Organic LETTERS

Letter

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Structural Revision of (+)-Uprolide F Diacetate Confirmed by Asymmetric Total Synthesis

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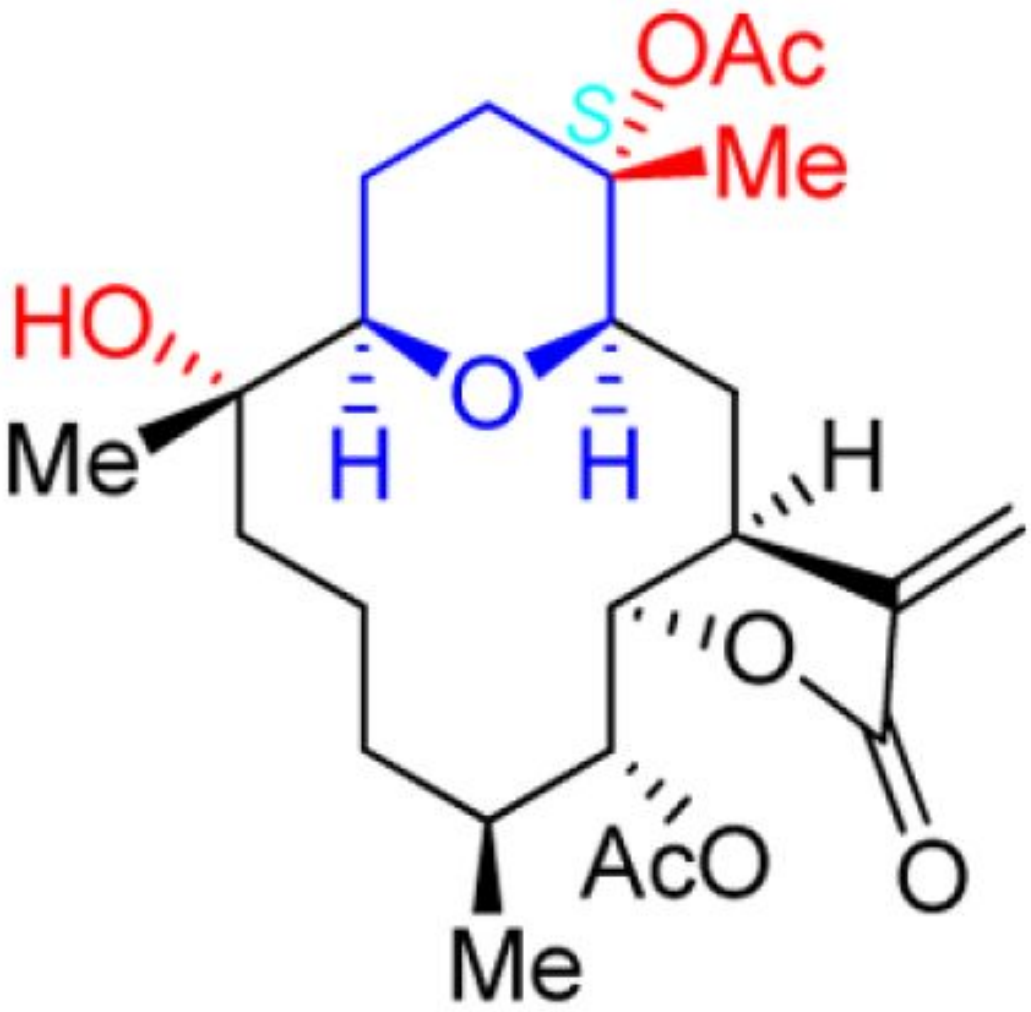
