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Supporting information for article:

Structural investigation of a pyrano-1,3-oxazine derivative and the phenanthridinone core moiety against BRD2 bromodomains

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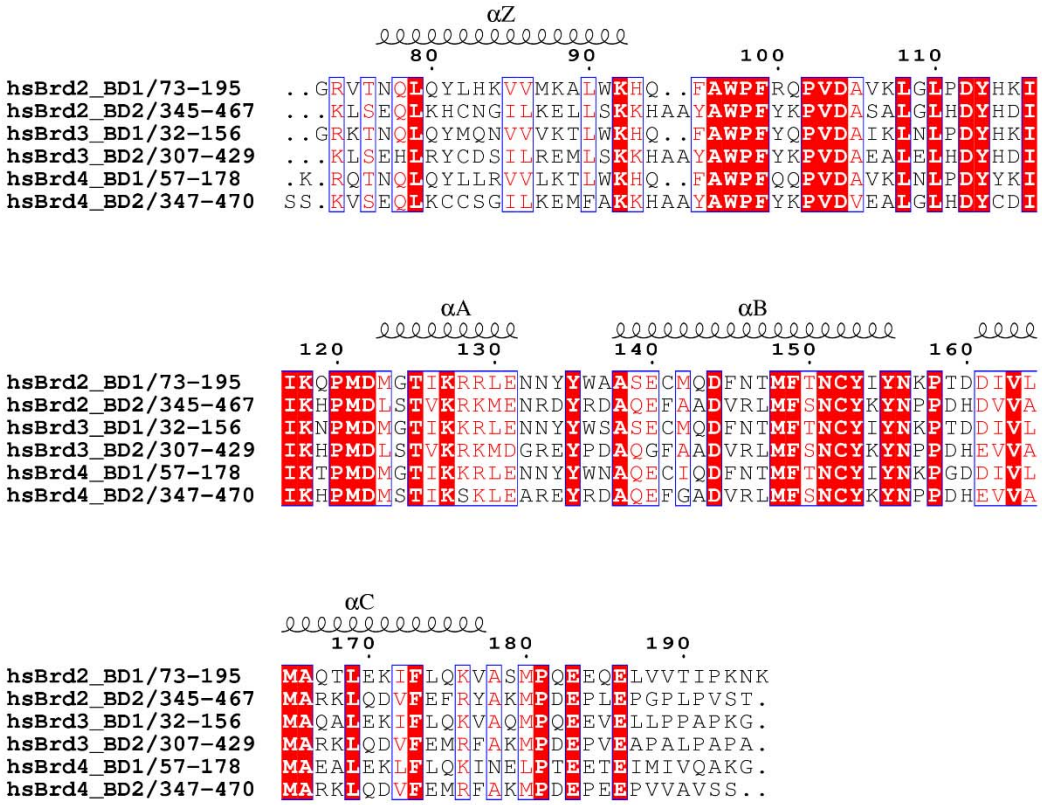

Figure S1 Multiple sequence alignment of tandem bromodomains of BET family proteins BRD2, BRD3 and BRD4. The alignment was produced by ClustalW (Larkins et al., 2007), and was manually modified. The white characters on the red background indicate identical residues; the red characters on the white background indicate completely homologous amino acids among the bromodomains. The figure was generated by ESpript (Robert and Gouet, 2014).

