CLAIMS

1. A biocatalyst for organic synthesis, comprising:

    a. a controlled porosity silica (CPS) as support material, wherein the support material has a pore diameter from about 20 to about 60 nm, a surface area from about 50 m^2/g to about 200 m^2/g and a pore volume from about 0.5 mL/g to about 2.0 mL/g;
    wherein the support material comprises an amino-functionalized surface; and

    b. one or more catalytically active enzyme(s) immobilized to the surface via non-covalent interactions.

2. The biocatalyst according to claim 1, wherein the enzyme(s) is/are selected from Table (A):

    Table A: immobilized enzymes

#	Enzyme name (*organism*)	Uniprot id/other ref.	EC Number
1	Lipase (*Thermomyces lanuginosus*)	O59952	3.1.1.3
2	Lipase CALB (*Pseudozyma antarctica*)	P41365	3.1.1.3
3	Sucrose phosphorylase (*Bifidobacterium adolescentis*)	A0ZZH6	2.4.1.7
4	Isopropanol dehydrogenase *(Thermoanaerobacter brockii)*	P14941	1.1.1.80
5	Fructose-6-phosphate aldolase (*Escherichia coli)*	P78055	4.1.2.-
6	Phenylalanine ammonia-lyase (*Petroselinum crispum)*	P24481	4.3.1.24
7	Xylose isomerase (*Thermotoga neapolitana*)	P45687	5.3.1.5
8	Triosephosphate isomerase (*Escherichia coli*)	P0A858	5.3.1.1
9	Glucose oxidase (*Aspergillus niger*)	P13006	1.1.3.4
10	Cholesterol oxidase (*Streptomyces sp*)	P12676	1.1.3.6
11	Galactose Oxidase (*Gibberella zeae*)	P0CS93	1.1.3.9
12	Choline oxidase (*Arthrobacter globiformis*)	Q7X2H8	1.1.3.17
13	Alcohol oxidase (*Candida boidinii*)	Q00922	1.1.3.13
14	L-alanine dehydrogemase (*Bacillus subtilis*)	Q08352	1.4.1.1
15	Alcohol dehydrogenase (*Saccharomyces cerevisia*)	P00330	1.1.1.1
16	Glucose-6-phosphate Dehydrogenase (*Leuconostoc mesenteroides*)	P11411	1.1.1.363
17	Glycerol dehydrogenase (*Citrobacter freundii*)	P45511	1.1.1.6
18	Sucrose phosphorylase (*Leuconostoc mesenteroides*)	Q59495	2.4.1.7
19	Formate dehydrogenase (*Candida boidinii)*	O13437	1.17.1.9
20	Phosphonate dehydrogenase (*Pseudomonas stutzeri)*	O69054	1.20.1.1
21	Glucose dehydrogenase (*Bacillus megaterium*)	P39484	1.1.1.47
22	Glucose dehydrogenase (*Thermoplasma acidophilum*)	P13203	1.1.1.47

