Predicting natural product value, an exploration of anti-TB drug space

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Supplementary information

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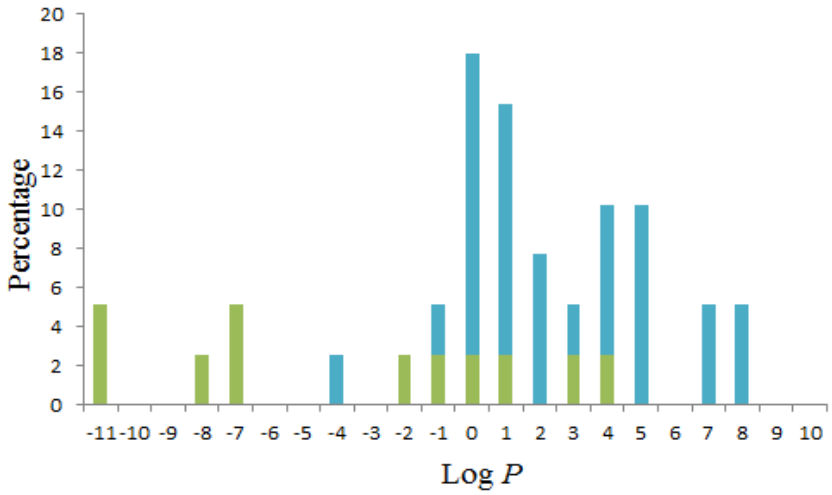


Figure S1 Distribution histogram of log *P* of the tuberculosis drugs. Nature derived TB drugs demonstrated in green and blue represent synthesized TB drugs.

