

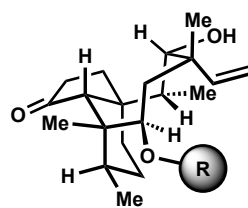
pleuromutilin (1)

- Tricyclic diterpenoid first isolated in 1951 from fungi of the *Clitopilus* genus

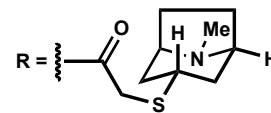
- Potent inhibitor of bacterial protein synthesis by binding to the bacterial ribosome.

- Modification of ester functionality (R) gives semisynthetic pleuromutilin derivatives, some of which are FDA-approved antibiotics

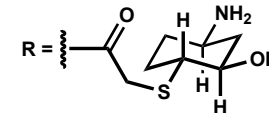
Nicholas J. Foy and Sergey V. Pronin*, *JACS* **2022**, *144*, 10174



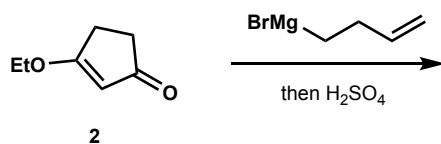
pleuromutilin derivatives:



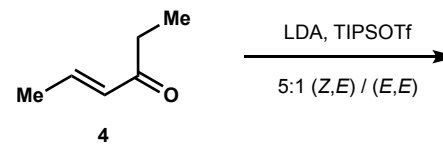
retapamulin (GSK), approved in 2007 for topical treatment of skin infections



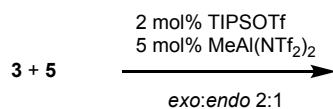
lefamulin (Nabriva), approved in 2019 for systematic treatment of bacterial infections in humans



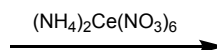
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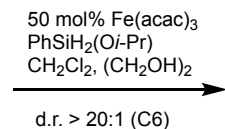
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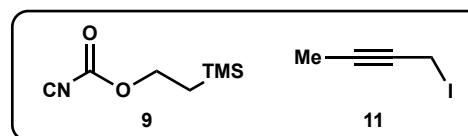
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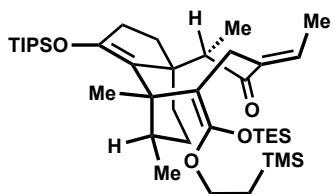
7



8



a) LDA, TIPSOTf
b) PPTS
c) LDA, Et₂O, 9

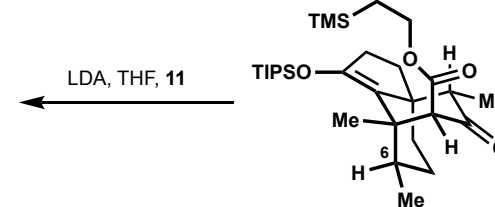


14

KHMDS, TESCI
reaction name?

Ti(Oi-Pr)₄
i-PrMgCl (2 equiv.)
pre-stirred to form...?

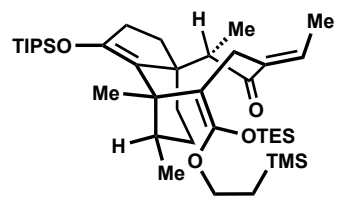
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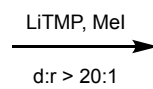
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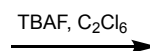
LDA, THF, 11



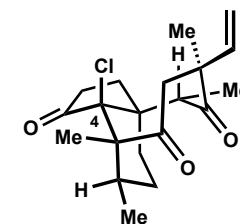
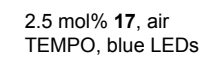
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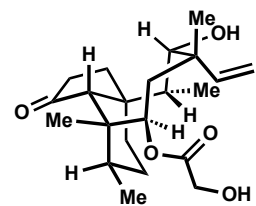
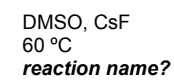
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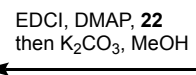
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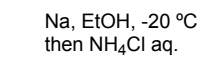
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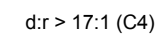
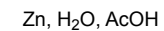
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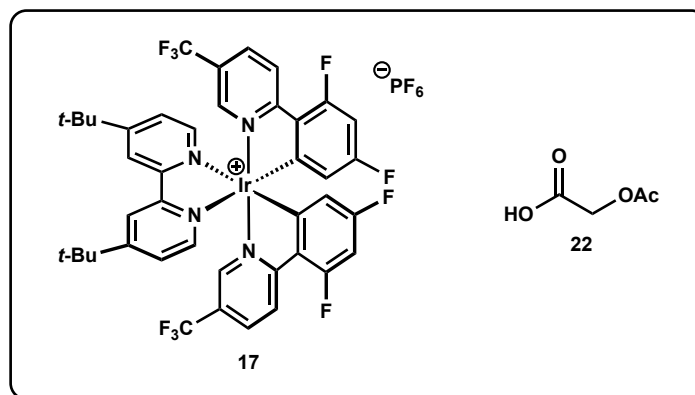
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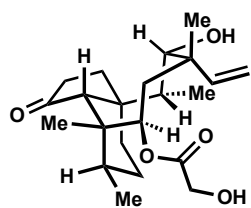


