

Rhodium-Catalyzed Reductive Mannich Coupling of Vinyl Ketones to N-Sulfonylimines Mediated by Hydrogen

Susan A. Garner and Michael J. Krische*

Department of Chemistry and Biochemistry, University of Texas at Austin, 1 University Station A5300, Austin, Texas 78712-1167

mkrische@mail.utexas.edu

Received April 18, 2007



Catalytic hydrogenation of methyl vinyl ketone (MVK) and ethyl vinyl ketone (EVK) in the presence of *N*-(*o*-nitrophenylsulfonyl)imines **8a**–**13a** at ambient pressure with tri-2furylphosphine-ligated rhodium catalysts enables formation of Mannich products **8b**–**13b** and **8c**–**13c** with moderate to good levels of *syn*-diastereoselectivity. As revealed by an assay of various *N*-protecting groups, excellent yields of reductive Mannich product also are obtained for *N*-arylimines **1a**–**4a**, although diminished levels of *syn*-diastereoselectivity are observed. Coupling of MVK to imine **8a** under a deuterium atmosphere provides *deuterio*-**8b**, which incorporates a single deuterium atom at the former enone β -position.

Following seminal studies by Revis (1987),^{2a} the reductive aldol reaction has become the topic of intensive investigation.¹ To date, catalysts for reductive aldol coupling based on rhodium,^{2,3} cobalt,⁴ iridium,⁵ ruthenium,⁶ palladium,⁷ copper,^{8,9} nickel,¹⁰ and indium^{11,12} have been devised. Related reductive Mannich couplings have received far less attention.¹³ The first reductive Mannich coupling was reported by Isayama (1992) and involves the cobalt-catalyzed coupling of ethyl crotonate to *N*-methylbenzaldimine mediated by phenylsilane.^{13a} Upon heating, this Mannich product is converted to the corresponding β -lactam. In 2002, Morken reported a related iridium-catalyzed reductive Mannich coupling of trifluorophenyl acrylate to PMP- protected aldimines mediated by silane that provides direct access to the β -lactam.^{13b} In the same year, Matsuda described a rhodium-catalyzed reductive Mannich coupling of acrylates to *N*-tosylaldimines.^{13c} The cobalt- and iridium-catalyzed Mannich couplings en route to β -lactams exhibit high levels of *syn* and *anti*-diastereoselectivity, respectively. Finally, an organo-catalytic reductive Mannich coupling employing a proline derived secondary amine catalyst mediated by Hantzsch ester recently was reported by Cordova.^{13d}

Using *elemental hydrogen* as the terminal reductant, we have developed a diverse set of catalytic reductive C–C couplings,^{1g} including hydrogen-mediated aldol couplings of vinyl ketones.³ For such aldol couplings, it was found that high levels of *syn*-diastereoselectivity could be achieved through the use of cationic rhodium catalysts ligated by tri-2-furylphosphine.^{3e-g} These studies suggest the feasibility of related reductive Mannich couplings mediated by hydrogen. Here, we report that catalytic hydrogenation of vinyl ketones in the presence of *N*-arylaldimines **1a**–**4a** delivers the products of reductive Mannich coupling in excellent yield. Additionally, we find that *N*-sulfonylimines **7a**–**13a** engage reductive Mannich coupling with high levels of *syn*-diastereoselectivity in moderate to good yield.

Our initial studies focused on the hydrogenative coupling of methyl vinyl ketone (MVK) to *N*-arylaldimines 1a-6a derived from *p*-nitrobenzaldehyde (Table 1). It was found that coupling of MVK to imine 1a derived from aniline gave the desired reductive Mannich product 1b in excellent yield, though poor

(3) For rhodium-catalyzed reductive aldol reaction mediated by hydrogen, see: (a) Jang, H. Y.; Huddleston, R. R.; Krische, M. J. J. Am. Chem. Soc. **2002**, 124, 15156. (b) Huddleston, R. R.; Krische, M. J. Org. Lett. **2003**, 5, 1143. (c) Koech, P. K.; Krische, M. J. Org. Lett. **2004**, 6, 691. (d) Marriner, G. A.; Garner, S. A.; Jang, H. Y.; Krische, M. J. J. Org. Chem. **2004**, 69, 1380. (e) Jung, C. K.; Garner, S. A.; Krische, M. J. Org. Lett. **2006**, 8, 5519. (f) Han, S. B.; Krische, M. J. Org. Lett. **2006**, 8, 5657. (g) Jung, C. K.; Krische, M. J. Org. Lett. **2006**, 128, 17051.

