Total Synthesis of (+)-Complanadine A Using an Iridium-Catalyzed Pyridine C-H Functionalization


By

Lakshmi Jeedimalla

October 15th, 2012
RICHMOND SAR PONG

- Was born on 23rd April, 1974 in Ghana.
- Graduated from Princeton University.
- Finished postdoctoral fellowship at California Institute of Technology.
- Joined the faculty at University of California Berkeley as an Assistant Professor and currently, working as an Associate Professor.
The Sarpong Group
Complanadine A

- One of the Lycopodium alkaloid
- Unsymmetrical dimer of Phleg-marine-derived alkaloid Lycodine.
Retro synthetic approach
Synthesis of 10 & 12:


Cascade for Synthesis of Complanadine monomer
Synthesis Of Boc protected Lycodine:

1. Reaction of 17 with Boc₂O, Et₃N in THF at 60 °C (65% yield over two steps).
2. Reaction of 8 with Pb(OAc)₄ in CHCl₃ at room temperature (84% yield).
3. Reaction of 7 with Tf₂O, pyridine at -78 °C to rt (72% yield).
4. Reaction of 18 with cat. Pd(OAc)₂, dppf, NH₄O₂CH, Et₃N in DMF at 60 °C (90% yield).
Final steps for the synthesis of Complanadine A

\[
\text{cat. } [\text{Ir(COD)(OMe)}]_2 / \text{dtBu-dipy} \\
[\text{B(pin)}]_2 \\
\text{THF, } 80^\circ \text{C} \\
75\% \\
\]

\[
\text{PdCl}_2(\text{dpdf}), \text{K}_3\text{PO}_4 \\
6\text{N HCl, } 70^\circ \text{C} \\
\text{42% yield} \\
\text{(over two steps)}
\]

Complanadine A (4)
Conclusion

- synthesis of Complanadine A was achieved in 8 steps from enamide 9 and acetal 12 with an yield of 42%.

- Potential access to other nature products like Lycodine, Lycoplanadine F, and Lycoplanadine G

- Seigel group also delivered a synthesis of this natural product and made it to JACS (back to back articles) within days of the Sarpong Group