3 h, 70%.
Supporting Table S1. Ligand efficiency.$^a$

|          | 1       | 4d      | (+)-JQ1  | NMP     |
|----------|---------|---------|----------|---------|
| IC$_{50}$ (M) |         |         |          |         |
| BRD4(1)  | $4.8 \times 10^{-6}$ | $3.4 \times 10^{-6}$ | $4.8 \times 10^{-6}$ | $1.6 \times 10^{-6}$ | $77 \times 10^{-9}$ | $34 \times 10^{-3}$ | $2.4 \times 10^{-1}$ |
| CREBBP   | 5.32    | 5.47    | 5.32     | 5.8     | 7.11    | 1.47     | 2.64     |
| pIC$_{50}$ | 0.39    | 0.40    | 0.39     | 0.43    | 0.32    | 0.30     | 0.53     |
| LE       | 19      | 19      | 19       | 19      | 31      | 7        | 7        |

$^a$ pIC$_{50} = -\log_{10} IC_{50}$

LE = $pIC_{50} \times 1.4$ (kcal/mol)

Heavy atom count
### Supporting Table S2. Data collection and refinement statistics.\(^a\)

| Data Collection | 3SVF | 3SVG | 3SVH |
|-----------------|------|------|------|
| **PDB ID**      | BRD4(1)/2 | BRD4(1)/4d | CREBBP/4b |
| **Space group** | P2\(_1\)2\(_1\)2\(_1\) | P2\(_1\)2\(_1\)2\(_1\) | P2\(_1\) |
| **Cell dimensions:** a, b, c (Å) | 43.56 48.98 60.28 | 37.66 44.19 77.85 | 42.36 61.92 58.42 |
| α, β, γ (deg)   | 90.00 90.00 90.00 | 90.00 90.00 90.00 | 90.00 111.38 90.00 |
| **Resolution (Å)** | 1.98 (2.08-1.98) | 1.68 (1.77-1.68) | 1.80 (1.90-1.80) |
| Unique observations | 9376 (1302) | 15429 (2207) | 24992 (3517) |
| Completeness (%) | 98.8 (96.4) | 99.8 (99.0) | 95.4 (92.4) |
| Redundancy       | 6.5 (5.2) | 4.4 (3.8) | 2.7 (2.7) |
| Rmerge           | 0.185 (0.745) | 0.067 (0.580) | 0.095 (0.265) |
| I/σ I            | 7.5 (2.0) | 13.5 (2.0) | 8.1 (3.4) |

| Refinement | 3SVF | 3SVG | 3SVH |
|------------|------|------|------|
| **Resolution (Å)** | 1.98 | 1.68 | 1.80 |
| R\(_{work}\) / R\(_{free}\) (%) | 17.7/22.6 | 17.6/21.5 | 18.8/22.9 |
| Number of atoms | 1054/23/86 | 1082/31/125 | 1986/80/232 |
| B-factors (Å\(^2\)) | 23.46/24.36/26.29 | 18.77/22.88/26.26 | 12.49/15.21/17.80 |
| (protein/other/water) | | | |
| r.m.s.d bonds (Å) | 0.016 | 0.015 | 0.015 |
| r.m.s.d angles (°) | 1.526 | 1.552 | 1.611 |
| Ramachadran Favoured (%) | 98.40 | 98.33 | 100.00 |
| Allowed (%) | 1.60 | 1.67 | 0.00 |
| Disallowed (%) | 0.00 | 0.00 | 0.00 |

\(^a\) Values in parentheses correspond to the highest resolution shell.

**Protein crystallization:** Aliquots of the purified proteins were set up for crystallization using a mosquito® crystallization robot (TTP Labtech, Royston UK). Coarse screens were typically setup onto Greiner 3-well plates using three different drop ratios of precipitant to protein per condition (100+50 nL, 75+75 nL and 50+100 nL). Initial hits were optimized further scaling up the drop sizes. All crystallizations were carried out using the sitting drop vapor diffusion method at 4 °C. CREBBP crystals with \(4b\) were grown by mixing 150 nL of the protein (10.6 mg/mL and 10 mM final ligand
concentration) with an equal volume of reservoir solution containing 0.25 M potassium thiocyanate, 10% PEG3350 and 5% ethylene glycol. BRD4(1) crystals with 2 were grown by mixing 50 nL of protein (10.3 mg/mL and 5 mM final ligand concentration) with 100 nL of reservoir solution containing 0.2 M sodium acetate, 0.1 M Bis-Tris pH 8.5, 20% PEG3350 and 10% ethylene glycol. BRD4(1) crystals with 4d were grown by mixing 75 nL of protein (9.9 mg/mL and 5 mM final ligand concentration) with an equal volume of reservoir solution containing 0.2 M sodium sulfate, 0.1 M BT-propane pH 8.5, 20% PEG3350 and 10% ethylene glycol. In all cases diffraction quality crystals grew within a few days.

