

FIG. 1. Synthesis of P1 and P2

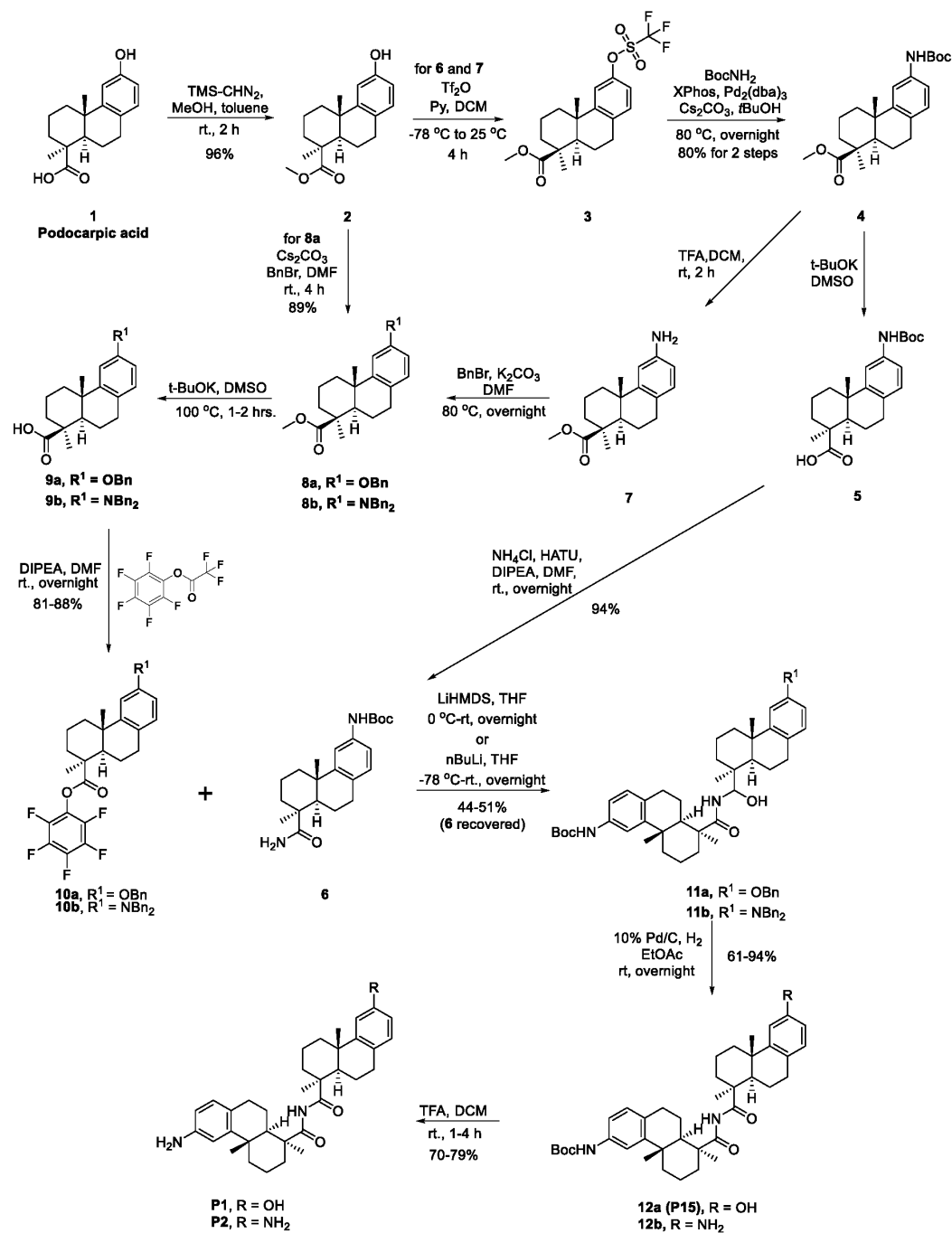


FIG. 2A. Synthesis of Payloads P3-P9, P13, P14, and P17