(4) For cobalt-catalyzed reductive aldol reaction, see: (a) Isayama. S.;
Mukaiyama, T. *Chem. Lett.* **1989**, 2005. (b) Baik, T. G.; Luis, A. L.; Wang,
L. C.; Krische, M. J. *J. Am. Chem. Soc.* **2001**, *123*, 5112. (c) Wang, L. C.;
Jang, H.-Y.; Roh, Y.; Lynch, V.; Schultz, A. J.; Wang, X.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 9448. (d) Lam, H. W.; Joensuu, P. M.; Murray,
G. J.; Fordyce, E. A. F.; Prieto, O.; Luebbers, T. *Org. Lett.* **2006**, *8*, 3729.
(5) For iridium-catalyzed reductive aldol reaction, see: (a) Zhao. C. X.;

Duffey, M. O.; Taylor, S. J.; Morken, J. P. *Org. Lett.* **2001**, *3*, 1829. (6) For ruthenium-catalyzed reductive aldol reaction, see: Doi, T.;

(i) For reliabilities and reductive and reduction, see: Doi, 17, Fukuyama, T.; Minamino, S.; Ryu, I. Synlett **2006**, *18*, 3013.

(7) For palladium-catalyzed reductive aldol reaction, see: (b) Kiyooka, S. I.; Shimizu, A.; Torii, S. *Tetrahedron Lett.* **1998**, *39*, 5237.

(8) For copper-promoted reductive aldol reaction, see: (a) Chiu, P.; Chen, B.; Cheng, K. F. *Tetrahedron Lett.* **1998**, *39*, 9229. (b) Chiu, P. *Synthesis* **2004**, *13*, 2210. (c) For copper-promoted reductive intramolecular Henry reaction, see: Chung, W. K.; Chiu, P. *Synlett* **2005**, *1*, 55. (d) For copper-promoted and -catalyzed reductive cyclizations of α,β -acetylenic ketones tethered to ketones, see: Chiu, P.; Leung, S. K. *Chem. Commun.* **2004**, 2308.

⁽¹⁾ For reviews encompassing the topic of reductive aldol coupling, see: (a) Motherwell, W. B. Pure Appl. Chem. 2002, 74, 135. (b) Huddleston, R. R.; Krische, M. J. Synlett 2003, 12. (c) Jang, H.-Y.; Huddleston, R. R.; Krische, M. J. Chemtracts 2003, 16, 554. (d) Jang, H.-Y.; Krische, M. J. Eur. J. Org. Chem. 2004, 19, 3953. (e) Jang, H.-Y.; Krische, M. J. Acc. Chem. Res. 2004, 37, 653. (f) Chiu, P. Synthesis 2004, 2210. (g) Ngai, M.-Y.; Krische, M. J. Metal Catalyzed Reductive Aldol Coupling. In Modern Reductions; Andersson, P., Munslow, I., Eds.; Wiley-VCH: Weinheim, Germany, 2007, in press.

⁽²⁾ For rhodium-catalyzed reductive aldol reaction mediated by silane, see: (a) Revis, A.; Hilty, T. K. *Tetrahedron Lett.* **1987**, *28*, 4809. (b) Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990**, *31*, 5331. (c) Taylor, S. J.; Morken, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 12202. (d) Zhao, C.-X.; Bass, J.; Morken, J. P. *Org. Lett.* **2001**, *3*, 2839. (e) Taylor, S. J.; Duffey, M. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (f) Fuller, N. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (f) Fuller, N. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (f) Fuller, N. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (f) Fuller, N. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528. (f) Fuller, N. O.; Morken, J. P. *Synlett* **2005**, 1459. (g) Emiabata-Smith, D.; McKillop, A.; Mills, C.; Motherwell, W. B.; Whitehead, A. J. *Synlett* **2001**, 1302. (h) Freiría, M.; Whitehead, A. J.; Tocher, D. A.; Motherwell, W. B. *Tetrahedron.* **2004**, *60*, 2673. (i) Nishiyama, H.; Shiomi, T.; Tsuchiya, Y.; Matsuda, I. *J. Am. Chem. Soc.* **2005**, *127*, 6972. (j) Ito, J. I.; Shiomi, T.; Nishiyama, H. *Adv. Synth. Catal.* **2006**, *348*, 1235. (k) Shiomi, T.; Ito, J.-I.; Yamamoto, Y.; Nishiyama, H. *Eur. J. Org. Chem.* **2006**, 5594. (l) Willis, M. C.; Woodward, R. L. *J. Am. Chem. Soc.* **2005**, *127*, 18012.