Data Collection and Structure Solution: All crystals were cryo-protected using the well solution supplemented with additional ethylene glycol and were flash frozen in liquid nitrogen. Data were collected in-house on a Rigaku FRE rotating anode system equipped with a RAXIS-IV detector at 1.52 Å. Indexing and integration was carried out using MOSFLM\(^3\) and scaling was performed with SCALA.\(^4\) Initial phases were calculated by molecular replacement with PHASER\(^5\) using the known models of BRD4(1) (PDB ID: 2OSS) and CREBBP (PDB ID: 3DWY). Initial models were built by ARP/wARP\(^6\) followed by manual building in COOT.\(^7\) Refinement was carried out in REFMAC5.\(^8\) In all cases thermal motions were analyzed using TLSMD\(^9\) and hydrogen atoms were included in late refinement cycles. Data collection and refinement statistics can be found in Supporting Table S2. The models and structure factors have been deposited with PDB accession codes: 3SVF (BRD4(1)/2), 3SVG (BRD4(1)/4d), 3SVH (CREBBP/4b).
Further General Experimental

Mass spectra of purchased 1 (Supporting Figure S1A, B) were obtained using an Agilent MSD-ToF electrospray ionisation orthogonal time-of-flight mass spectrometer. The sample was diluted 1:100 (v/v) in LC-MS grade acetonitrile and infused directly into the ion source at a flow rate of 3 µL per minute using a syringe pump. The instrument was configured with the standard ESI source and operated in positive ion mode. Data analysis was performed using Quantitative Analysis software (Agilent Technologies Inc).

LCMS of resynthesized 1 (Supporting Figure S1C) was obtained using a Waters Nano Acquity nano-LC system interfaced to a Waters Synapt mass spectrometer via an electrospray source. LC conditions were: Waters 1.7 µM BEH C18 75 µM × 150 mm column with a binary solvent system using water + 0.1% formic acid and MeCN. Data analysis was performed with using Synapt software (Waters Corporation).

Analytical thin layer chromatography (TLC) was carried out on Merck silica gel 60 F254 aluminum-supported thin layer chromatography sheets. Visualisation was by absorption of UV light (λ_max 254 nm), or thermal development after dipping in an aqueous solution of potassium permanganate, potassium carbonate and sodium hydroxide.

Flash column chromatography was performed on a Biotage SP1 or SP4 system using KP-Sil™ cartridges.

Anhydrous solvents were obtained under the following conditions: dry DMF and dry MeOH were purchased from Sigma-Aldrich UK in SureSeal™ bottles and used without further purification; anhydrous THF was distilled from sodium and benzophenone in a recycling still and stored over activated 3 Å molecular sieves under an argon atmosphere;
Dry DMAc (Sigma) was degassed by repeated freeze-thaw cycles and stored over activated 3 Å molecular sieves under an argon atmosphere. EtOH was degassed by repeated freeze-thaw cycles and stored under an argon atmosphere, but was not dried.

**Chemicals** were purchased from Acros UK, Sigma-Aldrich UK, Alfa Aesar UK, Fisher UK or Fluka UK. Where appropriate and if not stated otherwise, all non-aqueous reactions were performed in a flame-dried flask under an inert atmosphere of nitrogen or argon, using a double vacuum manifold with the inert gas passing through a bed of activated 4 Å molecular sieves and self-indicating silica gel. K$_2$CO$_3$ and Na$_2$CO$_3$ were dried in an oven prior to use. $N,O$-Dimethylhydroxylamine hydrochloride was dried in a vacuum desiccator prior to use.

**In vacuo** refers to the use of a rotary evaporator attached to a diaphragm pump. Brine refers to a saturated aqueous solution of sodium chloride. Petroleum ether refers to the fraction boiling between 30–40 °C unless otherwise stated.

**Synthesis and characterization of compounds 1, 7, 8, 10-13**

6-(3,5-Dimethylisoxazol-4-yl)-3-methyl-3,4-dihydroquinazolin-2(1H)-one 1

To a solution of 3-methyl-3,4-dihydroquinazolin-2(1H)-one (5.00 g, 31.0 mmol) in DMF (120 mL) was added $N$-bromosuccinimide (6.61 g, 37.1 mmol). The reaction was stirred at rt for 2 h then concentrated in vacuo. The resulting residue was resuspended in EtOAc, washed with H$_2$O (3 × 100 mL), dried and concentrated in vacuo. Purification by silica gel column chromatography (5:1 CH$_2$Cl$_2$:EtOAc) gave 6-bromo-3-methyl-3,4-dihydroquinazolin-2(1H)-one as a colorless solid (916 mg, 12%); mp 195–197 °C (EtOH); $^1$H NMR (500 MHz, DMSO-$D_6$) 2.85 (s, 3H) 4.39 (s, 2H), 6.70-6.74 (m, 1H), 7.28–7.32 (m, 2H), 9.33 (s, 1H); $^{13}$C NMR (125 MHz, DMSO-$D_6$) 33.8, 49.2, 112.0,
115.2, 120.3, 128.1, 130.4, 137.3, 153.3; HRMS m/z (ES<sup>+</sup>) found [M+H]<sup>+</sup> 240.9969, 
C<sub>9</sub>H<sub>10</sub>BrN<sub>2</sub>O<sup>+</sup> requires 240.9971; m/z (ES<sup>+</sup>) 263 ([<sup>79</sup>M+Na]<sup>+</sup>, 56), 265 ([<sup>81</sup>M+Na]<sup>+</sup>, 53), 295 ([<sup>79</sup>M+MeOH+Na]<sup>+</sup>, 12), 297 ([<sup>81</sup>M+MeOH+Na]<sup>+</sup>, 12), 503 ([<sup>79</sup>M+Na]<sup>+</sup>, 53), 505 ([<sup>79</sup>M+<sup>81</sup>M+Na]<sup>+</sup>, 100), 507 ([<sup>81</sup>M+Na]<sup>+</sup>, 52). Anal. Calcd for C<sub>9</sub>H<sub>9</sub>BrN<sub>2</sub>O: C, 44.8; H, 3.8; N, 11.6. Found: C, 44.8; H, 3.7; N, 11.6.