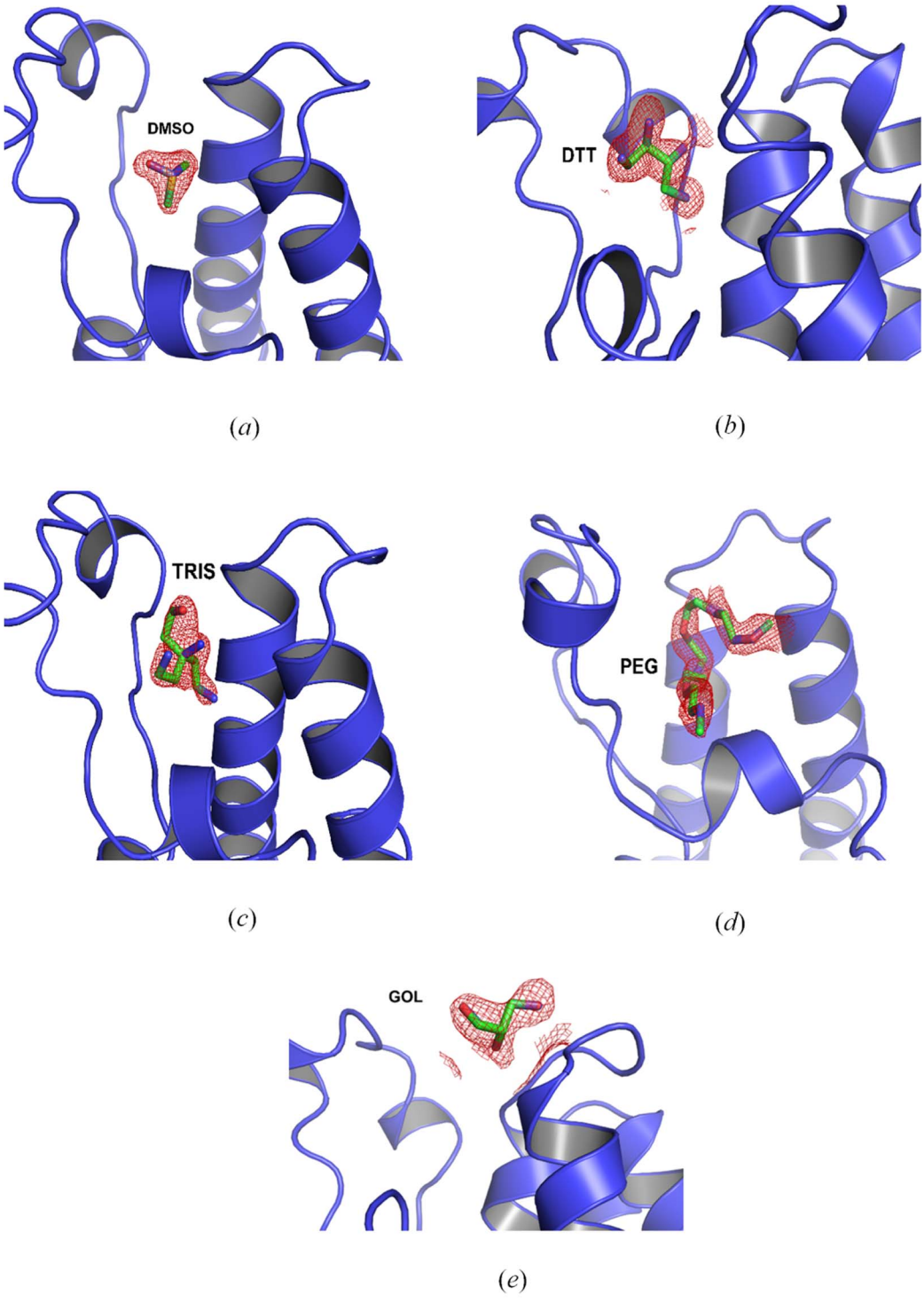

Figure S2 Various reagent/solvent/precipitant of protein buffers, crystallization reagent, ligand solvents, and cryo-protectant, observed in the binding pocket of BRD2 bromodomains. (*a*) Dimethyl sulfoxide (DMSO), (*b*) Dithiothreitol (DTT), (*c*) Tris buffer (TRIS), (*d*) Polyethylene glycol (PEG), and (e) Glycerol (GOL).

