Electronic Supplementary Information

Monosubstituted dually cationic cyclodextrins for stronger chiral recognition

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1. Instrumentation

All ^{1}HNMR spectra and mono-dimensional ^{1}HNMR spectra (TOCSY) were recorded on a Bruker AVANCE 500 MHz (Bio-Spin Corporation, Europe) spectrometer in DMSO-d_6. Data is expressed in parts per million (ppm) downfield shift from tetramethylsilane as internal reference and are reported as position (in ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant (*J* in Hz) and integration (number of protons). ^{13}CNMR spectra were recorded on a Bruker AVANCE 500 MHz spectrometer in $CDCl_3$ or DMSO-d_6 or D_2O with complete proton decoupling. Data is expressed in parts per million (ppm) shift relative to DMSO-d_6 (39.51 ppm) is reported as position (δ). Melting points were recorded on Beijing TECH brand melting point apparatus and are uncorrected. Electrospray Ionization spectra were acquired on a Finniga/AM TSQ Qurntum (Thermal, USA) time of flight mass spectrometer. Samples are presented in Methanol (or your solvent here) as a 100 *μl* loop injection by manual operation. Elemental analysis was carried out on a Perkin-Elmer 2400 CHN analyzer.

Beckman P/ACE MDQ CE unit (Fullerton, CA, USA) was used for all CE separations. 50 μm ID, 375 μm OD fused silica capillary was used with a total length of 59.2 cm (49 cm to the detector). Detection of analytes was carried out simultaneously at 214 nm, 254 nm and 280nm by using variable-wavelength PDA (Photodiode Array, 190-300 nm) detector. The electrosmotic flow (EOF) was measured with methanol as neutral marker. Samples were introduced hydrodynamically into the capillaryat 0.5 psi for 5 s. All experiments were performed under normal polarity with 15 kV applied voltage.

2. Synthesis of compound 3, 4, 8a and 9a.

*N-(2-Bromoethyl)phthalimide (**3a**).* Towards a solution of 1,2-dibromoethane (7.66 mL, 64.8 mmol) in acetone (20 mL) was added with **2** (4 g, 21.6 mmol) under N_2. The reaction mixture was stirred at 60^{o}C for 12 h under reflux. After cooling down to room temperature, KBr precipitate was removed via filtration. The filtrate was concentrated to ~10 mL. Recrystallization from ethanol afforded the title

compound **3a** (4.61 g, 84%) as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.89 (m, 2H, =CH_{ortho}), 7.77 (m, 2H, =CH_{meta}), 4.12 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-}N\text{-imine}}$), 3.63 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-bromo}}$).

*N-(3-bromopropyl)phthalimide (**3b**)*. White solid (yield 89%): ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.88 (m, 2H, =CH_{ortho}), 7.77 (m, 2H, =CH_{meta}), 3.85 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-imine}}$), 3.43 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-bromo}}$), 2.27 (m, 2H, *J* = 6.9 Hz, *J* = 6.6 Hz, -CH_2).

*N-(4-bromobutyl)phthalimide (**3c**)*. White solid (yield 83%): ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.86 (m, 2H, =CH_{ortho}), 7.73 (m, 2H, =CH_{meta}), 3.73 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-imine}}$), 3.45 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-bromo}}$), 1.89 (m, 4H, -CH_2).

*N-(6-bromohexyl)phthalimide (**3d**)*. White solid (yield 91%): ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.85 (m, 2H, =CH_{ortho}), 7.73 (m, 2H, =CH_{meta}), 3.69 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-imine}}$), 3.40 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-bromo}}$), 1.86 (m, 2H, -CH_2), 1.67 (m, 2H, -CH_2), 1.44 (m, 2H, -CH_2), 1.34 (m, 2H, -CH_2).

*N-[2-(1H-Imidazolyl)ethyl]phthalimide (**4a**)*.[13] To a suspension of sodium hydride (1.21 g, 50.46 mmol, 1.24 g of 97% mineral oil dispersion) in petroleum ether (20 mL) was bubbled with N_2 to remove the mineral oil. Freshly distilled DMF (25 mL) was added with stirring to dissolve the cleaned sodium hydride at 0^{o}C over 35 min. To the above solution was gradually added with a solution of imidazole (2.63 g) in DMF (40 mL) over 1 h. A solution of **3a** (12 g, 42.53 mmol) in DMF (160 mL) was then added dropwise. The reaction mixture was refluxed at 100^{o}C for 8 h. After removal of DMF, the syrupy residue was dissolved in dichloromethane, and washed with water at least three times. A further flush chromatography over silica gel with methanol/ethyl acetate (1/1, v/v) afforded the title compound **4a** (4.72 g, 46 %) as a white solid: m.p. 156^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.86 (m, 2H, =CH_{ortho}), 7.76 (m, 2H, =CH_{meta}), 7.46 (s, 1H, =CH-$_{2im}$), 7.07 (s, 1H, =CH-$_{4im}$), 7.00 (s, 1H, =CH-$_{5im}$), 4.33 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-}N\text{-im}}$), 4.08 (t, 2H, *J* = 6.6 Hz, -$CH_{2\text{-}N\text{-imine}}$).

*N-[3-(1H-imidazolyl)propyl]phthalimide (**4b**)*. White solid (yield 37%): m.p. 104^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.85 (m, 2H, =CH_{ortho}), 7.75 (m, 2H, =CH_{meta}), 7.57 (s, 1H, =CH-$_{2im}$), 7.04 (s, 1H, =CH-$_{4im}$), 6.99 (s, 1H, =CH-$_{5im}$), 4.01 (t, 2H, *J* = 6.9 Hz,

-$CH_{2\text{-}N\text{-im}}$), 3.73 (t, 2H, J = 6.9 Hz, -$CH_{2\text{-}N\text{-imine}}$), 2.18 (m, 2H, -$CH_2$).

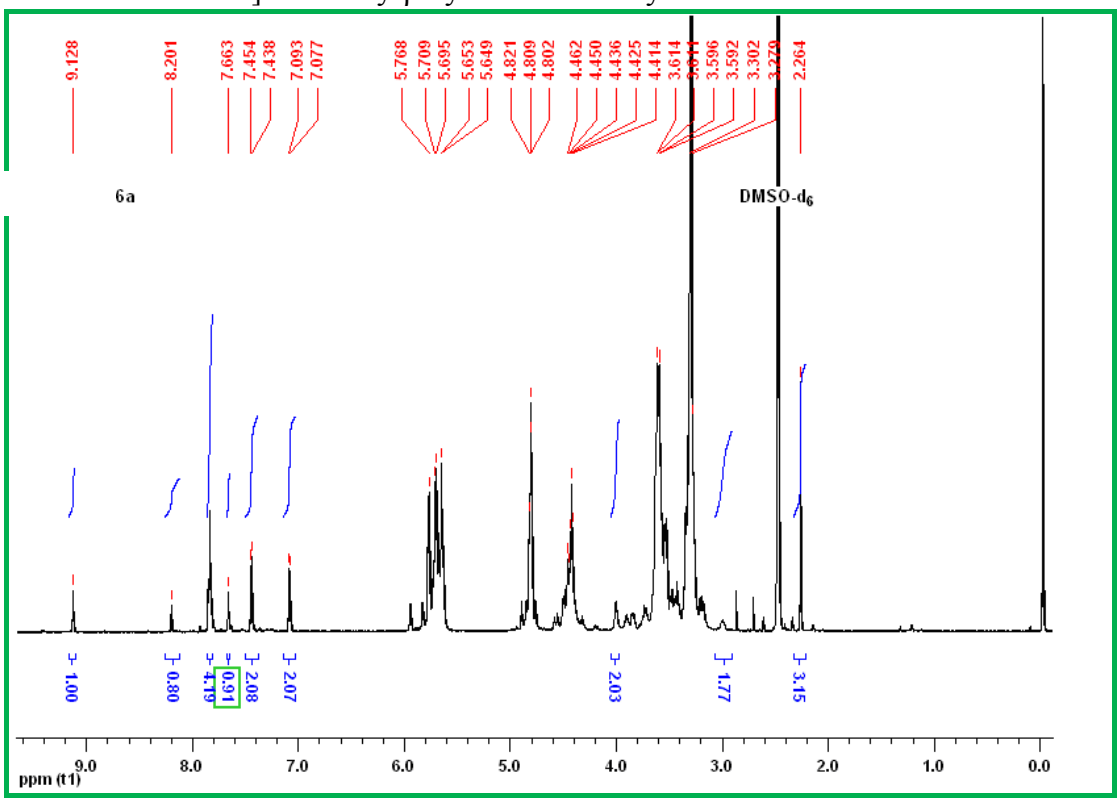
*N-[4-(1H-imidazolyl)butyl]phthalimide (**4c**)*. White solid (yield 43%): m.p. 84°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.83 (m, 2H, =CH_{ortho}), 7.72 (m, 2H, =CH_{meta}), 7.48 (s, 1H, =CH-$_{2im}$), 7.03 (s, 1H, =CH-$_{4im}$), 6.91 (s, 1H, =CH-$_{5im}$), 3.99 (t, 2H, J = 6.9 Hz, -$CH_{2\text{-}N\text{-im}}$), 3.71 (t, 2H, J = 6.9 Hz, -$CH_{2\text{-}N\text{-imine}}$), 1.84 (m, 2H, -$CH_2$), 1.68 (m, 2H, -$CH_2$).

