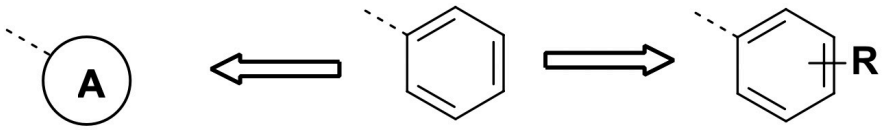
Key Organics
Chemistry | Innovation | Quality

SAR sets: Phenyl
Optimisation of potency & properties

Using small groups of pre-selected, off the shelf building blocks, our "SAR sets" can help:

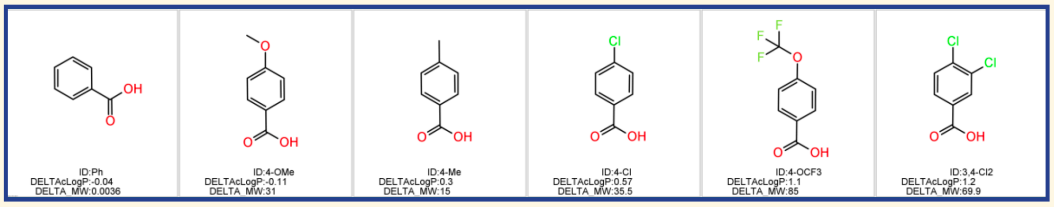
- **Develop structure-activity or structure-property relationships during hit-to-lead projects**
- **Identify compounds with improved properties (potency, physicochemical, ADME etc.)**



During the early stages of an optimisation project (e.g. 'Hit-to-Lead'), the focus is usually on increasing on-target potency of the compounds. Rapid and focused evaluation of differing substitution patterns on a compound to scope out spatial and electronic requirements of the ligand is important to help develop this understanding. Pre-selected sets of building blocks based on the original Topliss sequential batch evaluation process can enable this. Due to the nature of the evaluation and the groups used, the overall properties of the ligand may become MORE lipophilic and/or less physicochemically favourable during the process, this is why triage and selection of the most appropriate hits from a screen is important, to provide some latitude in compound properties (ΔcLogP & ΔMW shown). An example using the initial set of substituents proposed by Topliss is shown.

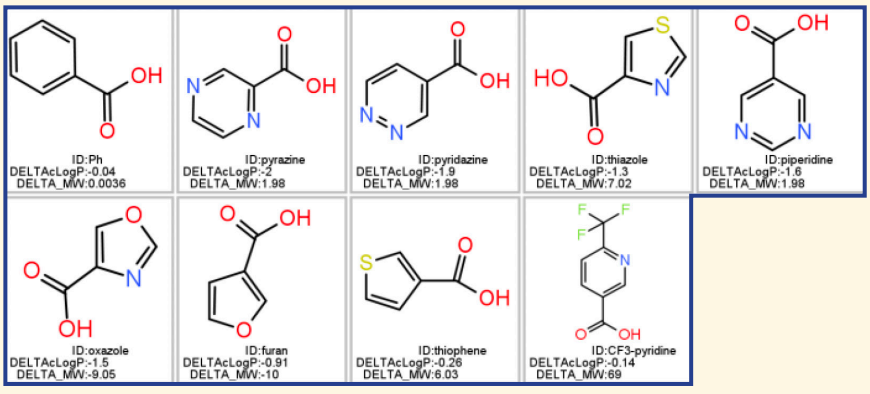
Reference: *Topliss, J. Med. Chem. 1977 (https://doi.org/10.1021/jm00214a001)*

SAR set T1
Initialy building blocks synthesis set (acids shown)

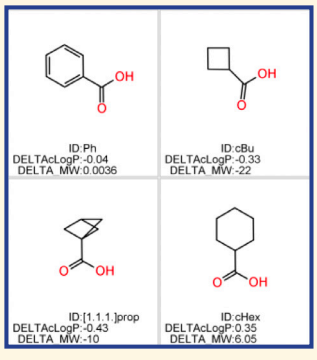


Other important aspects and properties of the hit compound can be evaluated in a comparable 'modular' manner using SAR sets. For example, the phenyl motif can be replaced with isosteric groups from a broad range of alternative structural classes to probe the effect on properties such as physicochemical, ADME or novelty. These isosteric replacements for the phenyl group have found use in the contemporary medicinal chemistry literature, and typically contain additional heteroatoms, modify the aromatic character and/or alter the 3D characteristics of the compound. Examples are shown below.