To a dry 2-5 mL microwave vial were added 8 (93 mg, 456 µmol), 6-bromo-3-methyl-3,4-dihydroquinazolin-2(1H)-one (100 mg, 415 µmol), Pd(OAc)<sub>2</sub> (1 mg, 4 µmol), RuPhos (6 mg, 13 µmol) and anhydrous Na<sub>2</sub>CO<sub>3</sub> (88 mg, 830 µmmol). The vial was sealed and purged with argon (3 × evacuate/fill). Degassed EtOH (2.3 mL) was added by syringe, and the mixture was heated at 110 °C for 3 h with microwave irradiation.

Purification of the crude reaction mixture by silica gel column chromatography (gradient elution, gradient 60 → 100% EtOAc/petroleum ether) gave 1 as a colorless solid (68 mg, 64%); mp 224-226 °C (MeOH); <sup>1</sup>H NMR (CDCl<sub>3</sub>) 2.24 (s, 3H), 2.38 (s, 3H), 3.07 (s, 3H), 4.50 (s, 2H), 6.83 (d, J = 8.1 Hz, 1H), 6.91 (s, 1H), 7.05 (dd, J = 8.1, 1.8 Hz, 1H), 8.15 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) 10.8, 11.5, 34.6, 50.8, 114.2, 116.1, 117.8, 123.8, 126.0, 129.1, 136.6, 154.5, 158.7, 165.0; HRMS m/z (ES<sup>+</sup>) found 280.1055; C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>NaO<sub>2</sub> requires M<sup>+</sup> 280.1056. m/z (ES<sup>+</sup>) 258 ([M+H]<sup>+</sup>, 28), 280 ([M+Na]<sup>+</sup>, 86), 312 ([M+Na+MeOH]<sup>+</sup>, 85), 537 ([2M+Na]<sup>+</sup>, 100). Anal. Calcd for C<sub>14</sub>H<sub>15</sub>N<sub>3</sub>NaO<sub>2</sub>: C, 65.4; H, 5.9; N, 16.3. Found: C, 65.2; H, 5.9; N, 16.2.

1-Bromo-3-ethoxybenzene 7

To a dry 2-5 mL microwave vial were added anhydrous K<sub>2</sub>CO<sub>3</sub> (829 mg, 6.00 mmol), 3-bromophenol (1.04 g, 637 µL, 6.00 mmol), EtBr (981 mg 672 µL, 9.00 mmol) and anhydrous MeOH (1.8 mL) under a nitrogen atmosphere. The vial was sealed, and the
mixture stirred at 120 °C for 20 min with microwave irradiation, then concentrated in vacuo. The residues were extracted with 40-60 °C petroleum ether (3 × 15 mL) and concentrated in vacuo to give 7 as a pale yellow oil (1.14 g, 95%); 1H NMR (500 MHz, CDCl₃) 1.42 (t, J = 7.0 Hz, 3H), 4.02 (q, J = 7.0 Hz, 2H), 6.83 (ddd, J = 8.1, 2.3, 1.0 Hz, 1H), 7.05-7.08 (m, 2H), 7.14 (dd, J = 8.1, 8.1 Hz, 1H); 13C NMR (100 MHz, CDCl₃) 14.7, 63.7, 113.6, 117.7, 122.8, 123.6, 130.5, 159.7; HRMS m/z (FI⁺) found M⁺ 199.9838, 201.9817; C₈H₇BrO requires M⁺ 199.9837, C₈H₈¹BrO requires M⁺ 201.9811. Anal. Calcd for C₈H₇BrO: C, 47.8; H, 4.5. Found: C, 47.7; H, 4.4.

Potassium (3,5-dimethylisoxazol-4-yl)trifluoroborate 8

To a suspension of 3,5-dimethylisoxazol-4-ylboronic acid (254 mg, 1.80 mmol) in MeOH (1.0 mL) at 0 °C was added KHF₂ (420 mg, 5.38 mmol). H₂O (1.20 mL) was then added dropwise. The solution was warmed to rt and stirred for 10 min, then concentrated and dried overnight in vacuo. The crude solid was purified by Soxhlet extraction (16 h) with acetone (15 mL). The collected solvent was concentrated in vacuo, and the residues redissolved the minimum amount of acetone (40 mL). The product was precipitated by the addition of Et₂O (60 mL) and collected by filtration. The filtrate was concentrated in vacuo, redissolved in acetone (5 mL) and further product was precipitated by the addition of Et₂O (20 mL) and collected by filtration. The combined solids were dried in vacuo to give 8 as a powdery colorless solid (312 mg, 85%); mp >275 °C (lit. >200 °C)¹⁰; 1H NMR (400 MHz, DMSO-D₆) 2.05 (s, 3H), 2.20 (s, 3H); 1¹B NMR (160 MHz, DMSO-D₆) 2.33 (q, J = 49 Hz); ¹⁹F NMR (470 MHz, DMSO-D₆) −134.8−134.2; m/z (ES⁻) 164 ([M-K]⁻, 100), 351 ([2M−2K+Na]⁻, 43), 367 ([2M−K]⁻, 22). Anal. Calcd for C₅H₆BF₃KNO: C,
29.6; H, 3.0; N, 6.9. Found: C, 29.7; H, 2.9; N, 6.8. These data are in good agreement with the literature values. 

