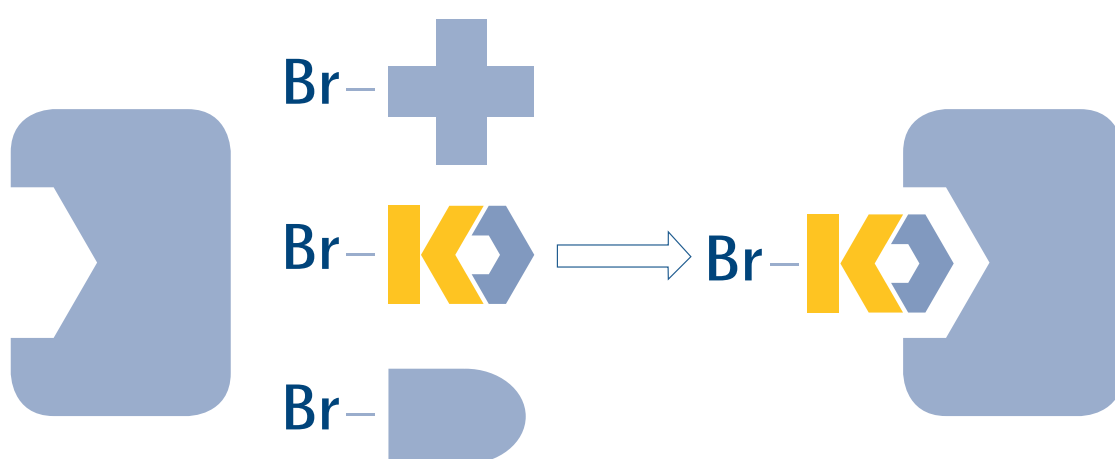


# BIONET Bromine Fragment Library



Key Organics have constructed a BIONET Bromine Fragment Library which includes 314 brominated fragments.

**Key features and benefits:**

- Measured solubility in PBS buffer  $\geq 100\mu\text{M}$  by  $^1\text{H}$  NMR
- Fragments soluble in DMSO at 200mM
- Purity  $\geq 95\%$
- Filtered for PAINS substructures
- Excludes fragments likely to form aggregates

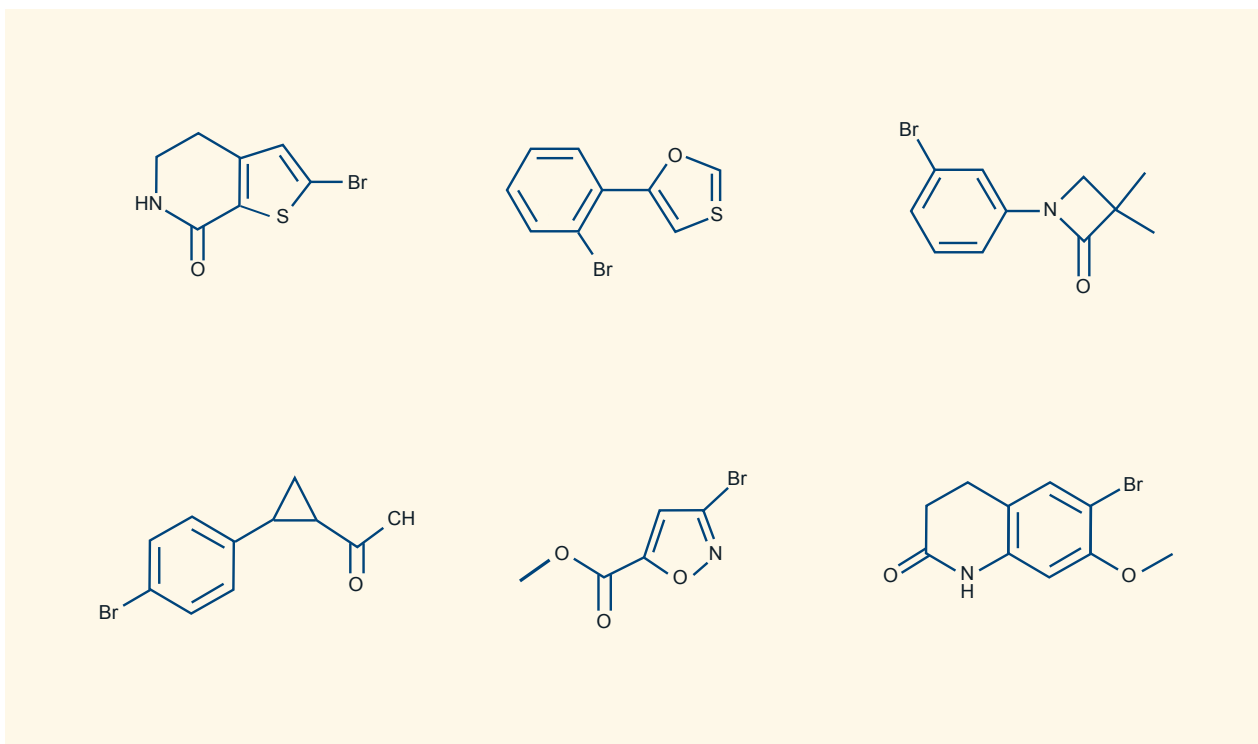
**The parameters used in the design of the library are:**