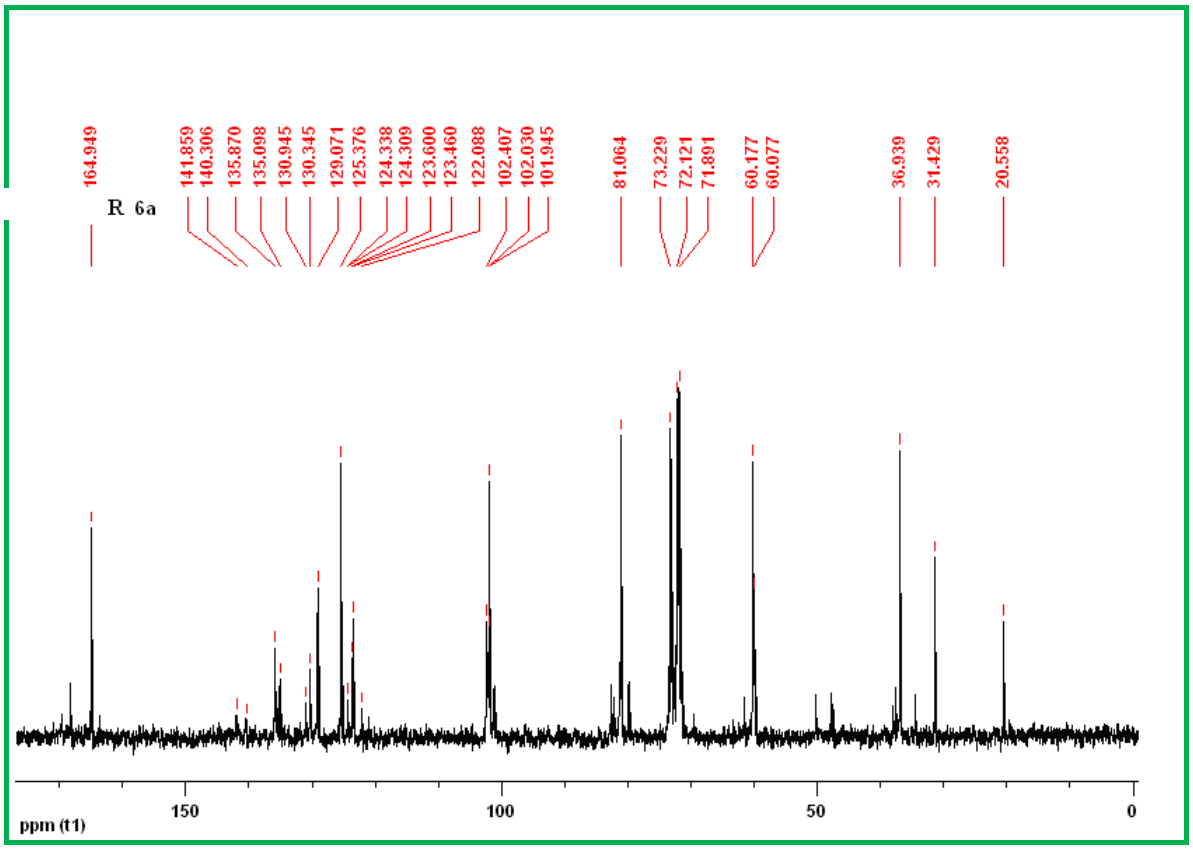
*N-[6-(1H-imidazolyl)hexyl]phthalimide (**4d**)*. White solid (yield 37%): m.p. 57°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.83 (m, 2H, =CH_{ortho}), 7.73 (m, 2H, =CH_{meta}), 7.45 (s, 1H, =CH-$_{2im}$), 7.03 (s, 1H, =CH-$_{4im}$), 6.89 (s, 1H, =CH-$_{5im}$), 3.92 (t, 2H, J = 4.2 Hz, -$CH_{2\text{-}N\text{-im}}$), 3.67 (t, 2H, J = 4.2 Hz, -$CH_{2\text{-imine}}$), 1.78 (m, 2H, -CH_2), 1.68 (m, 2H, -CH_2), 1.37 (m, 2H, -CH_2).

(1H-imidazol-1-yl)ethylamine (**8a**). A mixture solution of **4a** (0.17 g, 0.7 mmol), ethanol (10 mL), and hydrazine hydrate (0.039g, 0.77 mmol) was stirred at 80°C for 12 h. After cooling down to room temperature, hydrochloric acid (7.7 mmol) was added before refluxing the solution for another 5 h. Removal of the insoluble solid by filtration, the filtrate was concentrated and added with sodium hydroxide (7.7 mmol, 1 M) solution. Extracted with dichloromethane (3×15 mL), the collected solution was dried with $MgSO_4$ and evaporated to afford title compound as a colorless oil: ^{1}HNMR (500 MHz, DMSO-d_6) δ 7.59 (s, 1H, =CH-$_{2im}$), 7.14 (s, 1H, =CH-$_{4im}$), 6.86 (s, 1H, =CH-$_{5im}$), 3.93 (t, 2H, -$CH_{2\text{-}N\text{-im}}$), 2.51 (t, 2H, J = 6.9 Hz, -$CH_{2\text{-}N\text{-amine}}$).

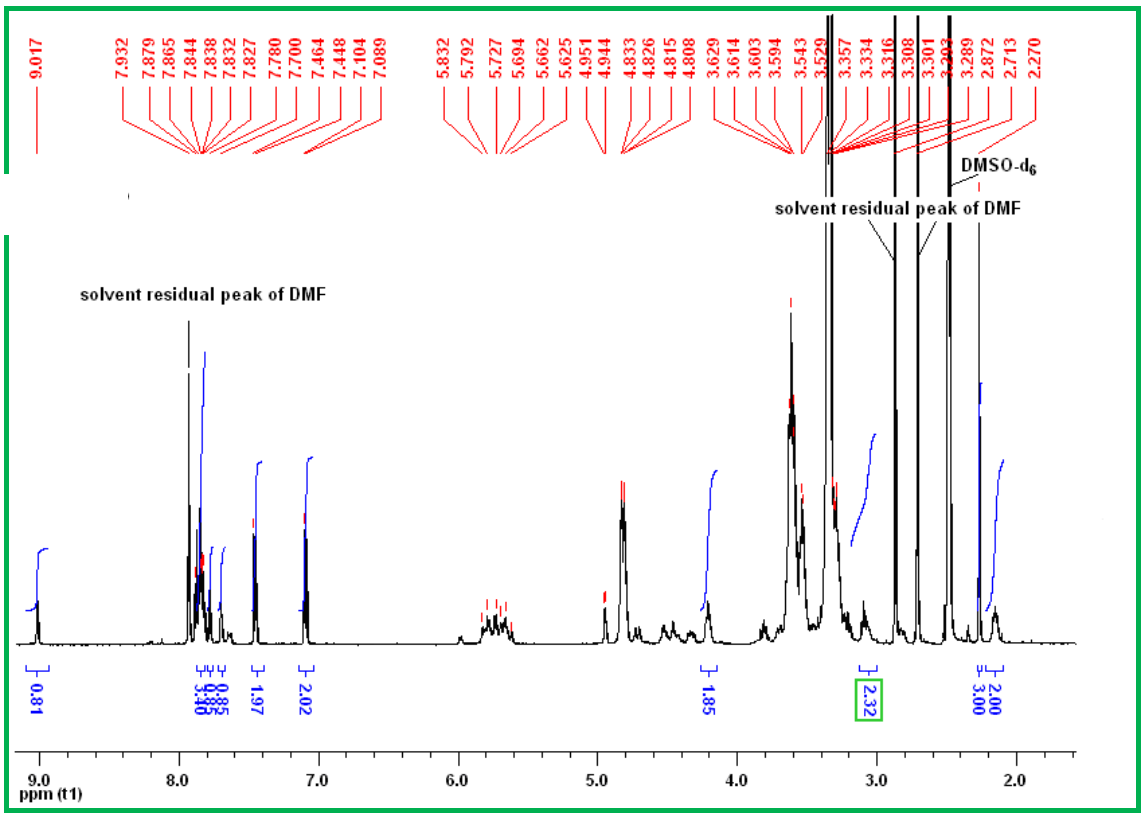
Mono-6^A-[2-(3-imidazolethyl)-ammonium]-6^A-deoxy-β-cyclodextrin chloride (**10a**). Similar synthetic approach as for **5** and **7** afforded the title compound as a white solid (82%): ^{1}H NMR (300 MHz, DMSO-$_{d6}$) δ 8.67 (s, 1H, =CH-2im), 8.28-8.24 (br, 2H, -NH_2), 7.60 (s, 1H, =CH-4im), 7.10 (s, 1H, =CH-5im), 8.02 (s, 2H), 7.94(s, 2H), 5.80-5.70 (m, 14H, OH-2 and OH-3), 4.96 (s, 1H, H-1), 4.83 (s, 6H, H-1), 4.51 (s br, 6H, OH-6), 4.14 (t, 2H, J = 6.6Hz, -CH_2); 4.03 (br, 1H, H-3'$_{CD}$), 3.64-3.36 (m, 27H, H-5$_{CD}$, H-3$_{CD}$ and H-6$_{CD}$), 3.36-3.26 (m, 14H, H-2$_{CD}$ and H-4$_{CD}$), 3.05 (t, 2H, J = 4.8Hz, -CH_2NH_2), 1.92 (t, 2H, J = 6.6Hz, J = 4.8 Hz, -CH_2).1399.4586; ESI-MS (m/z): calculated for [M^+] 1229.12, found 1228.86; Anal. Calcd for $C_{48}H_{80}ClO_{34}N_3$: C 45.09, H 6.31, N 3.29; found: C 45.89, H 6.32, N 3.26.

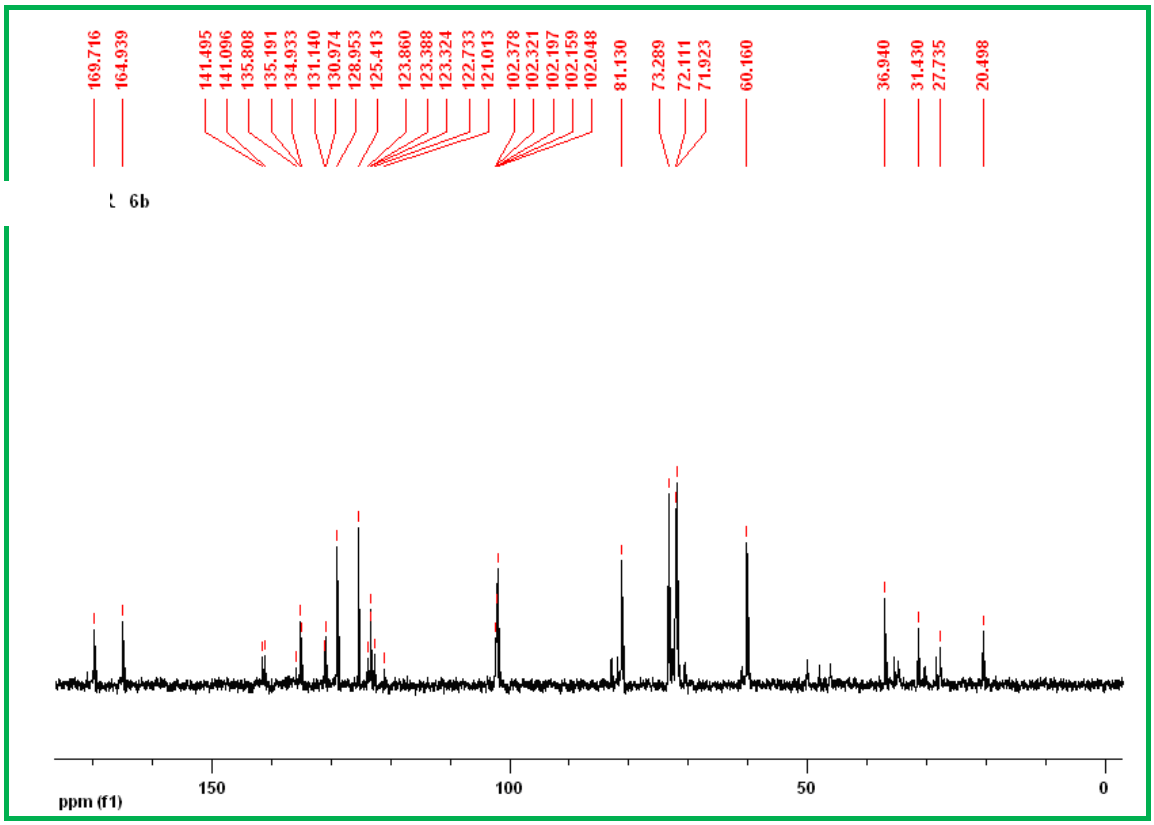
3. ^{1}H and ^{13}C NMR spectra of Mono-6^{A}-[3-(3-(1,3-dioxoisoindolin-2-yl)ethyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextr-in tosylate **5a**