**Ethyl 3-bromo-5-ethoxybenzoate 10**

To a dry 10–20 mL microwave vial were added 3-bromo-5-hydroxybenzoic acid 9 (1.30 g, 5.99 mmol), anhydrous K$_2$CO$_3$, anhydrous DMF (5 mL) and EtBr (1.96 g, 1.34 mL, 18.0 mmol) under a nitrogen atmosphere. The vial was sealed, and the mixture stirred at 100 °C for 15 min, then concentrated in vacuo. The mixture was diluted with H$_2$O (40 mL) and extracted with EtOAc (3 × 40 mL). The combined organic layers were washed with H$_2$O (2 × 120 mL) and brine (120 mL), dried (MgSO$_4$), filtered, and concentrated in vacuo to give 10 as an orange solid (1.57 g, 96%); mp 43-44 °C (EtOAc); $^1$H NMR (500 MHz, CDCl$_3$) 1.39 (t, $J$ = 7.2 Hz, 3H), 1.42 (t, $J$ = 7.0 Hz, 3H), 4.06 (q, $J$ = 7.0 Hz, 2H), 4.37 (q, $J$ = 7.2 Hz, 2H), 7.22 (dd, $J$ = 2.4, 1.8 Hz, 1H), 7.49 (dd, $J$ = 2.4, 1.5 Hz, 1H), 7.73 (dd, $J$ = 1.8, 1.5 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 14.3, 14.6, 61.4, 64.1, 114.1, 122.4, 122.6, 124.7, 133.0, 159.6, 165.3; HRMS m/z (ES$^+$) found [M+Na]$^+$ 294.9931, 296.9925, C$_{11}$H$_{13}$$^{79}$BrNaNO$_3$ requires M$^+$ 294.9940, C$_{11}$H$_{13}$$^{81}$BrNaNO$_3$ requires M$^+$ 296.9920; m/z (ES$^+$) 295 ([$^{79}$M+Na]$^+$, 100), 297 ([$^{81}$M+Na]$^+$, 97), 567 ([2$^{79}$M+Na]$^+$, 42), 569 ([$^{79}$M+$^{81}$M+Na]$^+$, 78), 571 ([2$^{81}$M+Na]$^+$, 37). Anal. Calcd for C$_{11}$H$_{13}$BrNO$_3$: C, 48.4; H, 4.8. Found: C, 48.3; H, 4.8.

**3-Bromo-5-ethoxybenzoic acid 11**

To a solution of 10 (500 mg, 1.83 mmol) in THF (2 mL) were added H$_2$O (1 mL) and LiOH (66 mg, 2.75 mmol), and the mixture was stirred for 23 h at rt. Aqueous HCl (1 M, 10 mL) was then added, and the mixture extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (30 mL), dried (MgSO$_4$), filtered, and
concentrated in vacuo to give 11 as a pale yellow solid (425 mg, 95%); mp 139-143 °C (EtOAc); $^1$H NMR (400 MHz, CDCl$_3$) 1.44 (t, $J = 7.0$ Hz, 3H), 4.09 (q, $J = 7.0$ Hz, 2H), 7.30 (dd, $J = 2.5$, 1.8 Hz, 1H), 7.55 (dd, $J = 2.5$, 1.4 Hz, 1H), 7.83 (dd, $J = 1.8$, 1.4 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$) 14.6, 64.2, 114.5, 122.8, 123.5, 125.3, 131.6, 159.7, 170.3; HRMS m/z (ES$^-$) found [M−H]$^-$ 242.9962, 244.9642; C$_9$H$_9^{79}$BrO$_3$ requires M$^-$ 242.9962, C$_9$H$_9^{81}$BrO$_3$ requires M$^-$ 244.9642; m/z (ES$^-$) 243 ([$^{79}$M], 96), 245 ([$^{81}$M$^-$], 100), 487 ([$^{79}$M$^-$], 6) 489 ([$^{79}$M+$^{81}$M]$^-$, 13), 491 ([$^{81}$M], 6), 509 ([$^{79}$M−2H+Na$^+$], 45), 511 ([$^{79}$M+$^{81}$M−2H+Na$^-$], 80), 513 ([$^{81}$M−2H+Na$^-$], 37). Anal. Calcd for C$_9$H$_9$BrO$_3$: C, 44.1; H, 3.7. Found: C, 44.0; H, 3.6.

3-Bromo-5-ethoxy-N-methoxy-N-methylbenzamide 12

To a dry flask containing 11 (353 mg, 1.44 mmol), N,O-dimethylhydroxylamine hydrochloride (285 mg, 2.92 mmol) and HBTU (576 mg, 1.52 mmol) were added anhydrous DMF (3.5 mL) and diisopropylethylamine (1.0 g, 1.3 mL, 7.46 mmol) at 0 °C under a nitrogen atmosphere. The mixture was warmed to rt and stirred for 14 h, then concentrated in vacuo. The residues were redissolved in EtOAc (50 mL), washed with citric acid (10% w/v, 2 × 50 mL), saturated aqueous NaHCO$_3$ (2 × 50 mL), H$_2$O (2 × 50 mL) and brine (50 mL), dried (MgSO$_4$), filtered, and concentrated in vacuo.

