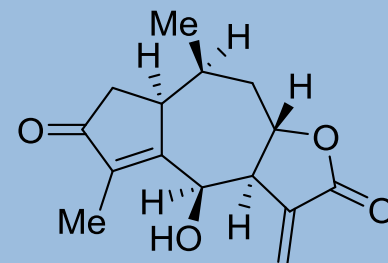


A Double Allylation Strategy for Gram-Scale Guaianolide Production: Total Synthesis of (+)-Mikanokryptin

X. Hu, K. S. Xu, T. J. Maimone *Angew. Chem. Int. Ed.* **2017**, *56*, 1624.

Melinda Mojzesová
University of Bern

02.02.2017, Journal Club



Mykanokryptin

Thomas J. Maimone (UC-Berkeley)

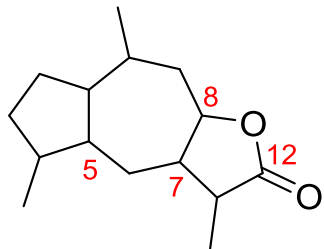
- ❖ B.S. University of California, Berkeley (2004, D. Trauner)
- ❖ Ph.D. The Scripps Research Institute, CA (2009, P. Baran)
- ❖ Postdoctoral Fellow, Massachusetts Institute of Technology (2009-2012, S. Buchwald)
- ❖ Since 2012 - Assistant Professor

- ❖ Research:
 - total synthesis of complex, biologically active natural products with relevance to issues of human health

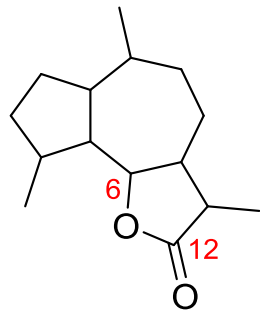


(+)-Mikanokryptin

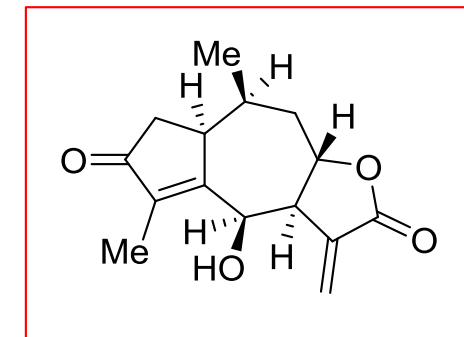
- ❖ first isolated in 1975 by Herz and co-workers from *Mikania scandens*
- ❖ belongs to the family of *trans*-fused 8,12-guaianolides