- Heavy atoms  $\leq 16$
- MW  $\leq 300$
- clogP  $\leq 3.3$
- Hydrogen bond donors  $\leq 3$
- Hydrogen bond acceptors  $\leq 4$
- tPSA  $\leq 70$
- Rotatable bonds  $\leq 3$

Properties were calculated using DataWarrior<sup>1</sup> and FAFDrugs4<sup>2</sup>.

The library excludes substructures identified as promiscuous or reactive by the following empirically determined rejection rules:

- Lilly MedChem Rules<sup>3</sup>
- PAINS<sup>4</sup>
- FAFDrugs4<sup>2</sup>



## <sup>1</sup>H NMR curation for fragment prioritisation and library characterization

<sup>1</sup>H NMR were employed to select compounds with the appropriate solution behavior to be amenable to rigorous biophysical analysis in physiologically relevant aqueous solution. Each singleton sample consisted of nominal 300  $\mu$ M compound in buffer (50 mM sodium phosphate pH 7.4, 100 mM NaCl). <sup>1</sup>H NMR spectra were acquired on a 600 MHz spectrometer equipped with a helium cryoprobe that significantly increased signal-to-noise. Simple 1D <sup>1</sup>H NMR spectra were acquired along with a series of 1D <sup>1</sup>H CPMG spectra, which were used to detect compounds showing potential aggregation in aqueous solution. The CMC Assist automation software allowed for an automatic readout of the fragment concentration that was experimentally derived from integrating the NMR resonances of each singleton sample and referencing to standardized samples using the ERETIC module (Bruker Spectrospin Inc.)<sup>10</sup>. The CMC Assist module also allowed for verification of each singleton spectrum to determine if the spectral attributes were consistent with the proposed primary structure of the corresponding fragment. This exercise was also complemented by an automated analysis using Spectral DB software (ACD Inc.).

## Key Organics Bromine Fragment Library exclude fragments likely to form aggregates

The spin-spin relaxation Carr-Purcell-Meiboom-Gill NMR experiment has been employed to detect and remove aggregate species from Key Organics BIONET Bromine Fragment library.<sup>5</sup>