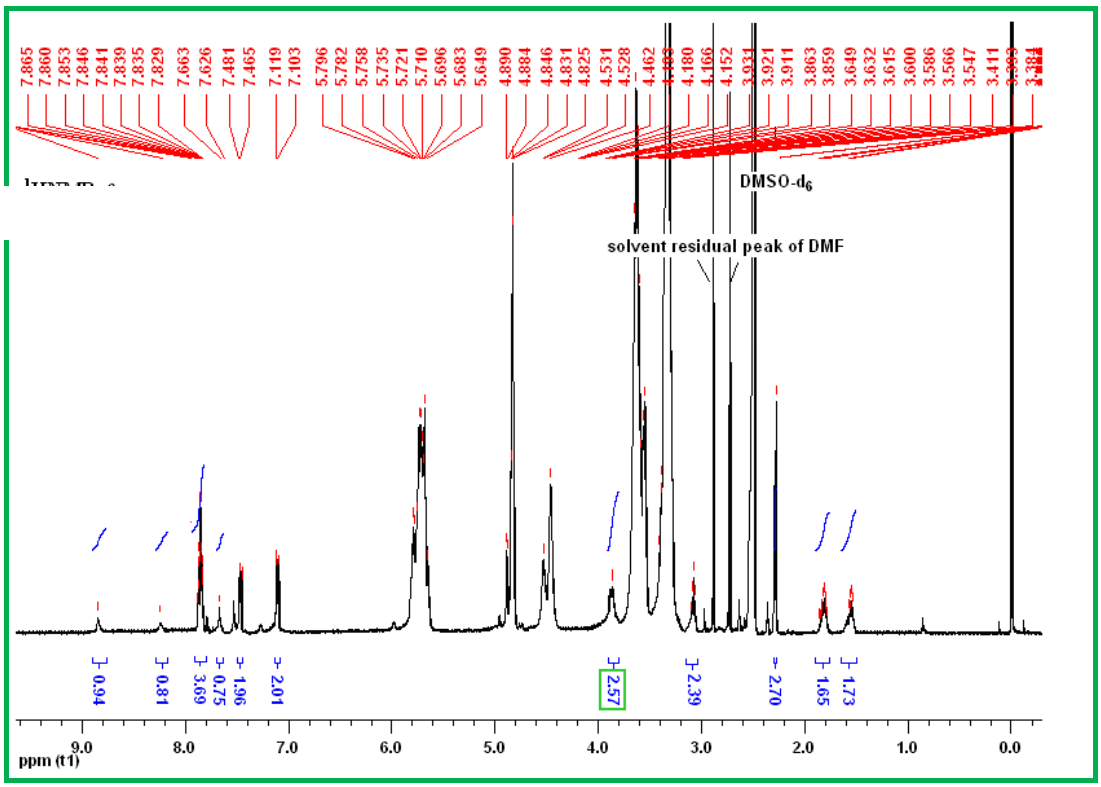


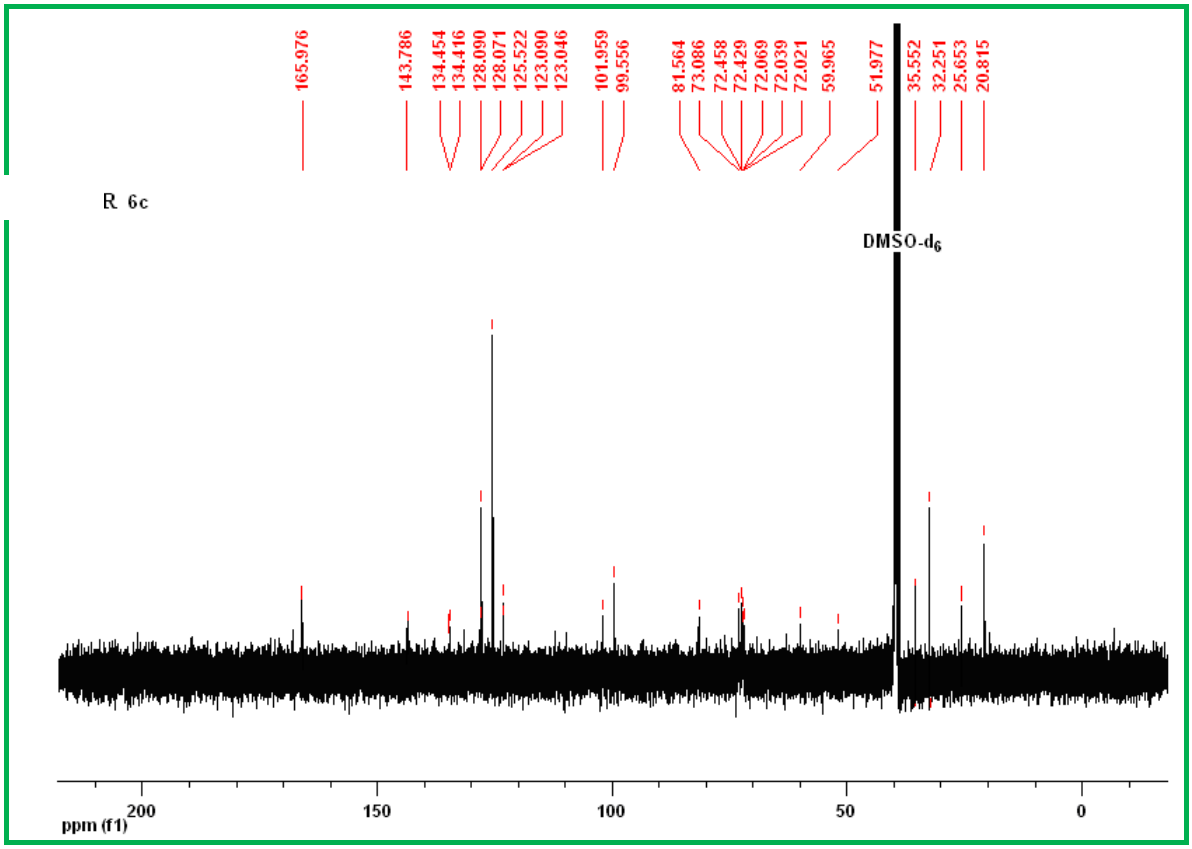
4. Mono-6^{A}-[3-(3-(1,3-dioxoisoindolin-2-yl)propyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodex-trin tosylate **5b**