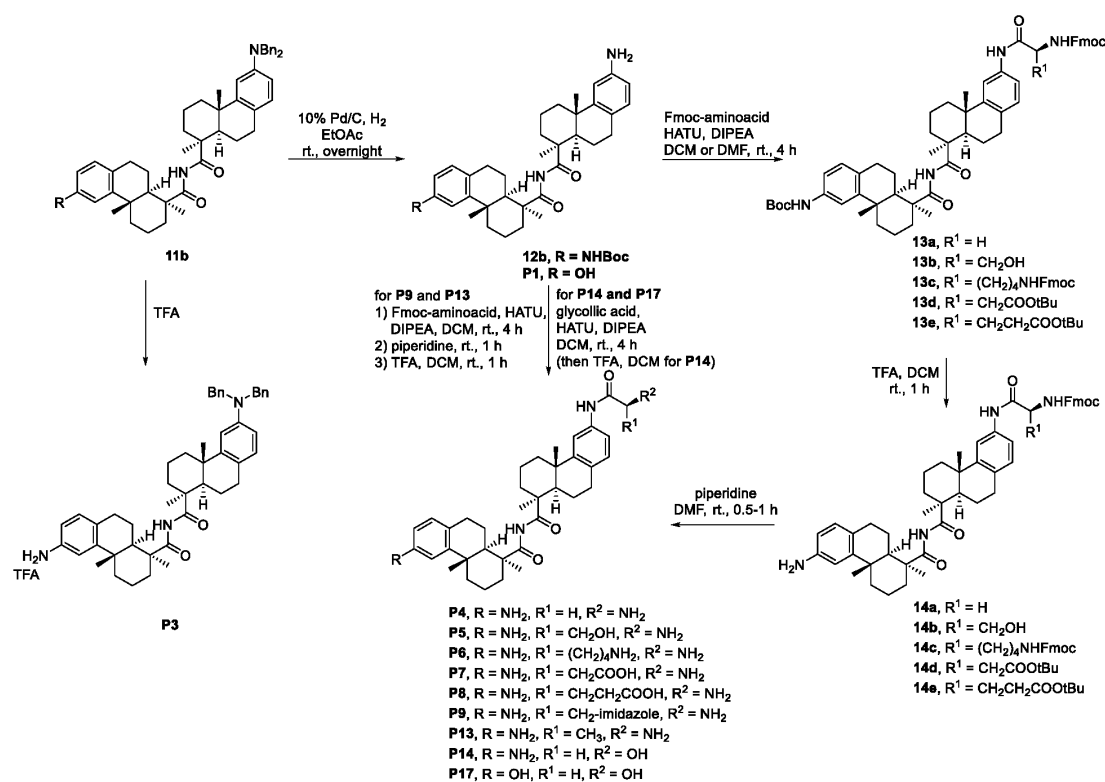


FIG. 2B. Synthesis of Payloads P10 and P11

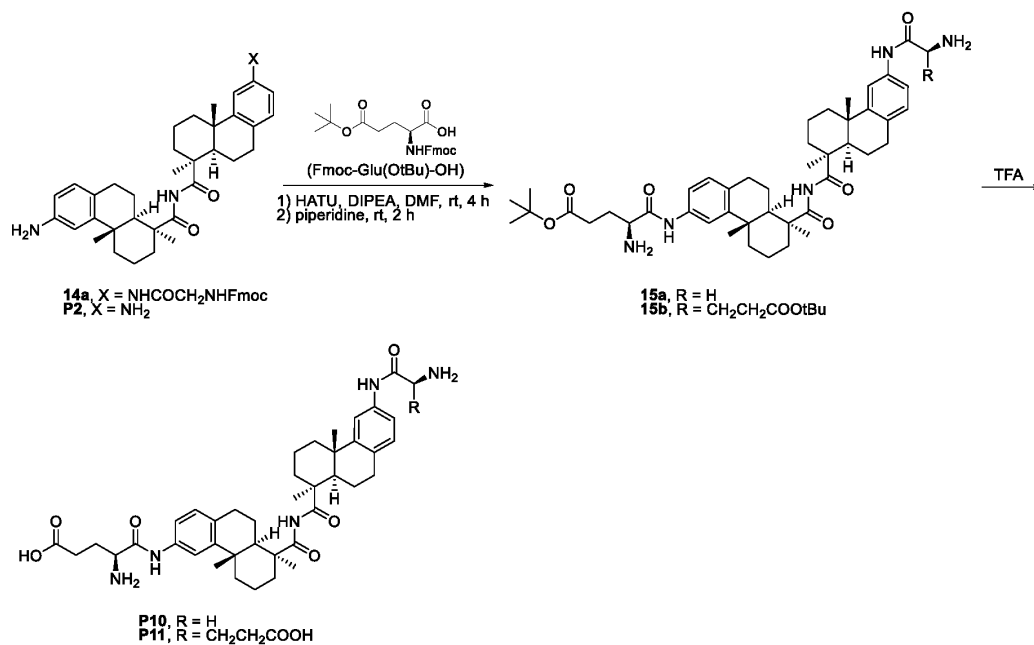


FIG. 2C. Synthesis of Payload P19