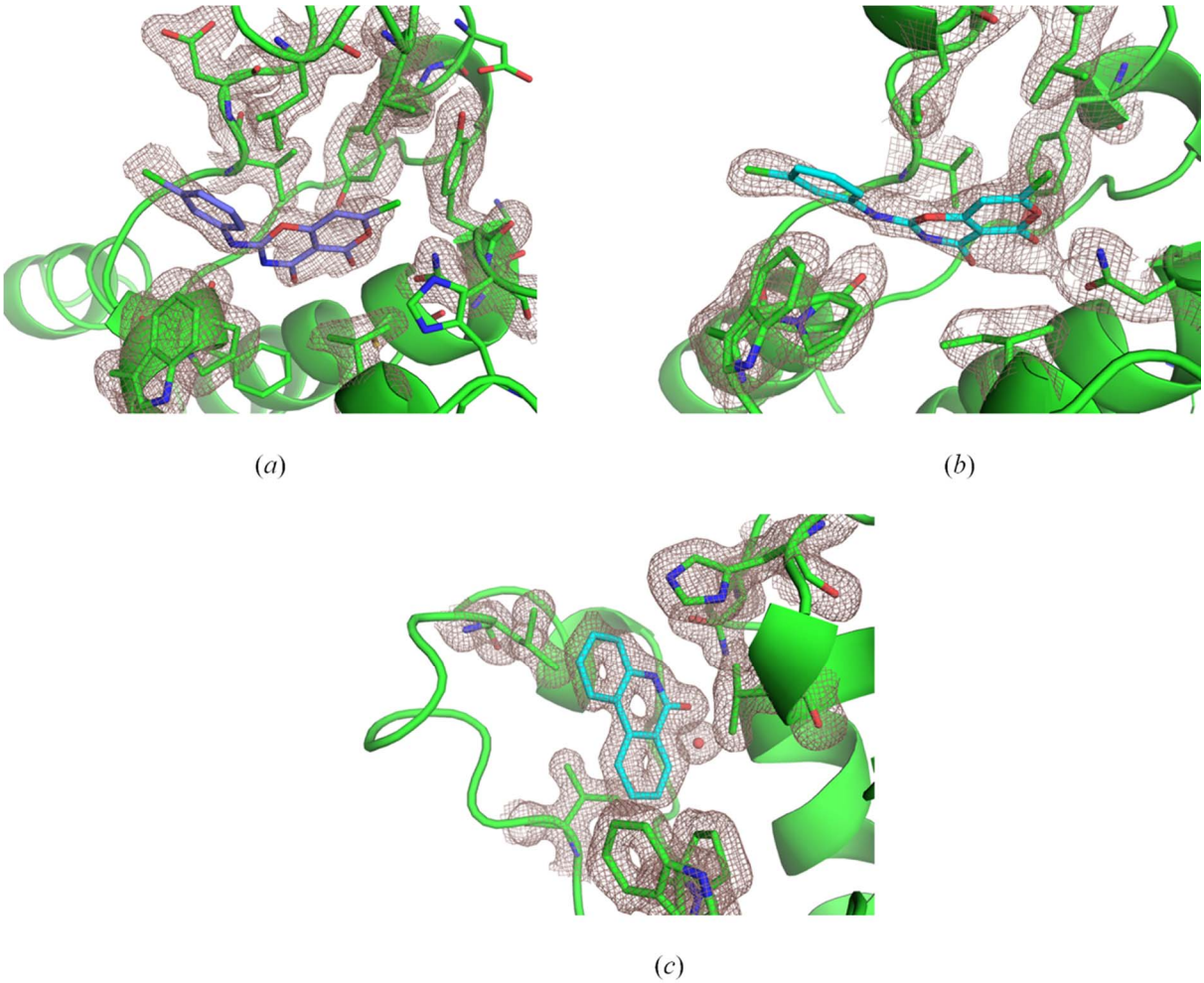

Figure S3 The structure of BRD2 bromodomains complexes. (*a*) The tertiary structure of the BRD2-BD2 complex with the compound NS5 bound to the active site. |2Fo|-|Fc| map contoured at 0.98 σ near the binding pocket of BD2. (*b*) The tertiary structure of the BRD2-BD1 complex with the compound NS5 bound to the active site. |2Fo|-|Fc| map contoured at 0.98 σ near the binding pocket of BD1. (*c*) The tertiary structure of the BRD2-BD2 complex with the compound L10a bound to the active site. |2Fo|-|Fc| map contoured at 1.0 σ near the binding pocket of BD2. The ligand and interacting residues are shown as sticks.

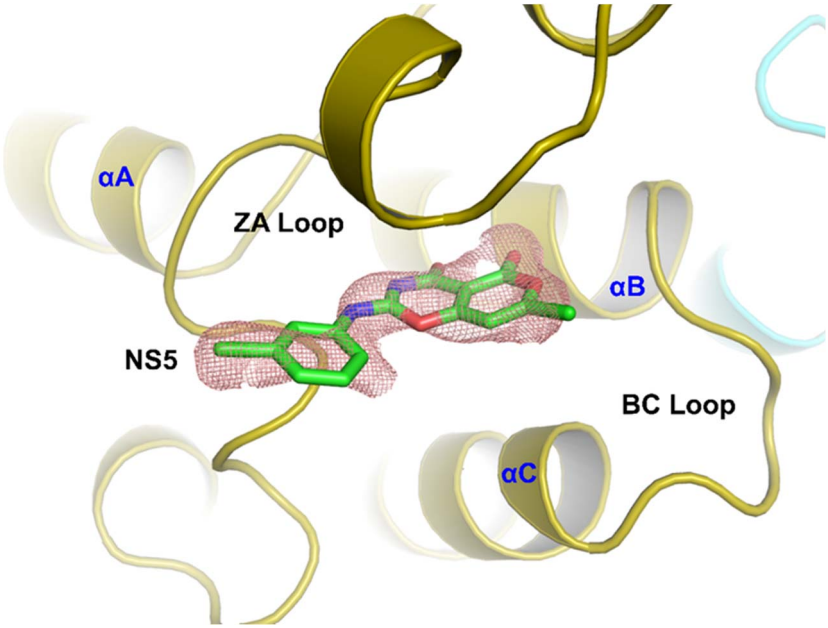

Figure S4 The crystal structure of BD1-NS5 complex. The Polder difference Fourier map of NS5 (contoured at 2.7 σ) in the Kac binding pocket of BD1 confirms the ligand binding that was reported in our previous structure (6JKE).

Larkin MA, Blackshields G, Brown NP, Chenna R, McGettigan PA, McWilliam H, Valentin F, Wallace IM, Wilm A, Lopez R, Thompson JD, Gibson TJ, Higgins DG. (2007). *Bioinformatics*, 23, 2947-2948.

Robert, X. and Gouet, P. (2014) *Nucleic Acids Res*. 42(W1), W320-W324.