Supplementary Material for Chemical Communications

A New Route to Fullerene Substituted Phenylalanine Derivatives

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Supplementary Materials

Synthesis of N-Ac-Fullerecine-(D-)Phe-OMe (3). Buckyketone (238 mg, 0.30 mmol) and Ac-Phe(4-NH_2)-OMe (85 mg, 0.36 mmol) and catalytic amount of *para*-benzosulfonic acid were added into a 250 mL Schlenk flask equipped with a magnetic stir bar. The starting mixture was pumped dry under vacuum. Then degassed fresh distilled toluene (150 mL) was charged into the flask under argon atmosphere. The flask was headed on a Soxhlet extractor filled with oven dried 4 Å molecular sieve. The reaction mixture was refluxed for overnight. After the heating stopped, the dark golden brown solution was filtered. The identity of the imine intermediate (**1**) was confirmed by IR and MALDI-MS. In a separate Schlenk flask equipped with a stir bar was placed phthalic acid (100 mg, 0.6 mmol) and the flask degassed under vaccuo. After addition of dry THF (10 mL) under argon, the flask was cooled to –78 °C using acetone-dry ice bath. The solution of compound **1** (0.2 mmol equivalent) was transferred in under inert atmosphere. After the solution was cooled to –78 °C, BH_3(THF) (1.2 mL, 1 M in THF, 1.2 mmol) was injected via a syringe. The reaction was continued for *ca*. 2 h. and quenched with MeOH (2 mL). The flask was then warmed to room temperature and ethyl acetate (25 mL) added. The reaction was washed by KOH (1 M) solution (50 mL, 0.6 mmol) and water (4 x 25 mL). The solvent was removed under reduced pressure and the resulting brown powder was further purified by flash silica gel column eluted by toluene/MeOH (10:1). Solvent evaporation yielded a dark brown solid. Yield (**3**): 133 mg, 44%. $^{13}C\{^1H\}$ NMR (toluene-d_8/methanol-d_4): δ 173.33 and 173.35 ($\underline{C}O_2Me$), 169.80, 158.19, 157.73, 157.36, 157.23, 146.69 [N(H)$\underline{C}$], 146.51, 146.27, 145.75, 145.74, 145.69, 145.66, 145.64, 142.85, 142.83, 142.44, 142.37, 142.36, 142.33, 141.93, 141.89, 140.62, 140.60, 140.59, 140.48, 136.47, 136.23, 135.31, 135.09, 130.74, 130.73, 113.99, 64.52 (C_{60}-sp^3), 63.84 (C_{60}-sp^3), 54.85 and 54.84 (α-$\underline{C}$H), 51.70 ($\underline{C}H_3$), 48.58 [$\underline{C}$(H)N], 41.53 ($\underline{C}H_2$), 37.71 ($\underline{C}H_2CH$), 35.56 ($\underline{C}H_2$), 31.07 ($\underline{C}H_2$), 22.92 ($\underline{C}H_3$).

Synthesis of N-Boc-Fullerecine-(D-)Phe-OH (4). Buckyketone (160 mg, 0.2 mmol) and Boc-Phe(4-NH_2)-OH (100 mg, 0.3 mmol) and catalytic amount of *para*-benzosulfonic acid were added into a 250 mL Schlenk flask equipped with a magnetic stir bar. The starting mixture was degassed under vacuum. Then degassed fresh distilled toluene/THF (4:1, 150 mL) was charged into the flask under argon atmosphere. The flask was headed on a Soxhlet extractor filled with oven dried 4 Å molecular sieve. The reaction mixture was refluxed for overnight. After the heating stopped, the dark golden brown solution was filtered by a cannula to a second Schlenk flask equipped with a magnetic stir bar. The identity of the imine intermediate (**2**) was confirmed by MALDI-MS. The resulting solution was hydrogenated by the general method described for compound **3** (see above). The reaction was washed by $KHCO_3$ solution in place of KOH. The final solution was concentrated and chromatographed on flash silica gel eluted by toluene/MeOH (20:1). Yield (**4**): 95 mg, 45%.

Deprotection of N-Ac-Fullerecine-(D-)Phe-OMe. Compound **3** (50 mg, 0.049 mmol) was added into a Schlenk flask equipped with a magnetic stir bar. The solid was degassed under vacuum and then dissolved in CH_2Cl_2 (25 mL) and cooled –10 °C under argon atmosphere. BBr_3 (5 mL, 1 M in CH_2Cl_2) was added drop wise through needle transfer when stirring. Dark brown precipitate showed up. Stirring continued at –10 °C for 1 hr and at 25 °C for 2 hr. The reaction was quenched by careful drop wise addition of water (25 mL). The solids stayed in between the interface of water and CH_2Cl_2. The solids was then centrifuged out, and washed by 6 M HCl (2 x 10 mL) with sonication. The residue was further washed with DI water (3 x 25 mL). The decanted liquid portion gave a clear yellow solution with indication of the produced fullerecine was soluble in H_2O (100 mg.L^{-1}). Yield (**5**): *ca.* 70%. $^{13}C\{^1H\}$ NMR (toluene-d$_8$/methanol-d$_4$): δ 174.20 ($\underline{C}O_2H$), 158.22, 157.80m 157.38, 157.29, 147.95, 147.93, 147.01 [N(H)$\underline{C}$], 146.76, 146.75, 146.71, 146.70, 146.55, 146.53, 146.51,146.31, 146.29, 146.20, 146.17, 146.134, 146.04, 146.03, 145.77, 145.76, 145.71, 145.69, 145.68, 145.66, 145.65,145.10, 145.09, 145.05, 143.53, 143.51, 142.87, 142.85, 142.83, 142.54, 142.51, 142.46, 142.43, 142.42, 142.39, 142.36, 142.35, 142.34, 142.22,141.95, 141.93, 141.92, 141.91, 141.90, 141.90, 140.61, 140.59, 140.49, 136.47, 136.25, 135.29, 135.13, 130.79 and 130.78 (*m*-C̲H), 126.21 and 126.20 (*p*-C̲), 114.06 and 114.05 (*o*-C̲H), 65.55 (C_{60}-sp^3), 63.91 (C_{60}-sp^3), 53.83 (α-C̲H), 48.61 and 48.60 [C̲(H)N], 41.43 (C̲H_2), 37.30 (C̲H_2CH), 35.55 (C̲H_2), 31.00 (C̲H_2).

