Evolution of a Synthetic Strategy for Complex Diterpenes from Euphorbiaceae and Thymelaeaceae

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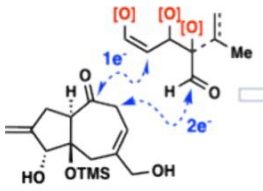
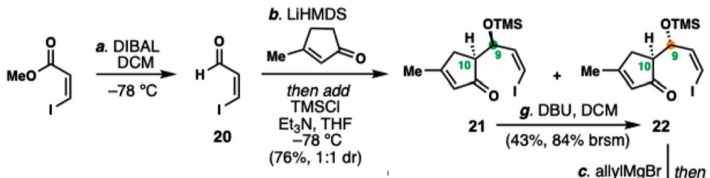


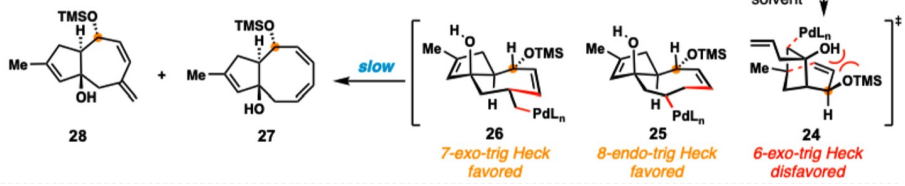


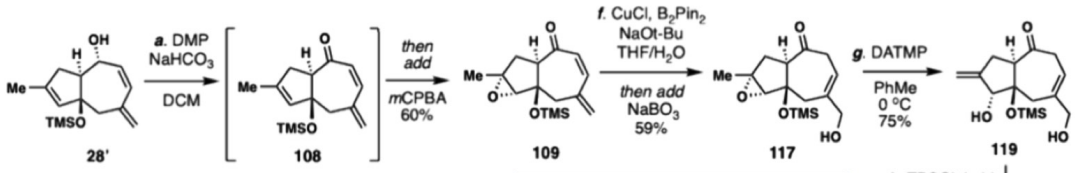
B Optimization of the Heck Reaction of **23** (step c')

Entry	Conditions	Results (Yield)[a]
1	$Pd(OAc)_2$, PPh_3, Et_3N, THF, 60 °C	**27** (20%) + **28** (30%)
2	$Pd(OAc)_2$, PPh_3, Et_3N, MeCN, 75 °C	**27** (15%) + **28** (40%)
3	$Pd(OAc)_2$, Na_2CO_3, TBAB, MeCN/H_2O, 70 °C	complex
4	$Pd(PPh_3)_4$, Et_3N, DMF, 80 °C	**28** (25%)
5	$Pd(PPh_3)_4$, Et_3N, MeCN, 75 °C	**28** (61%, 51%[b])
6	$Pd_2(dba)_3$, Et_3N, PhMe, 100 °C	**28** (<5%)
7	$Pd_2(dba)_3$, Et_3N, dppf, PhMe, 100 °C	complex

C Examination of Heck Reaction of **31** (step d')

Entry	Conditions	Results (Yield)[a]
1	$Pd_2(dba)_3$, Et_3N, PhMe, 80 °C	complex
2	$Pd(PPh_3)_4$, Et_3N, DMF, 80 °C	**33** (10%) + **34** (13%)
3	$Pd(PPh_3)_4$, Et_3N, MeCN, 75 °C	**33** (43%) + **34** (45%)
4	$Pd(PPh_3)_4$, K_2CO_3, MeCN, 75 °C	complex
5	$Pd(OAc)_2$, PPh_3, Et_3N, THF, 60 °C	**33** (30%) + **34** (35%) + **35**
6	$Pd(OAc)_2$, PPh_3, K_2CO_3, TBACl, PhMe, 80 °C	complex
7	$Pd(OAc)_2$, PPh_3, Et_3N, Ag_2CO_3, THF, 60 °C	complex





conjugate borylation/oxidation

ligandless Cu-catalyzed 1,6-

Entry	Conditions	Yield (ratio 109:117:118)
1	$Pt(PPh_3)_4$, B_2Pin_2, PhMe or THF, 80 °C 36 h	82% (1:1:1)
2	$(PPh_3)_3RhCl$, B_2Pin_2, PhMe or THF, rt to 80 °C 12 h	complex
3	$CuCl_2$, DMAP, B_2Pin_2, H_2O/THF, rt 24 h	<10% (complex)
4	PCy_3, B_2Pin_2, MeOH, rt 1 h	90% (1:3.7:9.4)
5	**39**, NaOt-Bu, B_2Pin_2, THF, rt 36 h	no rxn
6	CuCl, PCy_3, NaOt-Bu, B_2Pin_2, MeOH/THF, rt 24 h	no rxn
7	CuCl, *rac*-BINAP, KOt-Bu, B_2Pin_2, THF, rt 24 h	85% (1:1.4:1.2)
8	CuCl, **39**, NaOt-Bu, B_2Pin_2, THF, 0 °C to rt 3 h	81% (0:1.9:1)
9	CuCl, dppb, NaOt-Bu, B_2Pin_2, THF, rt 6 h	90% (0:2:1)
10	CuCl, dppf, NaOt-Bu, B_2Pin_2, THF, rt 24 h	85% (3:4:1)
11	CuCl, DPEphos, NaOt-Bu, B_2Pin_2, THF, rt 36 h	88% (6:3:1)
12	CuCl, KOt-Bu, B_2Pin_2, THF, rt 12 h	80% (5:4:1)
13	CuCl, NaOt-Bu, B_2Pin_2, THF, rt 12 h	84% (2:4:1)
14	CuCl, NaOt-Bu, B_2Pin_2, H_2O/THF, rt 12 h	80% (8:12:1)
15	CuCl, NaOt-Bu, B_2Pin_2, H_2O/THF, rt 36 h	**64% (0:11:1)**
16	$[Cu(PPh_3)_2F{\cdot}2MeOH]$, *rac*-BINAP, B_2Pin_2, PhMe or THF, rt 7 h	90% (0:1:1.6)