23	Laccase (*Bacillus subtilis*)	P07788	1.10.3.2
24	Alpha-galactosidase (*Thermotoga maritima*)	G4FEF4	3.2.1.22
25	Beta-galactosidase (*Bifidobacterium adolecentis*)	A1A399	3.2.1.23
26	Beta-galactosidase (*Aspergillus oryzae*)	Q2UCU3	3.2.1.24
27	Endo-1,4-beta-xylanase (*Aspergillus oryzae*)	Q9HFA4	3.2.1.8
28	Alpha-amylase (*Bacillus licheniformis*)	P06278	3.2.1.1
29	Xylose isomerase (*Streptomyces rubiginosus*)	P24300	5.3.1.5
30	Phosphoglucomutase (*Thermococcus kodakarensis)*	Q68BJ6	5.4.2.2
31	Glucose-6-phosphate isomerase (*Thermotoga maritima*)	Q9X1A5	5.3.1.9
32	Cellulase (*Acetivibrio thermocellus*)	P10477	3.2.1.4
33	Cellulase (*Thermoanaerobacterium*)	A0A0U4EBH5	3.2.1.4
34	Acid phosphatase (*Salmonella typhimurium*)	P26976	3.1.3.2
35	Polyphosphate—nucleotide phosphotransferase (*Erysipelotrichaceae bacterium*)	A0A3D5XRJ5	2.7.4.1
36	Amylosucrase (*Neisseria polysaccharea*)	Q9ZEU2	2.4.1.4
37	Glutamate—cysteine ligase (*Escherichia coli*)	P0A6W9	6.3.2.2
38	Glycerol kinase (*Escherichia coli*)	P0A6F3	2.7.1.30
39	Aminotransferase (*Chromobacterium violaceum*)	Q7NWG4	2.6.1.62
40	P450 (*Bacillus megaterium*)	P14779	1.6.2.4
41	Acid sugar phosphatase (*Bacillus subtilis*)	O32125	3.1.3.5
42	D-xylonate dehydratase (*Caulobacter vibrioides*)	Q9A9Z2	4.2.1.82
43	UDP-glucose 4-epimerase (*Chloroflexi bacterium*)	A0A7C4N9I7	5.1.3.2
44	Alkylhalidase (*Aspergillus niger*)	A2QL40	3.8.1.1
45	D-amino acid oxidase (*Sus scrofa*)	P00371	1.4.3.3
46	Adenylate kinase (*Homo sapiens*)	P13569	2.7.4.3
47	Alanine racemase (*Mycobacterium tuberculosis)*	P9WQA9	5.1.1.1
48	Haloalkane dehalogenase (*Xanthobacter autrophicus*)	P22643	3.8.1.5
49	Aromatic peroxygenase (*Agrocybe aegerita*)	B9W4V6	1.11.2.1
50	Acetase kinase (*Bacillus subtilis*)	P37877	2.7.2.1
51	Fatty acid peroxygenase (*Bacillus subtilis)*	O31440	1.11.2.4
52	Glycerol dehydratase (*Citrobacter freundii*)	P45514	4.2.1.30
53	Carbonic anhydrase (*Gallus gallus*)	P07630	4.2.1.1
54	Catalase (*Bacillus subtilis*)	P94377	1.11.1.6
55	Fructokinase (*Bacillus subtilis*)	O05510	2.7.1.4
56	NAD(P)H oxidase (*Sus scrofa*)	Q8HZK2	1.6.3.1
57	NAD(P)H oxidase *(Thermococcus kodakarensis)*	Q5JGP4	1.6.3.2
58	Hexokinase (*Saccharomyces cerevisiae*)	P04806	2.7.1.1
59	Amidase (*Arabidopsis thaliana*)	Q9FR37	3.5.1.4
60	Aminotransferase (*Arthrobacter species*)	F7J696	2.6.1.18
61	Amyloglucosidase 300L *(Aspergillus niger)*	Ref 1	3.2.1.3
62	Aminotransferase ATA_633 (*Arthrobacter species*)	Ref 2	2.6.1.26

Ref 1: Global Substance Registration System Ver 3.0.3 UNII record A370TYK9KO

Ref 2: Cuetos A et al. (2016) Angew Chem Int Ed 2016, **55**: 3144-3147

3. The biocatalyst according to any of the preceding claims, wherein the enzyme(s) are selected from list consisting of: *Thermomyces laguginosus* lipase (TLL, #1 in

Table A), *Candida antarctica* lipase (CalB, #2 in Table A), *Bifidobacterium adolescenti* sucrose phosphorylase (SucP, #3 in Table A), *Thermoanaerobacter brockii* secondary alcohol dehydrogenase (TbSADH, #4 in Table A), *Arthrobacter species* amine transaminase (ATA, #60 in Table A), *Leuconostoc mesenteroides* glycosyl transferase (GT, #18 in Table A), amyloglucosidase from *Aspergillus niger* (#61 in Table A), and aminotransferase (*Arthrobacter species*) (#62 in Table A); and their enzymatically active sequence variants.

4. The biocatalyst according to any of the preceding claims, wherein the support material surface comprises at least two different coatings, of which at least one provides the amino functionalization, wherein one of the coatings, which does not provide amino functionalization, provides a hydrophobic coating.

5. The biocatalyst according to claim 4, wherein the hydrophobic coating comprises alkyl moieties and/or aromatic moieties.

6. The biocatalyst according to claim 5, wherein the hydrophobic coating comprises C_{1-12} alkyl groups, most preferably C_{1-6} alkyl groups.

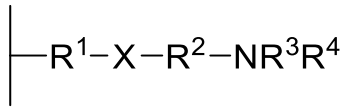
7. The biocatalyst according to any of the preceding claims, wherein the immobilized enzyme(s) is/are intermolecularly covalently linked by a linker comprising a bond selected from amino, amide, ester, ether, thioester, thioether, imidoamide, imidothioamide and thioamide.