TABLE 1. Hydrogen-Mediated Reductive Mannich Coupling ofMVK to N-Arylaldimines $1a-6a^a$



3	3a	NO_2	Н	99	1.2:1
4	4 a	Н	MeO	88	1:1
5	5a	Н	<i>i</i> -Pr	38	1.6:1
6	6a	Me	Me	11	2:1
^{<i>a</i>} Cited runs. See th	yields are of an supporting	isolated mate	erial and repr	esent the ave experimental	erage of two procedures

^{*a*} Cited yields are of isolated material and represent the average of two runs. See the Supporting Information for detailed experimental procedures. ^{*b*} Coupling to aldimine **2a** was conducted with 3 equiv of MVK in the absence of Li_2CO_3 .

levels of *syn*-diastereoselection were observed (Table 1, entry 1). In an effort to improve diastereoselectivity, variation of the electronic features of the N-aryl residue was explored. However, while aldimines 2a and 3a, derived from p-anisidine and *p*-nitroaniline, respectively, provide the reductive Mannich products 2b and 3b in excellent yield, the observed levels of syn-diastereoselection remained unsatisfactory (Table 1, entries 2 and 3). Finally, it was reasoned that aldimines incorporating sterically more demanding N-aryl residues might couple with greater levels of diastereoselection. Accordingly, aldimines 4a, 5a, and 6a were examined, which incorporate *o*-methoxyphenyl, o-isopropylphenyl, and o,o-dimethylphenyl N-aryl residues. Unfortunately, heightened levels of diastereoselection were not observed in couplings of MVK to 4a-6a, and the increased steric demand of substrates 5a and 6a adversely affected conversion and, hence, isolated chemical yield (Table 1, entries 4 - 6).

The relatively poor levels of diastereoselection in additions to the *N*-arylaldimines is potentially due to facile geometrical isomerism in the presence of the metal catalyst.¹⁴ Accordingly,

TABLE 2. Hydrogen-Mediated Reductive Mannich Coupling ofMVK to N-Arylsulfonylaldimines 7a and $8a^a$



^{*a*} Cited yields are of isolated material and represent the average of two runs. See the Supporting Information for detailed experimental procedures.

N-arylsulfonylimines, which are configurationally more stable, were examined as substrates. Gratifyingly, exposure of N-(ptoluenesulfonyl)imine 7a to conditions for hydrogenative coupling using MVK as the nucleophilic partner provides the desired Mannich adduct 7b in 70% yield with a 20:1 diastereomeric ratio favoring formation of the syn-diastereomer (Table 2, entry 1). The stereochemistry of 7b was corroborated by single-crystal X-ray diffraction analysis of a diastereomerically pure sample. Given the relatively facile cleavage of N-(nitrobenzenesulfonamides),¹⁵ the hydrogenative coupling of MVK to the N-(nitrobenzenesulfonyl)imine 8a was explored. The desired Mannich adduct 8b was produced in 78% yield with an 8:1 diastereomeric ratio, again favoring formation of the syn-diastereomer (Table 2, entry 2). Finally, using Rh-(COD)₂BF₄ as the catalyst precursor, a 95% yield of the desired Mannich adduct 8b was obtained with a diastereomeric ratio of 11:1 (Table 2, entry 3).

