Uncovering the Formation and Selection of Benzylmalonyl-CoA from the Biosynthesis of Splenocin and Enterocin Reveals a Versatile Way to Introduce Amino Acids into Polyketide Carbon Scaffolds

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[†] i i i (i), i i i , i , 1 , 300 1, i

[‡] i i i , i , i i , i i , i

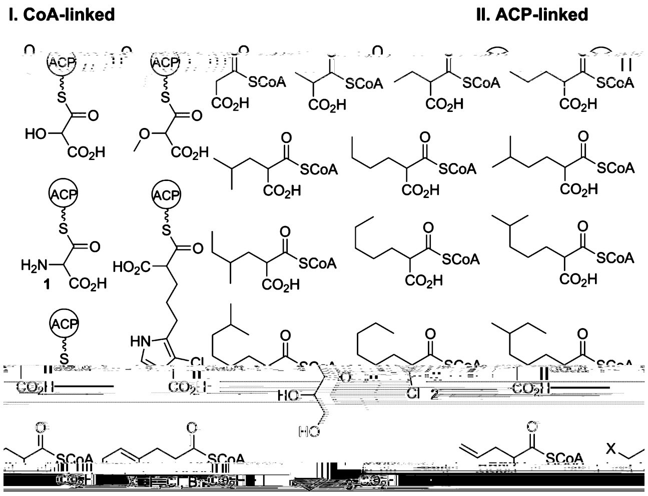

Figure 1. (1), (2), (3) (3)

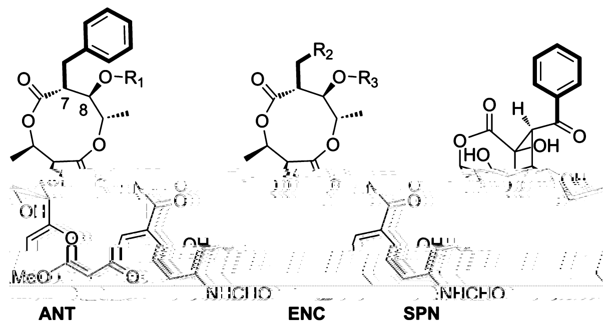

Figure 2.

RESULTS

Discovering Polyketides with Amino Acid Origin.

Cloning the Splenocin Biosynthetic Gene Cluster.