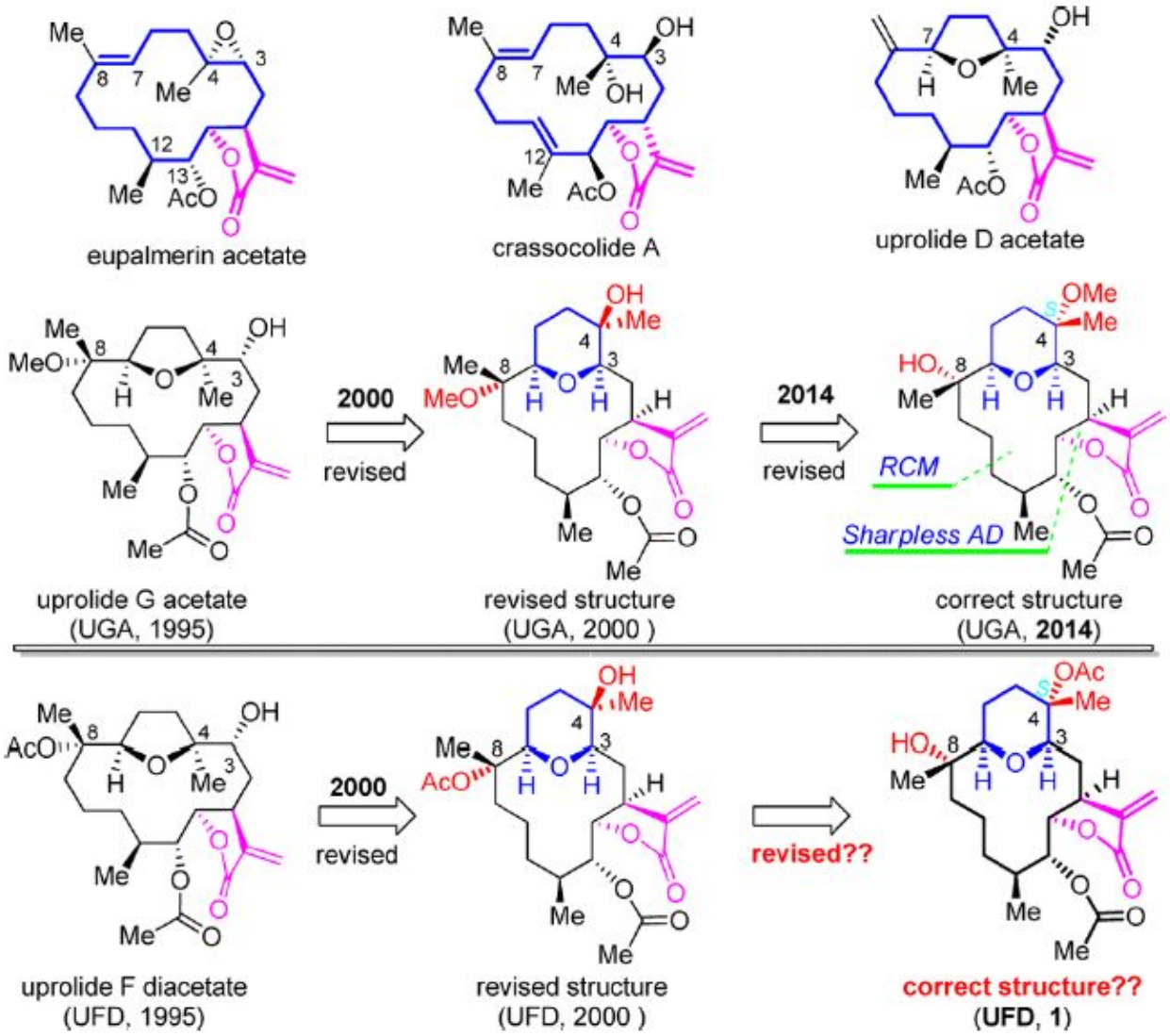
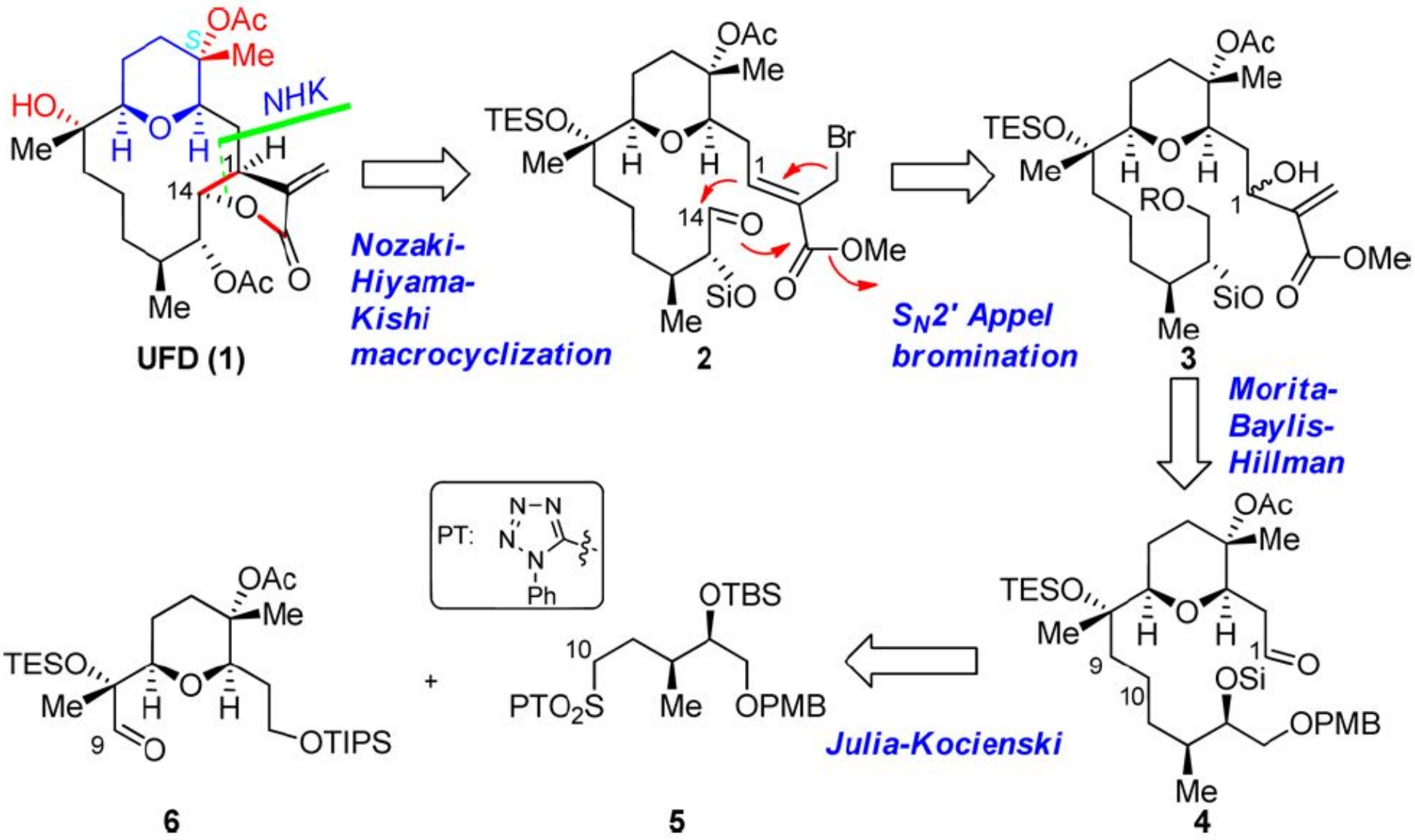
(+)-Uprolide F Diacetate (UFD)