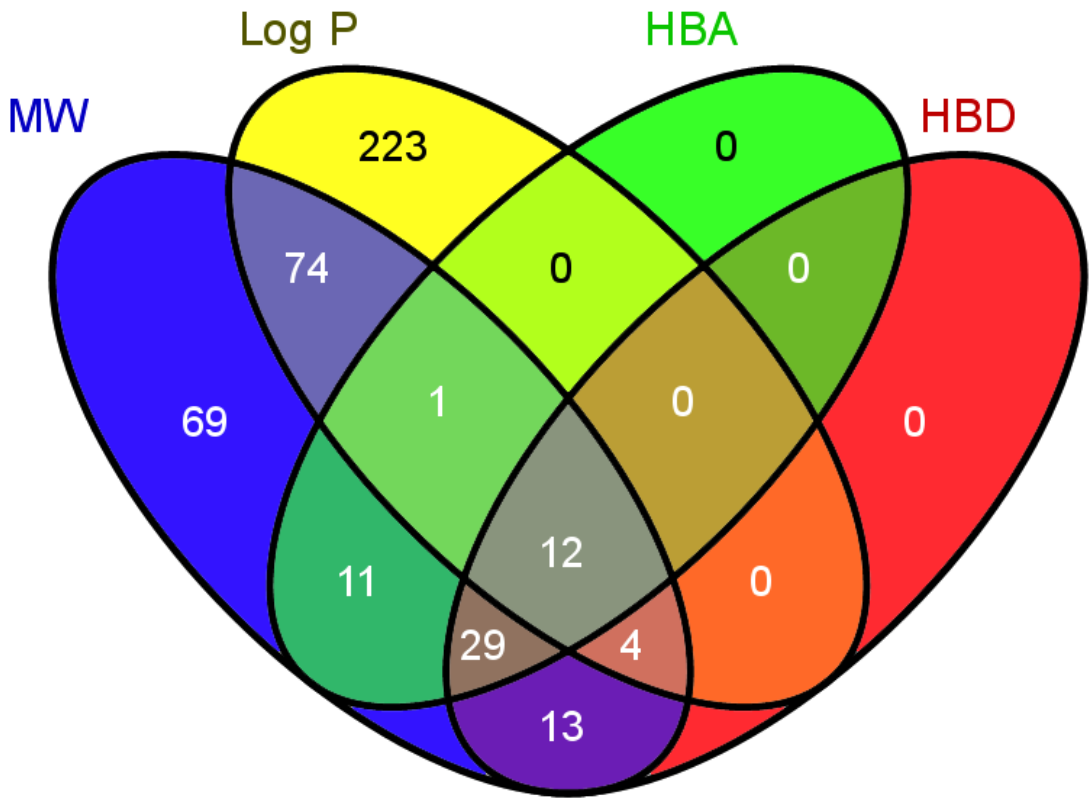


Figure S2 Venn diagram of Lipinski's physicochemical parameters for 949 anti-mycobacterium natural products. 