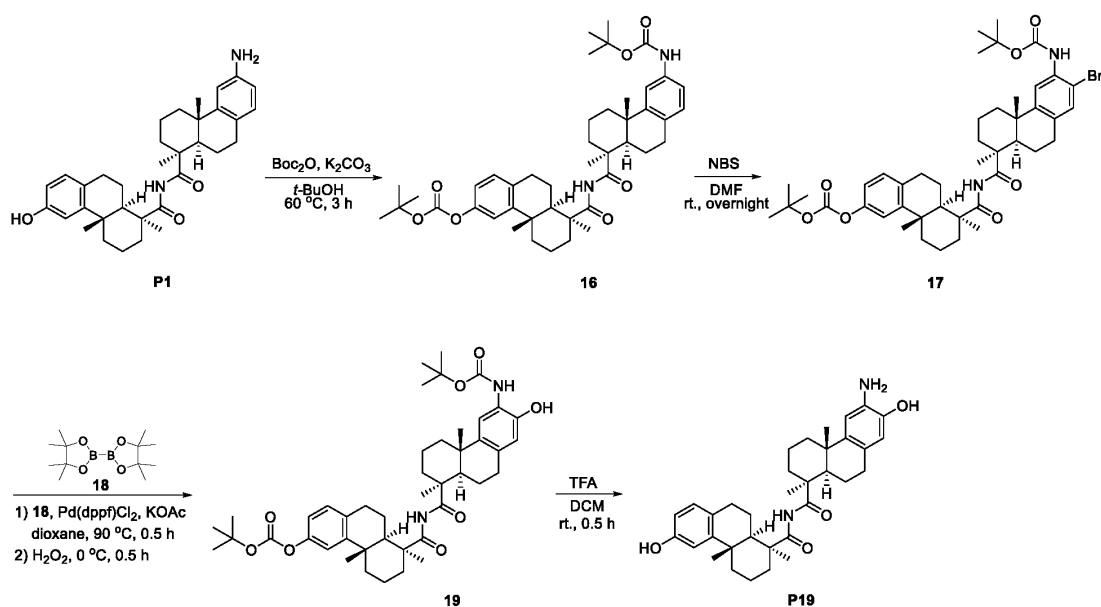
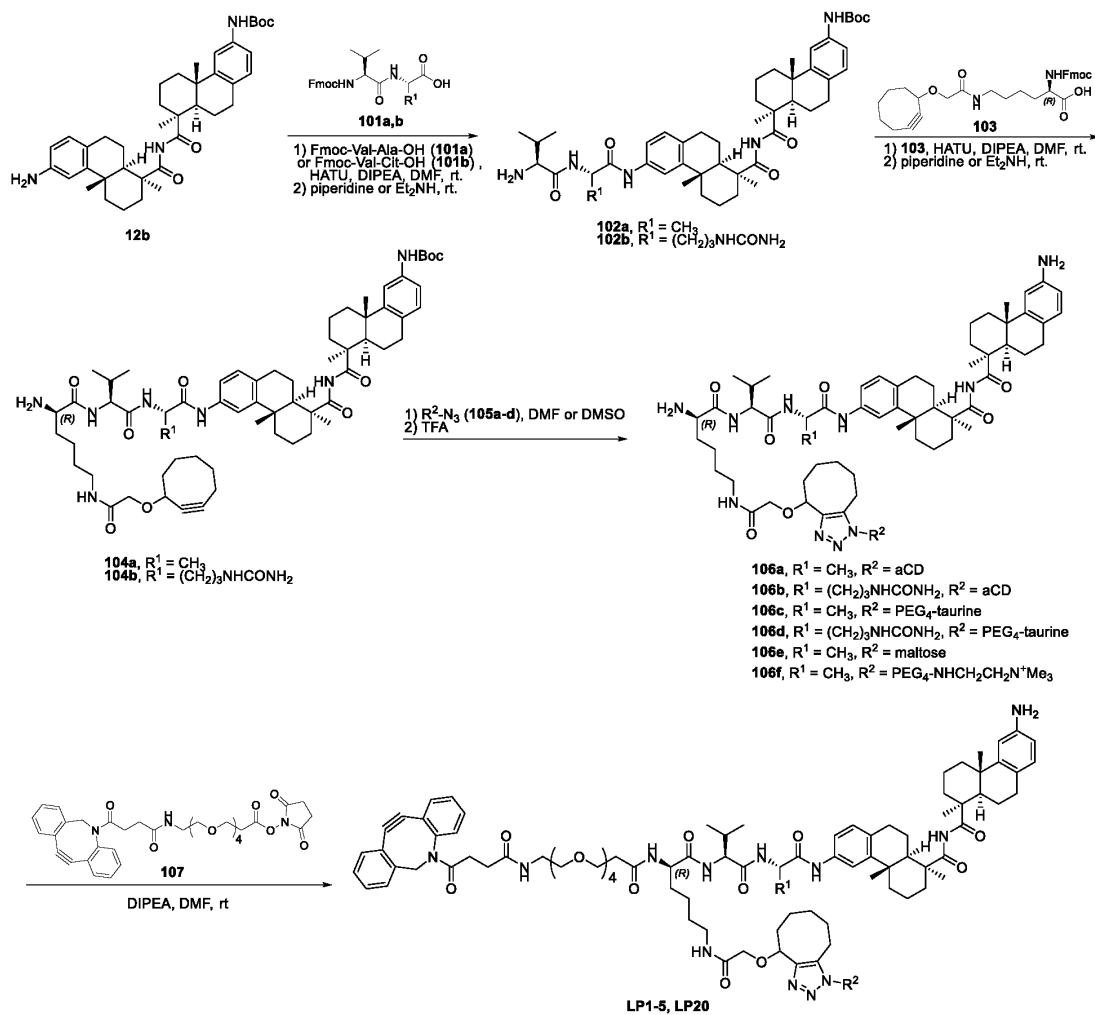
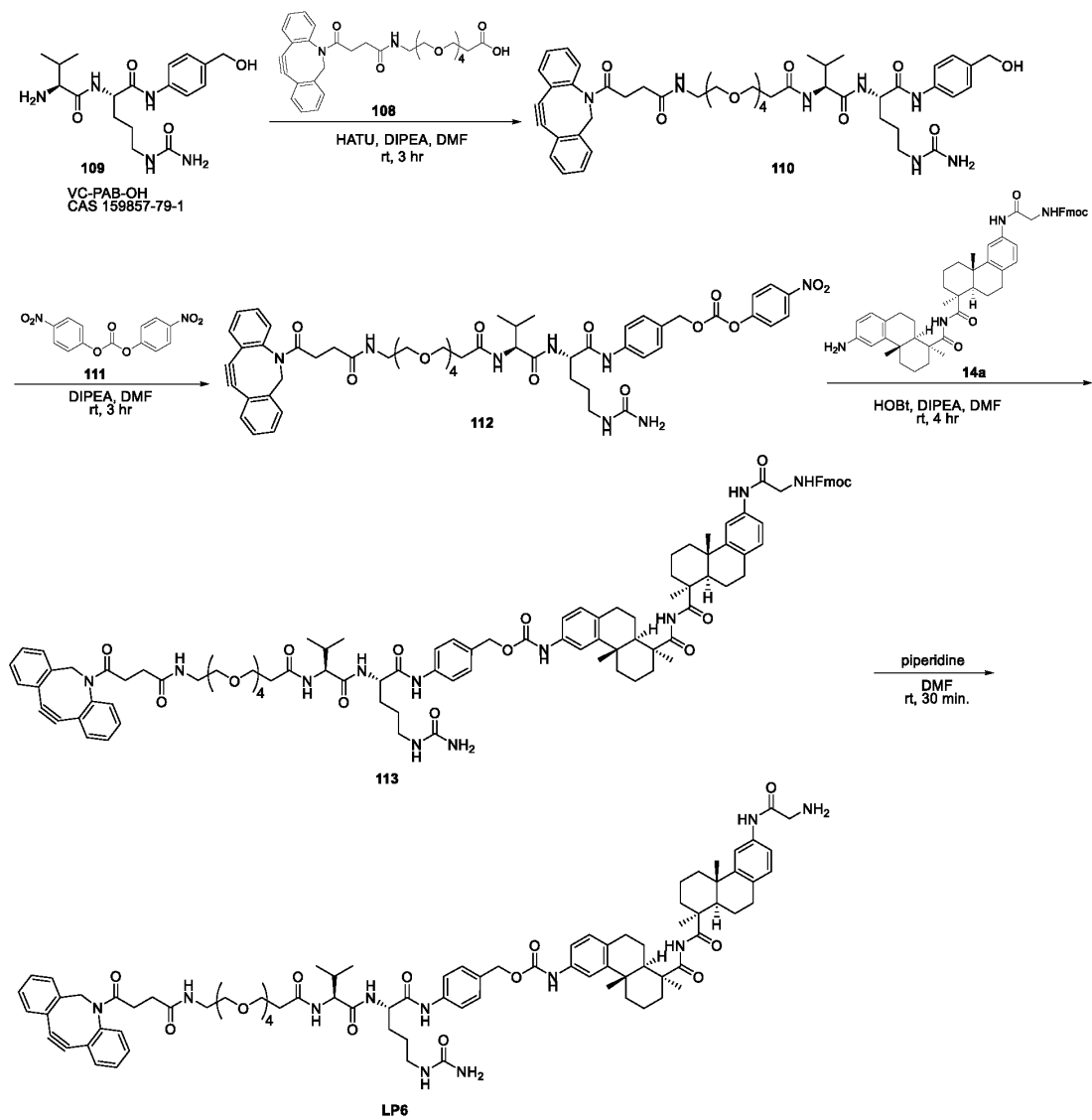


