ELECTRONIC SUPPLEMENTARY INFORMATION

A mass spectrometric investigation of novel quadruplex DNA-selective berberine derivatives†

a. Synthesis and characterisation of compound (**7**).

The berberine derivative **7** was synthesised according to the general procedure described[9] for **2**. An improved yield of **7** was obtained by carefully controlling the temperature regime in the final coupling and elimination step with 2-bromomethylnapthalene with 8-allyldihydroberberine. Compound **7** was prepared as follows: A solution of 8-allyldihydroberberine [1] (100.0 mg, 0.27 mmol) and 2-(bromomethyl)-naphthalene (59.0 mg, 0.27 mmol) in dry CH_3CN (3 ml) was heated at 60°C in a sealed vial. After 24 h, an aliquot was removed from the reaction and RP-HPLC analysis showed complete enamine alkylation. The vial was then heated to 100^{o}C and the reaction monitored by RP-HPLC for 2 days until all of the alkylated enamine intermediate had been consumed. The crude reaction was purified by semi-preparative RP-HPLC to yield the mixed Cl^-/Br^- salt of **7**. The mixed salt was redissolved in MeOH and stirred at rt for 2 h with excess Amberlite IRA-904 quaternary ammonium Cl^- anion exchange resin. The resin was filtered and solvent removed *in vacuo* to give **7** (74.5 mg, 58%) as a yellow solid; m.p. 144-145 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.23 (br.s, 2H, H-5), 4.05 (s, 3H, OCH_3), 4.25 (s, 3H, OCH_3), 4.81 (br.s., 2H, H-6), 4.95 (s, 2H, Ch_2Ph), 5.98 (s, 2H, OCH_2O), 7.06 (br.s, 1H, H-3′), 7.10 (br.s, 1H, H-12), 7.42 (s, 1H, H-4), 7.48(m, 4H, H-1′), 7.63 (d, J = 6.5, 1H, H-6′), 7.87-7.91 (m, 1H, H-4′), 8.0 (d, J = 6.5, 1H, H-5′), 9.95 (s, 1H, H-8). ^{13}C NMR (125 MHz, $CD_3OD/CDCl_3$): δ 29.5 (C5), 36.3 (CH_2), 56.5 (OCH_3), 57.9 (C6), 61.8 (OCH_3), 102.5 (OCH_2O), 108.3 (C4), 108.6 (C14), 120.3 (C13b), 121.8 (C3′), 121.9 (C8a), 126.2 (C6′), 126.3 (C7′), 126.5 (C1′), 126.6 (C11), 127.4 (C4′), 127.6 (C8′), 129.2 (C12), 131.1 (C4a′), 132.6 (C8a′, C12a), 133.9 (C2′), 136.8 (C13), 138.0 (C13a), 145.1 (C9), 147.4 (C3a), 150.3 (C14a), 150.8 (C10). HRMS (ES) *m/z* calculated for $C_{31}H_{26}N_1O_4$ $[M]^+$: 476.1866; found: 476.1862

[1] J. B. Bremner and S. Samosorn, *Aust. J. Chem.*, 2003, **56**, 871.

b. Relative abundances of each complex in mixtures containing ligands and D2, Q4, Q1 and Q2