513 compounds have no violation from Lipinski's parameters.

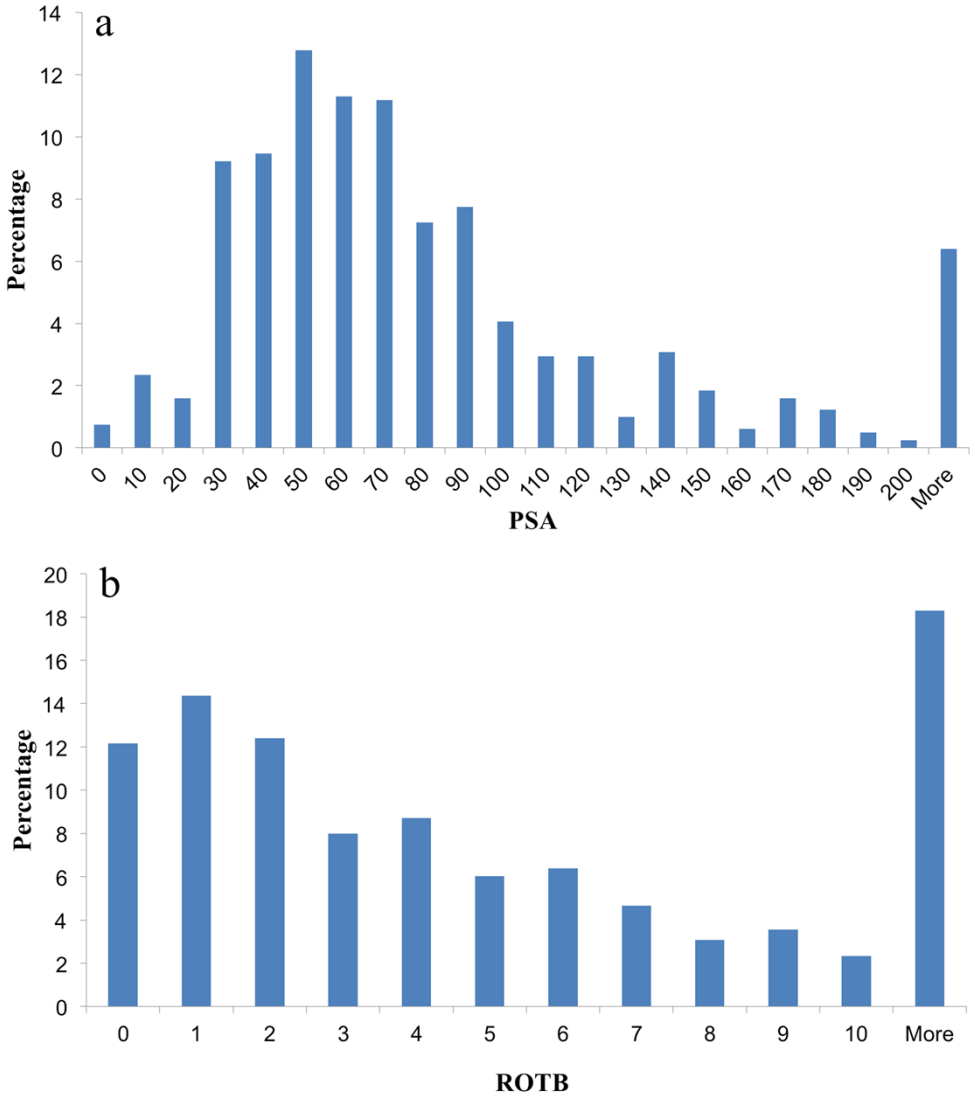
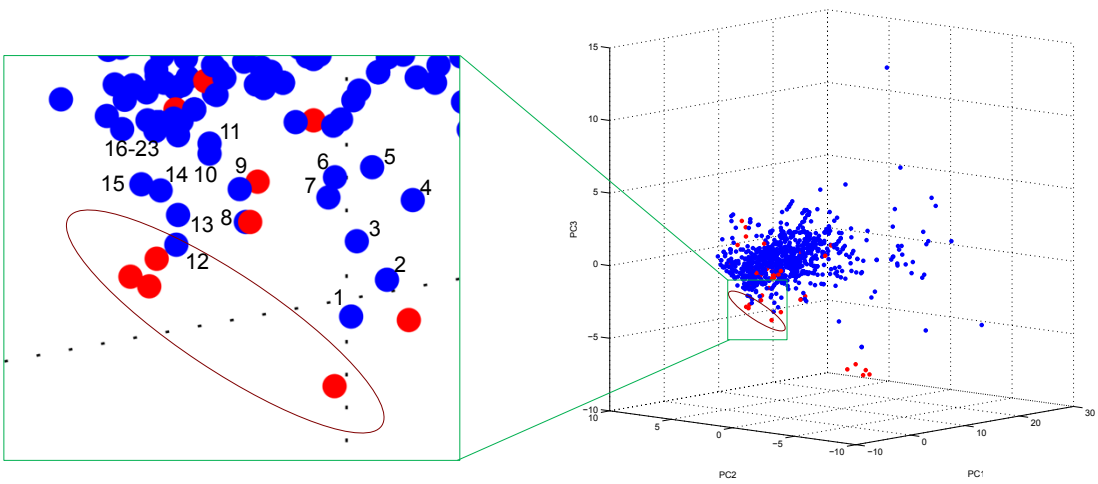


