E. A. VOIGHT,* H. YIN, S. V. DOWNING, S. A. CALAD, H. MATSUHASHI, I. GIORDANO, A. J. HENNESSY, R. M. GOODMAN, J. L. WOOD (GLAXOSMITHKLINE, KING OF PRUSSIA, USA; GLAXOSMITHKLINE, STEVENAGE, UK)

Target-Directed Synthesis of Antibacterial Drug Candidate GSK966587

**Org. Lett.** 2010, 12, 3422-3425.

### Synthesis of GSK966587

**Significance:** The eight-step synthesis of antibacterial agent GSK966587 (25% overall yield) required no protecting groups and involved only three isolated intermediates (C, G and J). Key steps were a Mizoroki–Heck reaction, a Negishi coupling, a directed ortho-metatation, and a Sharpless–Katsuki asymmetric epoxidation.

**Comment:** The directed ortho-metatation of naphthyridine D was strongly base-dependent. Problems included dianion formation, competing metatation at C6 as well as nucleophilic substitution of the fluorine atom. However, when (i-Pr)2N–ZnEt2Li was used as base, there was no dianion formation and only 4% metatation at C6 was observed.

---

**Chemical Structures:**

- **A**
- **B**
- **C**
- **D**
- **E**
- **F**
- **G**
- **H**
- **I**
- **J**
- **K**
- **L**

**Key Reactions:**

1. **Mizoroki–Heck coupling**
2. **Negishi coupling**
3. **Directed ortho-metatation**
4. **Sharpless–Katsuki asymmetric epoxidation**

---

**SYNFACTS Contributors:** Philip Kocienski

Synfacts 2010, 11, 1211-1211  Published online: 21.10.2010  DOI: 10.1055/s-0030-1258708; Reg-No.: K07310SF