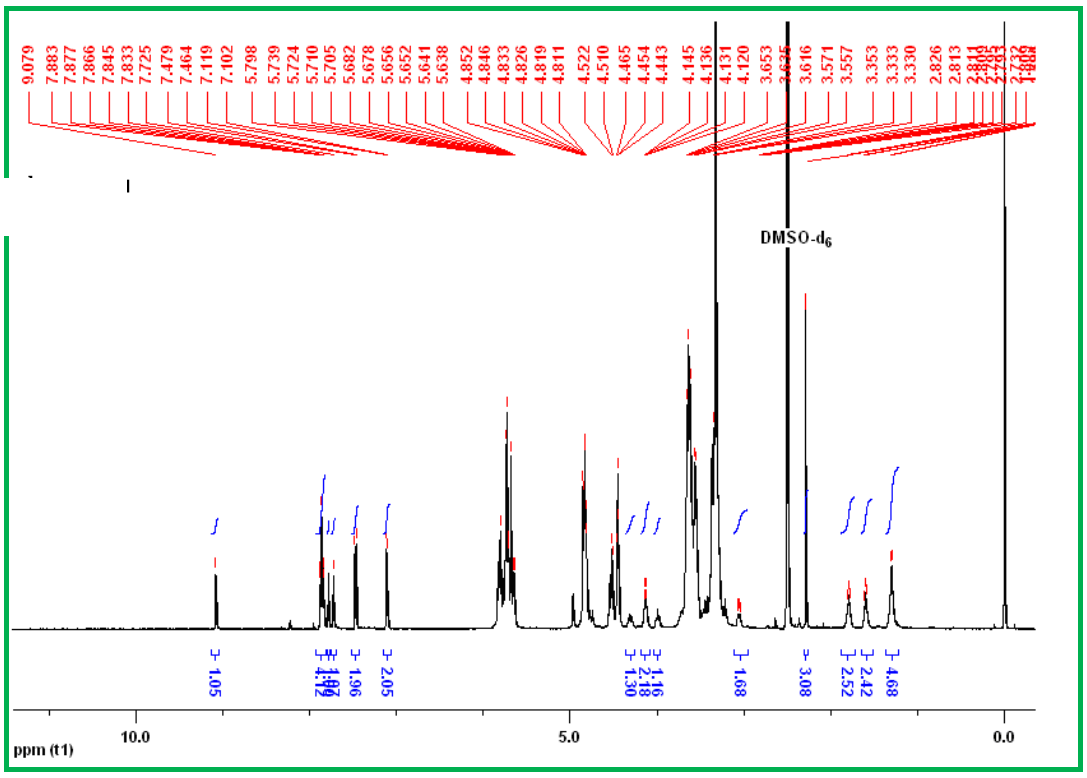


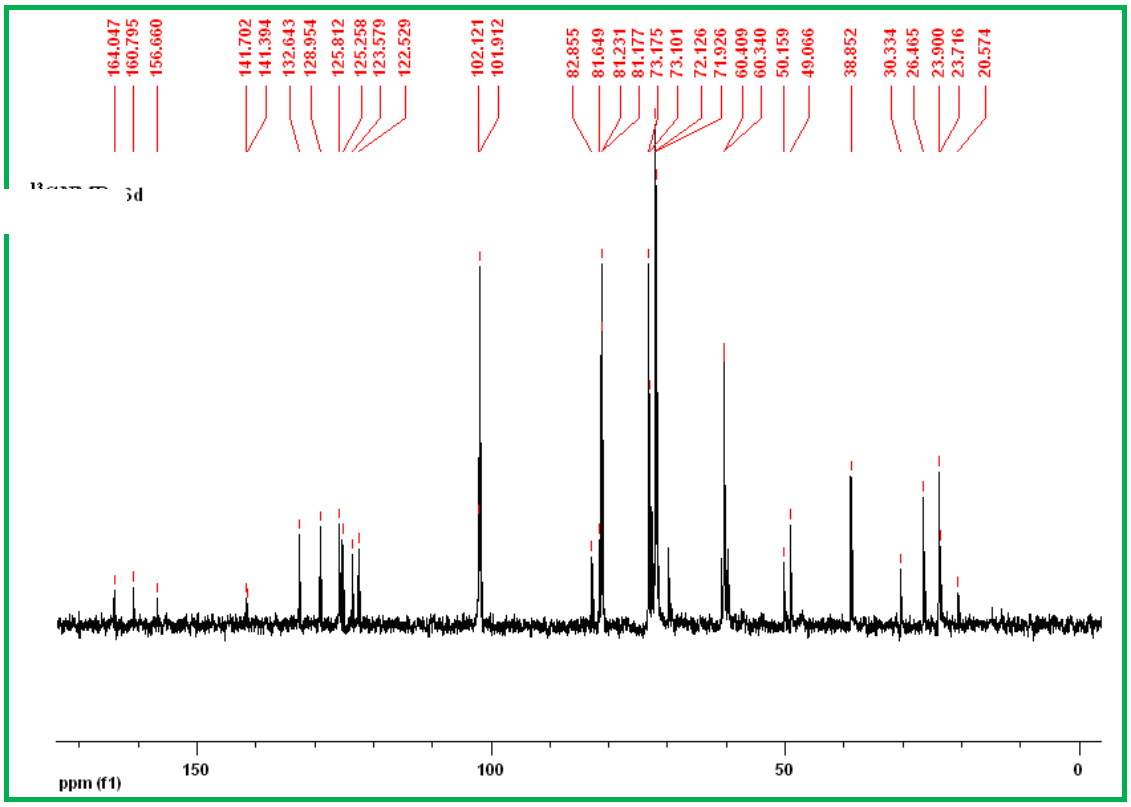
5. Mono-6^{A}-[3-(4-(1,3-dioxoisoindolin-2-yl)butyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate **5c**



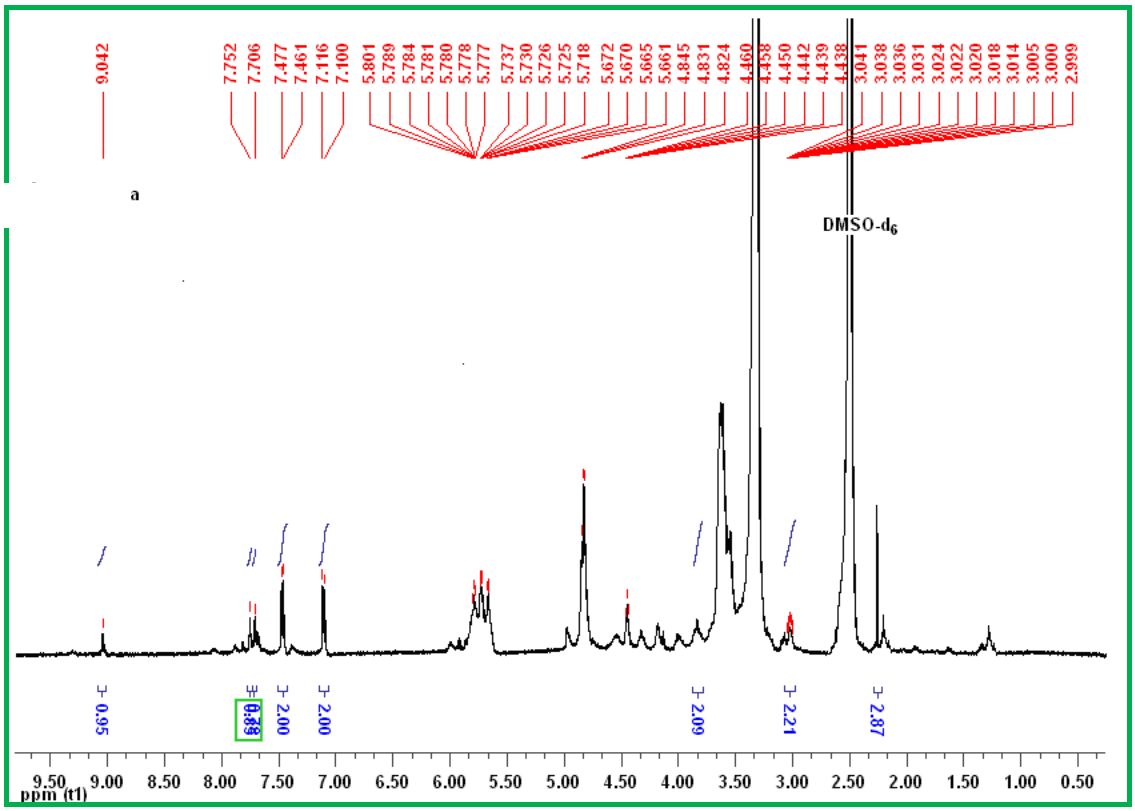


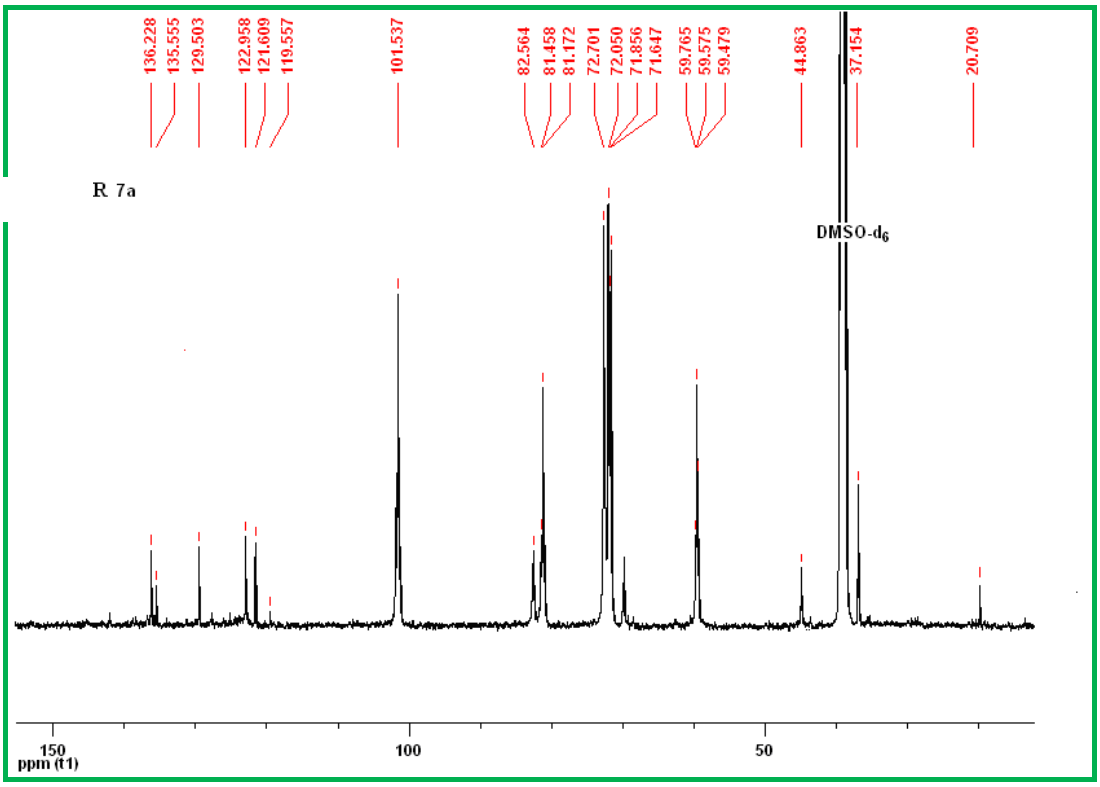
6. Mono-6^{A}-[3-(6-(1,3-dioxoisoindolin-2-yl)hexyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextr-in tosylate **5d**