DOI: 10.1021/jacs.5b00728
J. Am. Chem. Soc. 2015, 137, 4183−4190

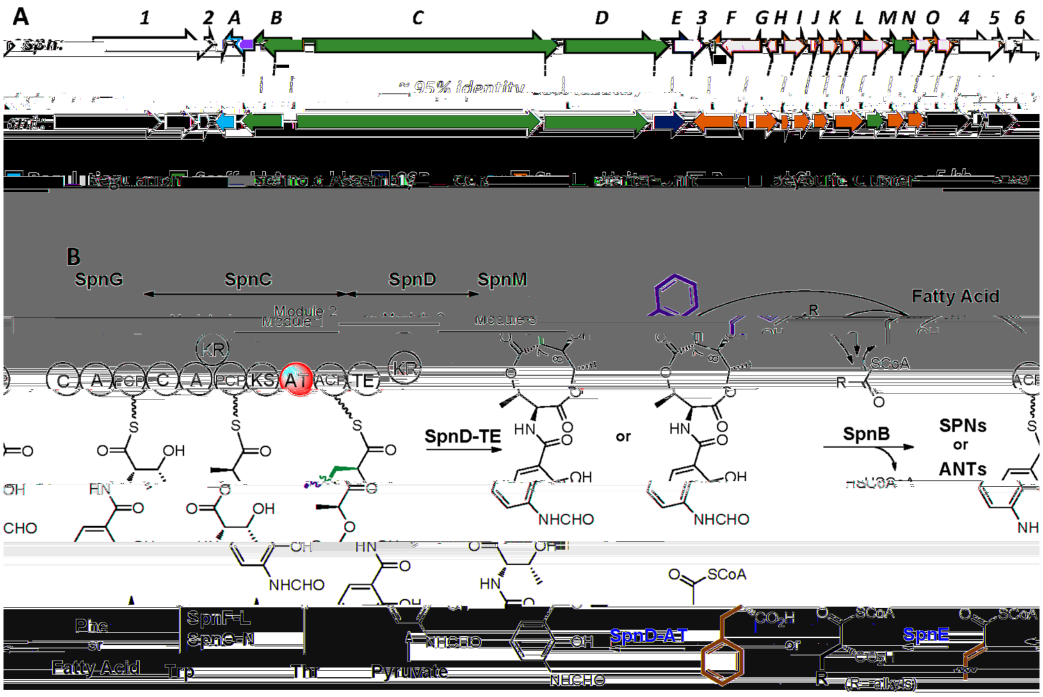

Figure 3. [illegible] 1. [illegible] 31. [illegible]

Table 1. Deduced Functions of ORFs in *spn* Biosynthetic Gene Cluster (Accession Number KP719128)

[illegible]	[illegible] (a.a.)	[illegible]	[illegible] (%)	[illegible]
1[a]	1 0	[illegible] -202	2	[illegible]
2[a]	1	[illegible] 22	3	[illegible]
[illegible]	1 3	[illegible] 22	100	[illegible]
[illegible]	33	[illegible] 22	2	[illegible]
[illegible]	2	[illegible] 22	[illegible]	[illegible]
[illegible]	12 3	[illegible] 22	[illegible]	[illegible]
[illegible]	0	[illegible] 22	[illegible]	[illegible]
3[a]	113	[illegible] −10	3	[illegible]
[illegible]	2	[illegible] 22	[illegible]	[illegible]
[illegible]	2	[illegible] 22	[illegible]	[illegible]
[illegible]	3 1	[illegible] 22	[illegible]	[illegible]
[illegible]	[illegible]	[illegible] 22	[illegible]	[illegible]
[illegible]	2 2	[illegible] 22	[illegible]	[illegible]
[illegible]	1 0	[illegible] 22	[illegible]	[illegible]
[illegible]	3	[illegible] 22	[illegible]	[illegible]
[illegible]	2	[illegible] 22	[illegible]	3- [illegible]
[illegible]	2 2	[illegible] 22	[illegible]	2,3- [illegible]
[illegible]	22	[illegible] 22	[illegible]	[illegible]
[a]	[illegible]	[illegible]	[illegible]	[illegible]
[a]	13	[illegible]	[illegible]	[illegible]
[a]	3	[illegible]	[illegible]	[illegible]

[a] [illegible]

[illegible] [11,12] [illegible] 3 [illegible] 3- [illegible]

[illegible] (3) [illegible] 2- [illegible]

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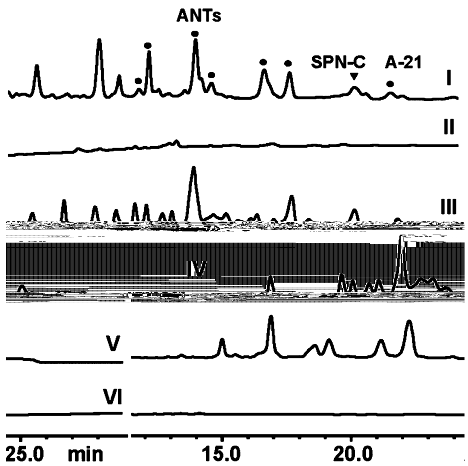

Figure 4.

