Supporting Information

Sensitive carbohydrate detection using Surface enhanced Raman Spectroscopy

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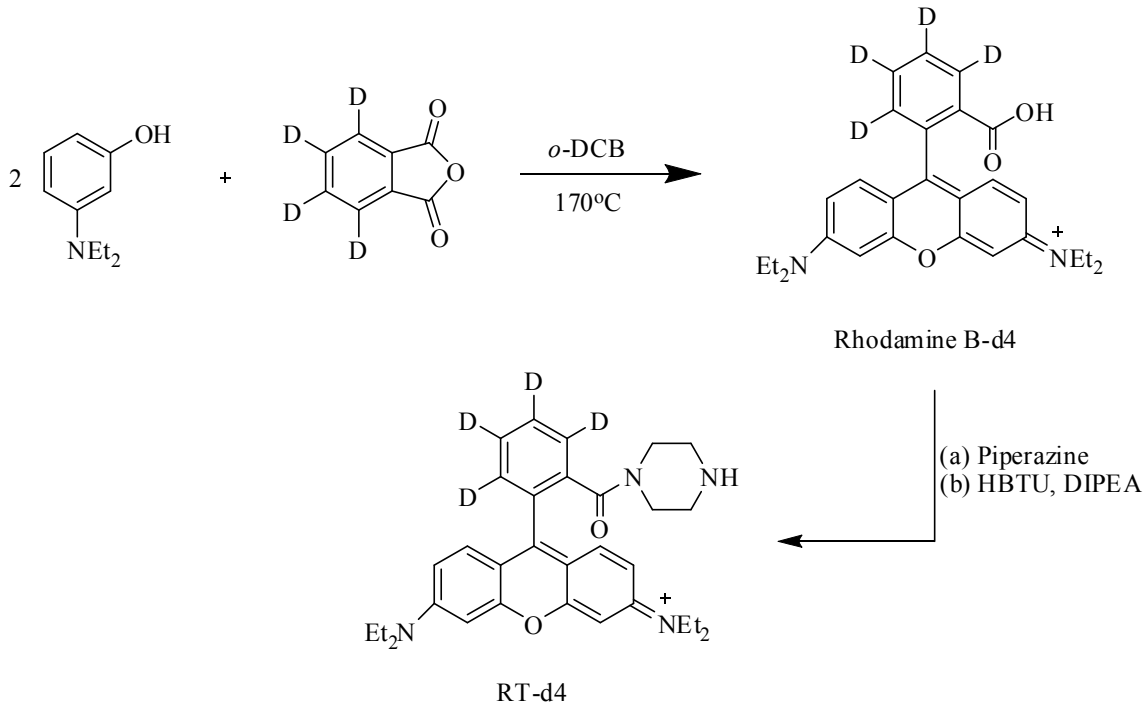
1. Synthesis of SERS tag RT-d_4:

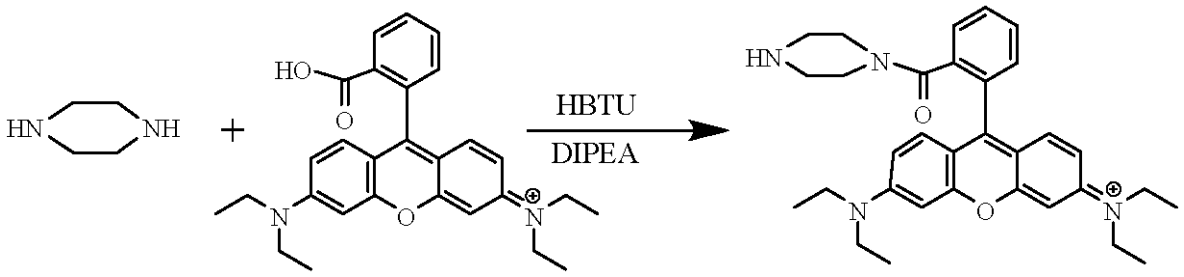


Preparation of Rhodamine B–d4: Pthalic anhydride (0.1g, 0.67mmol) was dissolved in *o*-dichlorobenzene followed by the addition of 3-(Diethylamino)phenol (0.1g, 0.66mmol). The mixture was heated to *ca* 170°C for hour, then another 0.1g of 3-(Diethylamino)phenol was added in portions over a period of 5hrs. After the addition was completed the reaction was stirred for five more hours and subsequently cooled to room temperature. The reaction was quenched by dilute sodium hydroxide, followed by addition of few drops of concentrated hydrochloric acid. *O*-dichlorobenzene was removed under reduced pressure and the crude product was purified by flash chromatography using dichloromethane/methanol (4.5/0.5) on silica to give 0.18g (56% yield) of dark purple RB-d4. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 6.67 (d, J = 9.0 Hz, 2H), 6.48 (d, J = 2.5 Hz, 2H), 6.39 (dd, J = 9.0 Hz, 2.5 Hz, 2H), 3.38 (q, J = 7.1 Hz, 8H), 1.18 (t, J = 7.0 Hz, 12H).