FIG. 3. General Synthesis of Linker and LP1-5 and LP20



LP	R ¹	R ²
LP1	CH ₃	αCD
LP2	(CH ₂) ₃ NHCONH ₂	αCD
LP3	CH ₃	PEG ₄ -taurine
LP4	(CH ₂) ₃ NHCONH ₂	PEG ₄ -taurine
LP5	CH ₃	Maltose
LP20	CH ₃	PEG ₄ -NHCH ₂ CH ₂ N ⁺ Me ₃

FIG. 4. Synthesis of LP6



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FIG. 5. Synthesis of LP7

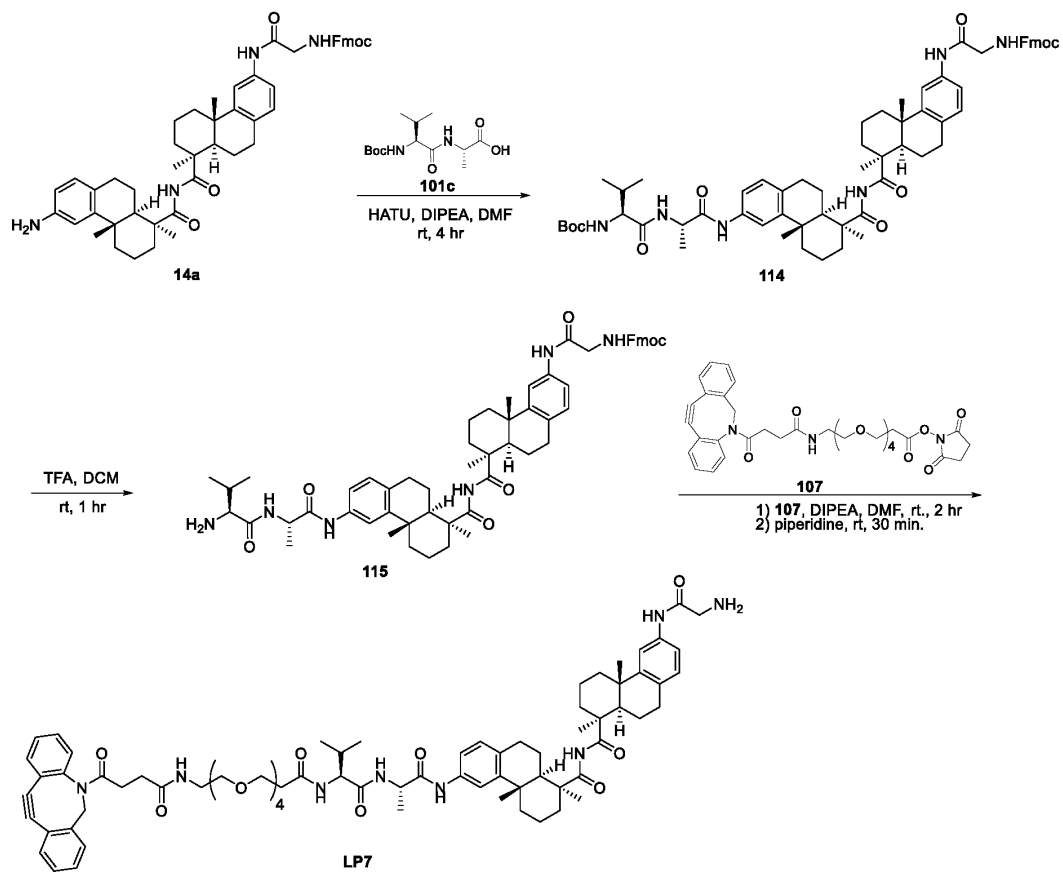


FIG. 6. Synthesis of LP8

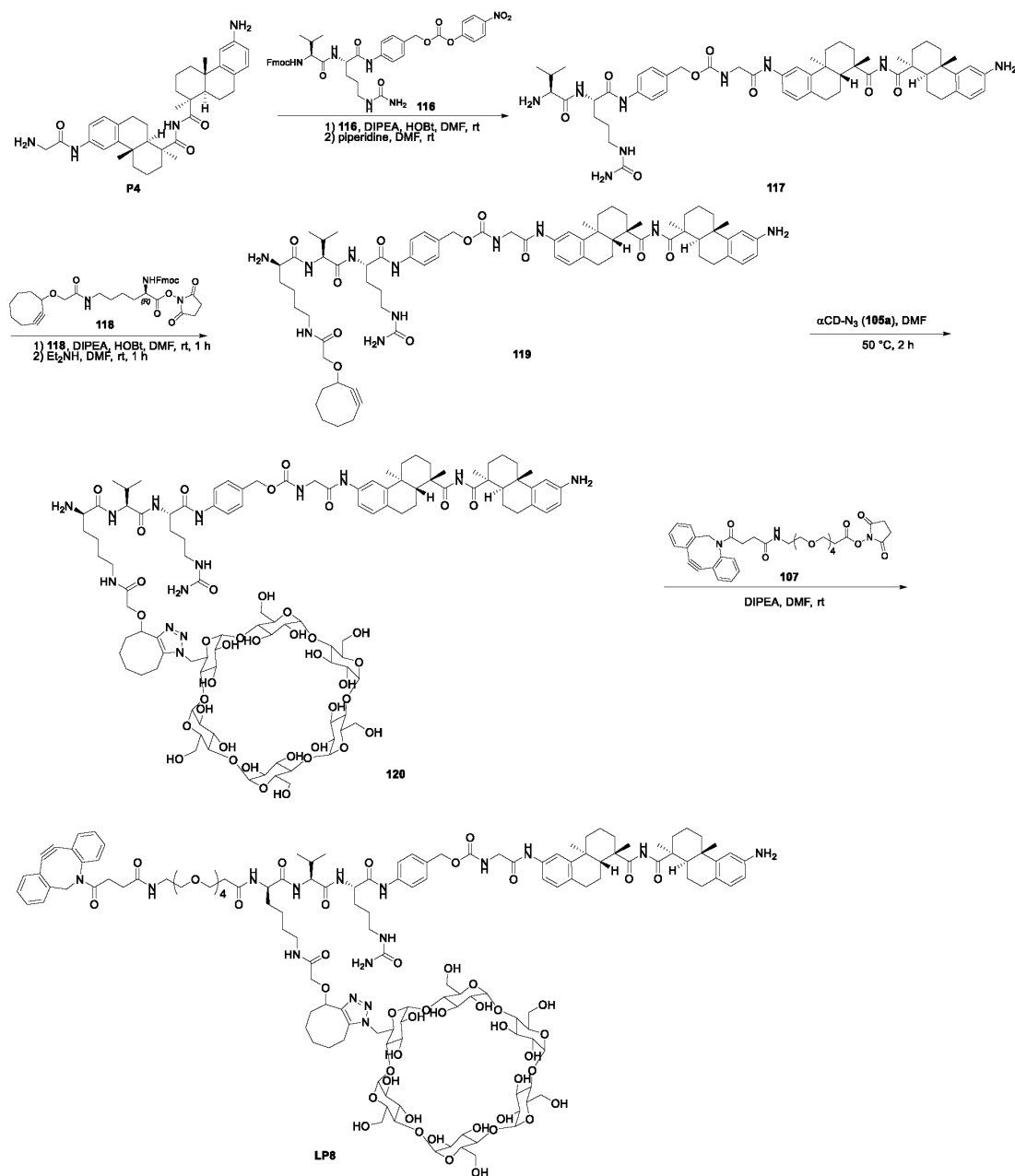
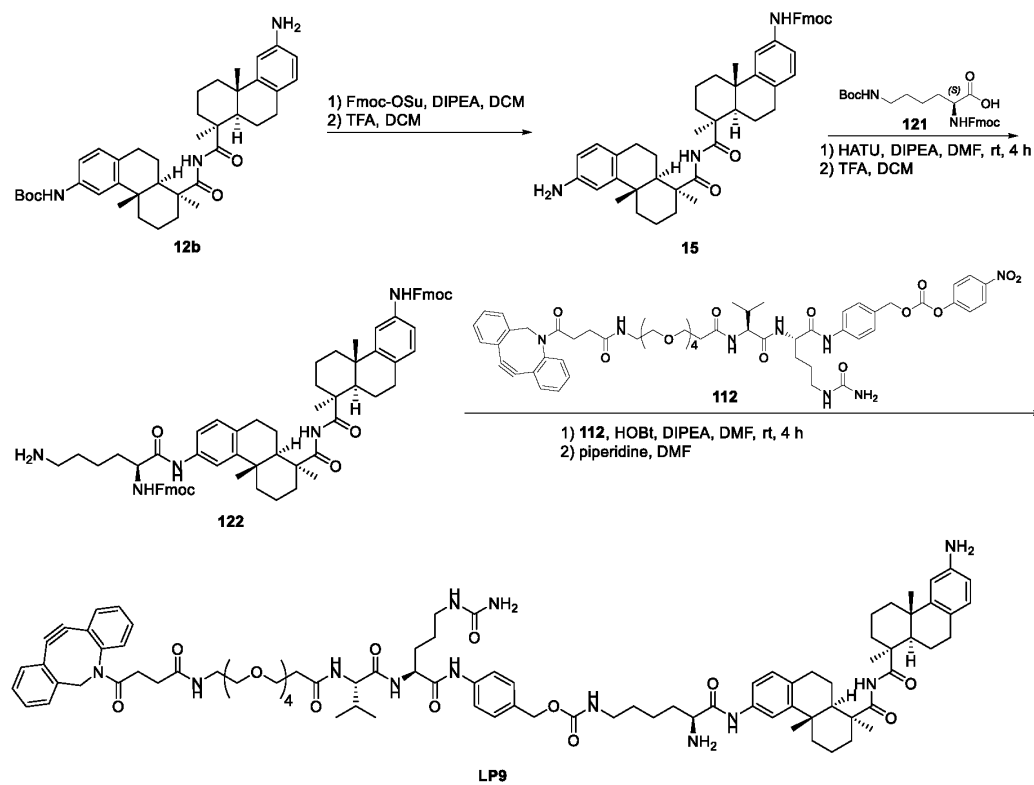