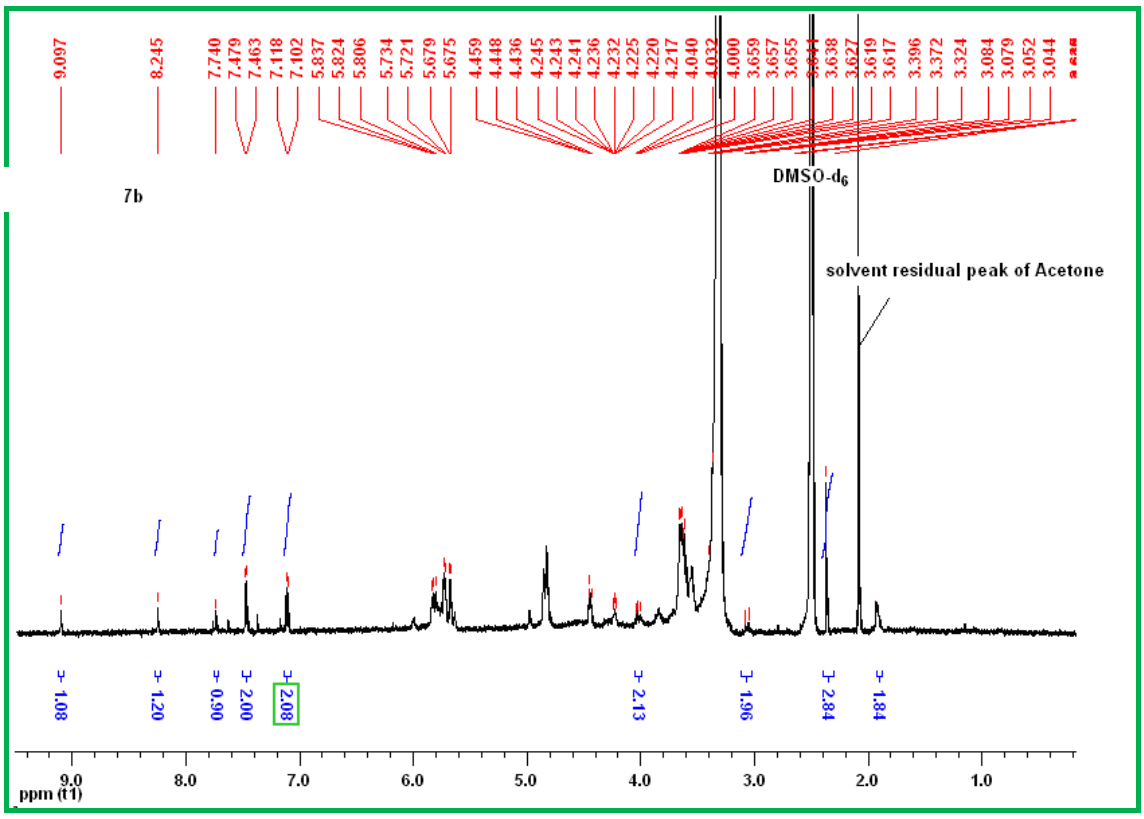


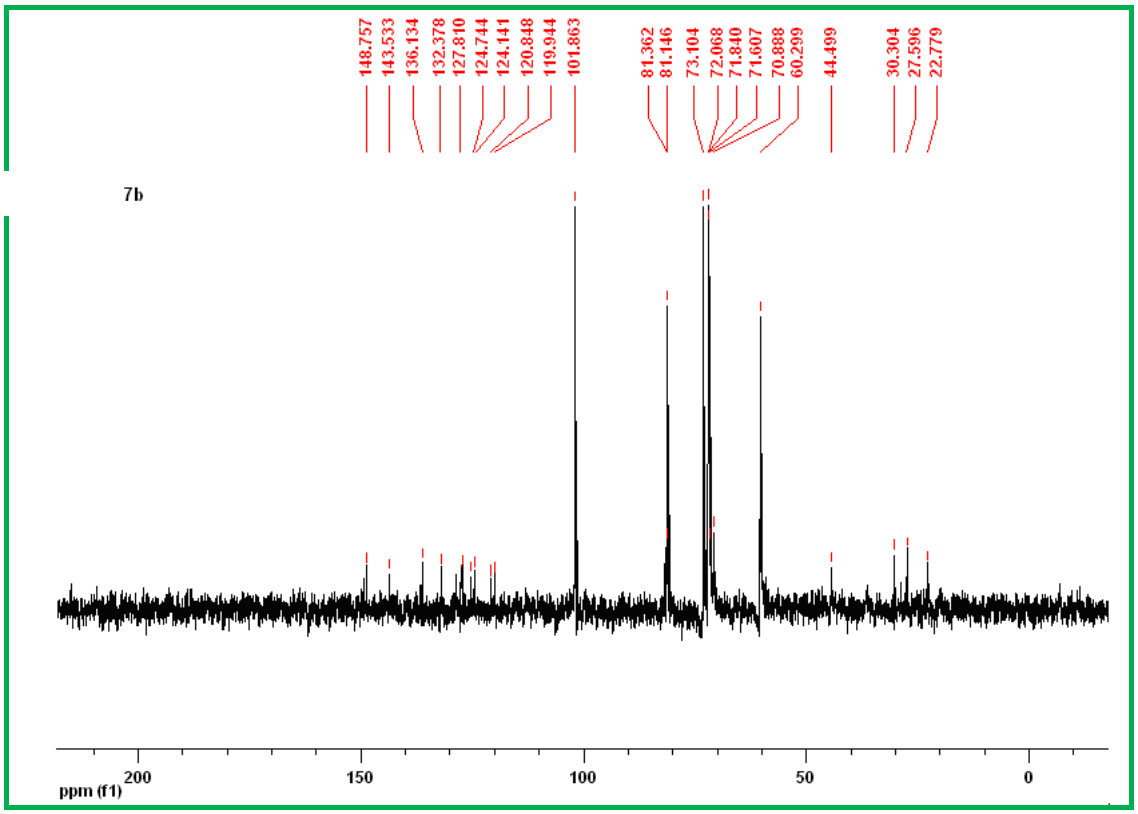
7. Mono-6^{A}-[3-(2-aminoethyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6a**



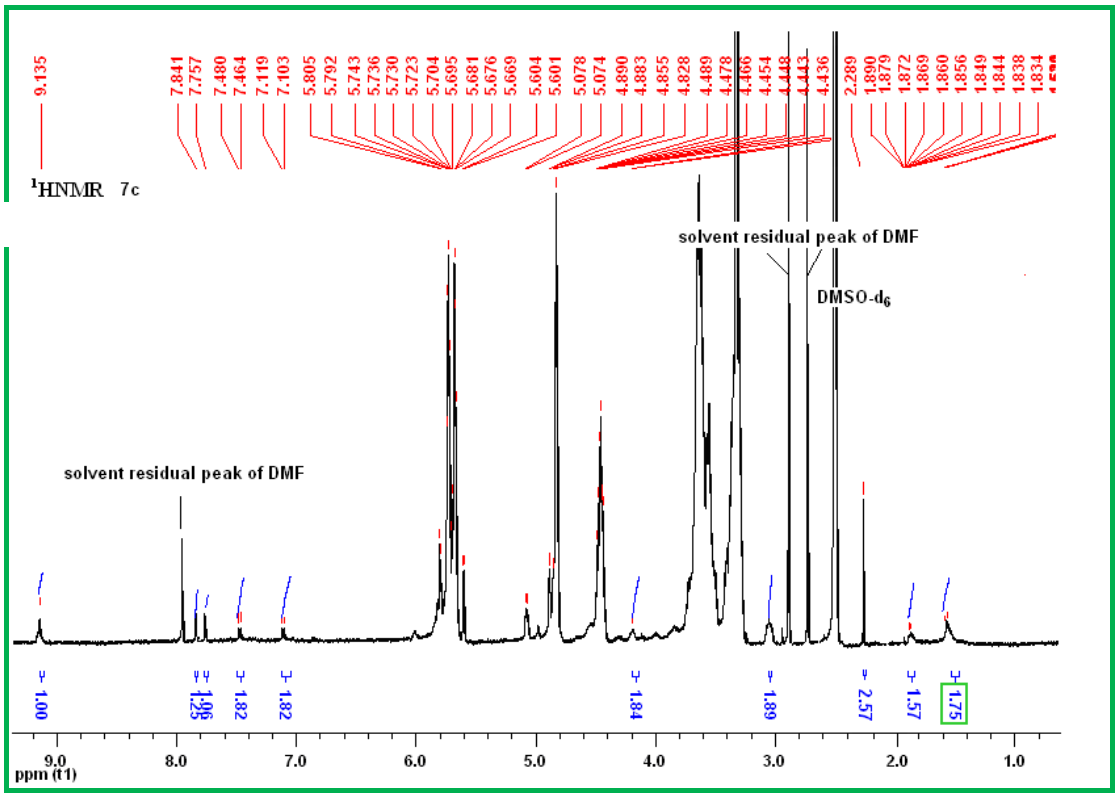


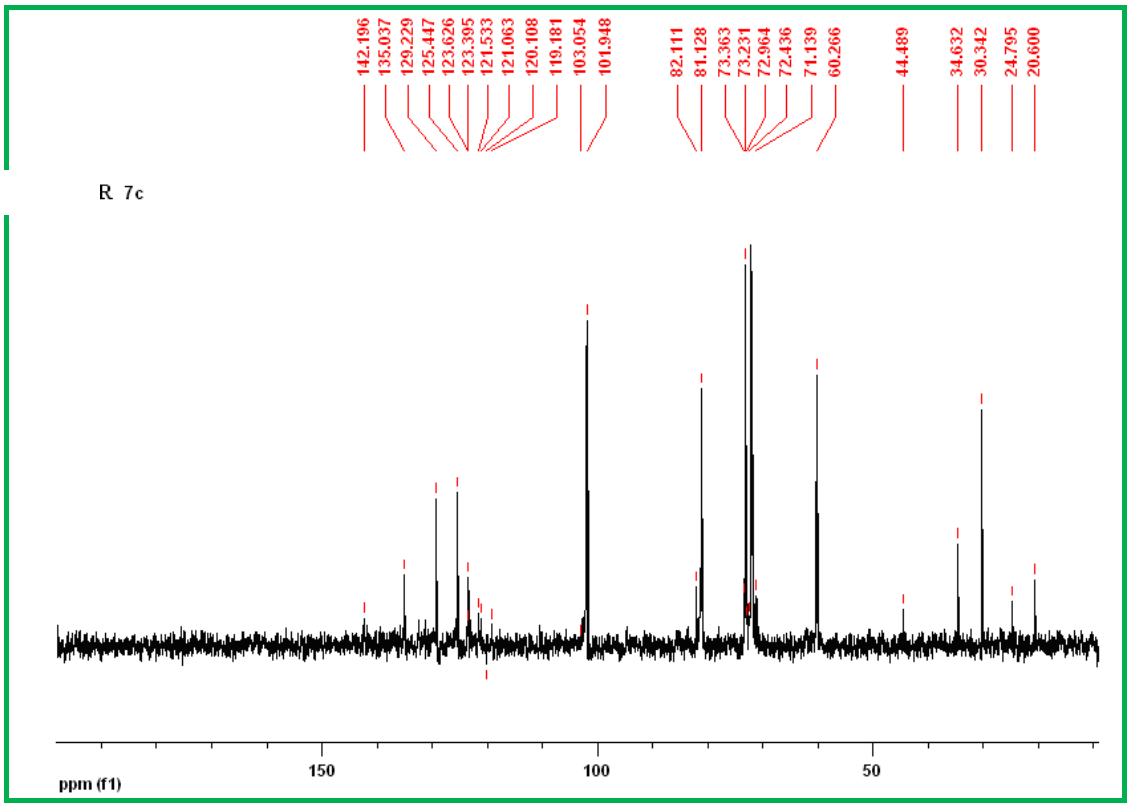
8. Mono-6^{A}-[3-(3-aminopropyl)-imidazolium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6b**