Figure S3 Distribution histogram of a) Polar surface area (PSA) and b) Rotatable bonds (ROTB) of the anti-mycobacterium natural products reported between 1990 and 2012 timeframe.



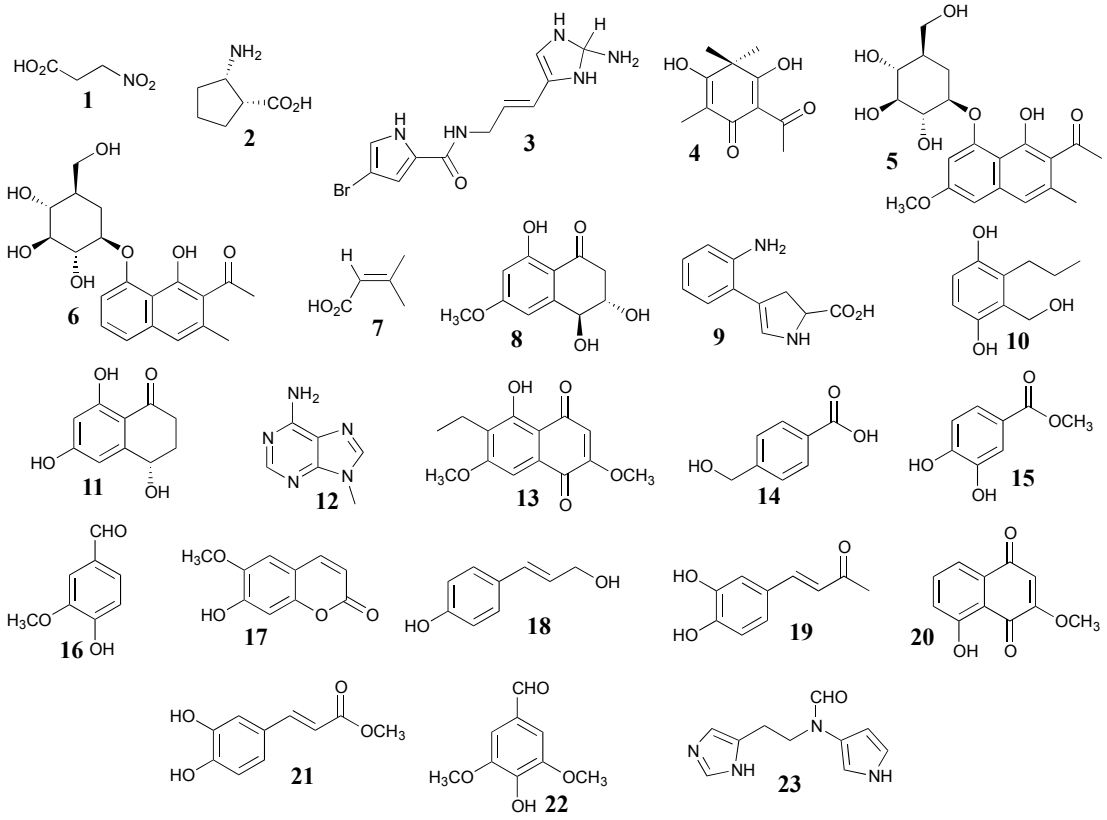
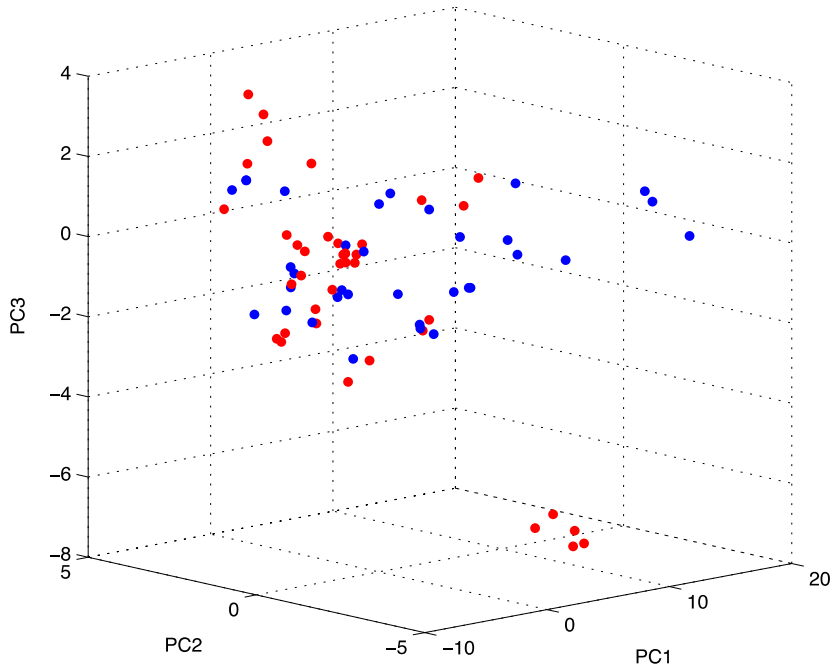
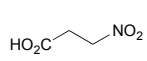