Purification by silica gel column chromatography (gradient elution, gradient 6 → 40% EtOAc/petroleum ether) gave 12 as a colorless oil (331 mg, 80%); $^1$H NMR (400 MHz, CDCl$_3$) 1.41 (t, $J = 7.0$ Hz, 3H), 3.34 (s, 3H), 3.57 (s, 3H), 4.03 (q, $J = 7.0$ Hz, 2H), 7.10-7.14 (m, 2H), 7.35-7.38 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 14.6, 33.7, 61.2, 64.0, 113.2, 119.9, 122.3, 123.1, 136.6, 159.3, 168.1; HRMS m/z (ES$^+$) found [M+Na]$^+$ 310.0055, 312.0034; C$_{11}$H$_{14}^{79}$BrNNaO$_3$ requires M$^+$ 310.0049, C$_{11}$H$_{14}^{81}$BrNNaO$_3$
requires $M^+ 312.0029$; $m/z$ (ES$^+$) 288 ([$^{79}M+H]^+$, 25), 290 ([$^{81}M+H]^+$, 24), 310
([$^{79}M+Na]^+$, 57), 312 ([$^{81}M+Na]^+$, 55), 597 ([$^{79}M+Na]^+$, 96), 599 ([$^{79}M+^{81}M+Na]^+$, 100), 601 ([$^{81}M+Na]^+$, 95). Anal. Calcd for C$_{11}$H$_{14}$BrNO$_3$: C, 45.9; H, 4.9; N, 4.9.
Found: C, 46.0; H, 4.8; N, 4.7.

1-(3-Bromo-5-ethoxyphenyl)ethanone 13

To a solution of 12 (250 mg, 868 µmol) in anhydrous THF (8 mL) under an argon atmosphere was added MeMgBr solution (1.0 M in dibutyl ether, 2.6 mL, 2.6 mmol) dropwise at 0 °C. The solution was warmed to rt and stirred for 15 h, then quenched with aqueous HCl (1 M, 15 mL). The mixture was extracted with EtOAc (3 × 15 mL), and the combined organic layers were washed with brine (50 mL), dried (MgSO$_4$), filtered, and concentrated in vacuo. Purification by silica gel column chromatography (gradient elution, gradient 3 → 30% Et$_2$O/petroleum ether) gave 13 as a colorless solid (181 mg, 86%); mp 40-41 °C (15% Et$_2$O/petroleum ether); $^1$H NMR (400 MHz, CDCl$_3$) 1.43 (t, $J = 7.0$ Hz, 3H), 2.57 (s, 3H), 4.07 (q, $J = 7.0$ Hz, 2H), 7.23-7.25 (m, 1H), 7.38-7.41 (m, 1H), 7.63-7.65 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) 14.6, 26.7, 64.2, 112.7, 122.5, 123.0, 123.8, 139.4, 159.8, 196.5; HRMS $m/z$ (ES$^+$) found [M+Na]$^+$ 264.9833, 266.9814; C$_{10}$H$_{11}$BrNaO$_2$ requires $M^+$ 264.9835, C$_{10}$H$_{11}$BrNaO$_2$ requires $M^+$ 266.9814; $m/z$ (ES$^+$) 265 ([$^{79}M+Na]^+$, 100), 267 ([$^{81}M+Na]^+$, 97). Anal. Calcd for C$_{10}$H$_{11}$BrO$_2$: C, 49.4; H, 4.6. Found: C, 49.6; H, 4.4.

Further characterization for compounds 3a-d, 4a-d

3,5-Dimethyl-4-phenyloxazole 3a

Anal. Calcd for C$_{11}$H$_{11}$NO: C, 76.3; H, 6.4; N; 8.1. Found: C, 76.4; H, 6.5; N, 8.0.

1-3-(3,5-Dimethylisoxazol-4-yl)phenylethanone 3b
Anal. Calcd for C_{13}H_{13}NO: C, 72.5; H, 6.1; N, 6.5. Found: C, 72.6; H, 6.2; N, 6.4.

4-(3-Ethoxyphenyl)-3,5-dimethylisoxazole 3c

$^{13}$C NMR (100 MHz, CDCl$_3$) 10.8, 11.6, 14.8, 63.5, 113.2, 115.6, 116.6, 121.3, 129.8, 131.7, 158.6, 159.2, 165.2. Anal. Calcd for C$_{13}$H$_{13}$NO: C, 71.9; H, 7.0; N, 6.5. Found: C, 72.0; H, 7.1; N, 6.4.

(RS)-1-(3-(3,5-Dimethylisozaxol-4-yl)phenyl)ethanol 3d

$^{13}$C NMR (100 MHz, CDCl$_3$) 10.8, 11.6, 25.4, 70.1, 116.6, 124.6, 126.1, 128.0, 128.9, 130.6, 146.6, 158.7, 165.2. Anal. Calcd for C$_{13}$H$_{13}$NO: C, 71.9; H, 7.0; N, 6.5. Found: C, 72.0; H, 7.0; N, 6.3.

Ethyl 3-(3,5-dimethylisoxazol-4-yl)-5-ethoxybenzoate 4a

$^{13}$C NMR (100 MHz, CDCl$_3$) 10.8, 11.6, 14.3, 14.7, 61.3, 63.9, 113.5, 115.9, 120.5, 122.5, 131.9, 132.3, 158.5, 159.2, 165.6, 166.1. Anal. Calcd for C$_{16}$H$_{19}$NO$_4$: C, 66.4; H, 6.6; N, 4.8. Found: C, 66.6; H, 66.5; N, 4.7.

3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxybenzoic acid 4b

$^{13}$C NMR (126 MHz, CDCl$_3$) 10.8, 11.6, 14.7, 64.0, 113.8, 115.7, 121.6, 123.1, 131.0, 132.1, 158.5, 159.3, 165.7, 171.1. Anal. Calcd for C$_{14}$H$_{15}$NO$_4$: C, 64.4; H, 5.8; N, 5.4. Found: C, 64.2; H, 5.9; N, 5.3.