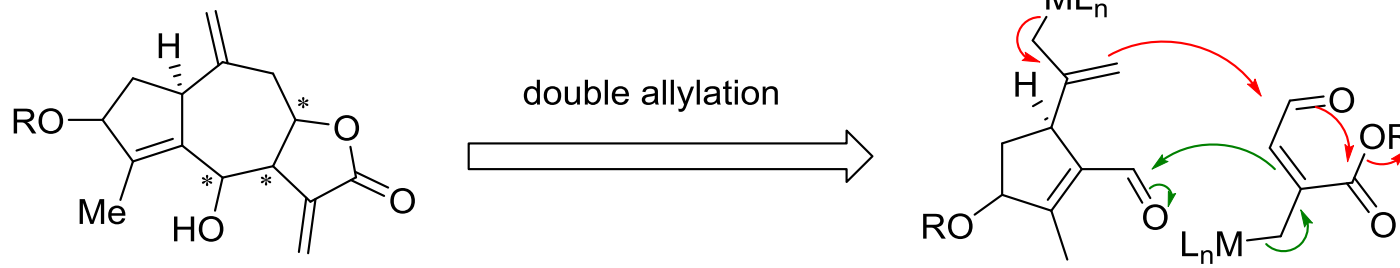
8,12-guaianolide



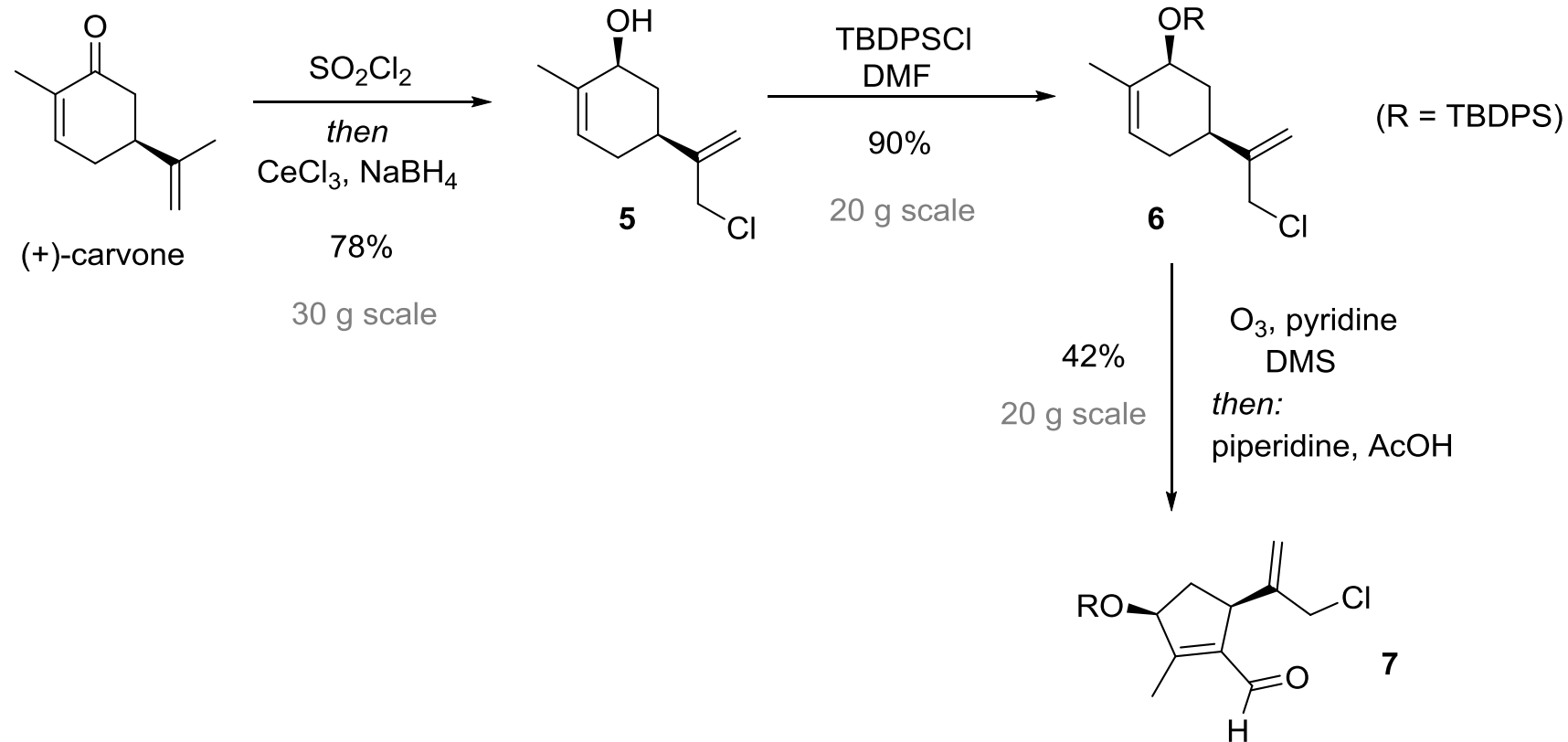
6,12-guaianolide



