

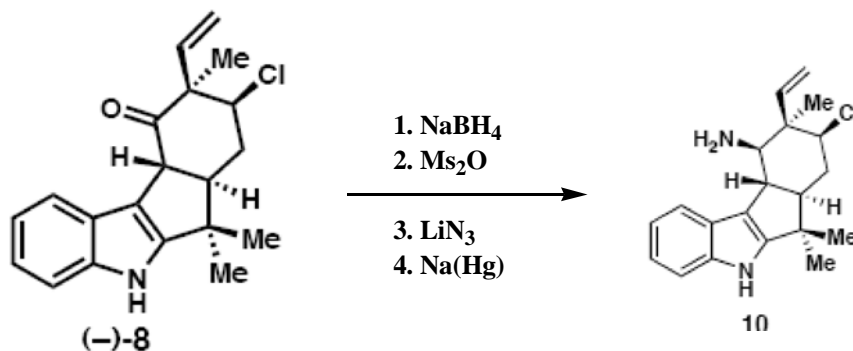
University of Massachusetts Boston
Department of Chemistry
Chemistry Doctoral Program
Green Chemistry Track
Written Qualifying Exam
June 18, 2007

Organic Chemistry II

Questions are based on the following article:

“Enantioselective Total Syntheses of Welwitindolinone A and Fischerindoles I and G”
Phil S. Baran and Jeremy M. Richter. *Journal of the American Chemical Society*, **2005**,
127(44), 15394-15396.

- (1) Propose a *reasonable* pathway (intermediate products) and classify the individual reactions (e.g. oxidation, reduction, A_E, S_N, A_{RSE}, A_N etc.) for the following reaction sequence. **(4 points)**



- (1) MeOH, NaBH₄ (1.5 equiv), 0 °C, 5 min;
 (2) then Ms₂O (2.0 equiv), py, 23 °C, 30 min, 69% overall;
 (3) DMF, LiN₃ (3.0 equiv), 120 °C, 48 h;
 (4) then EtOH, Na(Hg) (10 equiv), reflux, 4 h, 38% overall
- (2) Based on the available spectral data identify the compound from Scheme 1 (by its number) and assign the spectral data to the appropriate groups (NMR data to H and C atoms, major IR bands to functional groups). **(6 points)**

IR (film) ν_{max} : 2977, 1716, 1647, 1450, 1374, 1294, 1226, 1113, 987, 910, 860, 745 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ : 6.28 (dd, J = 17.6, 10.8 Hz, 1 H), 5.27 (d, J = 10.8 Hz, 1 H), 5.03 (d, J = 17.6 Hz, 1 H), 4.78 (s, 1 H), 4.72 (s, 1 H), 3.91 (dd, J = 12.4, 4.0 Hz, 1 H), 2.59 (t, J = 13.6 Hz, 1 H), 2.24 – 2.34 (m, 3 H), 2.10 – 2.16 (m, 1 H), 1.70 (s, 3 H), 1.32 (s, 3 H);