FIG. 7. Synthesis of LP9



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FIG. 8. Synthesis of LP10 and LP11

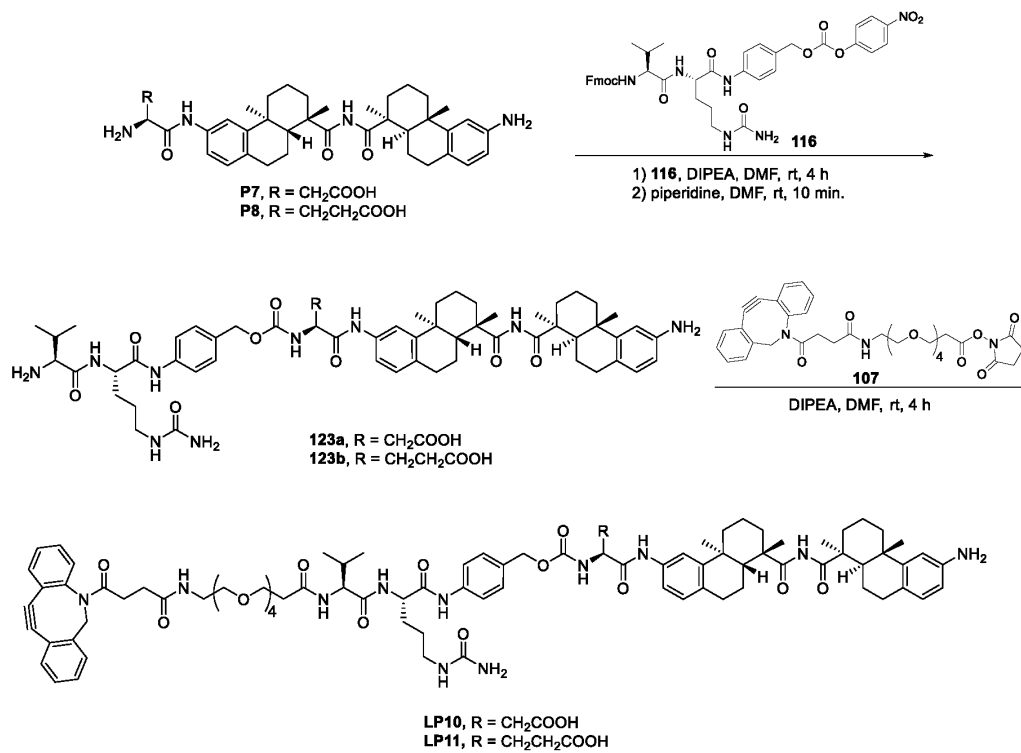
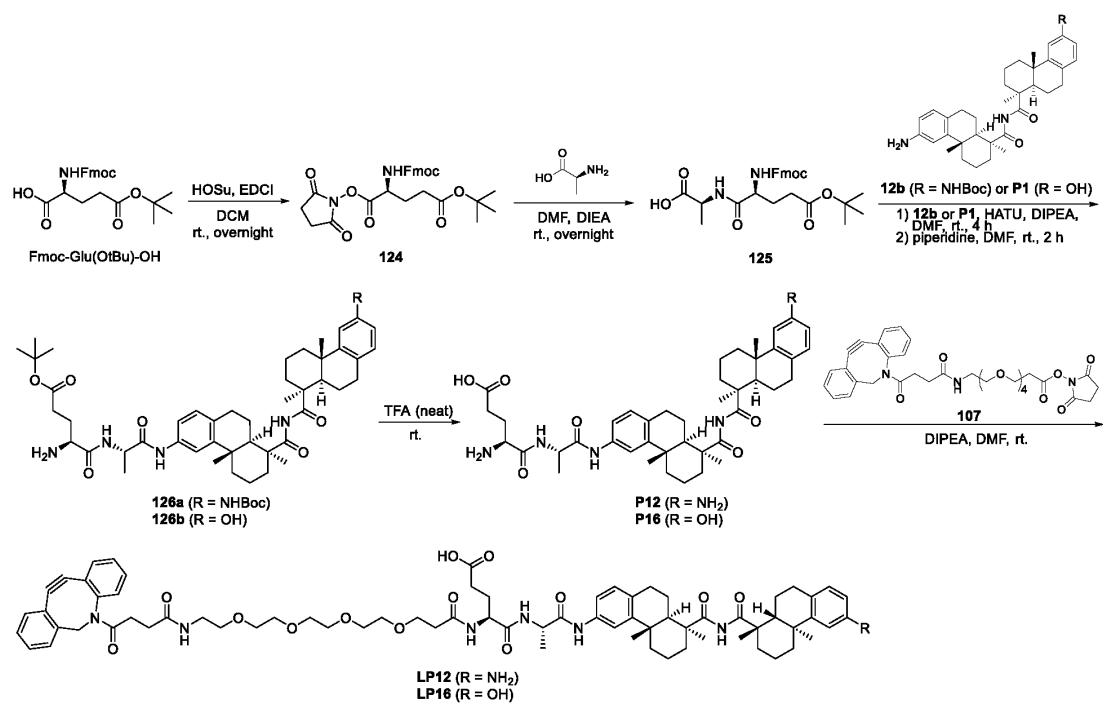