These optimized conditions were assayed against a diverse set of *N*-(nitrobenzenesulfonyl)imines. It was found that the hydrogenative Mannich coupling proceeds most efficiently for highly electrophilic *N*-(*o*-nitrobenzenesulfonyl)imines, even then requiring catalyst loadings of 10 mol % in most cases to enforce good conversion. Due to extended reaction times (24 h), Na₂-SO₄ was required to suppress imine hydrolysis and the formation of hydroxy-bridged dimers of rhodium. Ultimately, using commercially available MVK and EVK as pronucleophiles, *N*-(nitrobenzenesulfonyl)imines **8a**-**13a** were converted to the Mannich adducts **8b**-**13b** and **8c**-**13c**, respectively (Table 3).

To gain further insight into the reaction mechanism, the reductive coupling of MVK and *p*-nitrobenzaldimine **8a** was performed with elemental deuterium. The Mannich coupling product *deuterio*-**8b** incorporates a single deuterium atom at the former enone β -position. Deuterium incorporation at the α -carbon of the product is not observed, thus excluding Morita–Baylis–Hillman pathways en route to product. The strict incorporation of a single deuterium atom is consistent with a mechanism involving irreversible enolization via enone hydrometallation or enone-imine oxidative coupling to furnish an azarhodacyclopentane, which then hydrogenolytically cleaves to deliver product (Scheme 1).

⁽⁹⁾ For copper-catalyzed reductive aldol reaction, see: (a) Ooi, T.; Doda,
K.; Sakai, D.; Maruoka, K. *Tetrahedron Lett.* **1999**, 40, 2133. (b) Lam, H.
W.; Joensuu, P. M. A. Org. Lett. **2005**, 7, 4225. (c) Lam, H. W.; Murray,
G. J.; Firth, J. D. Org. Lett. **2005**, 7, 5743. (d) Deschamp, J.; Chuzel, O.;
Hannedouche, J.; Riant, O. Angew. Chem., Int. Ed. **2006**, 45, 1292. (e)
Chuzel, O.; Deschamp, J.; Chauster, C.; Riant, O. Org. Lett. **2006**, 8, 5943.
(f) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2006**, 47, 1403. (g) Zhao, D.; Oisaki, K.; Kanai, M.; Shibasaki, M. J. Am. Chem.
Soc. **2006**, *128*, 14440. (h) Welle, A.; Diez-Gonzalez, S.; Tinant, B.; Nolan,
S. P.; Riant, O. Org. Lett. **2006**, 8, 6059.

⁽¹⁰⁾ For nickel-catalyzed reductive aldol reaction, see: Chrovian, C. C.; Montgomery, J. *Org. Lett.* **2007**, *9*, 537.

⁽¹¹⁾ For a reductive aldol coupling employing stoichiometric quantities of indium reagent, see: Inoue, K.; Ishida, T.; Shibata, I.; Baba, A. *Adv. Synth. Catal.* **2002**, *344*, 283.

⁽¹²⁾ For indium-catalyzed reductive aldol reaction, see: (a) Shibata, I.; Kato, H.; Ishida, T.; Yasuda, M.; Baba, A. *Angew. Chem., Int. Ed.* **2004**, *43*, 711. (b) Miura, K.; Yamada, Y.; Tomita, M.; Hosomi, A. *Synlett* **2004**, 1985.

^{(13) (}a) Isayama, S. Yuki Gosei Kagaku Kyokaishi **1992**, 50, 190. (b) Townes, J.; Evans, M.; Queffelec, J.; Taylor, S. J.; Morken, J. P. Org. Lett. **2002**, 4, 2537. (c) Moraoka, T.; Kamiya, S.; Matsuda, I.; Itoh, K. Chem. Commun. **2002**, 1284. (d) Zhao, G.-L.; Cordova, A. Tetrahedron Lett. **2006**, 47, 7417.

^{(14) (}a) Eaton, D. R.; Tong, J. P. K. *Inorg. Chem.* **1980**, *19*, 740. (b) Lehn, J.-M. *Chem. Eur. J.* **2006**, *12*, 5910 and references cited therein.

⁽¹⁵⁾ For a review on the use of the nitrobenzenesulfonamides in organic synthesis, see: Kan, T.; Fukuyama, T. *Chem. Commun.* **2004**, 353.