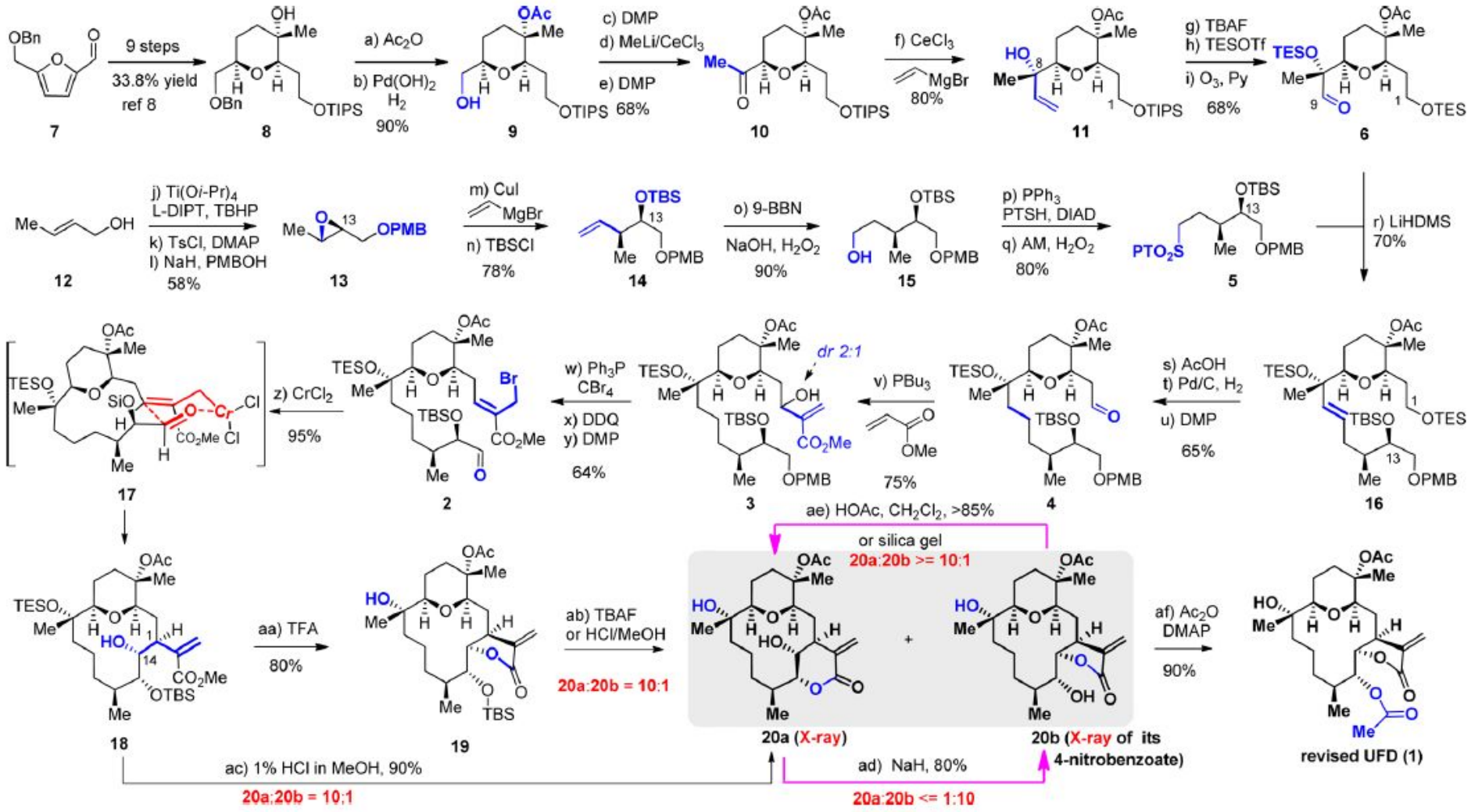
Представители α-метилен-γ-лактонсодержащих цембренов



