Significance: The synthesis of ent-ketorfanol depicted features a rhodium-catalyzed intramolecular C–H alkenylation/6π electrocyclization cascade (E → G → H) that provides the fused bicyclic 1,2-dihydropyridine H as a key intermediate. The torqueselectivity of the electrocyclization is a consequence of remote asymmetric induction provided by the isopropylidene-protected diol. Another noteworthy facet is the acid-catalyzed pinacol rearrangement/Friedel–Crafts alklylation (I → J).

Comment: Ketorfanol is a semisynthetic opioid that was previously derived from morphine or naloxone. It was never marketed. Because both enantiomers of diol B are readily available by Sharpless asymmetric dihydroxylation, both ketorfanol and ent-ketorfanol can be prepared in eleven steps and 9% overall yield without recourse to opiate modification. Note the use of the chlorine substituent in I to direct the regioselectivity of the Friedel–Crafts cyclization.