Supporting Information for

Development of a fluoride-responsive amide bond cleavage device that is potentially applicable to a traceable linker

Jun Yamamoto,[a,†] Nami Maeda,[a,†] Chiaki Komiya,[a] Tomohiro Tanaka,[b] Masaya Denda,[a] Koji Ebisuno,[a] Wataru Nomura,[b] Hirokazu Tamamura,[b] Youichi Sato,[c] Aiko Yamauchi,[c] Akira Shigenaga[a,d,*] and Akira Otaka[a,*]

[a] Department of Bioorganic Synthetic Chemistry, Institute of Health Biosciences and Graduate School of Pharmaceutical Sciences, The University of Tokushima, Shomachi, Tokushima 770-8505, Japan
[b] Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, Chiyoda-ku, Tokyo 101-0062, Japan
[c] Department of Pharmaceutical Information Science, Institute of Health Biosciences and Graduate School of Pharmaceutical Sciences, The University of Tokushima, Shomachi, Tokushima 770-8505, Japan
[d] JST, PRESTO, 4-1-8 Honcho, Kawaguchi, Saitama, 332-0012, Japan

[†]These authors contributed equally to this work.

E-mail:
shigenaga.akira@tokushima-u.ac.jp (A. Shigenaga)
aotaka@tokushima-u.ac.jp (A. Otaka)

Table of Contents

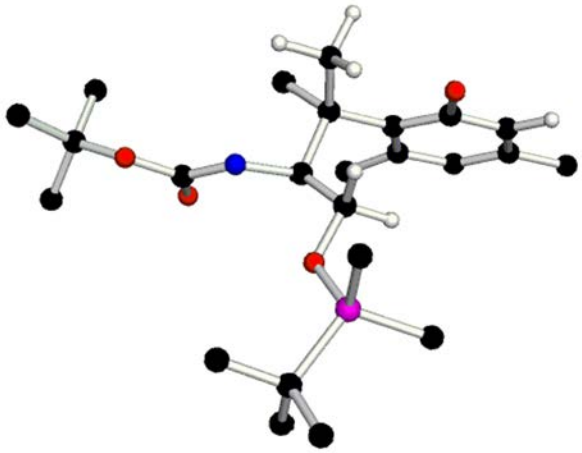

Figure S1. The MM2 energy minimized structure of phenol **2**. Some hydrogen atoms are omitted for clarity. C, H, N, O and Si atoms are shown as black, white, blue, red and magenta spheres, respectively. Generation of an initial structure and MM2 calculation were performed using ChemBio3D Ultra (CambridgeSoft). The figure was made using PyMOL (DeLano Scientific).

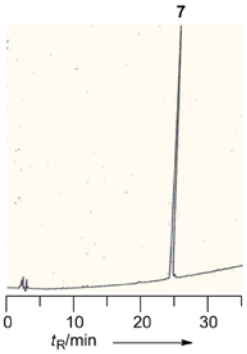

Figure S2. An HPLC profile of the FR traceable linker **7** after purification. HPLC conditions: Cosmosil $5C_{18}$-AR-II analytical column, linear gradient of 0.1% (v/v) TFA/MeCN in 0.1% (v/v) TFA aq., 50–90% over 30 min.

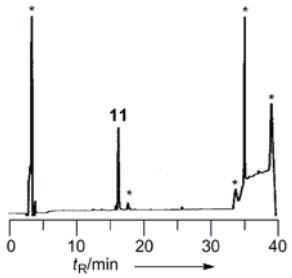

Figure S3. HPLC monitoring of a reaction of peptide **11** with KF followed by 3-bromobenzaldehyde. To peptide **11** (0.1 μmol) in Na phosphate buffer containing 6 M guanidine hydrochloride and 0.05 mM EDTA (200 mM phosphate, pH 7.6, 100 μL) were added KF (10 μmol), MESNa (10 μmol) and 3-bromobenzaldehyde (0.1 μmol). After 30 min of shaking at room temperature, the obtained mixture was analyzed by HPLC. HPLC conditions: Cosmosil $5C_{18}$-AR-II analytical column, linear gradient of 0.1% (v/v) TFA/MeCN in 0.1% (v/v) TFA aq., 5–30% over 30 mim, then 30–95% over 0.1 min followed by 95% for 6 min. *Non-peptidic peaks (These peaks were observed when the reaction mixture without peptide **11** was analyzed).