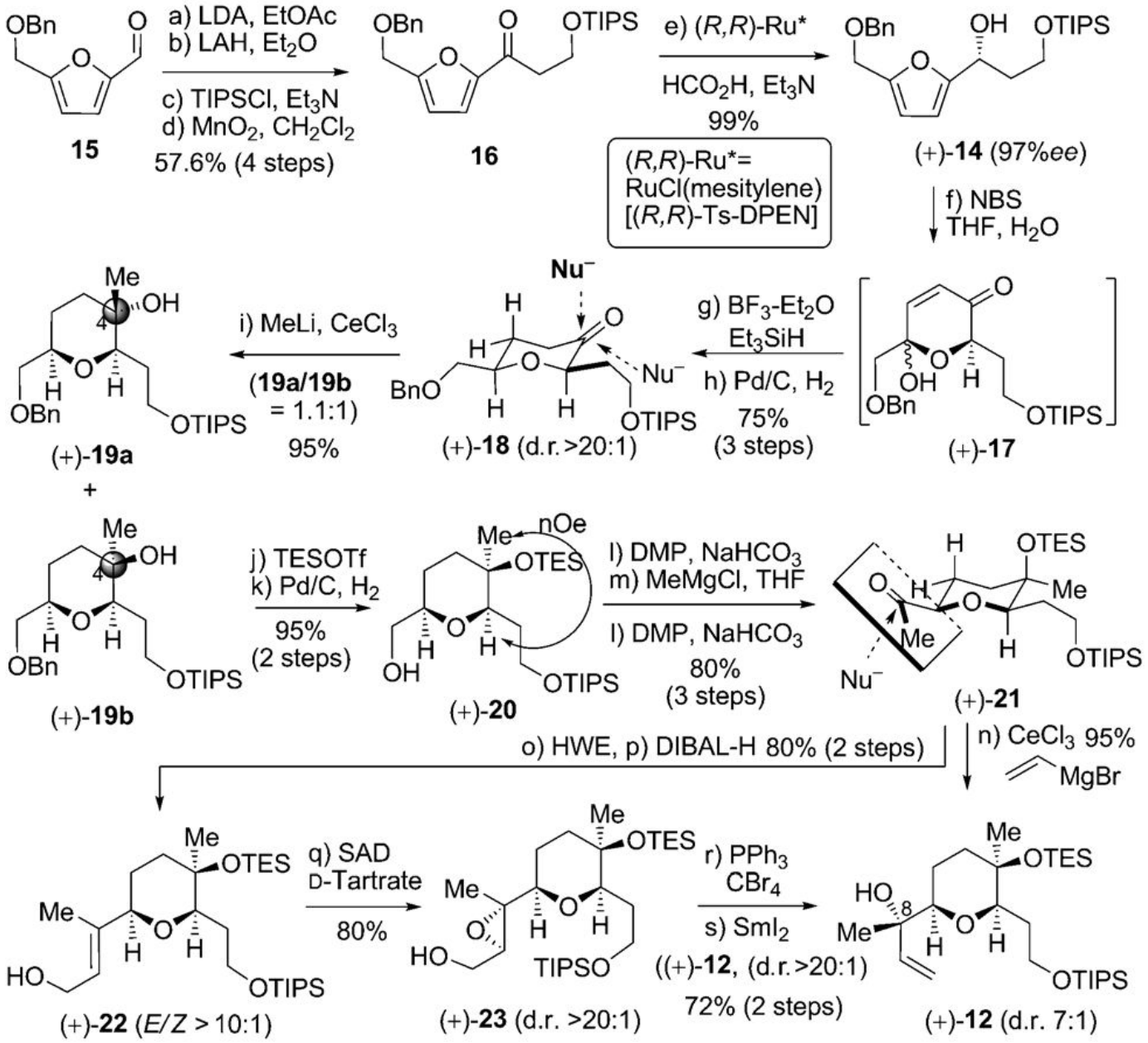
Ретросинтетический анализ



Полный синтез



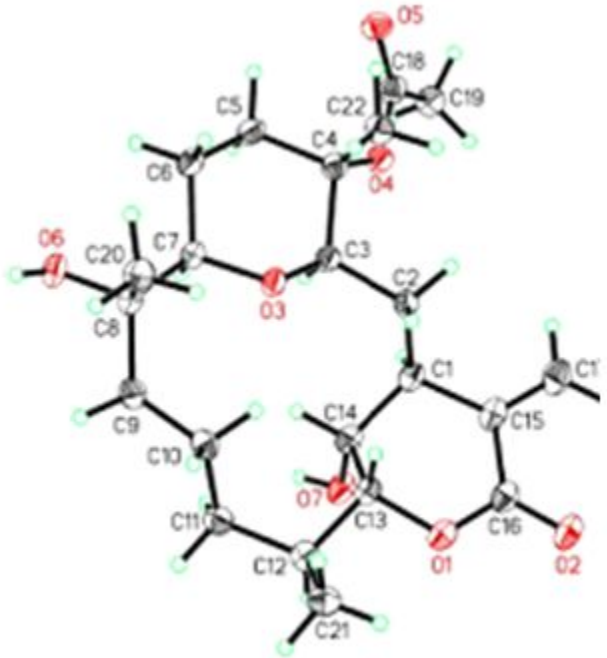
Синтез соединения 8 (со слайда №5)