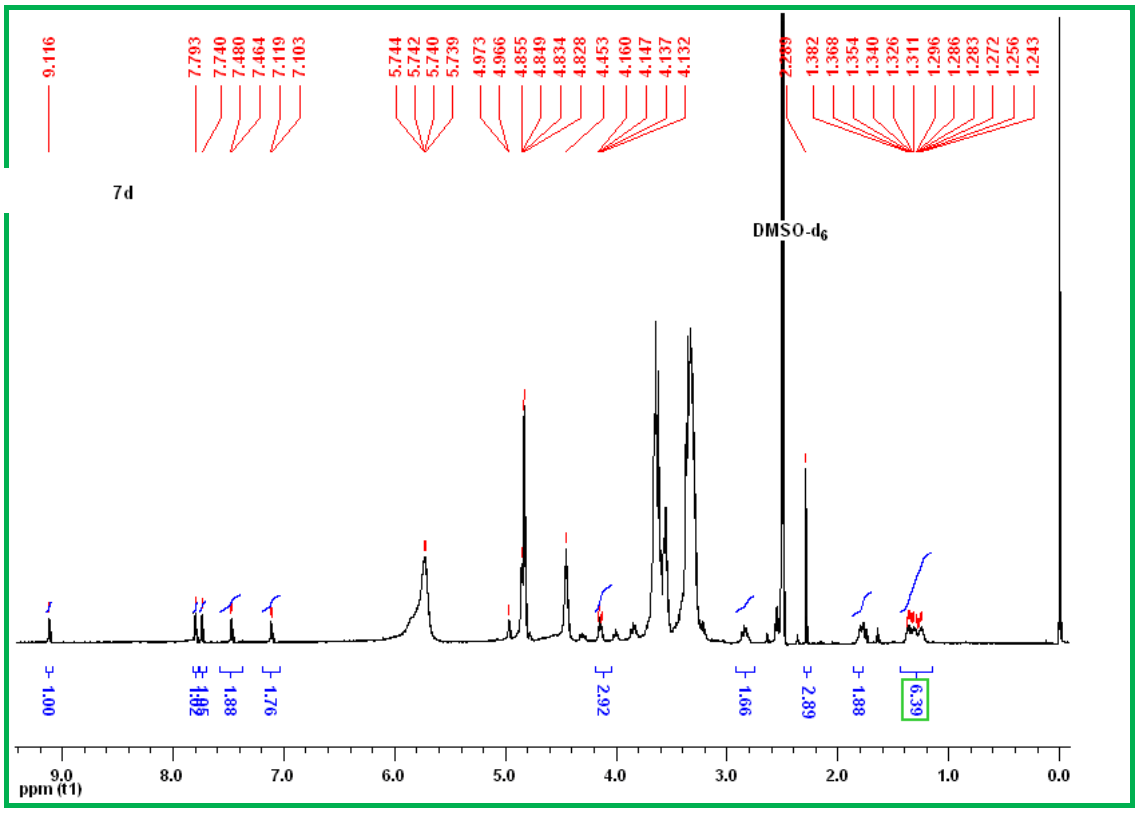


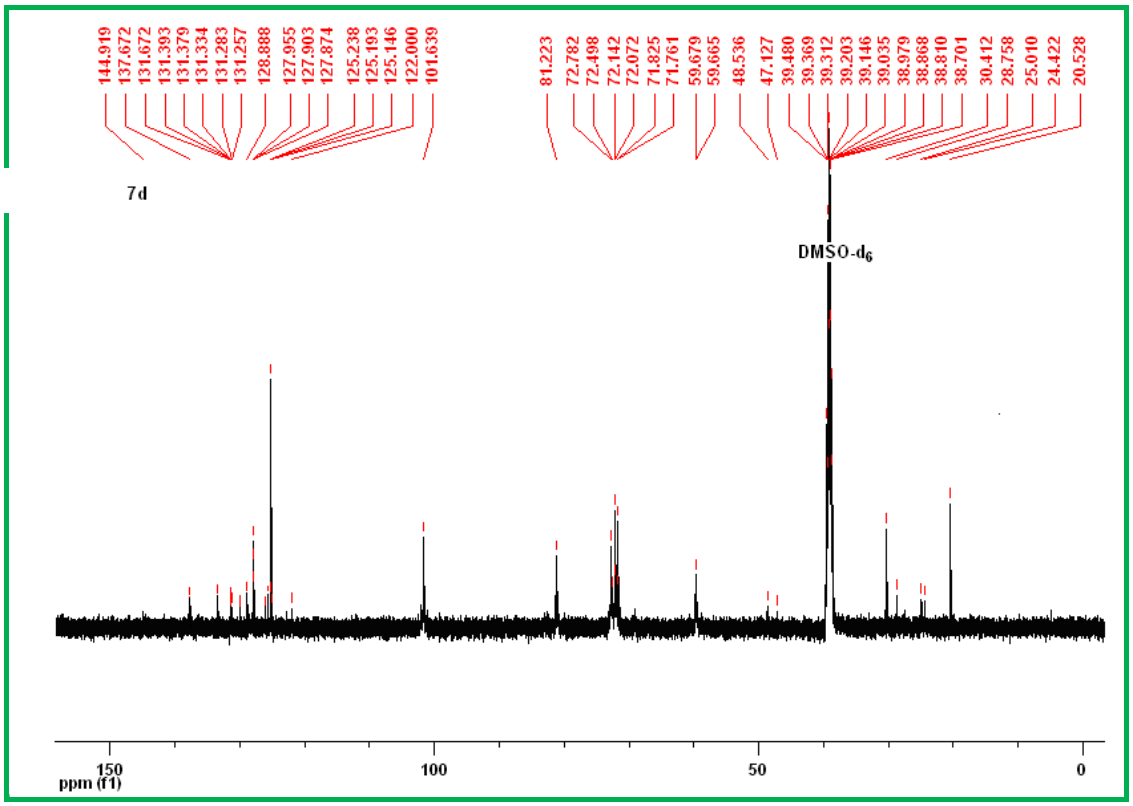
9. Mono-6^{A}-[3-(4-aminobutyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6c**