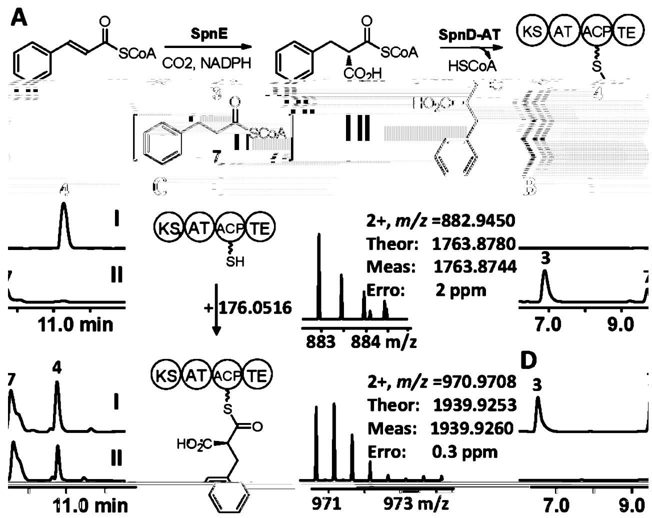

Figure 5.

Characterization of Benzylmalonyl-CoA as an Extender Unit and the selectivity of the AT Domain.

Correlation of Amino acid Origin to Benzylmalonyl-CoA Synthesis and Crosstalk of enc_c and *spn*.

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J. Am. Chem. Soc. 2015, 137, 4183−4190

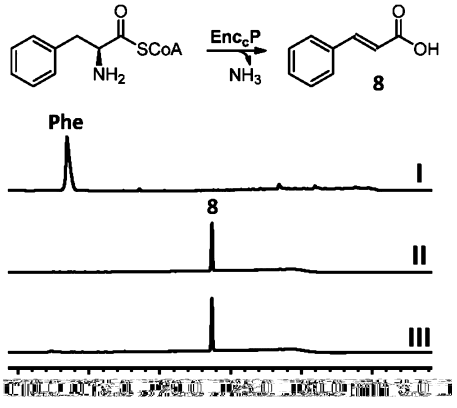

Figure 6. i . ( ) i ( ) i i (8) ( ) i .

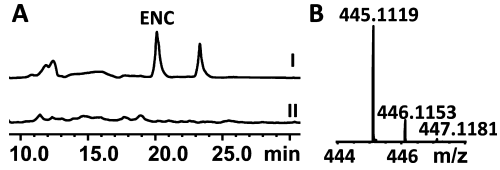

Figure 7. – i i . 31 ( ) 2 1 (Δ P) ( ). ( ) . ( ) .

Engineering *ant* Pathway to Produce SPN.

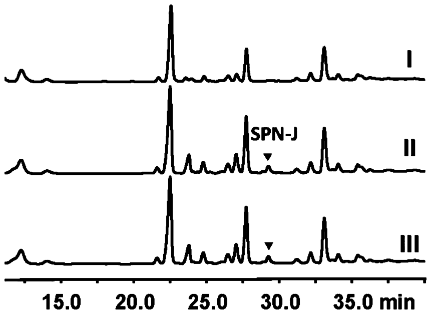

Figure 8. i 2110 i i (▼) i i i () i 2110 () 2 (2110 i $^{m}E^{*}$- P) () 2 (2110 i $^{m}E^{*}$- P- H).

(3)

DISCUSSION

Novel Strategy to Convert an Amino Acid into Polyketide Extender Unit. α ifi [23] α α α iff (1), fi β- [3] (2), ifi -2 [3] ifi ff (3). α α,β- α,β- α,β- ifi fi

(3) fi

Versatility for Converting Other Amino Acids into CoA-linked Extender Units, and Significance for Expanding Extender Unit Variety. [3,2] [3] (1). ffi fi fi ifi [2] *m*- [,2] β- ff ifi [13,20,2] α,β- α [3,i,13,2] 3-i ( ), ( ). (1 3 3 2,) [3i,2] ff

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J. Am. Chem. Soc. 2015, 137, 4183−4190

Broad Selectivity of the AT Domain and Potential to Introduce Structural Diversity into the Polyketide Scaffold.

(3).

■ CONCLUSION

(3)

■ ASSOCIATED CONTENT

Supporting Information

■ AUTHOR INFORMATION

Corresponding Author

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Author Contributions

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Notes

■ ACKNOWLEDGMENTS

(31322002, 312 011, 31 000 2), (-12−0 23), (13−1), (201 0 20 201 20).

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DOI: 10.1021/jacs.5b00728
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