

Group Problems

27 November 2018

Provide mechanisms for the following reactions and identify the intermediates.

1. C1CCCCC1=CNC(=O)OC(C)(C)C $\xrightarrow[\text{THF, rt, 1.5 h}]{\text{PhI=O (1.1 eq.)}}$ **A** $\xrightarrow[\text{reflux, 4 h}]{\text{PhMe}}$ C1CCCCC1=COC(=O)OC(C)C
87% **96%**
2. C12CCCCC1C(=O)C2C(=O)OCC $\xrightarrow[\text{THF, rt, 1 h}]{\text{KH, SeO}_2\text{Ph}}$ C12CCCCC1C(=O)C2C(=O)OCC $\xrightarrow[\text{THF, rt, 1 h}]{\text{KH, SeO}_2\text{Ph}}$ C12CCCCC1C(=O)C2C(=O)OCC
57% **59%**
3. C=CC(=O)O $\xrightarrow[\text{CH}_2\text{Cl}_2, \text{rt, overnight}]{\text{i) TsNHOTs (1.0 eq.), NaOAc (3.0 eq.), B (2.5 mol%)}}$ C[C@H]1N[C@@H](OC)C1O $\xrightarrow[\text{MeOH, rt, 6 h}]{\text{ii) NaOMe (1.8 eq.)}}$ C[C@H]1N[C@@H](OC)C1O
79%, 98% ee, >20:1 dr
B = C1CCN1C2=CC=C(C(F)(F)F)C(F)(F)F
4. C1CCCCC1CC(=O)N(C)C(C)C(=O)OCC $\xrightarrow[\text{CH}_2\text{Cl}_2, 0^\circ\text{C, 12 h}]{\text{i) Tf}_2\text{O (1.5 eq.), 2-fluoropyridine (2.0 eq.)}}$ C1CCCCC1CC(=O)OCC $\xrightarrow[\text{rt, 3 h}]{\text{ii) K-Selectride (3.0 eq.)}}$ C1CCCCC1CC(=O)OCC $\xrightarrow[\text{rt, 12 h}]{\text{iii) silica/CH}_2\text{Cl}_2/\text{H}_2\text{O}}$ C1CCCCC1CC(=O)OCC
86%, 91% ee
5. C#CC1=CC=C(C=C1)[N+](=O)[O-] $\xrightarrow[\text{diglyme, 120 }^\circ\text{C, 1 h}]{\text{(3.0 eq.) NaF (0.1 eq.)}}$ **[C]** $\xrightarrow[\text{rt, 3 h}]{\text{EtO}_2\text{C-CH=N}_2 (5.0 \text{ eq.}), \text{Et}_3\text{N (1.5 eq.)}}$ CCOC(=O)C1=CC=C(C=C1)N2C(=O)C(=C(C2)F)C3=CC=C(C=C3)[N+](=O)[O-]
72% (over 2 steps)

Retrosynthesis: Propose a retro- and forward synthesis of Duloxetine Hydrochloride (Cymbalta).