JOCNote

TABLE 3. Diastereoselective Hydrogen-Mediated Reductive Mannich Coupling of MVK and EVK to N-(o-Nitrophenyl)sulfonylaldimines $8a-13a^{a-h}$



^{*a*} Representative procedure: To a 13 mm × 100 mm test tube charged with Na₂SO₄ (0.78 mmol, 200 mol %), Fur₃P (0.094 mmol, 24 mol %), Rh(COD)₂OTf (0.039 mmol, 10 mol %), and imine (0.39 mmol, 100 mol %) was added dichloromethane (0.2 M). The test tube was sealed, and the reaction mixture was sparged with Ar(g) followed by H₂(g) for 20 s each. The reaction was placed under 1 atm of hydrogen using a balloon, and MVK (1.17 mmol, 300 mol %) was added to the reaction mixture and it was stirred for 24 h at 35 °C. The reaction mixture was evaporated onto silica, and the product was isolated by flash chromatography (SiO₂: EtOAc/hexane). ^{*b*} For **8b** the reaction was conducted with 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P in the absence of Na₂SO₄. ^{*c*} For **9b**, **10b**, and **11b** the reaction was conducted with 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P. ^{*f*} For **9c**, **10c**, and **11c** the reaction was conducted with 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P. ^{*f*} For **9c**, **10c**, and **11c** the reaction was conducted the 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P. ^{*f*} For **9c**, **10c**, and **11c** the reaction was conducted with 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P.

SCHEME 1. Reductive Mannich Coupling under a Deuterium Atmosphere



In summary, catalytic hydrogenation of methyl vinyl ketone (MVK) and ethyl vinyl ketone (EVK) in the presence of N-(nitrophenylsulfonyl)imines **8a**-14a at ambient pressure with tri-2-furylphosphine ligated rhodium catalysts enables formation of Mannich products **8b**-14b and **8c**-14c, respectively, with moderate to good levels of *syn*-diastereoselectivity. Future studies will focus on the development of improved second generation catalysts for hydrogen-mediated reductive Mannich coupling, enantioselective variants of the transformations reported herein, and the discovery of related C-C bond-forming hydrogenations.

Experimental Section

General Procedure for the Synthesis of *N***-Nosylaldimines.** *N*-Nosylaldimines were prepared according to the procedure established by Love.¹⁶ To a round-bottomed flask charged with aldehyde (100 mol %) and 2-nitrobenzenesulfonamide (100 mol %) was added tetraethylorthosilicate (113 mol %). The round-bottomed flask was equipped with a still head and heated to 160 °C under an atmosphere of argon. The reaction was allowed to stir for \sim 6 h during which time ethanol was collected in a receiving flask. The reaction was cooled to room temperature and then ethyl ether was added to the reaction mixture. The reaction mixture was stirred for several hours and was then filtered with the aid of cold ethyl ether. The crude imine was then crystallized from an appropriate solvent.

8a: ¹H NMR (400 MHz, CDCl₃) δ 7.84–7.89 (m, 3H), 8.20 (d, J = 9.9 Hz, 2H), 8.37 (d, J = 8.9 Hz, 2H), 8.43 (m, 1H), 9.18 (s, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 124.3, 125.0, 131.0, 132.3, 132.9, 135.2, 137.0, 148.6, 151.5, 171.2; HRMS calcd [M + 1] for C₁₃H₁₀N₃O₆S 336.0290, found 336.0296; FTIR (film) 1594, 1347, 1165, 1125, 1056, 839, 798, 748, 675, 590 cm⁻¹; mp 186–187 °C.

General Procedure for Intermolecular Hydrogen-Mediated Reductive Coupling of Methyl Vinyl Ketone and N-Nosylaldimines. To a 13 mm \times 100 mm test tube charged with Na₂SO₄ (0.78 mmol, 200 mol %), Fur₃P (0.094 mmol, 24 mol %), Rh-(COD)₂OTf (0.039 mmol, 10 mol %), and imine (0.39 mmol, 100 mol %) was added dichloromethane (0.2 M). The test tube was sealed and the reaction system was purged with argon and then with hydrogen for 20 s each. The reaction was placed under 1 atm of hydrogen using a balloon, and MVK (1.17 mmol, 300 mol %) was added to the reaction mixture. The reaction mixture was allowed to stir for 24 h, at which point the reaction mixture was

⁽¹⁶⁾ Love, B. E.; Raje, P. S.; Williams, T. C. Synlett. 1994, 493.

evaporated onto silica gel and the products were separated by column chromatography (SiO₂: EtOAc/hexane). For entry **8b** the reaction was conducted with 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P without Na₂SO₄. For entries **9b**, **10b**, and **11b** the reaction was conducted with 500 mol % MVK at 0.4 M DCM.