FIG. 9. Synthesis of P12 and LP12; and P16 and LP16



102a

127a (* = S-)
127b (* = R-)

1) 127, HATU, DIPEA, DMF, rt., 1 h
 2) TFA, DCM, rt., 1 h

128a (* = S-)
128b (* = R-)

107

DIPEA, DMF, rt., 4 h

LP13 (* = S-)
LP14 (* = R-)

129
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EDCI, DMF, rt., 20 h

130

Pd/C, H₂
 MeOH, rt., 20 h

131

132

DIPEA, DMF, rt., 2 h

133

1) PNPIC, DIPEA, DMF, rt.
 2) **Px2** (**Ser-P1**), DIPEA, DMF, rt.

LP15

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FIG. 9C. Synthesis of P18 and LP17 and LP18

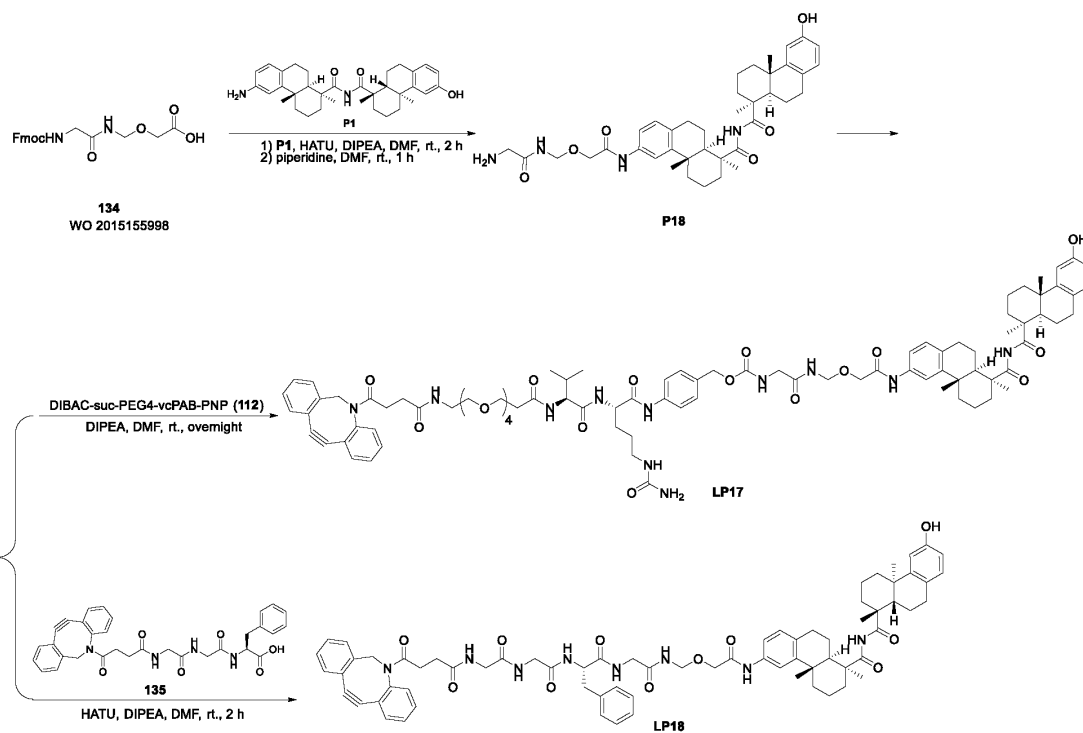


FIG. 9D. Synthesis of LP19

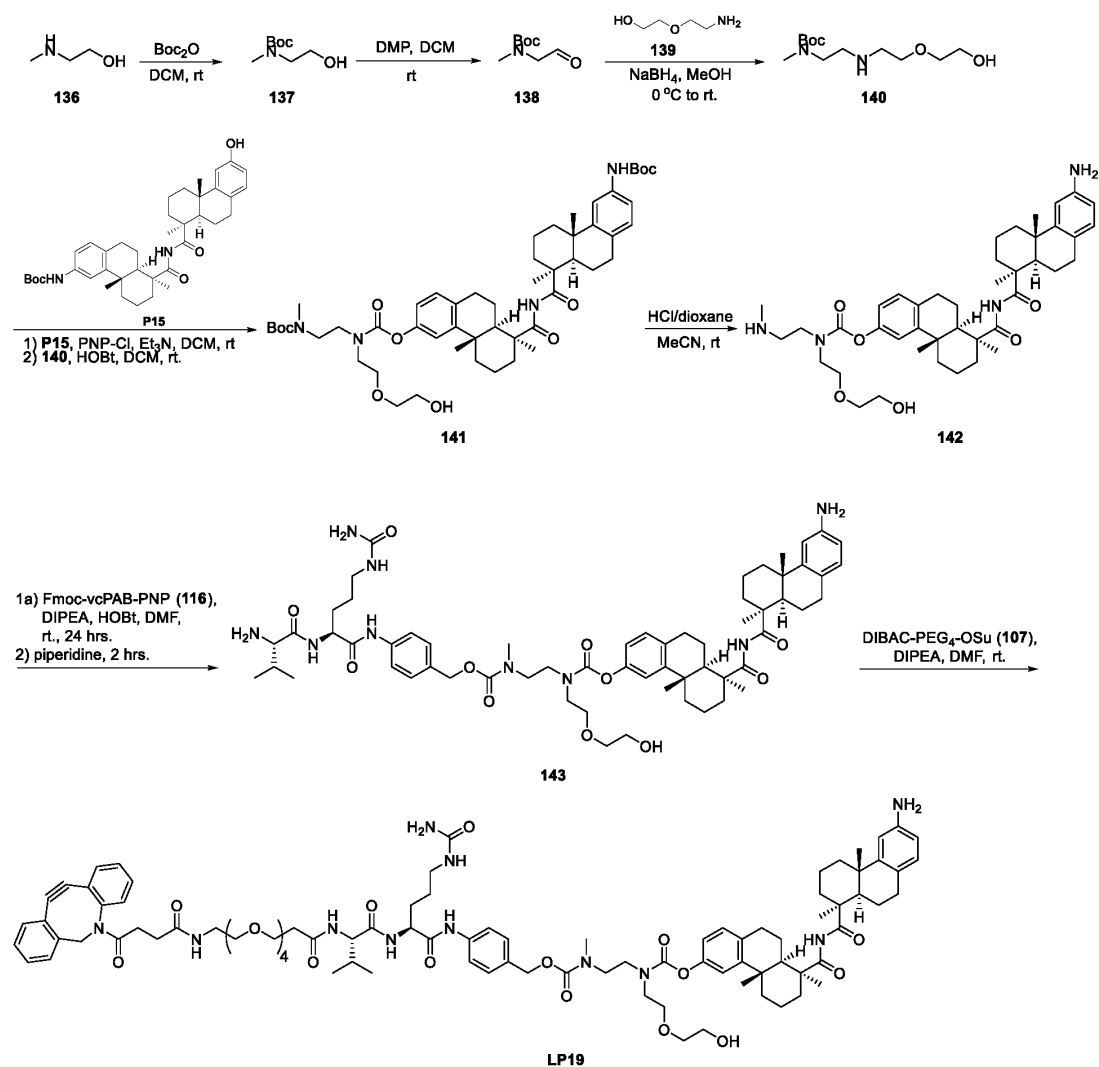


FIG. 10. Synthesis of Azide 105a

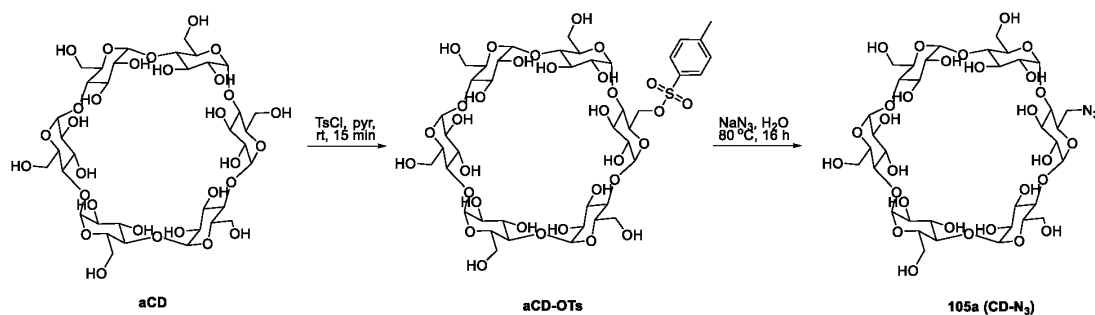


FIG. 11. Synthesis of Azide 105b

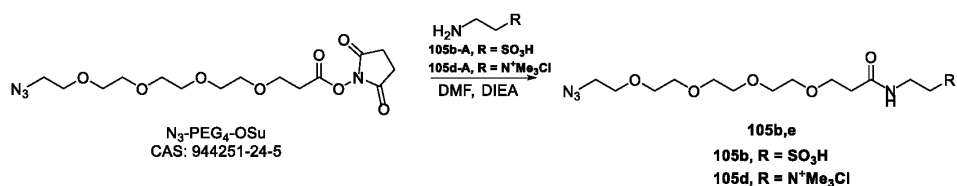


FIG. 12. Synthesis of intermediate 105c

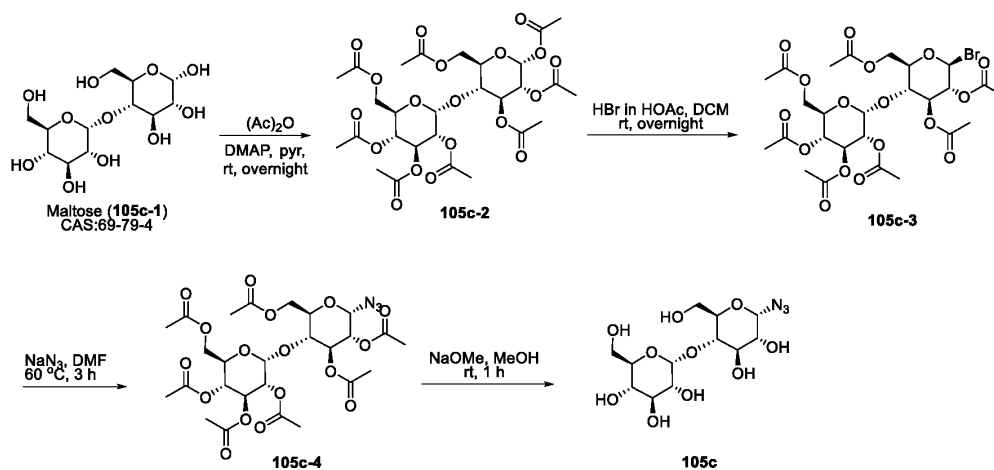


FIG. 13. Activation of Cholesterol Efflux by an anti-MSR1 ADC Having a P2 Payload