Figure S4 Anti-mycobacterium natural products next to the small molecular weight cluster of TB drugs. 1) MIC = 0.4 μg/ml ($H_{37}Ra$), 2) MIC = 4 μg/ml ($H_{37}Ra$), 3) MIC = 6.1 μg/ml ($H_{37}Rv$), 4) MIC = 50 μg/ml (*M. smegmatis*), 5) MIC = 8.9 μM ($H_{37}Ra$), 6) MIC = 26.6 μM ($H_{37}Ra$), 7) MIC = 36.0 μg/ml ($H_{37}Rv$), 8) MIC = 25 μg/ml ($H_{37}Ra$), 9) MIC = 0.5 μg/ml (*M. smegmatis*), 10) 25 μg/ml ($H_{37}Rv$), 11) MIC = 12.5 μg/ml ($H_{37}Ra$), 12) MIC = 6.25 μg/ml ($H_{37}Rv$), 13) MIC = 12.5 μg/ml ($H_{37}Ra$), 14) 22% inhibition at 6.25 μg/ml ($H_{37}Ra$), 15) 24% inhibition at 6.25 μg/ml ($H_{37}Ra$), 16) MIC = 12.5 μg/ml ($H_{37}Rv$), 17) MIC = 42 μg/ml ($H_{37}Rv$), 18) MIC = 50 mg/L (*M. smegmatis*), 19) MIC = 8 μM ($H_{37}Rv$), 20) MIC = 15.3 μM ($H_{37}Rv$), 21) MIC = 25 μg/ml ($H_{37}Ra$), 22) MIC = 25 μg/ml ($H_{37}Rv$), 23) MIC = 10 μg/ml (*M. intracellulare*).





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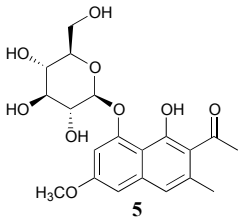

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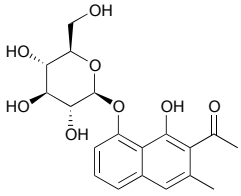

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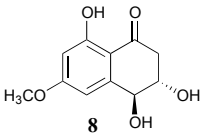

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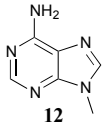

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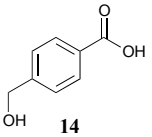

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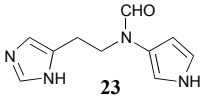

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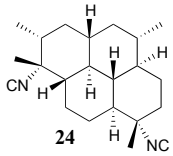

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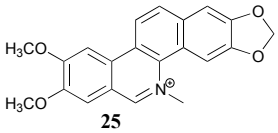

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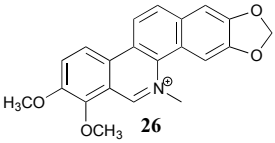

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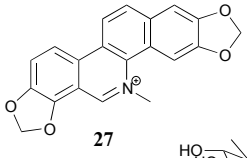

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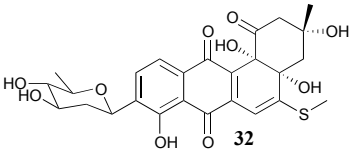

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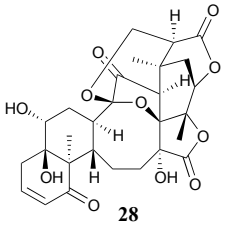

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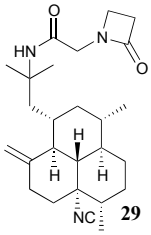

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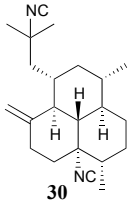

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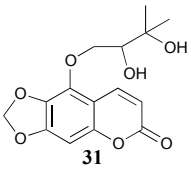

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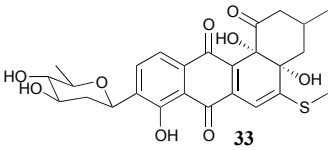

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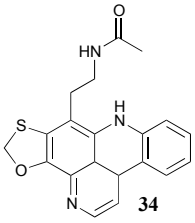

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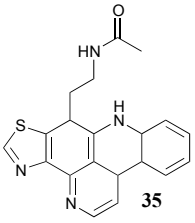

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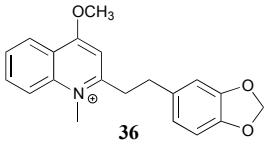

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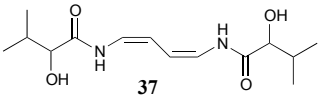

