

### PharmaBlock Whitepaper

Bridging molecules for innovative medicines

#### Bridge-Fused Rings as *m*-Phenyl Bioisosteres

In summary, while saturated *p*-phenyl isosteres are more and more popular in medicinal chemistry, *m*-phenyl and *o*-phenyl fragments do not have many 3-D-rich isosteres. As this review has shown, saturated *m*-phenyl isosteres such as bicyclo[2.2.1]heptane (B), bicyclo[2.1.1]hexane (C), bicyclo[3.1.1]heptane (D), and 2-oxabicyclo[2.1.1]hexane (E) are gaining popularity. As most 3-D-rich isosteres, they (a) have a higher degree of saturation for a molecule may increase receptor–ligand complementarity, which should mitigate off-target effects; (b) tend to have lower CYP450 inhibitions, thus reducing DDIs tendency; and (c) may have lower melting point and higher solubility; and (d) oxygen-containing isosteres have added advantage of lower lipophilicity. With many of those bridge-fused intermediates now commercially available, their utility in drug discovery is destined to bear fruits in the future.

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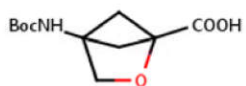
Bridge-Fused Rings as *m*-Phenyl Bioisosteres—Oxabicyclo[2.1.1]hexanes in Drug Discovery

PharmaBlock

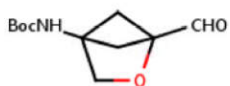
#### PharmaBlock Products-Oxabicyclo[2.1.1]hexanes

80,000+ building blocks, 63 series cover almost all the small molecule drug R&D needs

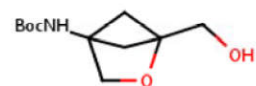
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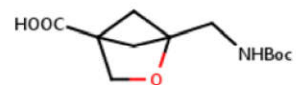
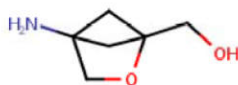
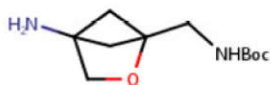
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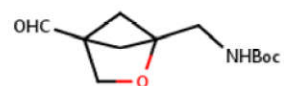
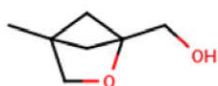
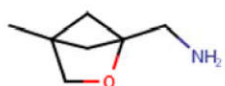
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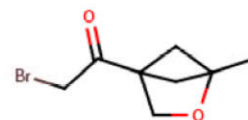
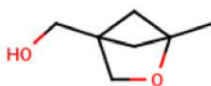
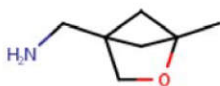
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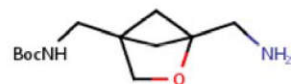
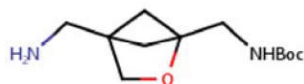
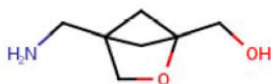
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