8b: ¹H NMR (400 MHz, d_6 -acetone) δ 1.23 (d, J = 7.0 Hz, 3H), 1.93 (s, 3H), 3.29–3.44 (m, 1H), 4.86 (d, J = 9.2 Hz, 1H), 7.43 (br s, 1H), 7.56 (d, J = 8.8 Hz, 2H), 7.63 (t, J = 7.9 Hz, 1H), 7.72 (t, J = 6.9 Hz, 1H), 7.77 (m, 1H), 7.88 (dd, J = 6.5, 1.4 Hz, 1H), 7.96 (d, J = 8.8 Hz, 2H); ¹³C NMR (75 MHz, d_6 -acetone) δ 14.5, 52.6, 60.5, 123.9, 125.5, 129.7,131.3, 133.3, 134.3, 134.7, 147.9, 209.3; HRMS calcd [M + 1] for C₁₇H₁₈N₃O₇S 408.0865, found 408.0866; FTIR (film) 3324, 3099, 2938, 1712, 1607, 1540, 1441, 1349, 1268, 1167, 1124, 1060, 854, 741, 593 cm⁻¹; mp 123–125 °C.

General Procedure for Intermolecular Hydrogen-Mediated Reductive Coupling of Ethyl Vinyl Ketone and N-Nosylaldimines. To a 13 mm \times 100 mm test tube charged with Na₂SO₄ (0.78 mmol, 200 mol %), Fur₃P (0.094 mmol, 24 mol %), Rh-(COD)₂OTf (0.039 mmol, 10 mol %), and imine (0.39 mmol, 100 mol %) was added dichloromethane (0.2 M). The test tube was sealed and the reaction system was purged with argon and then with hydrogen for 20 s each. The reaction was placed under 1 atm of hydrogen using a balloon, and EVK (1.95 mmol, 500 mol %) was added to the reaction mixture. The reaction mixture was allowed to stir for 48 h, at which point the reaction mixture was evaporated onto silica gel and the products were separated by column chromatography (SiO₂: EtOAc/hexane). For entry **8c** the reaction was conducted at 5 mol % loadings of Rh(COD)₂OTf and 12 mol % loadings of Fur₃P. For entries **9c**, **10c**, and **11c** the reaction was conducted with 500 mol % MVK at 0.4 M DCM.

8c: ¹H NMR (400 MHz, *d*₆-acetone) δ 0.70 (t, *J* = 7.1 Hz, 3H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.96–2.09 (m, 1H), 2.42–2.52 (m, 1H), 3.36–3.44 (m, 1H), 4.84 (d, *J* = 9.8 Hz, 1H), 7.46 (br s, 1H), 7.55 (d, *J* = 8.8 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.78 (dd, dd, *J* = 6.7, 1.4 Hz, 1H), 7.90 (dd, *J* = 6.5, 1.4 Hz, 1H), 7.98 (d, *J* = 8.8 Hz, 2H); ¹³C NMR (75 MHz, *d*₆-acetone) δ 6.5, 14.0, 35.4, 51.0, 60.0, 123.0, 124.6, 128.7, 130.5, 132.4, 133.4, 133.8, 147.0, 147.1, 147.3, 211.1; HRMS calcd [M + 1] for C₁₈H₂₀N₃O₇S 422.1022, found 422.1026; FTIR (film) 3324, 3099, 2978, 1711, 1606, 1540, 1500, 1443, 1349, 1169, 854, 593 cm⁻¹; mp 141–142 °C.

Acknowledgment is made to the Robert A. Welch Foundation, Johnson & Johnson, and the NIH-NIGMS (RO1-GM69445) for partial support of this research. Dr. Oliver Briel of Umicore of is thanked the generous donation of Rh- $(COD)_2BF_4$.

Supporting Information Available: Experimental details and spectral data for all new compounds (¹H NMR, ¹³C NMR, IR, HRMS) and single-crystal X-ray diffraction data corresponding to compound **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO070779W