Université de Montréal, Montréal, QC, Canada

THIRD INTERNATIONAL SYMPOSIUM
ON C–H ACTIVATION

May 30 – June 2, 2016

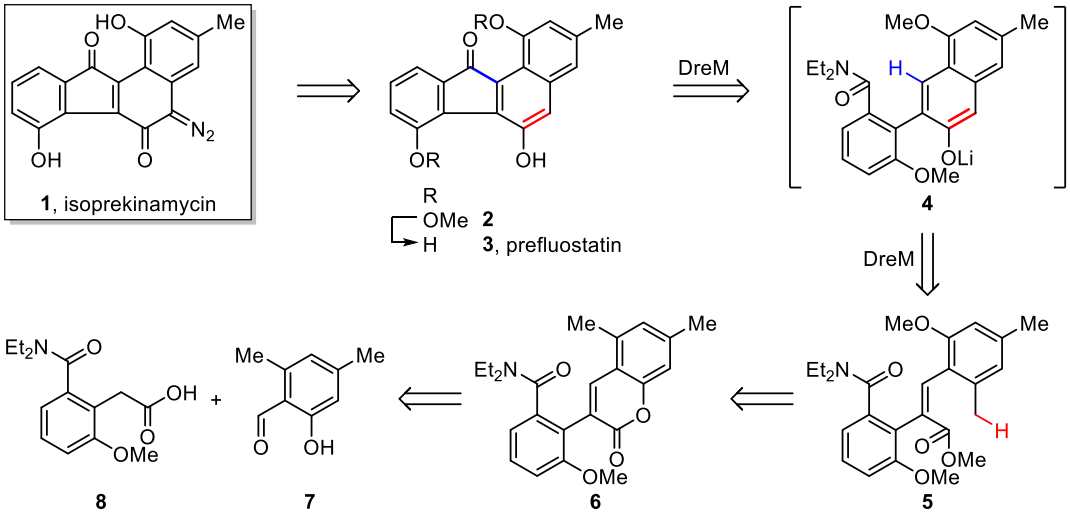
OR11 – Total Synthesis of Isoprekinamycin and Prefluostatin via a Double Directed remote Metalation (DreM) Cyclization

Timothy Hurst, Jignesh Patel, Chris Ziebenhaus, Matthew Kitching and Victor Snieckus*

Department of Chemistry, Queen's University, Kingston, Ontario, Canada K7L 3N6

E-mail: hurstt@queensu.ca

Isoprekinamycin (**1**, IPK) belongs to the rare benzo[*a*]fluorene class of natural products, and has been shown to possess potent antibacterial and antitumor properties.[1-3] IPK has previously been prepared in an 18-step linear sequence.[4] Herein we present our total synthesis of isoprekinamycin, which has been achieved in only 8 steps. The key step in this synthesis involves an unprecedented 'double DreM' cyclisation, allowing the construction of both the *beta*-naphthol and fluorenone ring systems in a single operation via the sequential functionalization of C(sp^3)–H (**5**→**4**) and C(sp^2)–H (**4**→**2**) bonds. The versatility of this route is further exemplified by the conversion of intermediate naphthol **2** into a second natural product, prefluostatin (**3**), by simple deprotection with BBr_3.



References

1. S. Omura, A. Nakagawa, H. Yamada, T. Hata and A. Furusaki *Chem. Pharm. Bull.* **1973**, *21*, 931-940.
2. S. J. Gould, N. Tamayo, C. R. Melville and Martha C. Cone *J. Am. Chem. Soc.* **1994**, *116*, 2207-2208.
3. P. J. Proteau, Y. Li, J. Chen, R. T. Williamson, S. J. Gould, R. S. Laufer and G. I. Dmitrienko *J. Am. Chem. Soc.* **2000**, *122,* 8325-8326.
4. W. Liu, M. Buck, N. Chen, M. Shang, N. J. Taylor, J. Asoud, X. Wu, B. B. Hasinoff and G. I. Dmitrienko *Org. Lett.* **2007**, *9*, 2915-2918.