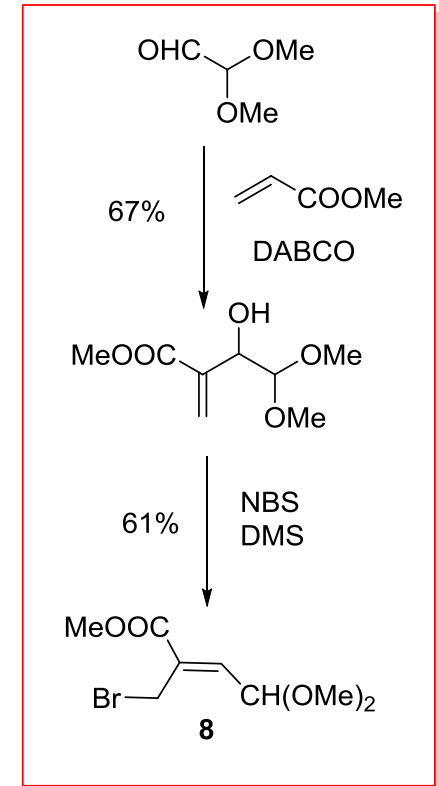
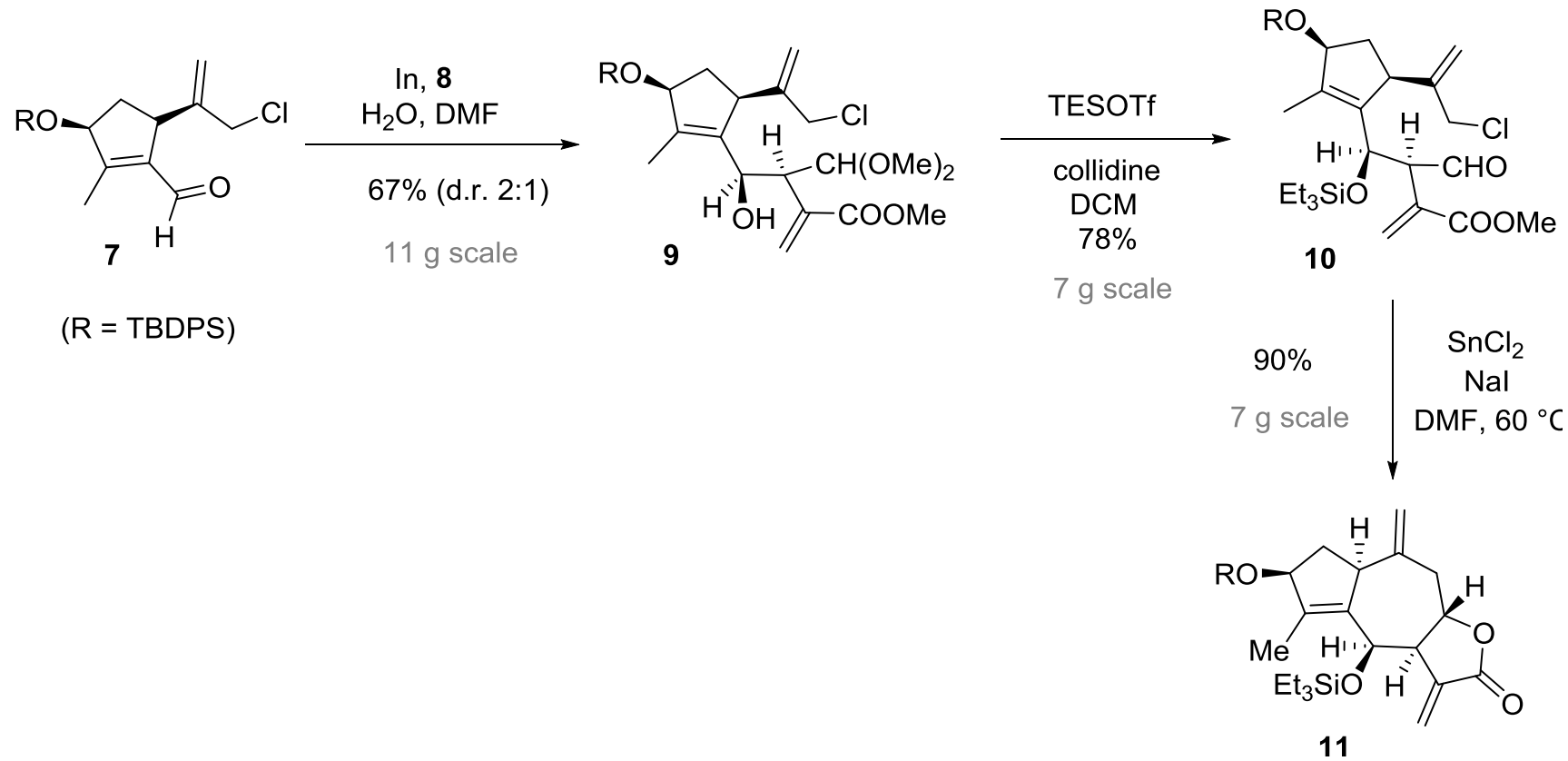
Developing a synthetic route...