Preparation of RT-d4: To a stirring solution of piperazine (100mg, 0.28 mmol) in dichloromethane (20 mL) was added HBTU (157 mg, 0.41 mmol), DIPEA (0.14 mL, 0.83 mmol) and rhodamine B-d4 (172 mg, 0.36 mmol). The reaction mixture was stirred at room temperature for 4.0 hrs and then quenched with dilute HCl. The organic layer was thoroughly washed with dilute HCl and brine, dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 30:1) to afford RT-d4 (174 mg, 80%) as a dark purple solid. ^{1}H NMR ($CDCl_3$, 600 MHz), δ (ppm). 7.24 (d, J = 9.6 Hz, 2H), 6.92 (d, J = 9.6 Hz, 2H), 6.74 (d, J = 1.8 Hz, 2H), 3.60 (m, 8H), 3.33 (br m, 4H), 2.67 (br s, 4H), 1.31 (t, J = 7.1 Hz, 12H).

2. Synthesis of SERS tag RT-d0:

The synthetic scheme of RT is shown below:



Scheme S1: Preparation of Rhodamine tag (RT)

Procedure: To a stirring solution of piperazine (0.35 gm,4.06 mmol) in dichloromethane (10 mL) was added HBTU (0.45 gm, 1.197 mmol), DIPEA (0.4 mL, 2.3 mmol) and rhodamine B (0.5 gm, 1.04 mmol). The reaction mixture was stirred at room temperature for 3 hr and then quenched with dilute HCl. The organic layer was thoroughly washed with dilute HCl and brine, dried over Na_2SO_4, and concentrated under vacuum. The crude product was purified by flash column chromatography (CH_2Cl_2/MeOH 30:1) to afford compound STM (0.41 gm, 72%) as a dark purple solid. ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): ^{1}H NMR (CD_2Cl_2, 300 MHz), δ (ppm): 7.74-7.68 (m, 2H), 7.62-7.56 (m, 1H), 7.39-7.32 (m, 1H), 7.17 (d, 2H, J = 9.5 Hz), 6.91 (dd, 2H, J = 9.5, J = 2.4 Hz), 6.74 (d, 2H, J = 2.4 Hz), 3.75-3.45 (m, 12H), 3.15-3.03 (br S, 4H), 1.29 (t, 12 H, J = 7.1 Hz).

3. Mass spectrum of RTd_4 and RTd_4-glucose:

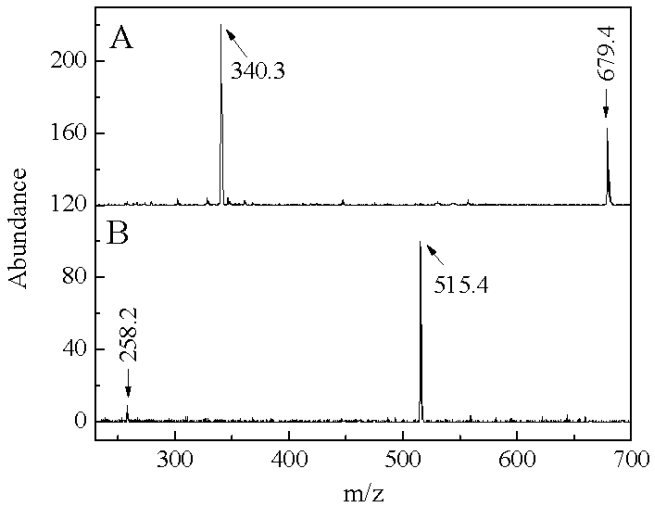


Figure S1: The mass spectrum of purified (A) RTd_4-glucose and (B) RTd_4. The m/z peak of 679.4 and 340.3 in spectrum A corresponds to the singly (M^+) and doubly charged (M^++H^+) RTd_4-glucose respectively. The 515.4 and the 258.2 peaks corresponds to the singly (M^+) and doubly charged (M^++H^+) RTd_4.

4. UV-Vis spectra of RT before and after glycan conjugation

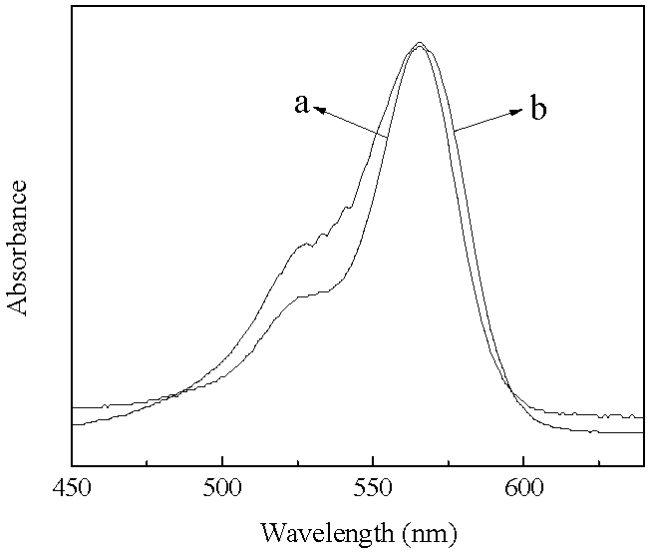


Figure S2: The UV-Vis spectra of RT (a) before and (b) after conjugation with carbohydrate.

