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

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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 $C(sp^3)-H (5\rightarrow 4)$ and $C(sp^2)-H (4\rightarrow 2)$ 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 $\text{BBr}_3$.

References