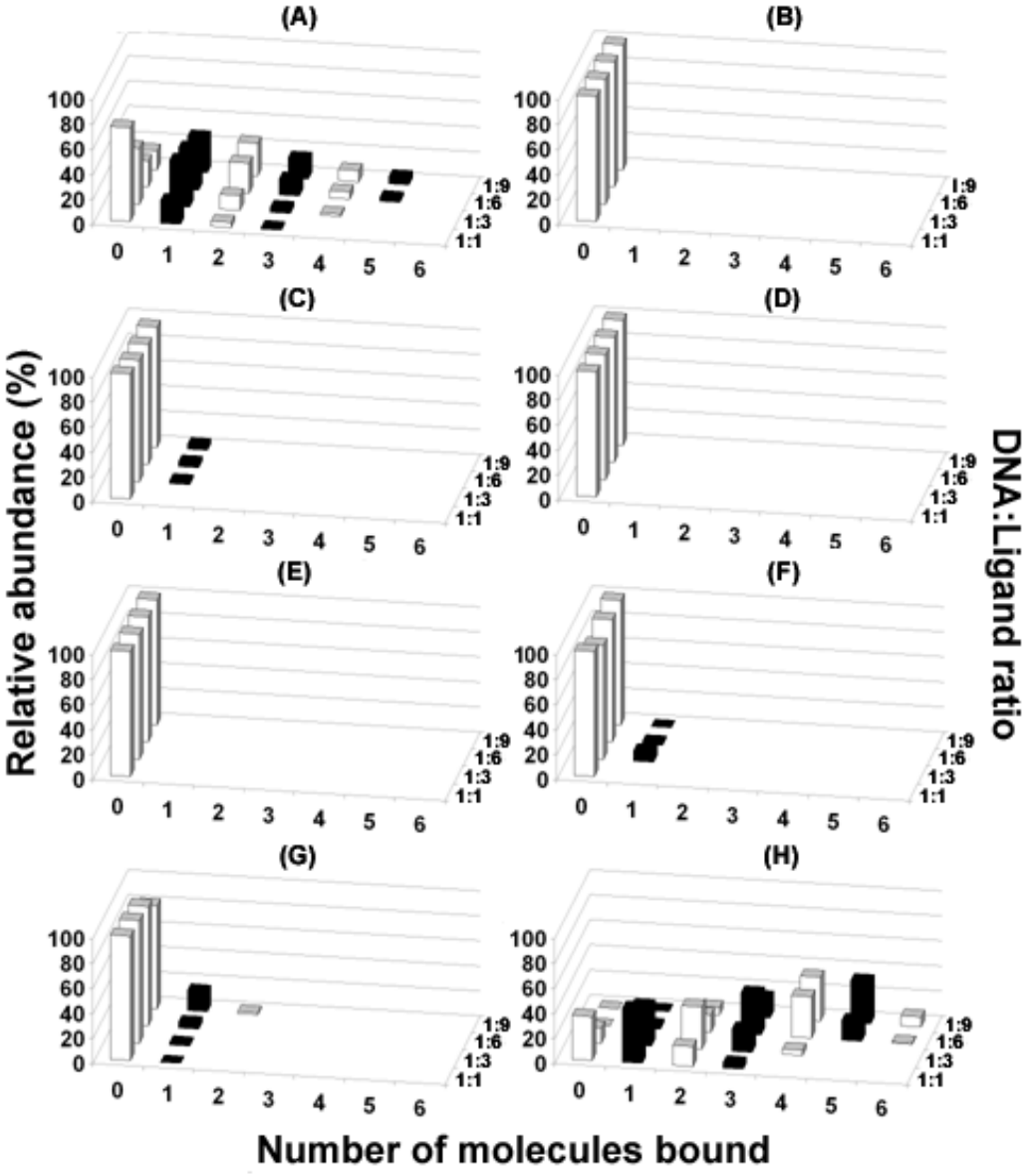

Fig. S1. Relative abundances of D2 duplex DNA-ligand complexes in 1:1-1:9 mixtures determined from negative ion ESI mass spectra. The data were obtained by summing the intensities of all ions from a particular DNA-ligand complex and expressing it as a percentage of the sum of the intensities of all DNA (free + bound) in the ESI mass spectra. (A) **1** (B) **2** (C) **3** (D) **4** (E) **5** (F) **7** (G) **6** (H) Dn

