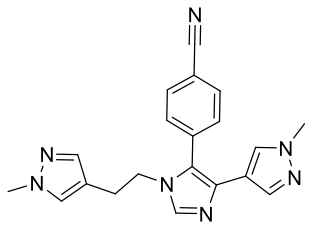
Product data sheet

MedKoo Cat#: 406642 Name: BAZ2-ICR CAS#: 1665195-94-7 Chemical Formula: $C_{20}H_{19}N_7$ Exact Mass: 357.17019 Molecular Weight: 357.41	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
BAZ2-ICR is an excellent chemical probe for functional studies of the BAZ2 bromodomains in vitro and in vivo. The bromodomain containing proteins BAZ2A/B play essential roles in chromatin remodeling and regulation of noncoding RNAs. BAZ2-ICR has IC50 (BAZ2A) = 130 nM; IC50(BAZ2B) = 180 nM; logD = 1.05; solubility 25 mM (D2O) and F = 70%.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	18.58	51.99
DMF	20.0	55.96
DMF:PBS (pH 7.2) (1:1)	0.5	1.40
Ethanol	13.37	37.41

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.80 mL	13.99 mL	27.98 mL
5 mM	0.56 mL	2.80 mL	5.60 mL
10 mM	0.28 mL	1.40 mL	5.60 mL
50 mM	0.06 mL	0.28 mL	0.56 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Drouin L, McGrath S, Vidler LR, Chaikuad A, Monteiro O, Tallant C, Philpott M, Rogers C, Fedorov O, Liu M, Akhtar W, Hayes A, Raynaud F, Müller S, Knapp S, Hoelder S. Structure enabled design of BAZ2-ICR, a chemical probe targeting the bromodomains of BAZ2A and BAZ2B. J Med Chem. 2015 Mar 12;58(5):2553-9. doi: 10.1021/jm501963e. Epub 2015 Feb 26. PMID: 25719566; PMCID: PMC4441536.

In vivo study

1. Drouin L, McGrath S, Vidler LR, Chaikuad A, Monteiro O, Tallant C, Philpott M, Rogers C, Fedorov O, Liu M, Akhtar W, Hayes A, Raynaud F, Müller S, Knapp S, Hoelder S. Structure enabled design of BAZ2-ICR, a chemical probe targeting the bromodomains of BAZ2A and BAZ2B. J Med Chem. 2015 Mar 12;58(5):2553-9. doi: 10.1021/jm501963e. Epub 2015 Feb 26. PMID: 25719566; PMCID: PMC4441536.

7. Bioactivity

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Biological target:

BAZ2-ICR is a BAZ2A/B bromodomains inhibitor with IC50s of 130 nM and 180 nM, and Kds of 109 nM and 170 nM, respectively.

In vitro activity

To investigate whether 13 (BAZ2-ICR) can displace BAZ2 bromodomains from chromatin in living cells, this study performed a fluorescence recovery after photobleaching (FRAP) assay utilizing GFP-tagged BAZ2A full length protein transfected into human osteosarcoma cells (U2OS). As a control this study used a mutant (N1873F) that does not bind KAc containing peptides and therefore mirrors the behavior of inhibitor bound BAZ2A. In addition, this study used the histone deacetylase (HDAC) inhibitor SAHA to increase overall levels of histone acetylation, resulting in a sufficient window measuring differences in recovery time and demonstrating the acetylation dependence of the FRAP experiments (Figure 6). Importantly, 1 μM 13 reduced the recovery time of the wild-type (wt) construct to a level similar to the dominant negative mutant, confirming that 13 inhibits BAZ2A in cells.

Reference: J Med Chem. 2015 Mar 12; 58(5): 2553–2559. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4441536/

In vivo activity

Compound 13 (BAZ2-ICR) showed very high solubility (25 mM in D2O), a measured log D of 1.05, high stability in mouse microsomes, and permeation in the CaCo-2 model (see SI) and thus a suitable profile for oral and intravenous gavage. This study therefore performed a full mouse pharmacokinetic experiment. In agreement with the in vitro data, 13 showed 70% bioavailability and moderate clearance (~50% of mouse liver blood flow) and volume of distribution (see SI). This set of data therefore suggested that 13 is suitable for modulating BAZ2A and BAZ2B in vivo.

Reference: J Med Chem. 2015 Mar 12; 58(5): 2553–2559. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4441536/