

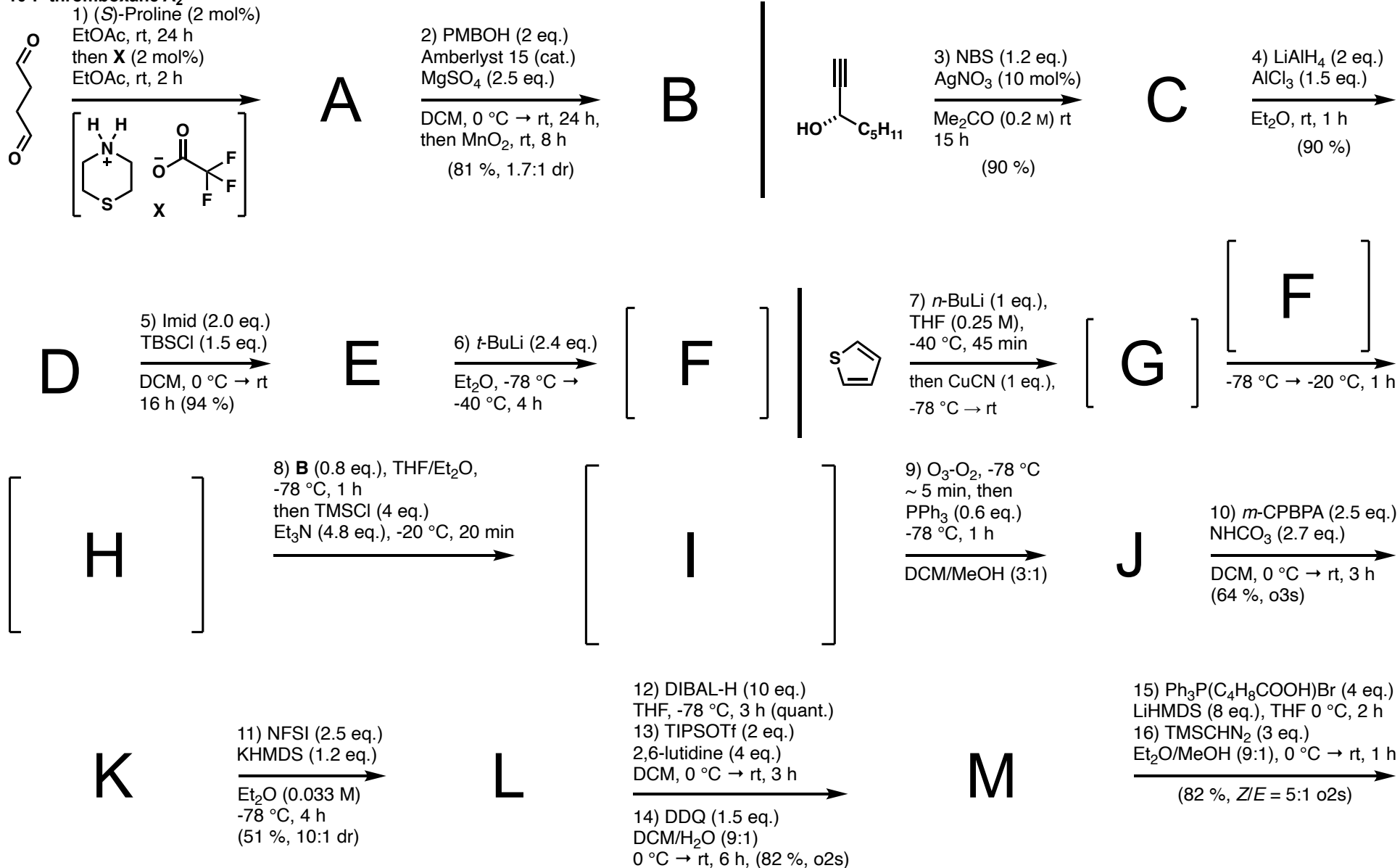
Synthesis, Stability, and Biological Studies of Fluorinated Analogues of Thromboxane A₂

21.02.24

Changcheng Jing, Shahida Mallah, Ella Kriemen, Steven H. Bennett, Valerio Fasano, Alastair J. J. Lennox, Ingeborg Hers, and Varinder K. Aggarwal

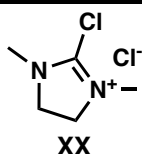
ACS Central Science 2020 6 (6), 995-1000 DOI: 10.1021/acscentsci.0c00310

10-F-thromboxane A₂



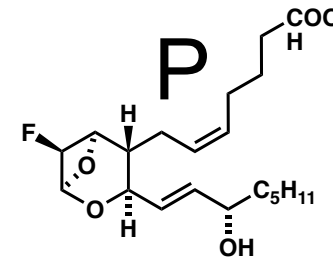
N

17) TBAF (3 eq.), AcOH (1.5 eq.)
THF, 0 °C, 1 h, (98 %)
18) **XX** (4 eq.), DIPEA (6 eq.)
MeCN, 0 °C → rt, 4 h, (α/β = 2.8:1)
19) Ag₂O (6 eq.), 1,4-dioxane
4 Å MS, 80 °C, 12 h (52 % o2s)



O

20) NaOH_{aq.} (1 M, 250 eq.)
1,4-dioxane, 0 °C → rt, 1 h
21) TBAF (3 eq.), THF,
0 °C → rt, 12 h, (78 % o2s)

10-F₂-thromboxane A₂

K

22) NFSI (4 eq.)
KHMDS (2.4 eq.)
Et₂O (0.1 M)
-78 °C, 4 h, (40 %)

Q

23) DIBAL-H (10 eq.)
THF, -78 °C, 3 h (quant.)
24) TIPSOTf (2 eq.)
2,6-lutidine (4 eq.)
DCM, 0 °C → rt, 4 h
25) DDQ (1.5 eq.)
DCM/H₂O (9:1)
0 °C → rt, 6 h, (84 %, o2s)

R

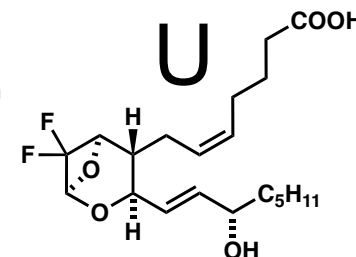
26) Ph₃P(C₄H₈COOH)Br (4 eq.)
LiHMDS (8 eq.), THF 0 °C, 2 h
27) TMSCHN₂ (3 eq.)
Et₂O/MeOH (9:1), 0 °C → rt, 1 h
(73 %, Z/E = 5:1 o2s)

S

28) Ac₂O (2 eq.), py (4 eq.), DMAP
(0.5 eq.), DCM, 0 °C → rt, 3 h (97 %)
29) TBAF (3 eq.), AcOH (1.5 eq.)
THF, 0 °C, 1 h (94 %)
30) MsCl (1.5 eq.), Et₃N (10 eq.), DCM
0 °C → rt, 1.5 h (96 %, α/β = 1:2)
31) ^tBuOK (2 eq.), THF/ⁱPrOH, 4 Å MS
0 °C → rt, 3 h (67 %)
32) TBAF (3 eq.), THF, 0 °C → rt 12 h
(94 %)

T

32) NaOH_{aq.} (1 M, 300 eq.)
1,4-dioxane, 0 °C → rt, 24 h



Unexpected reaction:

M

33) Ph₃P(C₄H₈COOH)Br (4 eq.)
^tBuOK (8 eq.), THF 40 °C, 1 h
(67 %)

V