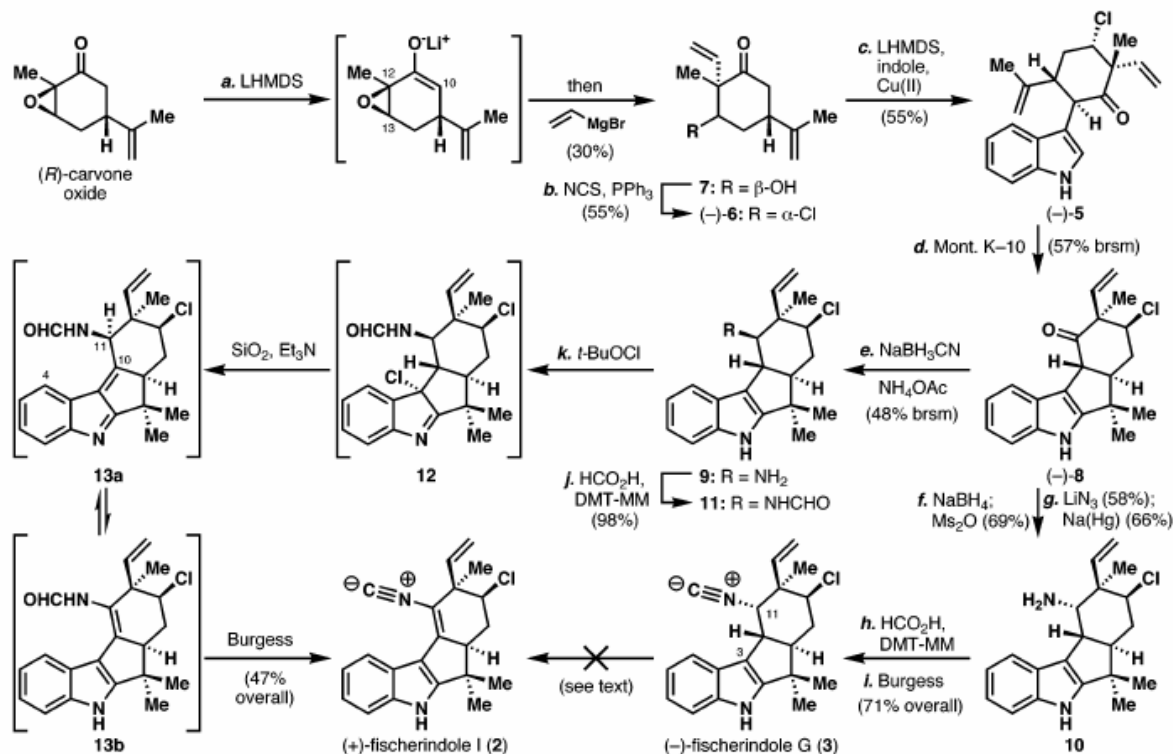
¹³C NMR (100 MHz, CDCl₃) δ : 207.3, 145.5, 136.6, 118.4, 110.8, 66.5, 57.9, 43.0, 42.0, 37.7, 21.1, 20.3;

LRMS (GC-MS) [M + H⁺] 213, found 213.

Green Chemistry: (2 points)

Select the steps from Scheme 1 that you find the most environmentally benign and the one that you rate the most harmful. Explain the reasons for your selections in both cases.

Scheme 1. Short, Enantioselective Total Syntheses of (+)-2 and (–)-3^a



^a Reagents and conditions: (a) LHMDS (1.2 equiv), THF, -78°C , 30 min; -15°C , CH_2CHMgBr (2.0 equiv), 15 min, 30%; (b) THF, PPh_3 (1.0 equiv), NCS (1.0 equiv), 18 h, 55%; (c) indole (2.0 equiv), LHMDS (3.1 equiv), THF, -78°C , 30 min, then $\text{Cu(II)2-ethylhexanoate}$ (1.5 equiv), -78 to 23°C , 15 min, 55%; (d) DCE, Montmorillonite K-10 clay (10 equiv), microwave irradiation, 120°C , 6 min, filter, then repeat, 40% + 30% recovered 5; (e) THF, MeOH , NaCNBH_3 (10 equiv), NH_4OAc (40 equiv), 7 days, 26% 9 + 46% 8; (f) MeOH , NaBH_4 (1.5 equiv), 0°C , 5 min; then Ms_2O (2.0 equiv), py, 23°C , 30 min, 69% overall; (g) DMF, LiN_3 (3.0 equiv), 120°C , 48 h; then EtOH , Na(Hg) (10 equiv), reflux, 4 h, 38% overall; (h) HCO_2H (1.3 equiv), CDMT (1.4 equiv), DMAP (cat.), NMM (1.4 equiv), CH_2Cl_2 , 23°C , 30 min, 87%; (i) PhH , Burgess reagent (2.0 equiv), 23°C , 30 min, 82%; (j) same as (h), 98%; (k) THF, TEA (1.0 equiv), $t\text{-BuOCl}$ (1.5 equiv), 0°C , 10 min, then $\text{SiO}_2/\text{Et}_3\text{N}$ (PTLC), then PhH , Burgess reagent (2.0 equiv), 23°C , 30 min, 47% overall; (l) CDMT = 2-Chloro-4,6-dimethoxy-1,3,5-triazine; DCE = 1,2-dichloroethane; DMF = N,N -dimethylformamide; DMAP = 4-(dimethylamino)pyridine; IBX = o -iodoxybenzoic acid; LHMDS = lithium hexamethyldisilazide; Ms = methanesulfonyl; NCS = N -chlorosuccinimide; NMM = N -methylmorpholine.