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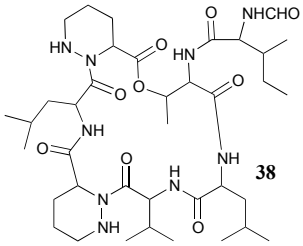

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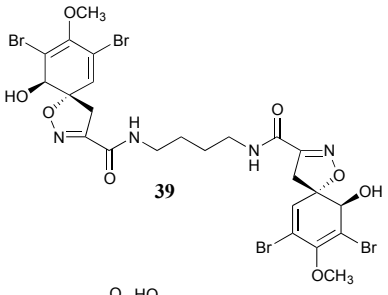

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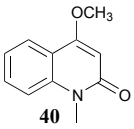

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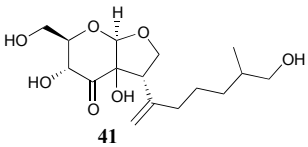

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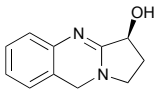

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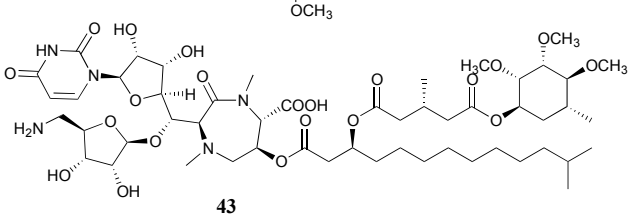

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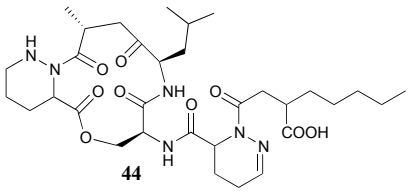

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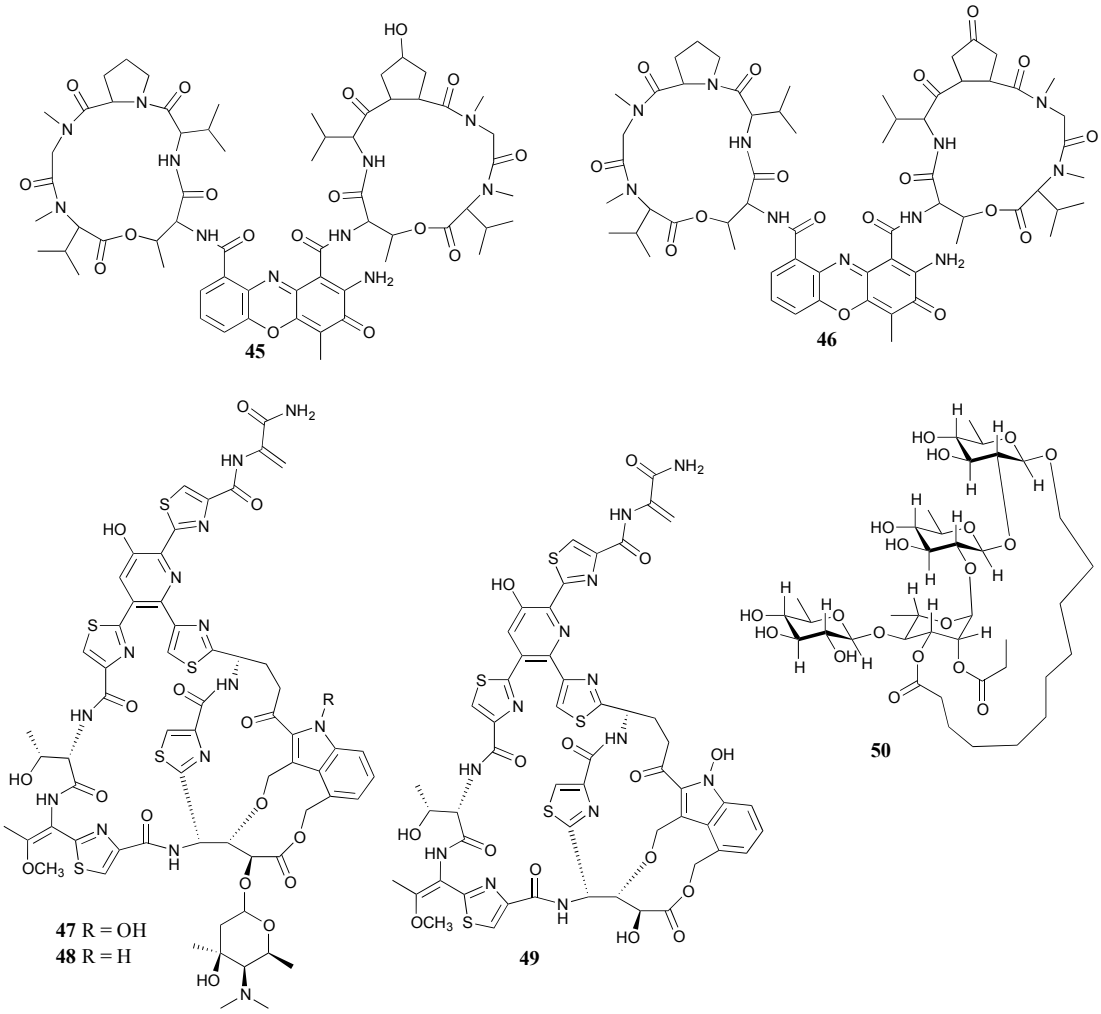

