Supplementary information

Diversity of enzymatic SAM-dependent methylation of aromatic compounds.

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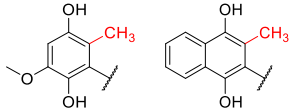
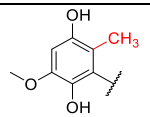
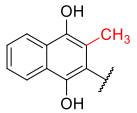
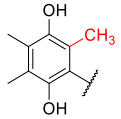
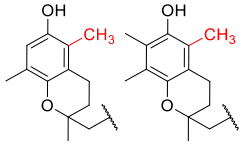
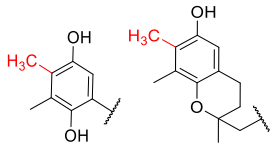
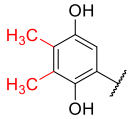
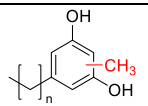
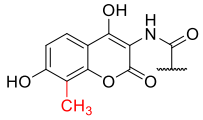
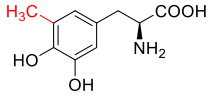
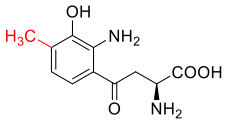
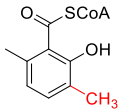
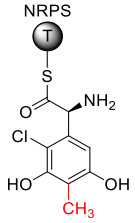
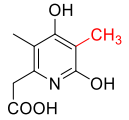
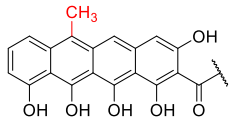
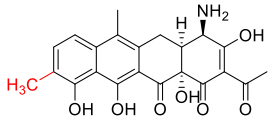
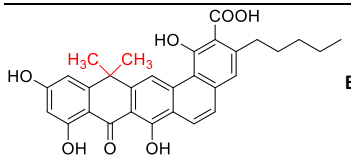
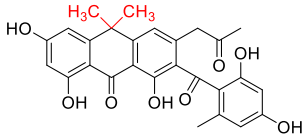
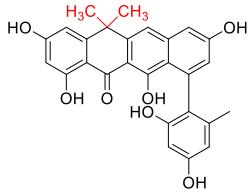
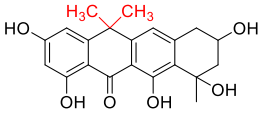
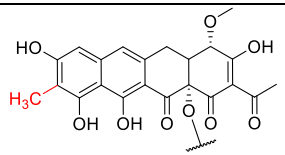
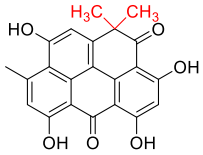
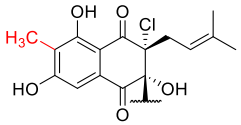
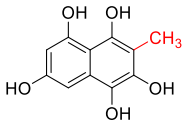
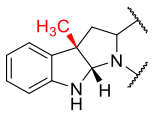
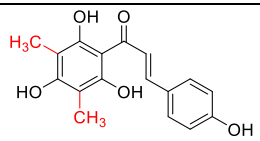
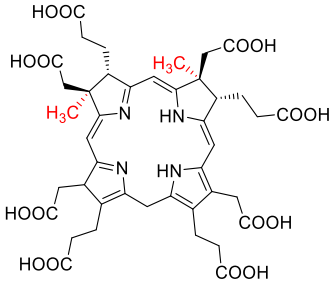
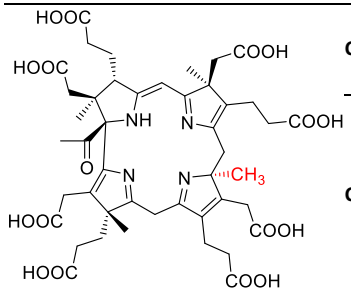
Table S1: Canonical SAM-dependent C-methyltransferases catalyzing aromatic C-methylation.