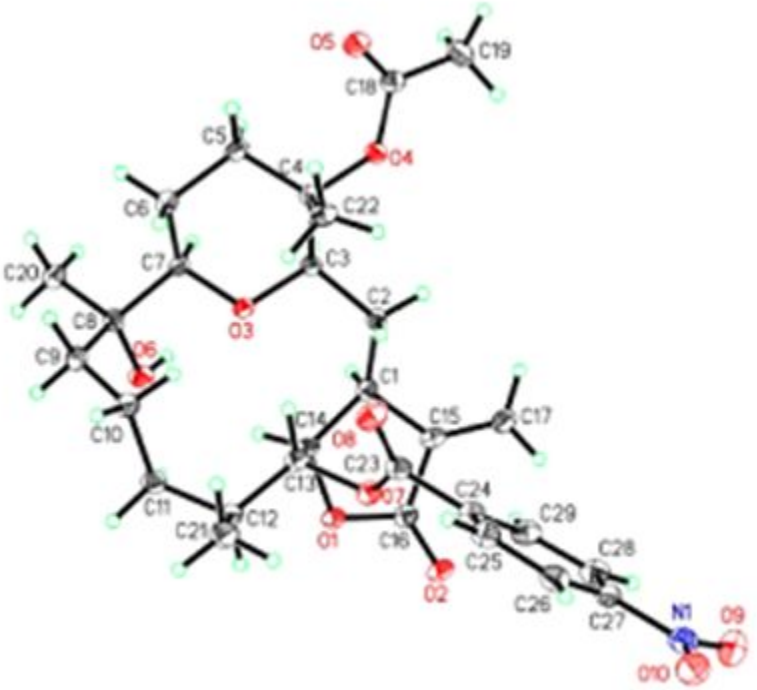
Условия

(a) Ac2O (1.5 equiv), iPr2NEt (2.0 equiv), DMAP (1.0 equiv), CH2Cl2, rt, 4 h, 90%; (b) 10 wt % Pd(OH)2/C (10 mol %), H2 (1.0 atm), EtOAc/MeOH = 1/4, rt, 2 h, 100%; (c) DMP (1.2 equiv), NaHCO3 (5.0 equiv), CH2Cl2, rt, 1 h, 95%; (d) CeCl3 (3.0 equiv), MeLi (2.0 equiv), THF, −78 °C, 1 h, 80%; (e) DMP (1.2 equiv), NaHCO3 (5.0 equiv), CH2Cl2, rt, overnight, 90%; (f) CeCl3 (3.0 equiv), vinylMgBr (2.0 equiv), THF, −78 °C, 1 h, 80%; (g) Bu4NF (1.5 equiv), THF, rt, 3 h, 90%; (h) TESOTf (2.4 equiv), 2,6-lutidine (6.0 equiv), CH2Cl2, −78 °C, 1 h, 95%; (i) O3, pyridine (4.0 equiv), −78 °C, 30 min, 80%; (j) Ti(OiPr)4 (5 mol %), (+)-diisopropyl L-tartrate (6 mol %), tBuOOH (2.0 equiv), CH2Cl2, −20 °C, 2 h; (k) TsCl (1.2 equiv), Et3N (2.0 equiv), DMAP (10 mol %), CH2Cl2, rt, overnight, 61% over 2 steps; (l) NaH (5.0 equiv), PMBOH (2.0 equiv), DMF, rt, overnight, 95%; (m) CuI (1.3 equiv), vinylMgBr (6.0 equiv), Et2O, −78 °C → rt, 80%; (n) TBSCl (1.25 equiv), imidazole (2.5 equiv), DMF, rt, overnight, 98%; (o) 9-BBN (3.0 equiv), THF, rt, overnight, then 3 N NaOH, 30 wt % H2O2, rt, 6 h, 90%; (p) PPh3 (1.5 equiv), PTSH (1.5 equiv), DIAD (1.5 equiv), THF, rt, overnight, 90%; (q) Ammonium molybdate tetrahydrate (10 mol %), 30 wt % H2O2 (10 equiv), EtOH, rt, overnight, 90%; (r) sulfone 5 (1.25 equiv), LHMDS (1.25 equiv), THF, −78 °C → rt, 2 h, 70%; (s) AcOH/THF/H2O = 1/4/1, rt, 4 h, 80%; (t) 10 wt % Pd/C (10 mol %), H2 (1.0 atm), EtOAc, rt, 2 h, 90%; (u) DMP (1.2 equiv), NaHCO3 (5.0 equiv), CH2Cl2, rt, 1 h, 90%; (v) methyl acrylate (2.0 equiv), PBu3 (20 mol %), THF, rt, overnight, 75%; (w) CBr4 (6.0 equiv), PPh3 (6.0 equiv), iPr2NEt (12.0 equiv), CH2Cl2, rt, overnight, 80%; (x) DDQ (1.5 equiv), pH = 7.0 buffer, CH2Cl2, rt, 2 h; (y) DMP (1.33 equiv), NaHCO3 (5.0 equiv), CH2Cl2, rt, 1 h, 80% over 2 steps; (z) CrCl2 (20 equiv), 4 Å molecular sieves, THF, rt, 16 h, 95%; (aa) MeOH (10 equiv), CF3COOH/CH2Cl2 = 1/4, rt, 1 h, 80%; (ab) Bu4NF (2.0 equiv), THF, rt, 2 h, 80%; or 1% concn HCl in MeOH, rt, 2 h, 90%; (ac) 1% concn HCl in MeOH, rt, 4 h, 90%; (ad) NaH (3.0 equiv), THF, rt, 2 h, 80%; (ae) HOAc/CH2Cl2 = 1/4, rt, 24 h, 85%; (af) Ac2O (15.0 equiv), iPr2NEt (30 equiv), DMAP (3.0 equiv), CH2Cl2, rt, 1 h, 90%.

РСА 20a и 4-нитробензоатпроизводного 20b (21)



20a



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