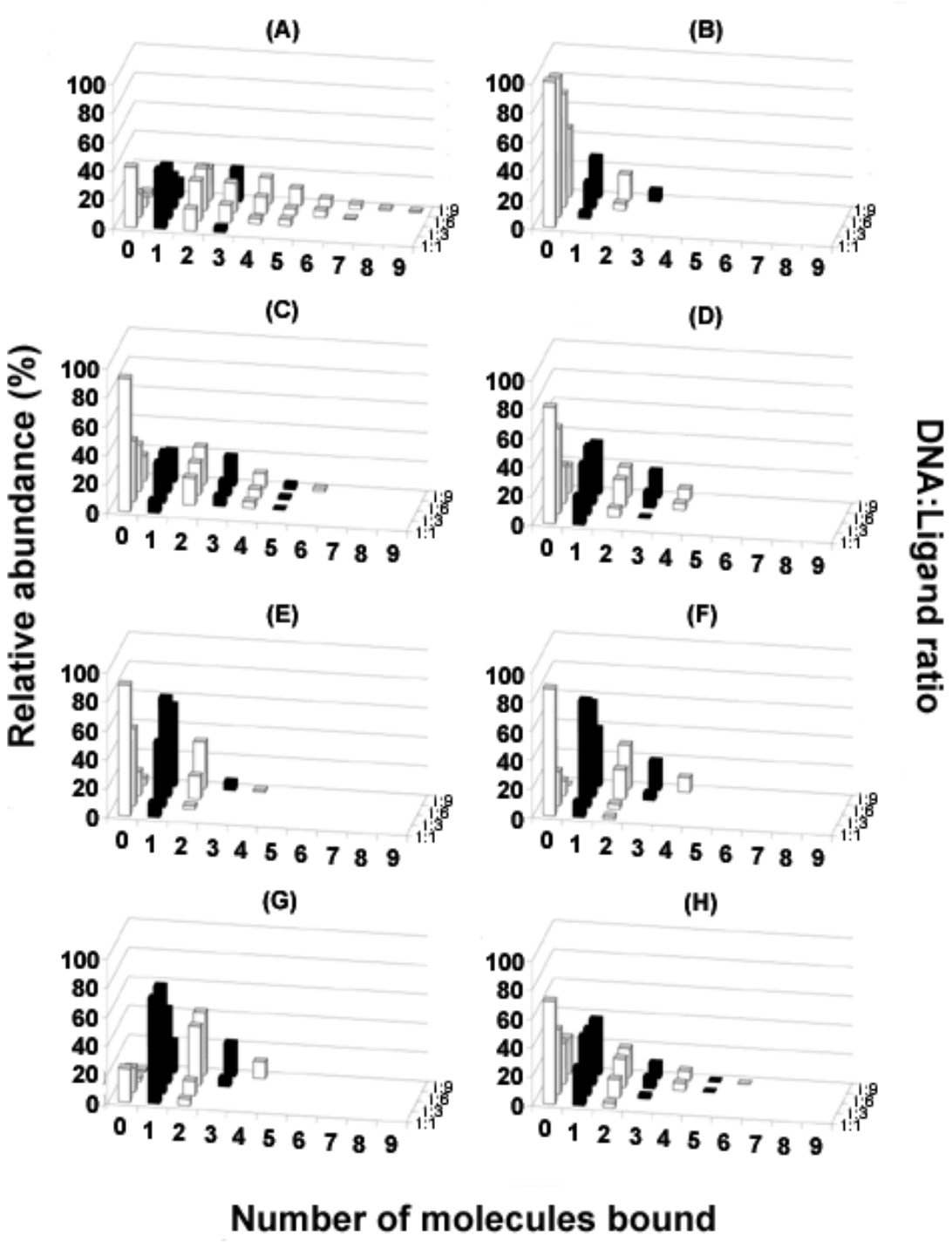

Fig. S2. Relative abundances of Q4 qDNA DNA-ligand complexes in 1:1-1:9 mixtures determined from negative ion ESI mass spectra. The data were obtained by summing the intensities of all ions from a particular DNA-ligand complex and expressing it as a percentage of the sum of the intensities of all DNA (free + bound) in the ESI mass spectra. (A) **1** (B) **2** (C) **3** (D) **4** (E) **5** (F) **7** (G) **6** (H) Dn

