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Directed Evolution of Cytochrome c for Carbon–Silicon Bond Formation: Bringing Silicon to Life
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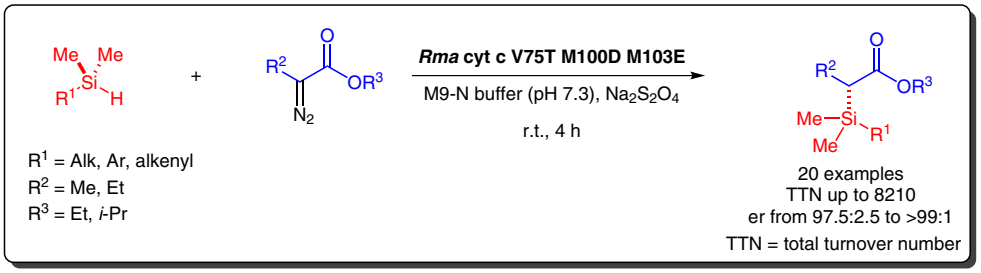
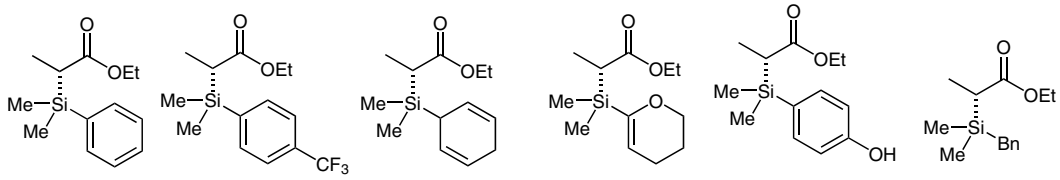
Asymmetric Enzymatic Carbon–Silicon Bond Formation

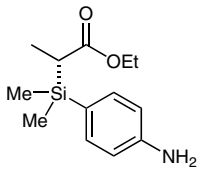


Selected examples:



2520 TTN, er > 99:1 | 140 TTN, er > 99:1 | 630 TTN, er = 99:1 | 930 TTN, er = 99:1 | 910 TTN, er > 99:1 | 740 TTN, er > 99:1

Application to *in vivo* synthesis:



using
E. coli expressing **Rma cyt C V75T M100D M103E**

0.1 mmol scale; 70% isolated yield; er = 99:1

Significance: The insertion of carbenes into silicon–hydrogen bonds under physiological conditions is reported by the Arnold group. Three selective modifications of the active site of cytochrome c from *Rhodothermus marinus* resulted in a highly active catalyst (*Rma* cyt c, V75T M100D M103E) that gave the desired products with remarkable total turnover numbers (≤8210) and enantioselectivities (er > 97.5:2.5). The transformation was performed *in vivo* on a preparative scale by using *Escherichia coli* expressing the mutant enzyme.

Comment: Despite the high abundance of carbon and silicon, no known lifeform can form a bond between these two elements. The authors impressively showed that just three modifications of the wild-type enzyme can force nature to create this unusual bond with extraordinary efficiency. Interestingly, no cyclopropanation, cyclopropenation or insertion into O–H or N–H bonds occurs when the required functional groups are present. The system achieved a 15-fold higher activity and chemoselectivity than the best synthetic catalysts.

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Category
Organo- and Biocatalysis

Key words
carbenes
directed evolution
heme protein
carbon–silicon bond formation
cytochrome c
enzyme modification