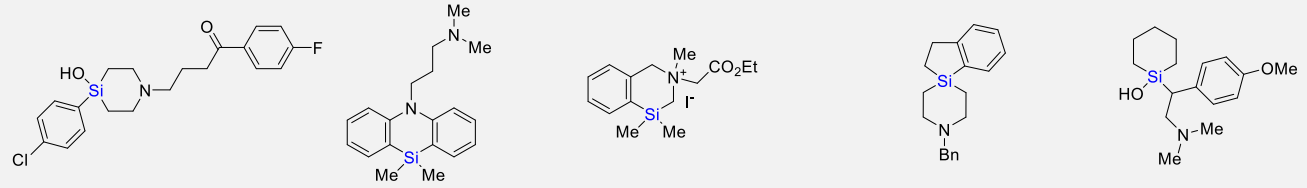
Silicon-Containing Building Blocks for Drug Design

Introduction

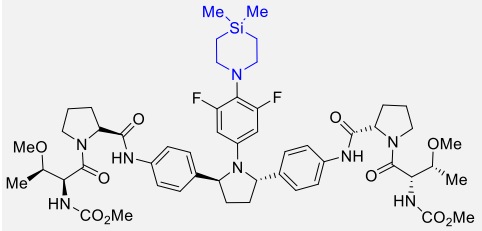
Silicon-containing compounds have been largely ignored in drug design until recently.[1] Silicon can be considered a bioisostere of carbon and hence offers an innovative avenue in drug discovery. For example, C/Si exchange in drug-like scaffolds provides an exciting approach in medicinal chemistry to improve ADME/Tox profile and to enhance potency of the biologically active compounds (Figure 1).[2-6] Herein we have designed and synthesized a library of silicon-containing building blocks for drug design.



Sila-haloperidol | Sila-dimetracrine | Sila-analogue of tetrahydroisoquinoline | Spirocyclic σ-receptor ligand | Sila-venlafaxine

Figure 1. Examples of silicon-containing molecules of medicinal interest.

Design



- Silicon-containing NS5A inhibitor;
- Pan-genotypic activity against GT1-6 HCV;
- Improved activity against GT6a HCV;
- High liver distribution.

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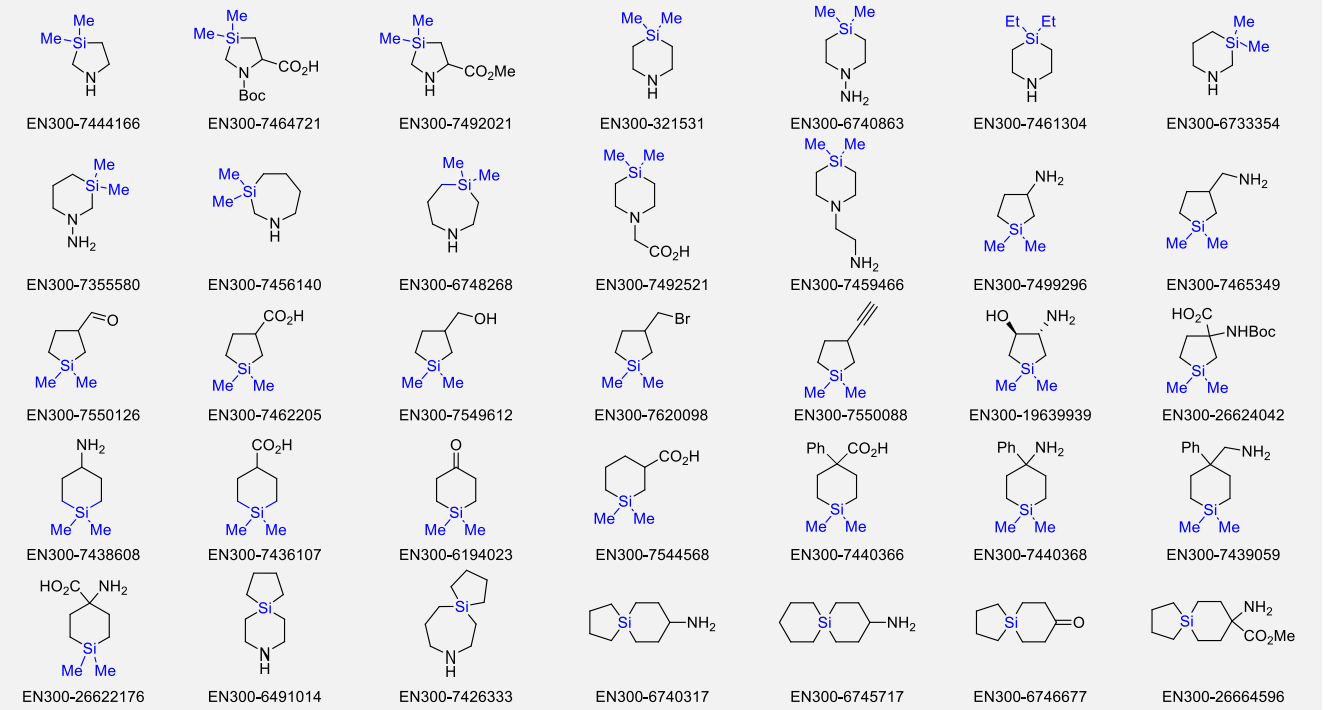
Advantages of "Silicon Switch":

- Bond length C–C = 1.54 Å, C–Si = 1.87 Å → changes in the interactions with specific proteins;
- Increase in lipophilicity;
- Si prefers higher coordination numbers → access to compounds for which corresponding carbon analogs are not available.

We offer more than 30 of silicon-containing building blocks from stock on a 5-10 g scale.



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EN300-7438608 | EN300-7436107 | EN300-6194023 | EN300-7544568 | EN300-7440366 | EN300-7440368 | EN300-7439059

EN300-26622176 | EN300-6491014 | EN300-7426333 | EN300-6740317 | EN300-6745717 | EN300-6746677 | EN300-26664596

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