	C-MT Name	Origin and protein sequence accession number	Substrates	Natural product/ Biosynthetic pathway	Comment	Literature
	**UbiE/MenG**	*Escherichia coli* (ABJ03312)	2-methoxy-6-polyprenyl-1,4-benzoquinol; dimethyl-menaquinol	ubiquinone; menaquinone	Class I SAM MT	1
	**Coq5**	*Saccharomyces cerevisiae* (DAA09788)	2-methoxy-6-polyprenyl-1,4-benzoquinol	ubiquinone	Class I SAM MT PDB: 4OBW	2
	**DPhQ-MT** (MenG)	*Arabidopsis thaliana* (AEE30377); *Phelipanche aegyptiaca* (QXL99850)	2-phytyl-1,4-naphthoquinone	phylloquinone	Class I SAM MT; name 'DPhG-MT' adapted from Stutts *et al.*[3], frequently referred to in literature/ genomic databases as 'MenG'	4, 5, 6
	**MpqE**	*Nitrospira inopinata* ENR4 (WP_082633614.1)	plastoquinole	2-methyl-plastoquinone	Class I SAM MT	7
	**γ-TMT**	*Arabidopsis thaliana* (AAD02882)	γ-tocopherol; δ-tocopherol	tocopherol	Class I SAM MT	8, 9, 10, 11
	'VTE3-type' **MPBQ-/MSBQ-MT**	*Arabidopsis thaliana* (BAB62076)	2-methyl-6-phytyl-benzoquinone (MPBQ); 2-methyl-6-solanyl-1,4-benzoquinone (MSBQ)	tocopherol; plastoquinone	Class I SAM MT	12, 13, 9
	'Synechocystis type' **MPBQ-/MSBQ-MT**	*Synechocystis* sp. PCC6803 (BAA18485)	2-methyl-6-phytyl-benzoquinone (MPBQ); 2-methyl-6-solanyl-1,4-benzoquinone (MSBQ)	tocopherol; plastoquinone	Class I SAM MT; name MPBQ-/MSBQ-MT also referred to in literature as 'Sll0418' or 'PlqQ'	12, 13
	**MpqQ**	*Nitrospira inopinata* ENR4 (WP_062482398.1)	2-solanyl-1,4-benzoquinone	2-methyl-plastoquinone	Class I SAM MT	7

	**Mtr$_{GmCg}$**	*Gimesia maris* (QGQ32756)	pentadecyl- and heptadecyl-resorcinol	alkylresorcinols	Class I SAM MT	14
	**CouO**	*Streptomyces rishiriensis* (AAG29793)	aminocoumarin derivative	coumermycin	Class I SAM MT PDB: 5M58	15, 16
	NovO	*Streptomyces niveus* (AAF67508)	aminocoumarin derivative	novobiocin	Class I SAM MT PDB: 5MGZ	15, 17
	**SfmM2**	*Streptomyces lavendulae* (ABI22137)	L-tyrosine; D-tyrosine; L-dopa	saframycin A	Class I SAM MT	18, 19
	SacF/SfcF	*Pseudomonas fluorescens* (AAL33761)	L-tyrosine; D-tyrosine; L-dopa	safracin B	Class I SAM MT	19, 20
	NapS	*Streptomyces lusitanus* (AGD80625)	L-tyrosine	naphthyridinomycin	Class I SAM MT	21
	Cya9	*Streptacidiphilus griseoplanus* (BAO84882)	L-tyrosine	cyanocydine	Class I SAM MT	22
	**SibL**	*Streptosporangium sibiricum* (ACN39735)	(D/L)-3-hydroxykynurenine	sibiromycin	Class I SAM MT PDB: 4U1Q, 4QVG, 4X3Q	23, 24
	Orf19	*Streptomyces refuineus* (ABW71850)	(D/L)-3-hydroxykynurenine; L-tyrosine; D-tyrosine; L-dopa	anthramycin	Class I SAM MT	25
	AcmI	*Streptomyces chrysomallus* (ADG27364)	3-hydroxy-D-kynurenine; L-tyrosine; L-*meta*-tyrosine; L-dopa	actinomycin B	Class I SAM MT	26, 27
	AcmL	*Streptomyces chrysomallus* (ADG27351)	3-hydroxy-D-kynurenine; L-tyrosine; L-*meta*-tyrosine; L-dopa	actinomycin B	Class I SAM MT	26, 27
	**MdpB1**	*Actinomadura madurae* (ABY66020)	6-methylsalicylyl-CoA	maduropeptin	Class I SAM MT CoA-activated substrate	28, 29
	PokMT1	*Streptomyces diastatochromogenes* (ACN64833)	6-methylsalicylyl-CoA	polyketomycin	Class I SAM MT CoA-activated substrate	30
	**TotM**	*Streptomyces pactum* (ATL73035)	3,5-dihydroxy-phenylglycine (NRPS T-domain-bound)	totopotensamide	Class I SAM MT; MT domain of PKS/NRPS TotB1	31, 32
	Orf23	*Amycolatopsis* sp. MJM2582 (AHF20598)	3,5-dihydroxy-phenylglycine (NRPS T-domain-bound)	ristocetin	Class I SAM MT; MT domain of PKS/NRPS TotB1	33
	**HcgC**	*Methanococcus maripaludis*; *Methanocaldococcus jannaschii* (AAB98480)	6-carboxymethyl-5-methyl-4-hydroxy-2-pyridinol	FeGP-cofactor	Class I SAM MT PDP: 5D5O, 5D4U, 5D4V	34, 35