8. The biocatalyst according to any of claims 1-7, wherein the enzyme(s) is/are immobilized to the surface via an interaction mediated by a chelated metal ion.

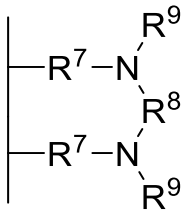
9. The biocatalyst according to claim 8 wherein the chelated metal ion is selected from Ni^{2+}, Cu^{2+}, Mg^{2+}, Fe^{3+} and Zn^{2+}.

10. The biocatalyst according to any of the preceding claims, wherein the intermolecular covalent linker, when present, does not comprise imine bonds.

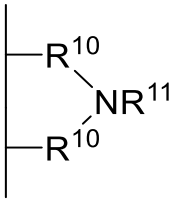
11. The biocatalyst according to any of the preceding claims, wherein the amino-functionalized surface comprises a structure of formula (I), (II) or (III):



(I)



(II)



(III)

wherein

R^1 is C_{1-6} alkanediyl; and wherein R^1 provides a covalent attachment to the silica surface (the vertical line on the left);

X is a bond (i.e., X is absent) or is a phenyl ring;

R^2 is C_{1-6} alkanediyl;

R^3 is W;

R^4 is W or is selected from the group consisting of C_{1-10} alkyl, C_{5-7} cycloalkyl, phenyl, phenyl-C_{1-6}-alkyl, amino-C_{2-8} alkyl, *N*-(phenyl)amino-C_{2-8} alkyl and *N*-(phenyl-C_{1-6}-alkyl)amino-C_{2-8} alkyl, and aminocarbonyl, wherein each amino is substituted with W; and wherein phenyl, at each instance, is optionally substituted with one or more substituents C_{1-4} alkyl;
or R^3 and R^4, together with the nitrogen atom to which they are attached, combine to form a 5- to 7-membered heterocyclic ring which may contain one or more unsaturated bonds and which may contain one more additional heteroatoms;
or R^3 and R^4 together form $=CR^5R^6$, wherein R^5 and R^6 are each independently C_{1-4} alkyl;

Each R^7 is independently C_{1-6} alkanediyl; and wherein R^7 provides a covalent attachment to the silica surface (the vertical line on the left);

R^8 is C_{1-3} alkanediyl;

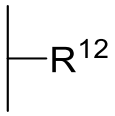
Each R^9 is independently W or is selected from the group consisting of C_{1-4} alkyl and hydroxy-C_{1-4} alkyl;

Each R^{10} is independently C_{1-6} alkanediyl; and wherein R^{10} provides a covalent attachment to the silica surface (the vertical line on the left);

R^{11} is W or is selected from the group consisting of C_{1-10} alkyl, C_{5-7} cycloalkyl, phenyl, phenyl-C_{1-6}-alkyl, amino-C_{2-8} alkyl, *N*-(phenyl)amino-C_{2-8} alkyl and *N*-(phenyl-C_{1-6}-alkyl)amino-C_{2-8} alkyl, and aminocarbonyl, wherein each amino is substituted with W; and wherein phenyl, at each instance, is optionally substituted with one or more substituents C_{1-4} alkyl; and

each W is hydrogen.

12. The biocatalyst according to any of the preceding claims, wherein the amino-functionalized surface comprises a structure of formula (I), as defined above, in combination with a structure of formula (IV):