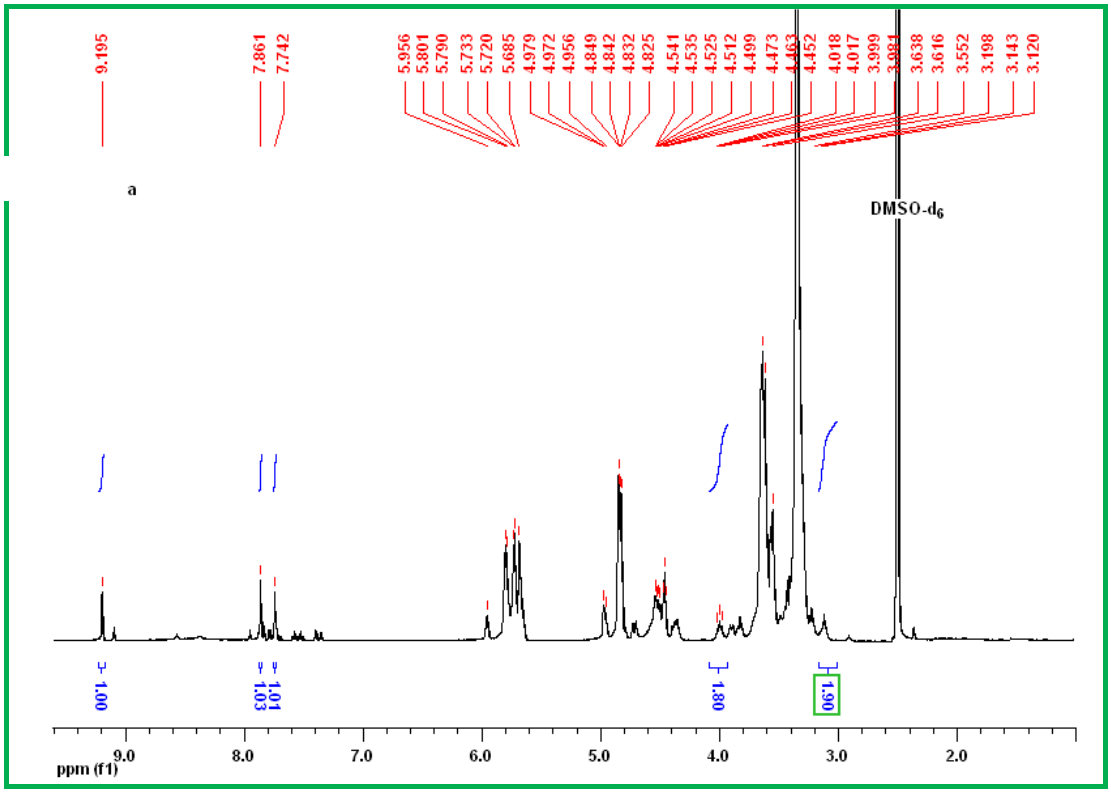


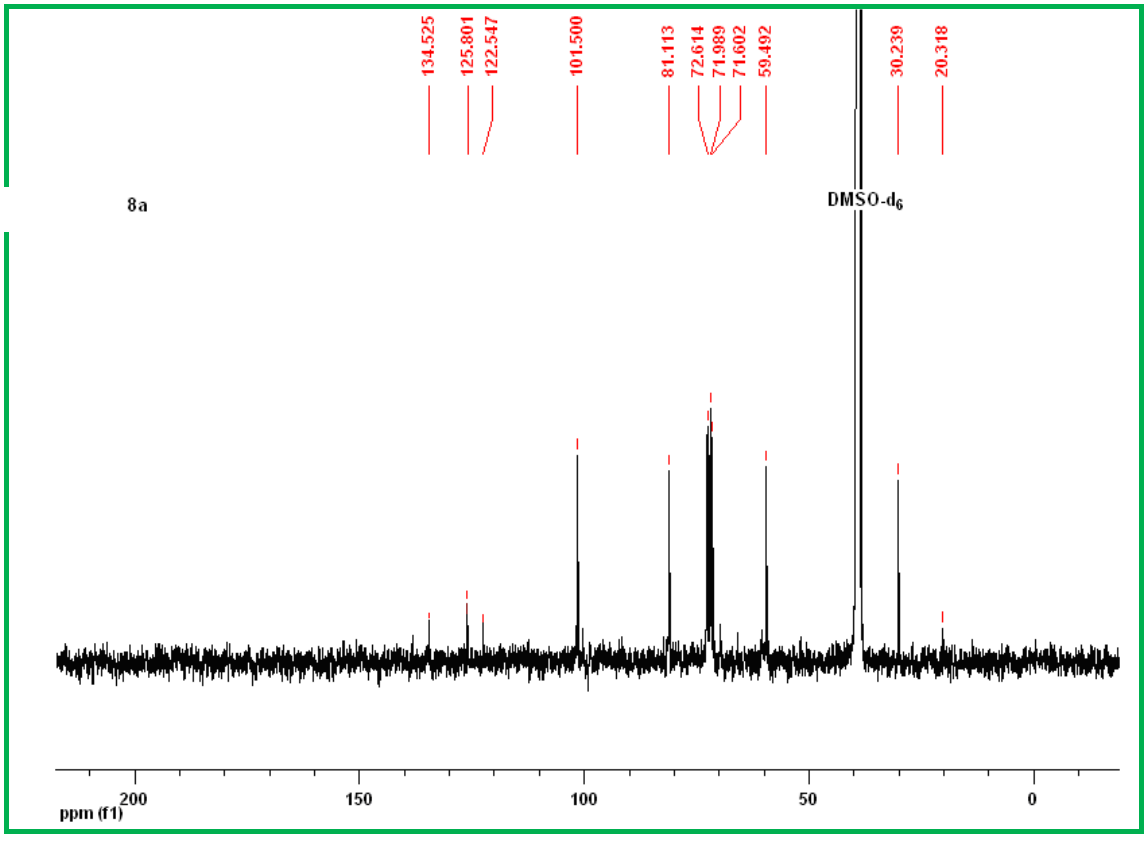
10. Mono-6^{A}-[3-(6-aminohexyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6d**



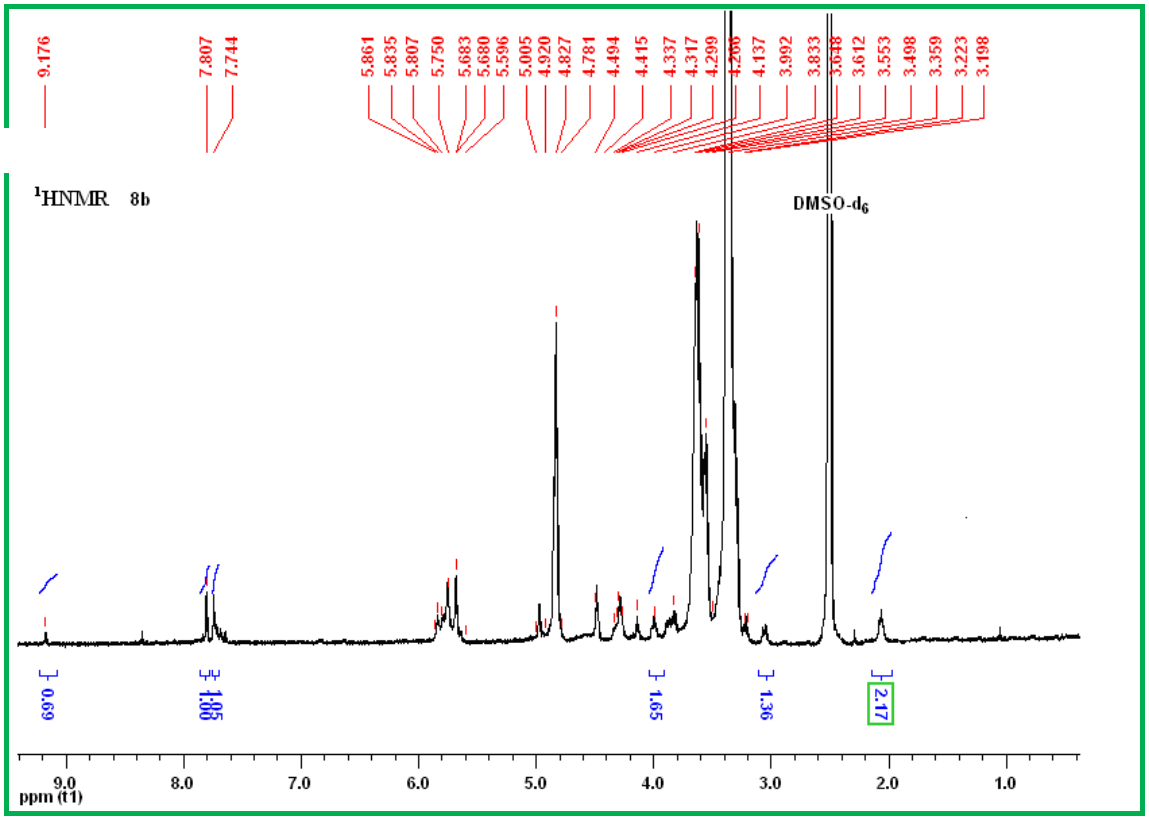


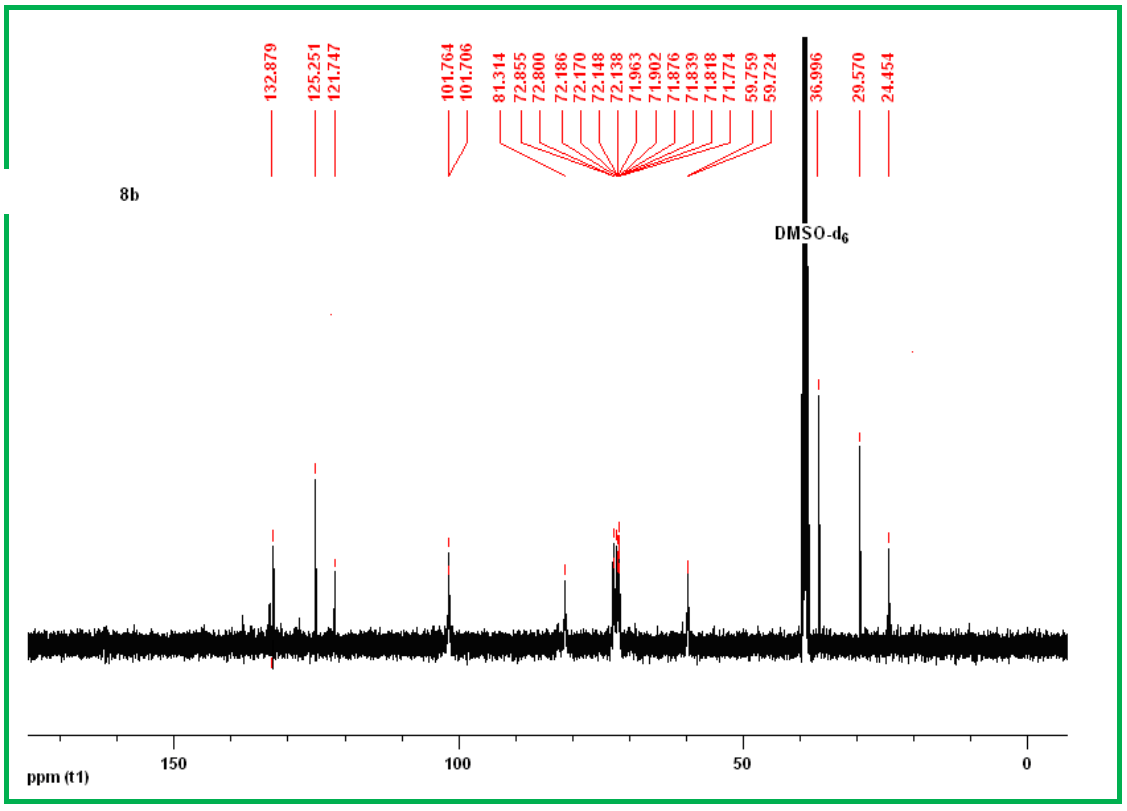
11. Mono-6^{A}-[3-(2-ammonioethyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7a**



