P. H. Carter* et al. (Bristol-Myers Squibb Company, Princeton, USA)
Use of a Conformational-Switching Mechanism to Modulate Exposed Polarity: Discovery of CCR2 Antagonist BMS-741672

**Synthesis of BMS-741672**

![Diagram of the synthesis process]

**Significance:** BMS-741672 is a chemotactic chemokine receptor 2 (CCR2) antagonist that is of interest for the treatment of inflammatory, cardiovascular, and metabolic diseases. The discovery synthesis depicted (>20 steps) is based on construction of the all-cis 1,2,4-triaminocyclohexane core using a Curtius rearrangement (A → B), an iodolactamization (D → E), and a Hoffman rearrangement (K → L).

**Comment:** The synthesis of lactam G was previously developed by Bristol-Myers Squibb (C. L. Campbell et al. J. Org. Chem. 2009, 74, 6368), and a shorter large-scale route to BMS-741672 was subsequently reported that delivered 50 kg of API for clinical evaluation (J. Deerberg et al. Org. Process Res. Dev. 2016, 20, 1949).