5. UV-Vis spectra of RT dissolved in different pH solutions

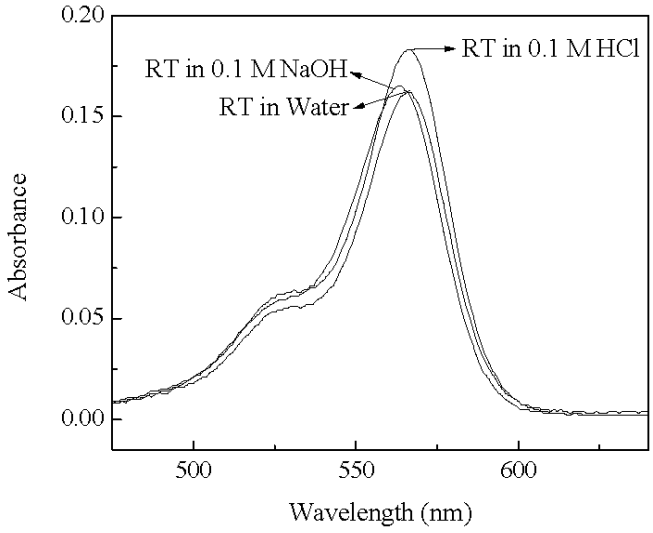


Figure S3: UV-Vis spectra of RT in 0.1 M HCl, 0.1 M NaOH, and water.

6. SERS spectra of RT-glucose and RTd_4-glucose:

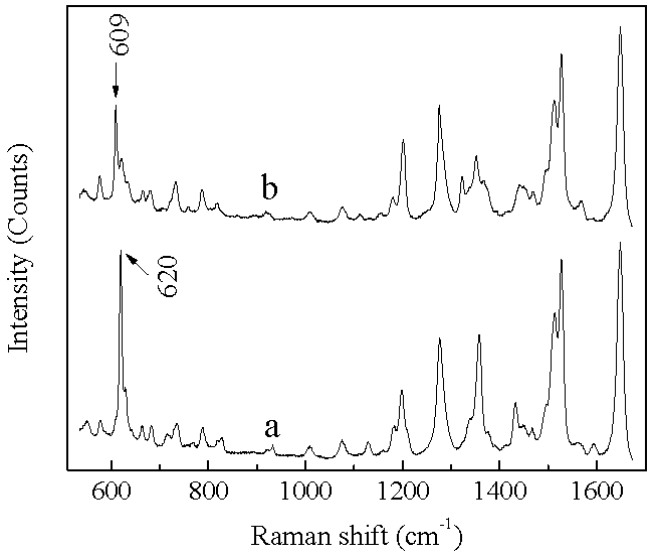


Figure S4: SERS spectra of (a) RT-glucose and (b) RTd_4-glucose.

7. Fluorescence spectra of RT-glucuronic acid:

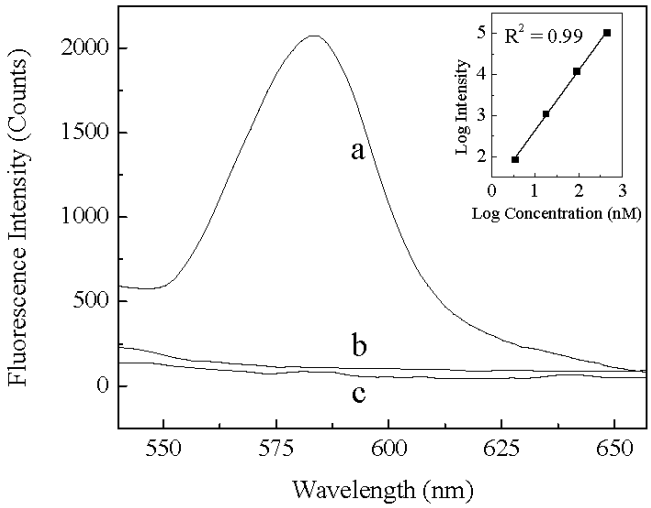


Figure S5: Fluorescence spectra of RT-glucuronic acid with concentration of (a) 7 nM and (b) 1 nM. The spectrum (c) is the background fluorescence spectrum. Inset showing the correlation between fluorescence intensity and sample concentration.