	**OxyF**	*Streptomyces rimosus* (AAZ78330)	pretetramid	oxytetracycline	Class I SAM MT	36
	CtcK	*Streptomyces aureofaciens* (AEI98654)	pretetramid	chlortetracycline	Class I SAM MT	37
	ChdMI	*Amycolatopsis sulphurea* (AHD25937)	tetracyclic polyketide	chelocardin	Class I SAM MT	38
	SsfM4	*Streptomyces* sp. SF2575 (ADE34484)	pretetramid	SF2575	Class I SAM MT	39
	PokMT2	*Streptomyces diastatochromogenes* (ACN64843)	tetracyclic polyketide	polyketomycin	Class I SAM MT	40
	**ChdMII**	*Amycolatopsis sulphurea* (AHD25930)	tetracyclic polyketide	chelocardin	Class I SAM MT	38
	**BenF**	*Streptomyces* sp. (CAM58795)	pentangular polyketide	benastatin	Class I SAM MT geminal dimethylation	41
	**FasT**	uncultured bacterium (AEM44262); *Streptomyces kanamyceticus* CGMCC 4.1441	phenylanthrone core	fasamycin	Class I SAM MT geminal dimethylation	42, 43, 44
	Abx$_{(+)}$M	*Actinomycetes* sp. MA7150 (AUO15565); *Streptomyces* sp. FJS 31-2; *Streptomyces* sp. FXJ 1.264	phenylanthrone core	anthrabenzoxocinones	Class I SAM MT geminal dimethylation	45, 44, 46
	Abx$_{(-)}$M	*Streptomyces* sp. MA6657 (AUI41033)	phenylanthrone core	anthrabenzoxocinones	Class I SAM MT geminal dimethylation	45, 44
	**ForT**	*Streptomyces formicae* KY5 (AQP25568)	phenylnaphthacene	formicamycins	Class I SAM MT geminal dimethylation	47
	AccT	*Streptomyces* sp. MA37 (QKO28699)	phenylnaphthacene	accramycin	Class I SAM MT geminal dimethylation	48
	**TamO**	environmental DNA AZ60 (AFY23046)	tetracyclic polyketide	tetarimycine A/B	Class I SAM MT geminal dimethylation	49

