Supporting Information to Accompany:

**A Practical Synthesis Renin Inhibitor MK-
1597 (ACT-178882) *via* Catalytic
Enantioselective Hydrogenation and
Epimerization of Piperidine Intermediate**

Carmela Molinaro,^{†} Scott Shultz,[‡] Amélie Roy,[†] Stephen Lau,[†] Thao Trinh,[†] Rémy
Angelaud,[†] Paul D. O'Shea,[†] Stefan Abele,[§] Mark Cameron,[‡] Ed Corley,[‡] Jacques-
Alexis Funel,[§] Dietrich Steinhuebel,[‡] Mark Weisel[‡] and Shane Krska[‡]*

[†]*Department of Process Research, Merck, 16711 Autoroute Transcanadienne, Kirkland,
Québec, Canada, H9H 3L1.*

[‡]*Department of Process Research, Merck, P.O. Box 2000, Rahway, NJ 07065, USA.*

[§]*Department of Process Research Chemistry, Actelion Pharmaceuticals Ltd,
Gewerbestrasse 16, 4123 Allschwil, Switzerland.*

carmela_molinaro@merck.com

Table of contents

General information	S2
Ligand structures.....	S3
Copies of ^1H NMR and ^{13}C NMR	S4-S34

General Information. Reactions were carried out under an atmosphere of dry nitrogen. Reagents and solvents were used as received from commercial sources. ^1H NMR spectra were recorded on 400 MHz or 500 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (acetone- d_6 : δ 2.04, dmso- d_6 : δ 2.49, chloroform- d : δ 7.24). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), integration and coupling constants (Hz). ^{13}C NMR spectra were recorded on a 100 MHz or 125 MHz spectrometer with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference (acetone- d_6 : δ 206.0, dmso- d_6 : δ 39.5, chloroform- d : δ 77.0). ^{19}F NMR spectra were recorded on 375 MHz spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with α,α,α -trifluorotoluene added as an internal reference (δ – 67). A% indicates the area percent observed on a HPLC trace at 220 nm. Assay yields are reported relative to an HPLC standard.

Structures of ligands used in the asymmetric hydrogenation :**AND Enantiomer** **W009-1** **J004-1**

MK-1597-AcOH