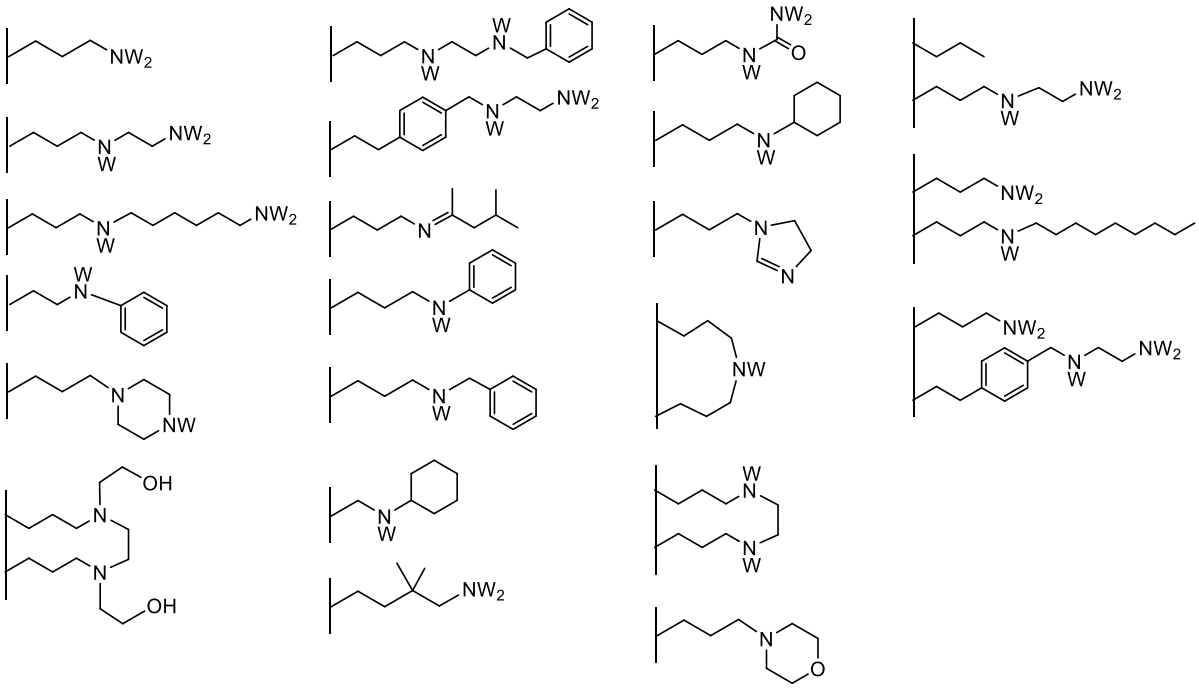
(IV)

wherein R^{12} is selected from C_{1-12} alkyl and amino-C_{1-6} alkyl.

13. The biocatalyst according to any of the preceding claims, wherein the surface does **not** contain any functional groups that may chelate a metal ion apart from the amino groups.

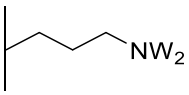
14. The biocatalyst according to any of the preceding claims, wherein the surface comprises amino-functionalized aliphatic moieties.

15. The biocatalyst according to any of the preceding claims, wherein the amino-functionalized surface comprises any of the following structures, wherein each W is hydrogen:

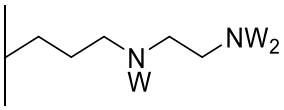


16. The biocatalyst according to any of the preceding claims, wherein the amino-functionalized surface comprises any of the following structures, wherein each W is hydrogen:

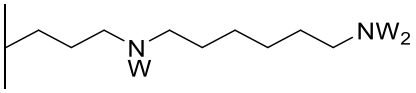
(1)



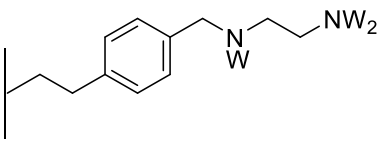
(2)



(3)



(4)



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17. A method for synthesis of an organic compound, comprising:

    a. providing a biocatalyst according to any of the claims 1-16, placed in a reactor;

    b. feeding a precursor to the organic compound to the flow reactor, whereby the immobilized enzyme(s) catalyze(s) a reaction/reactions resulting in the synthesis of the organic compound; and

    c. recovering the organic compound.

18. The method according to claim 17, wherein the reactor is a batch reactor or a continuous flow reactor, preferably a continuous flow fixed bed reactor.

19. A method of manufacturing a biocatalyst according to any of claims 1-16, comprising:

    a. providing one or more catalytically active enzyme(s);

    b. providing a controlled porosity silica (CPS) as support material, wherein the support material has a pore diameter from about 20 to about 60 nm, a surface area from about 50 m^2/g to about 200 m^2/g and a pore volume from about 0.5 mL/g to about 2.0 mL/g, said support material comprising an amino-functionalized surface; and

    c. non-covalently immobilizing the one or more enzyme(s) on the support material.

20. The method according to claim 19, further comprising:
    selecting a bifunctional cross-linking reagent capable of producing **amino, amide or thioamide bonds when reacted with enzymes, and**
    covalently cross-linking the enzyme(s) using the bifunctional reagent, wherein the bifunctional reagent preferably is a bis-epoxide, an imidoester, or a N-hydroxysuccinimide ester.