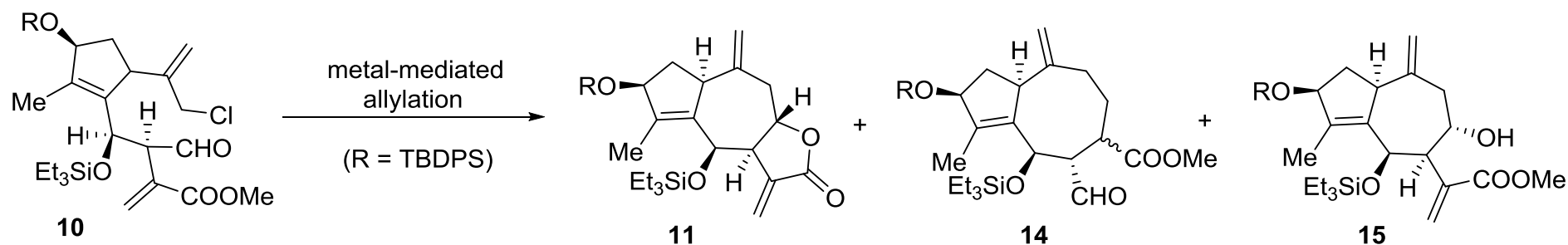
Forward Synthesis – western fragment



Forward Synthesis – allylation reactions

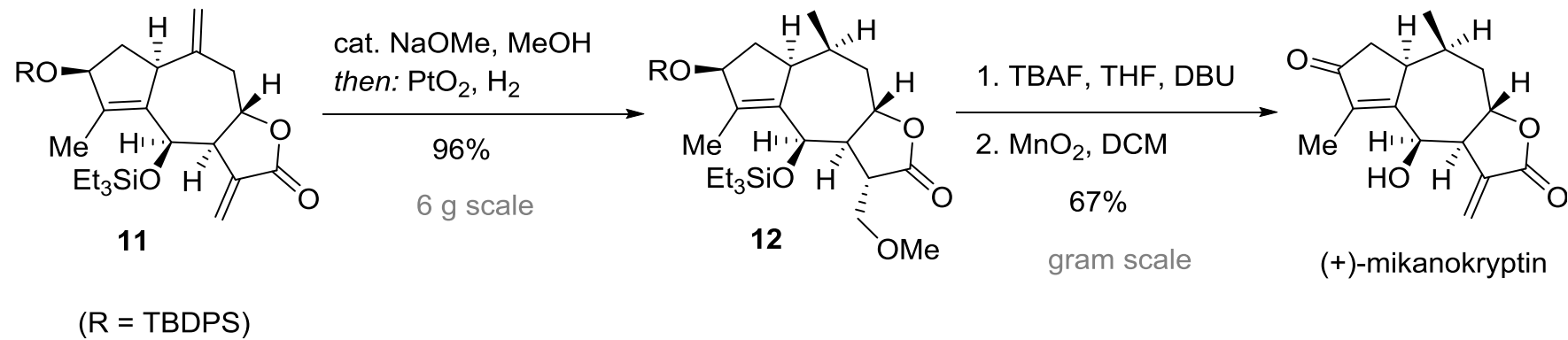


Metal-mediated allylation conditions



Entry	Conditions ^[a]	Yield [%] ^[b]			rsm ^[c]
		11	14	15	
1	CrCl ₂ , cat. NiCl ₂ , DMF, 60 °C	10 ^[d]	17	–	–
2	In ⁰ , NaI, DMF, 60 °C	13 ^[e]	–	–	–
3 ^[f]	NaI; SmI ₂ , HMPA–THF, –78 °C	27 ^[d]	17	–	–
4 ^[f]	NaI; Zn ⁰ , aq. NH ₄ Cl, THF, rt	0	51	–	34
5 ^[f]	NaI; Mg ⁰ , cat. (CH ₂ Br) ₂ , THF, rt	0	–	–	–
6 ^[f]	NaI; <i>i</i> PrMgCl, THF, 0 °C	0	–	–	–
7 ^[f]	NaI; SnCl ₂ , DMF, rt	53 ^[e]	–	20	9
8 ^[g]	SnCl ₂ , NaI, DMF, 60 °C	90 ^[e]	–	–	–

Forward Synthesis – redox manipulations



Conclusion

- ❖ short (8 steps), enantiospecific, gram-scale total synthesis of mikanokryptin from (+)-carvone in 6% overall yield
- ❖ first gram-scale synthesis of guaianolides
- ❖ through variation of allylation processes, the synthesis of other 8,12-guaianolides should be possible