2003
08 Advanced Synthesis
AGM Barrett

The course will outline and discuss several total syntheses to illustrate strategic planning. The use of reagents for asymmetric synthesis and organometallic transformations will be highlighted.

Summary of Topics

1. Gilvocarcin

Total synthesis of gilvocarcin (Suzuki). Stereoselective C-glycoside synthesis; benzyne-furan cycloadditions; intramolecular palladium catalysed coupling chemistry.

2. *N*-Acetylneuraminic Acid

Total synthesis of the sialic acids KDN and *N*-acetylneuraminic acid. Ring closing metathesis; desymmetrisation; carboxylic acid masking.

3. (-)-Histrionicotoxin

Total synthesis of (-) histrionicotoxin (Stork). Brown allylboration; epoxide spiroannulation and related reactions; (*Z*)-iodomethylenylation; Weinreb-Woodward-Vorbruggen amide synthesis; palladium catalysed coupling reactions.

4. Strychnine

"The heroic ring by ring forging of the original strychnine assembly, which required 27 steps, resolution of enantiomers, and the use of three degradation products of the natural alkaloid as relays, now stands as an instructive inspiration for the design of synthetic alternatives" (Comments by M.E. Kuehne, 1993, on the classic synthesis of strychnine by R.B. Woodward). True or false? An overview of a recent total synthesis (Rawal). Pyrroline-diene Diels Alder reactions; allylation; palladium catalysed cyclisations; isostrychnine synthesis and conversion into strychnine.

5. The Endiandric Acid Cascade

Total synthesis of endiandric acids A, B, C and D (Nicolaou). Acetylene coupling; semi-hydrogenation; cascade electrocyclisations and cycloadditions; biomimetic synthesis.

6. (-)-Roxaticin

Total synthesis of (-) roxaticin (Rychnovsky). Asymmetric hydrogenation; Brown allylboration; 1,3-dioxanes in stereocontrolled 1,3-diol assembly; polyene construction; macrocyclisation.

References

1. Matsumoto, T.; Hosoya, T.; Suzuki, K. *J. Am. Chem. Soc.* **1992**, *114*, 3568.

2. Voight, E.A.; Rein, C.; Burke, S.D. *J. Org. Chem.* **2002**, *67*, 8489.

3. Stork, G.; Zhao, K. *J. Am. Chem. Soc.* **1990**, *112*, 5875.

4. Rawal, V.H.; Iwasa, S. *J. Org. Chem.* **1994**, *59*, 2865 and references therein. Bodwell, G.J.; Li, J. *Angew. Chem. Int. Ed.* **2002**, *41*, 3261.

5. Nicolaou, K.C.; Petasis, N.A.; Zipkin, R.E.; Uenishi, J. *J. Am. Chem. Soc.* **1982**, *104*, 5555. Nicolaou, K.C.; Petasis, N.A.; Uenishi, J.; Zipkin, R.E. *J. Am. Chem. Soc.* **1982**, *104*, 5557. Nicolaou, K.C.; Zipkin, R.E.; Petasis, N.A. *J. Am. Chem. Soc.* **1982**, *104*, 5558. Nicolaou, K.C.; Petasis, N.A.; Zipkin, R.E. *J. Am. Chem. Soc.* **1982**, *104*, 5560.

6. Rychnovsky, S.D.; Hoye, R.D. *J. Am. Chem. Soc.* **1994**, *116*, 1753.