	**CmmMII**	*Streptomyces griseus* (CAE17532)	premithramycin	chromomycin A3	Class I SAM MT	50
	MtmMII	*Streptomyces argillaceus* (CAK50790)	premithramycin	mithramycin	Class I SAM MT	51
	**RemG**	*Streptomyces resistomycificus* (CAE51172)	unusual polyketide	resistomycin	Class I SAM MT; geminal dimethylation	52
	**NapB5**	*Streptomyces aculeolatus* (ABS50465); *Streptomyces* sp. CNQ-525 (ABS50493)	1,3,6,8-tetrahydroxynaphthalene (T_4HN) derivative	napyradiomycins	Class I SAM MT	53
	Mcl21	*Streptomyces* sp. CNH-189 (AGH68906)	1,3,6,8-tetrahydroxynaphthalene (T_4HN) derivative	merochlorin C/D	Class I SAM MT	54
	Fur6	*Streptomyces* sp. KO-3988 (BAE78974)	1,2,4,5,7-pentahydroxynaphthalene	furaquinocin A/D/C	Class I SAM MT; PDB: 8HAR	55, 56
	**Fur6**	*Streptomyces reveromyceticus* SN-593 (BBA98098)	1,2,4,5,7-pentahydroxynaphthalene	furaquinocin I/J	Class I SAM MT	57
	Fnq27	*Streptomyces virginiae* (CAL34105)	1,3,6,8-tetrahydroxynaphthalene (T_4HN) derivative	furanonaphthoquinone I	Class I SAM MT	58
	PsmD	*Streptomyces griseofuscus* (AHL44342)	indole derivative	physostigmine	Class I SAM MT; *β*-cap domain in addition to class I MT Rossmann fold; cyclisation; PDB: 7ZGT, 7ZKH, 7ZKG	59, 60, 61
	**NozMT**	*Nocardiopsis* sp. CMB-M0232 (UYF26243)	indole derivative	nocardioazine B	Class I SAM MT; multifunctional MT (N- and C-methylation); cyclisation	62
	StspM1	*Streptomyces* sp. HPH0547 (QEO60445)	cycloditryptophan	pyrroloindole alkaloid (ditryptophan 2,5-diketopiperazine)	Class I SAM MT; C3-methylation +cyclisiation	63
	SgMT	*Streptomyces griseoviridis* (GGT26788)	cycloditryptophan	pyrroloindole alkaloid (ditryptophan 2,5-diketopiperazine)	Class I SAM MT; C3-methylation +cyclisiation; PDB: 9GDJ	64

	**RdCMT**	*Rhododendron dauricum* (XTP75405)	naringenin chalcone	farerrol	Class I SAM MT; PDB: 9KUS	65
	**CysG**	*Salmonella enterica;* *Escherichia coli* (CAA32419)	uroporphyrinogen-III	siroheme	Class III MT; urophorphyrinogen III MT; MT core domain and dehydrogenase-ferrochelatase module; PDB: 1PJQ	66, 67
	Met1P	*Saccharomyces cerevisiae* (CAA82148)	uroporphyrinogen-III	siroheme	Class III MT; urophorphyrinogen III MT	68
	SirA	*Bacillus megaterium* (CAD48921)	uroporphyrinogen-III	siroheme	Class III MT; urophorphyrinogen III MT	69
	UPM1	*Arabidopsis thaliana* (AAB92676)	uroporphyrinogen-III	siroheme	Class III MT; urophorphyrinogen III MT	70
	NirE	*Pseudomonas aeruginosa* (BAA12682)	uroporphyrinogen-III	heme d_1	Class III MT; urophorphyrinogen III MT; PDB: 2YBO	71
	CobA	*Pseudomonas denitrificans* (AAA25773)	uroporphyrinogen-III	vitamin B12	Class III MT; urophorphyrinogen III MT; PDB: 1S4D	72, 73
	UroM	*Thermus thermophiles* (BAD71856)	uroporphyrinogen-III	vitamin B12	Class III MT; urophorphyrinogen III MT; PDB: 1VE2, 1V9A	74
	**CobM**	*Pseudomonas denitrificans;* *Rhodobacter capsulatus* (AAC16190)	precorrin-4	vitamin B12	Class III MT; cobalt-precorrin-4-MT; PDB: 3NDC	75
	CbiF	*Bacillus megaterium* (CAA04314)	Co-precorrin-4	vitamin B12	Class III MT; cobalt-precorrin-4-MT; PDB: 1CBF	76

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