1-(3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxyphenyl)ethanone 4c

$^{13}$C NMR (126 MHz, CDCl$_3$) 10.8, 11.6, 14.7, 26.7, 63.9, 112.3, 115.9, 120.5, 121.5, 132.2, 138.9, 158.5, 159.5, 165.6, 197.5. Anal. Calcd for C$_{15}$H$_{17}$NO$_3$: C, 69.5; H, 6.6; N, 5.4. Found: C, 69.6; H, 6.7; N, 5.3.
(RS)-1-(3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxyphenyl)ethanol 4d

$^{13}$C NMR (100 MHz, CDCl$_3$) 10.8, 11.6, 14.8, 25.4, 63.6, 70.1, 110.3, 114.4, 116.6, 118.3, 131.8, 148.1, 158.6, 159.4, 165.2. Anal. Calcd for C$_{15}$H$_{19}$NO$_3$: C, 68.9; H, 7.3; N, 5.3. Found: C, 69.1; H, 71; N, 5.5.

References

1. Fall, Y.; Reynaud, C.; Doucet, H.; Santelli, M., Ligand-Free-Palladium-Catalyzed Direct 4-Arylation of Isoxazoles Using Aryl Bromides. *Eur. J. Org. Chem.* 2009, 2009, 4041-4050.

2. Sarju, J.; Danks, T. N.; Wagner, G., Rapid microwave-assisted synthesis of phenyl ethers under mildly basic and nonaqueous conditions. *Tetrahedron Lett.* 2004, 45, 7675-7677.

3. Leslie, A. G. W.; Powell, H. *MOSFLM*, 7.01; MRC Laboratory of Molecular Biology: Cambridge, 2007.

4. Evans, P. *SCALA - scale together multiple observations of reflections*, 3.3.0; MRC Laboratory of Molecular Biology: Cambridge, 2007.

5. McCoy, A. J.; Grosse-Kunstleve, R. W.; Storoni, L. C.; Read, R. J., Likelihood-enhanced fast translation functions. *Acta Crystallogr. Sect. D. Biol. Crystallogr.* 2005, 61, 458-464.

6. Perrakis, A.; Morris, R.; Lamzin, V. S., Automated protein model building combined with iterative structure refinement. *Nat. Struct. Biol.* 1999, 6, 458-463.
7. Emsley, P.; Cowtan, K., Coot: model-building tools for molecular graphics. *Acta Crystallogr. Sect. D. Biol. Crystallogr.* 2004, 60, 2126-2132.

8. Murshudov, G. N.; Vagin, A. A.; Dodson, E. J., Refinement of macromolecular structures by the maximum-likelihood method. *Acta Crystallogr. Sect. D. Biol. Crystallogr.* 1997, 53, 240-255.

9. Painter, J.; Merritt, E. A., Optimal description of a protein structure in terms of multiple groups undergoing TLS motion. *Acta Crystallogr. Sect. D. Biol. Crystallogr.* 2006, 62, 439-450.

10. Molander, G. A.; Canturk, B.; Kennedy, L. E., Scope of the Suzuki-Miyaura Cross-Coupling Reactions of Potassium Heteroaryltrifluoroborates. *J. Org. Chem.* 2008, 74, 973-980.
6-bromo-3-methyl-3,4-dihydroquinazolin-2(1H)-one

Current Data Parameters
NAME  bromodihydroquinazolinone
EXPRO  1
PROCNO  1

F2 - Acquisition Parameters
Date_  20110721
Time  22.04
INSTROM  avc500
PROBBWD  5 mm CPOU1.13C
FULLPROG  zg30
TD  65536
SOLVENT  DMSO
NS  16
DG  2
SWH  10330.578 Hz
FIDRES  0.157632 Hz
AQ  3.1719923 sec
RG  4
DM  48.400 usec
DE  6.00 usec
TE  298.0 K
D1  1.00000000 sec
TD0  1

--------- CHANNEL f1 ---------
NUC1  1H
P1  9.60 usec
PL1  -6.00 dB
PL1W  15.1999981 W
SFQ1  500.3003896 MHz

F2 - Processing parameters
SI  32768
SF  500.3000000 MHz
NDW  EM
SSB  0
LB  0.30 Hz
GB  0
PC  1.00
6-bromo-3-methyl-3,4-dihydroquinazolin-2(1H)-one
6-(3,5-dimethylisoazol-4-yl)-3-methyl-3,4-dihydroquinazolin-2(1H)-one 1
6-(3,5-dimethylisoxazol-4-yl)-3-methyl-3,4-dihydroquinazolin-2(1H)-one 1
4-(3-Ethoxyphenyl)-3,5-dimethylisoxazole 3c
NAME 039
EXPER 04
PROCWO 1
Date_ 20101204
Time 22.17
INSTIRM EX040
PRBODY 9 mm QNP 1H13
POLPROD EX909
ID 32948
REVEXT 2031
NS 256
DS 4
DW 26778.610 Hz
FIDRES 0.198689 Hz
AG 0.6225988 sec
MS 37360
DW 19.100 ussec
DE 7.900 ussec
TE 350.00 ussec
D1 1.00000000 sec
D11 0.030000 sec
TD 1

---------- CHANNEL #1 ----------
H1C 9.50 ussec
P1 0.00 ussec
SF01 100.6450391 MHz