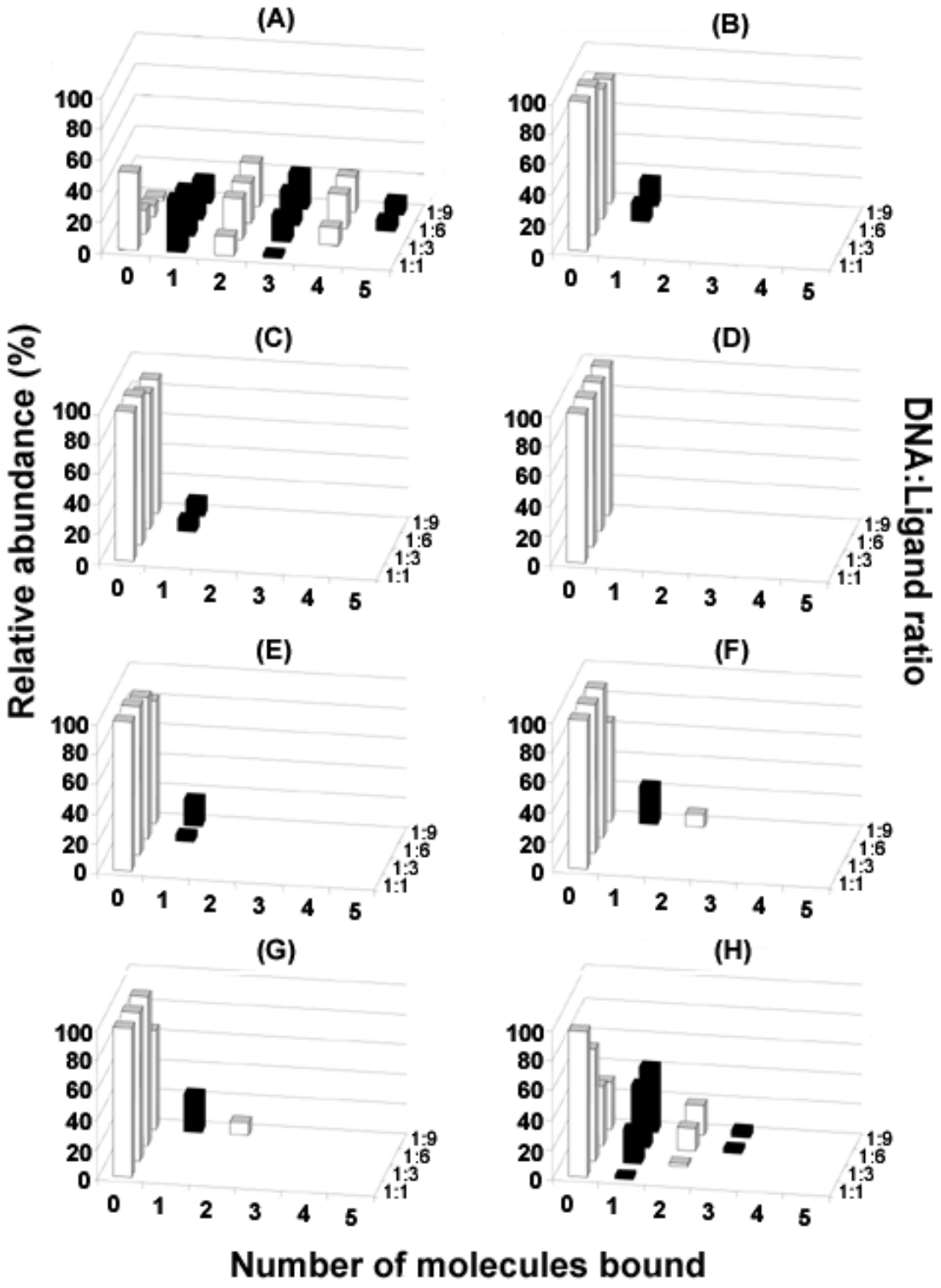

Fig. S3. Relative abundances of Q1 qDNA DNA-ligand complexes in 1:1-1:9 mixtures determined from negative ion ESI mass spectra. The data were obtained by summing the intensities of all ions from a particular DNA-ligand complex and expressing it as a percentage of the sum of the intensities of all DNA (free + bound) in the ESI mass spectra. (A) **1** (B) **2** (C) **3** (D) **4** (E) **5** (F) **7** (G) **6** (H) Dn