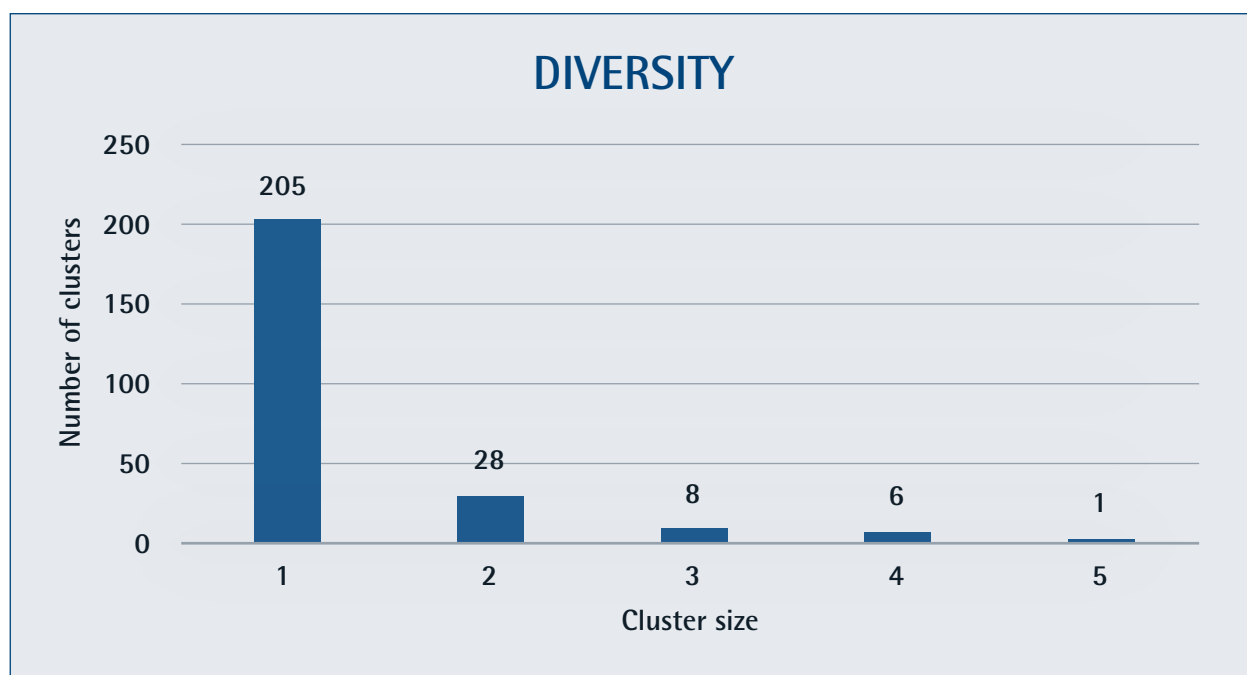
Small molecules can self-assemble in aqueous solution into a wide range of nanoentity types and sizes each having their own unique properties. This has important consequences in the context of drug discovery including issues related to nonspecific binding, off-target effects, and false positives and negatives. The spin-spin relaxation Carr-Purcell-Meiboom-Gill NMR experiment is sensitive to molecular tumbling rates and can expose larger aggregate species that have slower rotational correlations. The strategy easily distinguishes lone-tumbling molecules versus nanoentities of various sizes. The technique is highly sensitive to chemical exchange between single molecule and aggregate states and can therefore be used as a reporter when direct measurement of aggregates is not possible by NMR.

### Overview of calculated properties of the final library

Property	Average	Min	Max
Molecular Weight	220	161	290
Heavy Atom Count	11.3	7	16
tPSA	35.3	3.2	66
cLogP	1.7	-0.4	3.3
H-bond acceptors	2.3	1	4
H-bond donors	0.9	0	3
Rotatable bonds	0.9	0	3

### Diversity Statistics:

# clusters at 0.85 similarity = 205 singletons. 248 clusters / 314 fragments = 79%



## Fragment hits and SAR by catalogue

Key Organics can certainly help regarding following up on any hits, whether that is via SAR by catalogue, where we can search BIONET and commercial space for analogues of compounds of interest or via custom or contract synthesis. For those analogues available through other vendors, we can offer a compound management service to provide the following services:

- Compound Procurement
- Compound Weighing
- Compound Dissolution
- Automated Reformatting & Plating
- Compound Shipping & Logistics to in-house & partner testing laboratories
- Quality Control

**The BIONET Bromine Fragment Library is available custom-weighted in milligram or micromolar quantities. Customers can purchase the entire library or select any number of compounds as required.**

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### References

1. DataWarrior: An Open-Source Program for Chemistry Aware Data Visualization and Analysis. *J Chem Inf Model* **2015**.
  2. FAFDrugs4: M.; Miteva, S.; Violas, M.; Montes, D.; Gomez, P.; Tuffery, B.; Villoutreix. *Nucleic Acids Research*. **2006**, 34 (2), W738–W744.
  3. Rules for identifying potentially reactive or promiscuous compounds. Bruns et al, *J. Med. Chem.* **2012** (53).
  4. Baell, J. B.; Holloway, G. A. *J. Med. Chem.* **2010**, 53 (7), 2719–2740.
  5. Yann Ayotte, Victoria M. Marando, Louis Vaillancourt, Patricia Bouchard, Gregory Heffron, Paul W. Coote, Sacha T. Larda, and Steven R. LaPlante, *J. Med. Chem.* **2019**, 62, 7885–7896.
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**BIONET**  
Fragment Libraries

**Key Organics**  
Chemistry | Innovation | Quality

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