---------- CHANNEL #2 ----------
CPSPGR2 50.18015
N1 18
P2 0.00 ussec
P1 0.00 ussec
P1 19.00 ussec
P1 19.00 ussec
SF02 400.761658 MHz
SF 37360
SF 100.6303118 MHz
NOW 36100
SBB 0
LB 1.00 ussec
GB 0
PC 1.40

4-(3-Ethoxyphenyl)-3,5-dimethylisoxazole 3c
(RS)-1-((3,5-Dimethylisoxazol-4-yl)phenyl)ethanol 3d
(RS)-1-(3-(3,5-Dimethylisoxazol-4-yl)phenyl)ethanol 3d
Ethyl 3-(3,5-dimethylisoxazol-4-yl)-5-ethoxybenzoate 4a
Ethyl 3-(3,5-dimethylisoxazol-4-yl)-5-ethoxybenzoate 4a
3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxybenzoic acid 4b
3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxybenzoic acid 4b
1-(3-(5-Dimethylisoxazol-4-yl)-5-ethoxyphenyl)ethanone 4c

NAME  042
EXPNO  1
PROCNO  1
Date,  20101217
Time  12.12
INSTRUM  avs500
PPOBHD  5 mm CPDUL 13C
PULPROG  zg30
TD  65536
SOLVENT  CDCl3
NS  16
DS  2
SWH  10330.578 Hz
FIDRES  0.157632 Hz
AQ  3.1719923 sec
RG  4
DW  48.400 usec
DE  6.00 usec
TE  298.0 K
DI  1.0000000 sec
TDO  1

---------- CHANNEL f1 ----------
NOC1  1H
P1  9.60 usec
PL1  -6.00 dB
PLW  15.19999981 W
SF01  500.3030896 MHz
SI  12768
SF  500.3000240 MHz
CDW  EM
SSB  0
LR  0.30 Hz
GR  0
PC  1.00

ppm
1-(3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxyphenyl)ethanone 4c
(RS)-1-(3-(3,5-Dimethylisoxazol-4-yl)-5-ethoxyphenyl)ethanol 4d

Current Data Parameters
NAME: 046 wash
EXPMO: 1
PROCNO: 1

F2 - Acquisition Parameters
Date_: 20110503
Time_: 10.11
INSTRUM: dpx400
PROBES: 5 mm Dual 1H/1
PULPROG: zg60
TD: 32768
SOLVENT: CDC13
NG: 16
DG: 2
SWH: 5592.841 Hz
P1PRES: 0.170680 Hz
AQ: 2.9295092 sec
RG: 143.7
DM: 89.400 usec
DE: 17.00 usec
TE: 300.0 K
D1: 1.0000000 sec

-------- CHANNEL f1 --------
NUC1: 1H
P1: 7.30 usec
PL1: 0.00 dB
SPO1: 400.1320007 MHz

F2 - Processing parameters
SI: 32768
SF: 400.1330182 MHz
MDM: EM
SSB: 0
LB: 0.30 Hz
GB: 0
PC: 0.60
(RS)-1-(3,5-Dimethylisoxazol-4-yl)-5-ethoxyphenyl)ethanol 4d
1-Bromo-3-ethoxybenzene 7
1-Bromo-3-ethoxybenzene 7

NAME 005
EXPRO 2
PROCNO 1
Date_ 20101011
Time 16.19
INSTRUM aq400
PROBMD 5 mm QNP 1H/13
PULPROG zgpg30
TD 32768
SOLVENT d2o
NS 256
DS 1
SWH 26178.010 Hz
FIDRES 0.798889 Hz
AQ 0.6259198 sec
RG 32768
DW 19.100 usec
DE 7.50 usec
TE 300.0 K
D1 1.00000000 sec
D11 0.00000000 sec
TDD 1

======== CHANNEL f1 ========
NUC1 13C
P1 9.50 usec
PL1 0.00 dB
SFO1 100.6403931 MHz

======== CHANNEL f2 ========
CPDPDG2 wait:16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 19.00 dB
PL13 25.00 dB
SFO2 400.2016008 MHz
SI 32768
SF 100.6303718 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
Ethyl 3-bromo-5-ethoxybenzoate 10
Ethyl 3-bromo-5-ethoxybenzoate 10

NAME 009
SNIPRO 1
SNIPRO 2
Date 20101013
Time 10:10
INSTRUM AV6400
PUED 5 mm QNP 16113
PULPROG 294030
TD 32768
SOLVENT CDCl3
NS 256
DS 1
SW 26178.015 Hz
T1RES 0.298689 ms
AQ 0.029198 sec
INEQ 0.001
DW 19.100 usec
DS 7.50 usec
GS 300.0 Hz
DI 1.000000000 sec
D11 0.000000000 sec
ISO 1

--------- CHANNEL F1 ---------
N1C1 15C
P1 10.00 usec
P21 0.00 dm
SPO1 100.6400993 MHz

--------- CHANNEL F2 ---------
C13C2 13C
P123 90.00 usec
P212 10.00 dm
P213 10.00 dm
SPO2 600.281000 MHz
ST 32768
SP 100.639718 MHz
PG1 1.00 Hz
GR 1.40
3-Bromo-5-ethoxybenzoic acid 11

NAME  014 C
EXPNO  1
PROCNO  1
Date_  20101101
Time  17.36
INSTRNM  avc3600
PROBND  5 mm CPDUL 13C
PULPROG  zgpg30
TD  65536
SOLVENT  CDC13
NS  512
DS  2
SWM  31250.000 Hz
FIDRES  0.476837 Hz
AQ  1.0486259 sec
RG  912
DW  16.000 usec
DE  20.00 usec
TE  298.1 K
DI  2.00000000 sec
D11  0.03000000 sec
T00  1