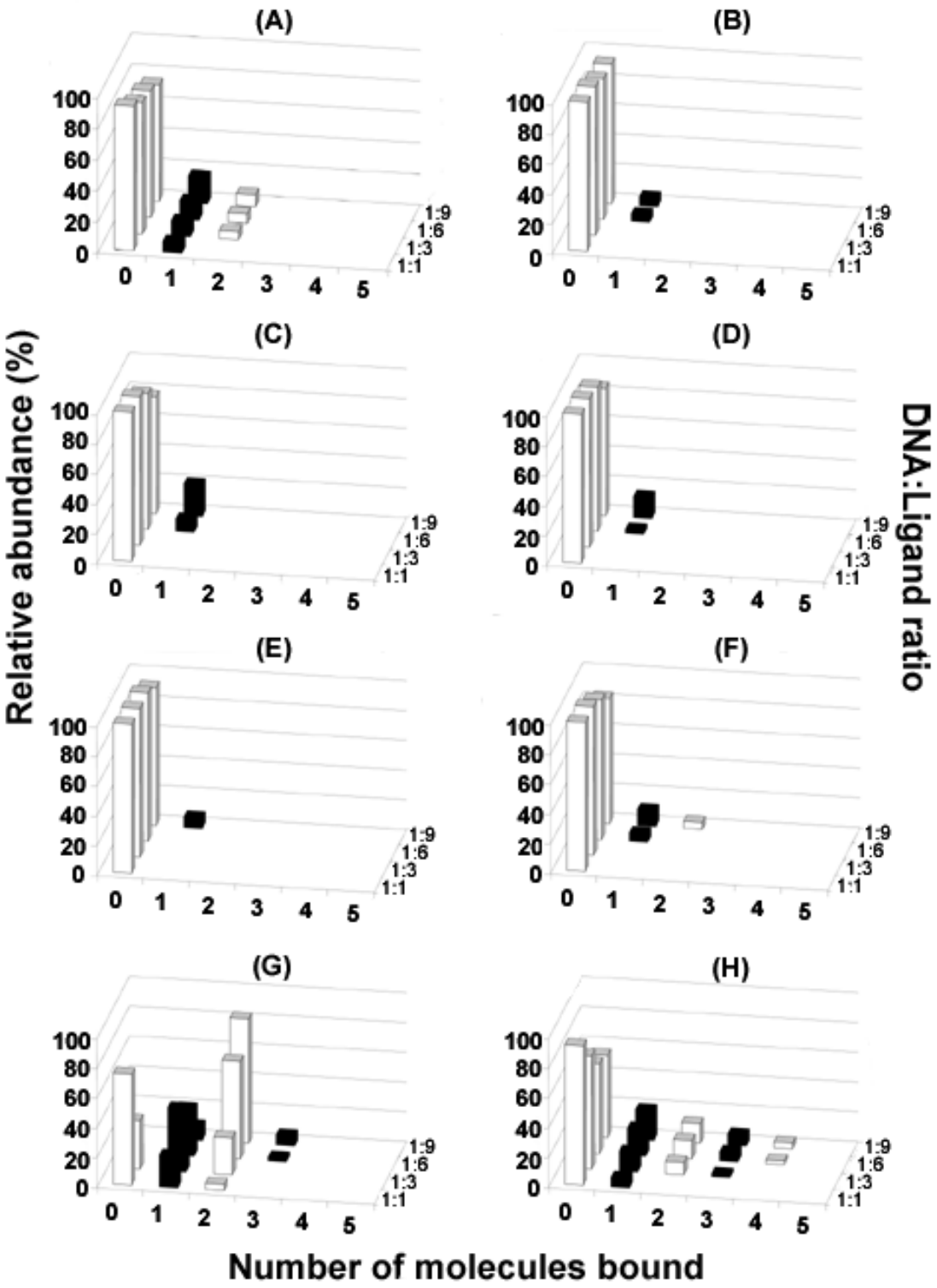

Fig. S4. Relative abundances of qDNA Q2 DNA-ligand complexes in 1:1-1:9 mixtures determined from negative ion ESI mass spectra. The data were obtained by summing the intensities of all ions from a particular DNA-ligand complex and expressing it as a percentage of the sum of the intensities of all DNA (free + bound) in the ESI mass spectra. (A) **1** (B) **2** (C) **3** (D) **4** (E) **5** (F) **7** (G) **6** (H) Dn

c. Comparison of number of ammonium ions associated with qDNA in the presence or absence of Berb (**1**) or (**7**).

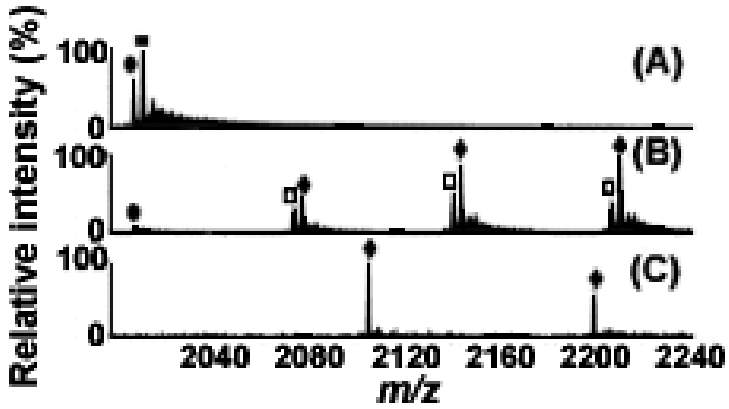

Fig. S5. Negative ion ESI mass spectra of Q4 alone and with **1** or **7** showing the region *m/z* 2000-2240 highlighting the 5^- ions. (A) Q4 alone (B) Q4 and **1** in a 1:9 mixture (C) Q4 and **7** in a 1:9 mixture. ●$[Q4+\underline{3}NH_4^+\text{-}8H]^{5-}$; ■ $[Q4+\underline{4}NH_4^+\text{-}9H]^{5-}$; □ $Q4+\underline{3}NH_4^+$ + n ligand-8H]$^{5-}$; ◆ $[Q4+\underline{4}NH_4^+$ + n ligand-9H]$^{5-}$; n = 1.