Reference: *Subbaiah & Meanwell J. Med. Chem. 2021 (https://doi.org/10.1021/acs.jmedchem.1c01215)*



SAR set HetAr: Heteroaromatic isosteric replacements (acids shown)



SAR set cAlk: Cycloalkyl isosteric replacements (acids shown)

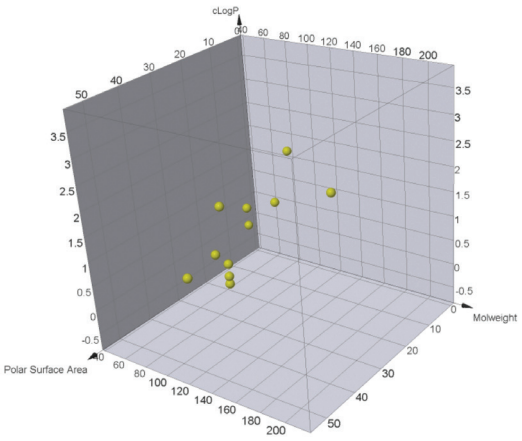
Key Organics routinely undertakes synthesis of bespoke or non-commercial compound(s) on either a custom fee-for-service (FFS) or contract (FTE) basis to provide dedicated support during the Hit Identification, Hit-to-Lead and Lead Optimisation phases for your discovery program.

Please visit our shop at: www.keyorganics.net

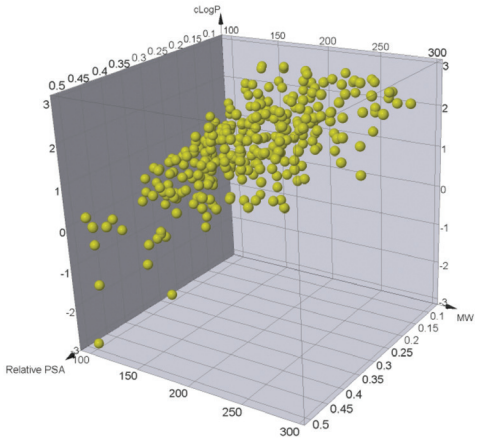
T: +44 (0)1840 212137 E: enquiries@keyorganics.net

- Key Organics can provide SAR sets of all the common functionalities, acids, anilines, halides, boronates, sulfonyl chlorides etc
- Sets can be expanded to meet customer needs eg. wider SAR exploration
- Scaffold "Decorator" sets of e.g. small amines can also be provided to further explore SAR
- Compounds provided in desired format, plates, barcoded vials etc
- Compounds provided in mg or mmol quantities ("Reaction Ready")

SAR set HetAr:
Heteroaromatic isosteric replacements (acids shown) *clogP v Mwt v PSA*



Decorator set amines:
clogP v Mwt v PSA



Service Offerings	Product Areas
Key Organics Chemistry Services	BIONET Chemistry Products
• Collaborative R&D • FTE Services • Custom Synthesis • Process R&D/Scale-up • Analytical Chemistry • Consultancy	• Intermediates • Fragment Libraries • Biochemicals • Screening Compounds • >275,000 Compounds

- ☑ Global client base spanning the Life Sciences industries for over 30 years
- ☑ Wholly-owned subsidiary of the well-established Tennant Group
- ☑ >275,000 innovative compounds in our collection
- ☑ Outstanding customer support, technical expertise & back-up
- ☑ Guaranteed IP security and confidentiality
- ☑ Reassuringly-high levels of performance
- ☑ >400 years' collective R&D experience of synthetic chemistry and drug discovery
- ☑ High proportion of client retention and loyalty

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