Figure S5 Anti-mycobacterium natural products possessing Log *P* values between -1 and 1. 1) MIC = 0.4 μg/ml ($H_{37}Ra$), 5) MIC = 8.9 μM ($H_{37}Ra$), 6) MIC = 26.6 μM ($H_{37}Ra$), 8) MIC = 25 μg/ml ($H_{37}Ra$), 12) MIC = 6.25 μg/ml ($H_{37}Rv$), 14) 22% inhibition at 6.25 μg/ml ($H_{37}Ra$), 23) MIC = 10 μg/ml (*M. intracellulare*), 24) MIC = 8 μg/ml ($H_{37}Rv$), 25) ≥ 94% inhibition at 12.5 μg/ml ($H_{37}Rv$), 26) ≥ 94% inhibition at 12.5 μg/ml ($H_{37}Rv$), 27) ≥ 94% inhibition at 12.5 μg/ml ($H_{37}Rv$), 28) MIC = 32 μg/ml ($H_{37}Rv$), 29) MIC = 15.3 μg/ml ($H_{37}Rv$), 30) MIC = 2 μg/ml ($H_{37}Rv$), 31) MIC = 64 μg/ml ($H_{37}Ra$), 32) MIC = 3.13 μg/ml ($H_{37}Ra$), 33) MIC = 12.5 μg/ml ($H_{37}Ra$), 34) MIC = 17 μM ($H_{37}Rv$), 35) MIC = 34 μM ($H_{37}Rv$), 36) MIC = 6.25-50 μg/ml (*M. tuberculosis*), 37) MIC = 6.25 μg/ml (*M. tuberculosis*), 38) MIC = 3.12 μg/ml (*M. vaccae*), 39) MIC = 6.25-25 μg/ml ($H_{37}Rv$), 40) MIC = 6.25-50 μg/ml (*M. tuberculosis*), 41) MIC = 64 μg/ml (*M. tuberculosis*), 42) MIC = 6-64 μg/ml (*M. tuberculosis*), 43) MIC = 3.13-50 μg/ml (*M. tuberculosis*), 44) MIC = 12.5 μg/ml ($H_{37}Rv$), 45) MIC = 8 μg/ml ($H_{37}Rv$), 46) MIC = 1 μg/ml ($H_{37}Rv$), 47, 48 and 49) MIC = ≤ 0.008 μg/ml (*M. tuberculosis*), 50) MIC = 25 μg/ml ($H_{37}Rv$).