--------- CHANNEL f1 ---------
NC1  13C
P1  9.50 usec
PL1  -4.40 dB
PL1W  28.15752029 W
SF1  125.8131151 MHz

--------- CHANNEL f2 ---------
CPDPEG2  waitz16
NCC2  1H
PCPD2  80.00 usec
PL2  -6.00 dB
PL12  12.42 dB
PL13  18.42 dB
PL2W  15.19999961 W
PL12W  0.21869738 W
PL13W  0.05493430 W
SF2  500.3020012 MHz
SI  12768
SF  125.8005638 MHz
WDM  EM
SSB  0
LB  1.00 Hz
GB  0
PC  1.40
3-Bromo-5-ethoxy-N-methoxy-N-methylbenzamide 12

NAME   022 H and HMBC
EXPNO   1
PROCNO   1
Date   20101208
Time   5.45
INSTRUM   av500
PROBBD   5 mm CPDUL 13C
PULPROG   zg30
TD   65536
SOLVENT   CDC13
NS   16
DS   2
SWH   10330.578 Hz
FIDRES   0.157632 Hz
AQ   3.1719923 sec
RG   4
DW   48.400 usec
DE   6.00 usec
TE   298.0 K
D1   1.00000000 sec
TD0   1

---------- CHANNEL r1 ----------
NUC1   1H
P1   9.60 usec
PL1   -6.00 dB
PLW   15.19999981 W
SF01   500.3030896 MHz
SI   32768
SF   500.3000240 MHz
CDW   EM
SSB   0
LS   0.30 Hz
GR   0
PC   1.00
3-Bromo-5-ethoxy-N-methoxy-N-methylbenzamide 12

```
NAME   022
EXPNO  2
PROCNO 1
Date_  2010104
Time_  12:10
INSTNUM av600
PFBMOD 3 mm QNP 30:13
WBFMOD 0:800008
ID_  32:248
DEV1NT CD2L3
NS_  256
DS_  4
DW_  26178810 Hz
FIDRES 0.78899888 Hz
AQ_  0.6259988 sec
NS_  32768
DW_  19.100 ussec
DE_  7.500 ussec
TE_  300.0 ussec
D1_  1.000000000 sec
D11_  0.000000000 sec
TR0_  1

---------- CHANNEL #1 ----------
NUC1_ 13C
P1_  9.50 ussec
P1L_  5.00 ussec
SPD1_ 100.6403931 MHz

---------- CHANNEL #2 ----------
CPWPNQ2_ 14F
NUC2_ 19
PCP02_ 80.000000000 ussec
PL2_  0.00 ussec
PL12_  12.000000000 ussec
PL13_  12.000000000 ussec
SFQ2_ 400.2016000 MHz
Si_  32768
SF_  100.6303718 MHz
NOW_ 231 MHz
SSB_ 0
LB_  1.000000000 ussec
GB_  0
PC_  1.40
```

```
OMe

EtO

\[\text{N} - \text{Me} \]

\[\text{Br} \]

S44
```
1-(3-Bromo-5-ethoxyphenyl)ethanone 13

| Parameter       | Value        |
|-----------------|--------------|
| Ac              | EtO          |
| Br              | EtO          |

**NAME:** 027  
**EXPNO:** 1  
**PROCNO:** 1  
**Date:** 20101113  
**Time:** 1.29  
**INSTRUM:** av400  
**PROBNO:** 5 mm QNP 18/13  
**PULPROG:** zg60  
**TD:** 650.36  
**SOLVENT:** CDC13  
**NS:** 16  
**DS:** 2  
**SWH:** 8278.146 Hz  
**FIDRES:** 0.126314 Hz  
**AQ:** 3.9584243 sec  
**MG:** 228.1  
**DW:** 60.400 usec  
**DE:** 7.50 usec  
**TE:** 380.0 K  
**D1:** 1.00000000 sec  

--- CHANNEL f1 ---
**NUC1:** 1H  
**P1:** 9.00 usec  
**PL1:** 0.00 dB  
**SPD:** 400.2024714 MHz  
**SR:** 32768  
**SF:** 400.2000028 MHz  
**WDW:** EM  
**SSB:** 0  
**LB:** 0.30 Hz  
**GB:** 0  
**PC:** 1.00
1-(3-Bromo-5-ethoxyphenyl)ethanone 13

NAME 027
EXPN0 2
RNCNO 1
Data_ 2B10111
Time 1.37
INSTRHM av400
PREPROC 5mm QNP 38u13
TFROG 38
TD 33768
SOLVENT CDCl3
NS 256
DS 4
DWN 26178.010 Hz
FIDRES 0.198089 Hz
AQ 0.6259988 sec
RS 32768
DW 19.100 usec
DE 7.90 usec
TE 150.0
DI 1.00000000 sec
D11 0.03000000 sec
TD0 1

====== CHANNEL f1 ======
NUC1 13C
P1 9.50 usec
P2 0.00 usec
SF1 100.640331 MHz

====== CHANNEL f2 ======
CPUSRG2 wa13114
NUC2 1H
PC120 80.00 usec
PL1 0.00 dB
PL2 19.00 dB
PL3 25.00 dB
SF2 400.201600 MHz
ST 32768
SF 100.630318 MHz
NOW EM
SSB 0
SB 1.00 Hz
GB 0
PC 1.40