Coupling of N-Boc-Fullerecine-Phe-OH with NH_2-Gly-OEt. Compound **4** (26 mg, 0.024 mmol) was mixed with NH_2-Gly-OEt (154 mg, 0.1 mmol) dissolved in 4:1 DCM/DMF (5 mL). HBTU (45 mg, 0.1 mmol) coupling reagents and a couple of drops NEt_3 were added thereafter. The solution was sonicated for 2 hr. The solution was concentrated first and then precipitated by the addition of Et_2O (30 mL), resulting a brown solid, which was separated centrifuge (4400 rpm for 30 min.) and washed by MeOH (2 x 25 mL). Yield (**6**): >90% (not isolated).

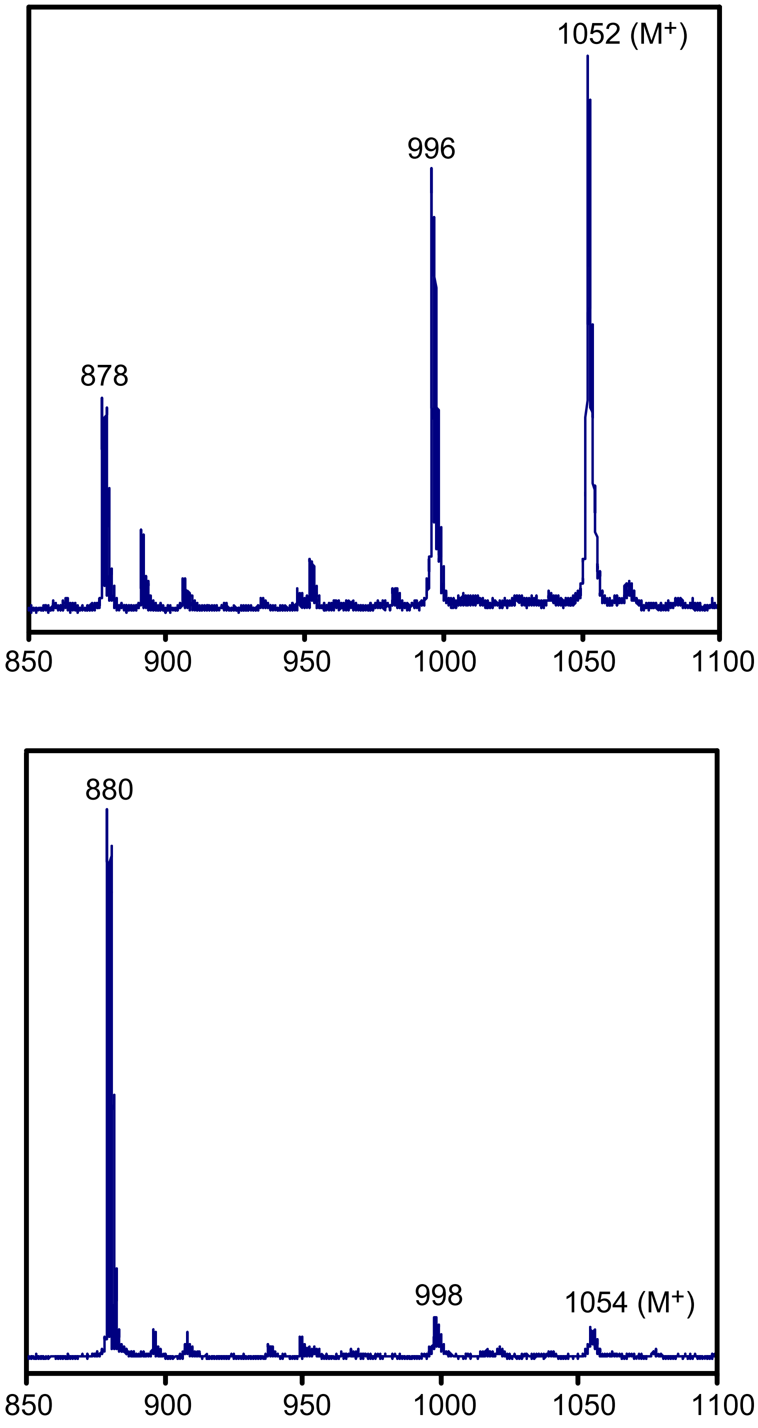

Figure S1. MALDI-TOF MS of compounds **3** (top) and **4** (bottom).