Current biochemical understanding regarding the metabolism of acinetobactin, the major siderophore of the human pathogen *Acinetobacter baumannii*, and outlook for discovery of novel anti-infectious agents based thereon

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Supplementary Figure 1. Structures of fimsbactins and baumannoferrins, other siderophores for *Acinetobacter baumanii*.
Supplementary Scheme 1. Total synthesis of acinetobactin. Currently, two synthetic routes have been devised by Takeuchi and Kim laboratories\textsuperscript{1,2} and they share a common theme in that two fragments, oxazoline acid and N-hydroxy histamine derivatives, are prepared first and a subsequent combination between them followed by global deprotection completes the total synthesis. (A) Preparation of oxazoline acid fragment S\textsubscript{5} by Takeuchi laboratory involving a condensation between imidate S\textsubscript{3} and L-Thr-OBn to construct the oxazoline ring of S\textsubscript{4}. (B) Preparation of oxazoline acid fragment S\textsubscript{10} by Kim laboratory, in which the oxazoline ring of S\textsubscript{9} was constructed by dehydrative cyclization from S\textsubscript{8} using a molybdenum oxide catalyst. (C) Preparation of N-hydroxy histamine fragment S\textsubscript{15}. Takeuchi laboratory accessed this fragment directly from histamine S\textsubscript{11} involving replacement of a primary amine group with chloride followed by a nucleophilic substitution with protected hydroxyl amine precursor S\textsubscript{13}. Kim and co-workers undertook a different approach involving a Cu(II)-promoted de novo imidazole formation (S\textsubscript{18} $\rightarrow$ S\textsubscript{14}) from simple alkenyl halide precursor S\textsubscript{16}. (D) Completion of total syntheses of Ab-Oxa (1) and Ab-Isox (2). Both research laboratories used the same methods to finish the syntheses initiated by amide formation between oxazoline acid fragment S\textsubscript{5} or S\textsubscript{10} and N-hydroxy histamine fragment S\textsubscript{15}. Global deprotection based on hydrogenolysis successfully yielded Ab-Oxa (1). Then, this compound could be readily converted to Ab-Isox (2) by simple reflux in methanol, corroborating the biosynthetic proposal by Walsh and co-worker described in the main text.
References