20



19





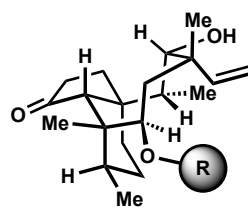
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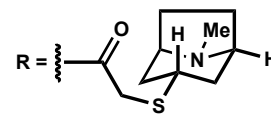
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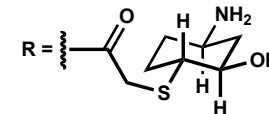
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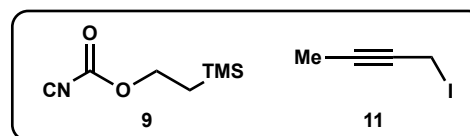
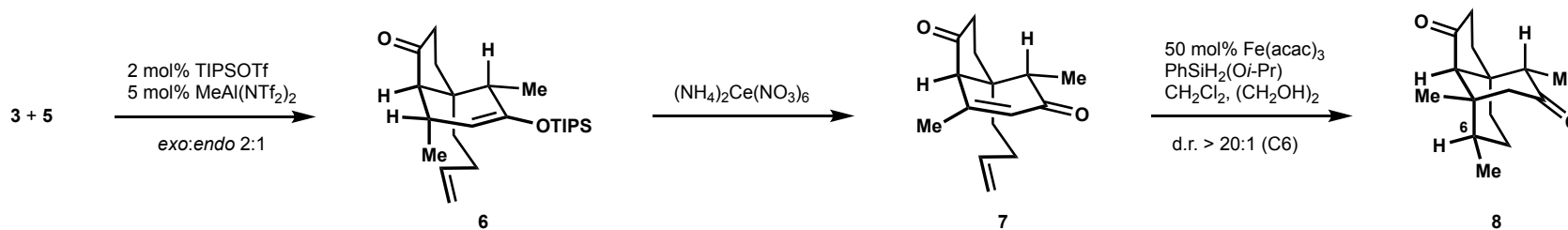
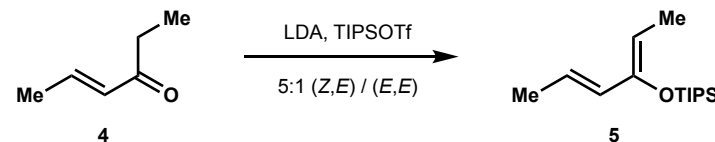
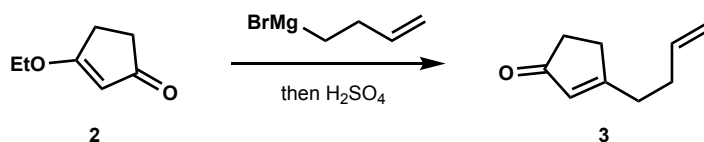
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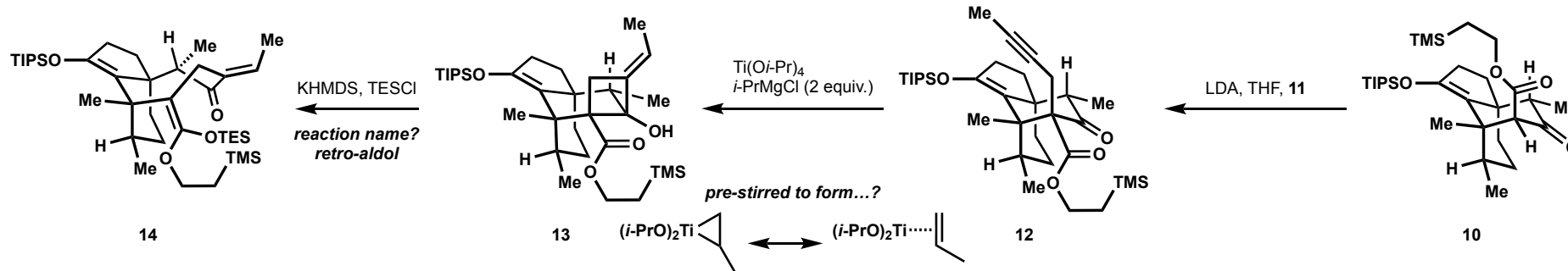
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reaction name?
retro-aldol

pre-stirred to form...?