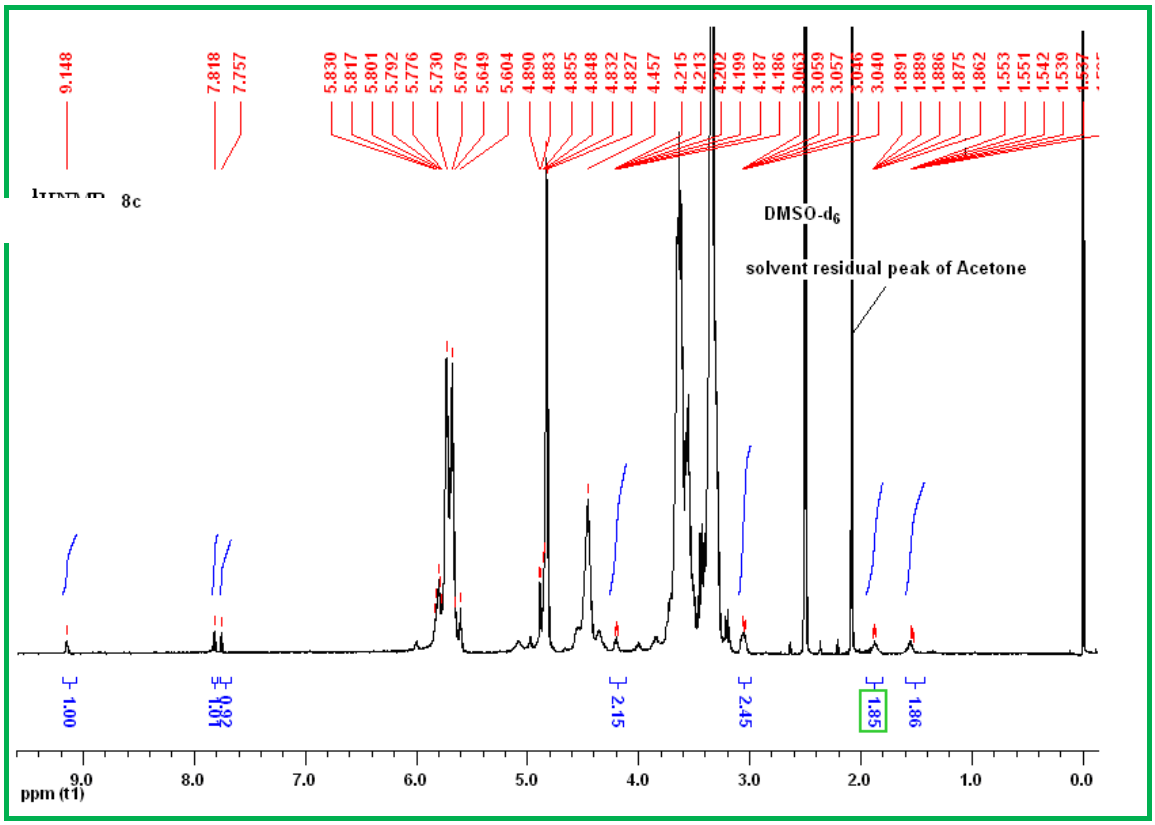


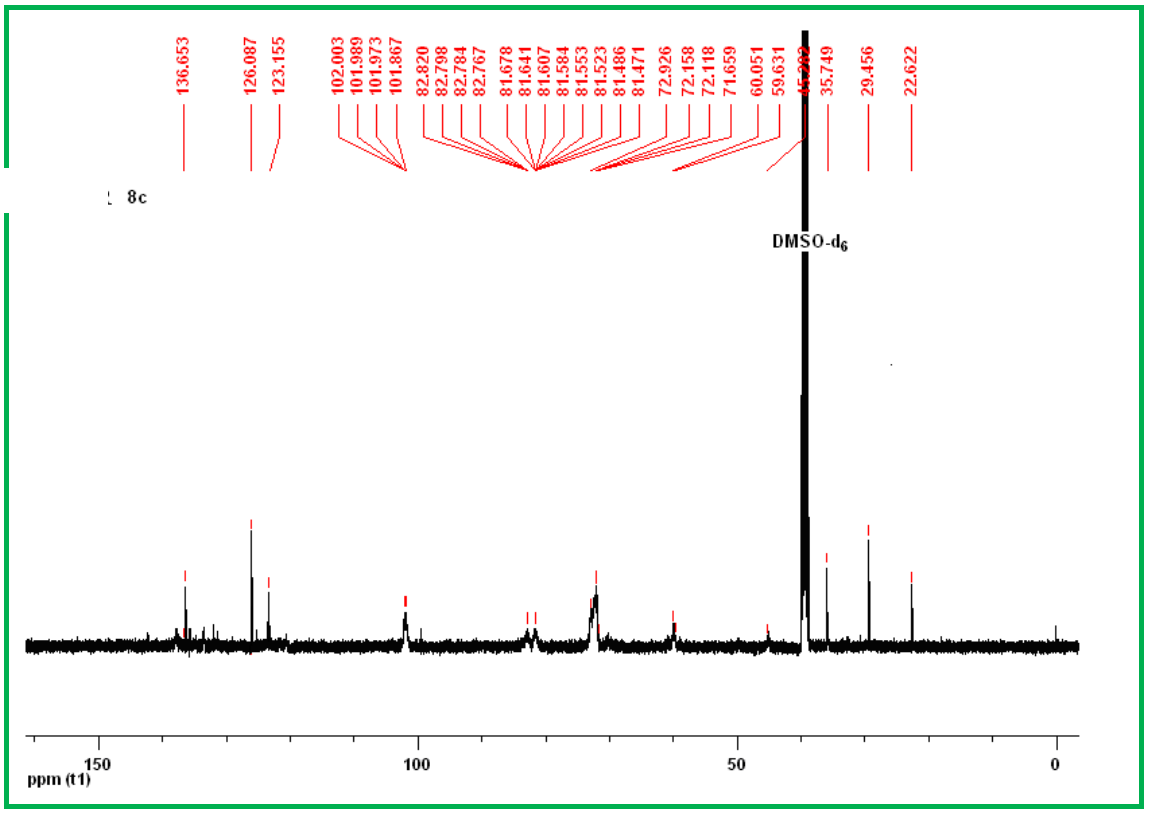
12. Mono-6^{A}-[3-(3-ammoniopropyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7b**



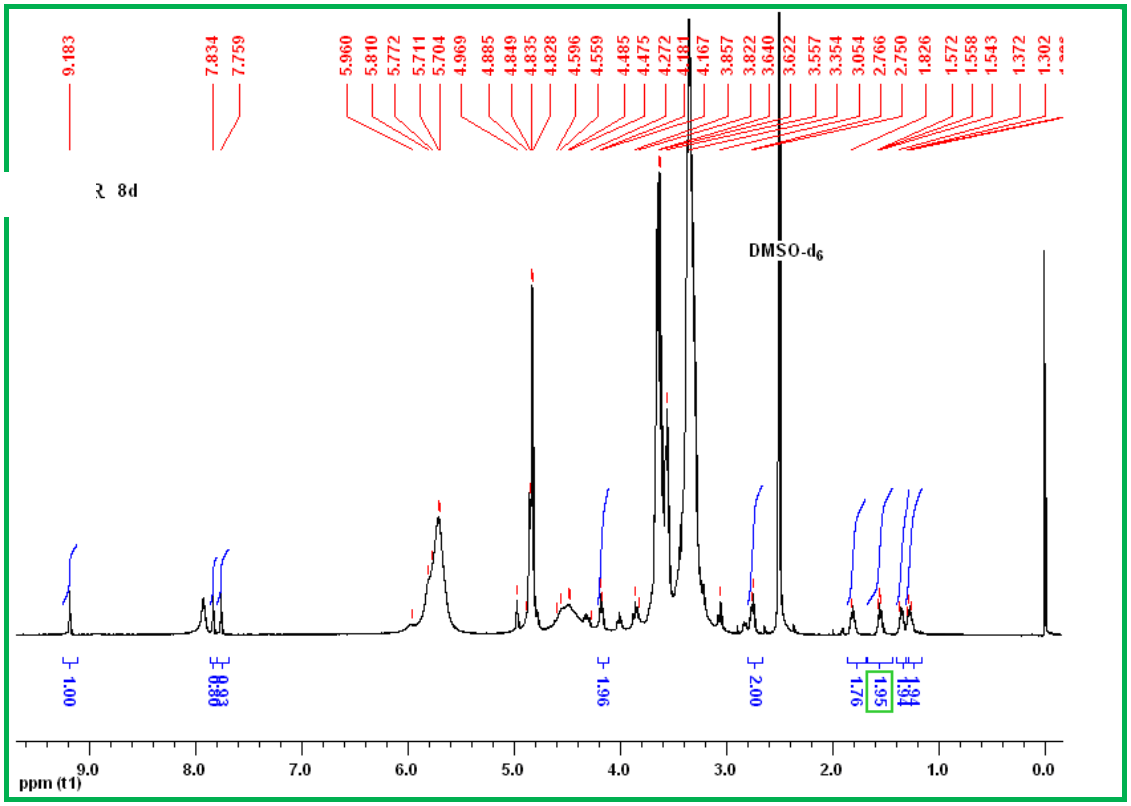


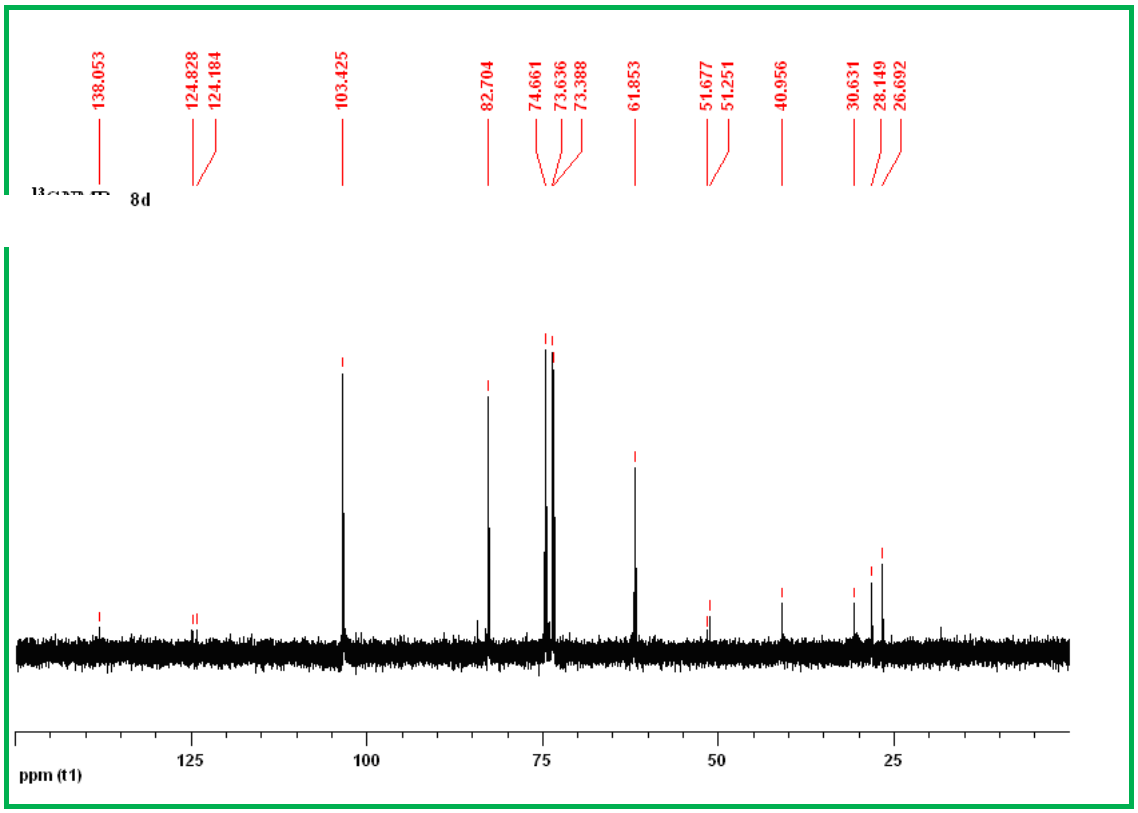
13. Mono-6^{A}-[3-(4-ammoniobutyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7c**





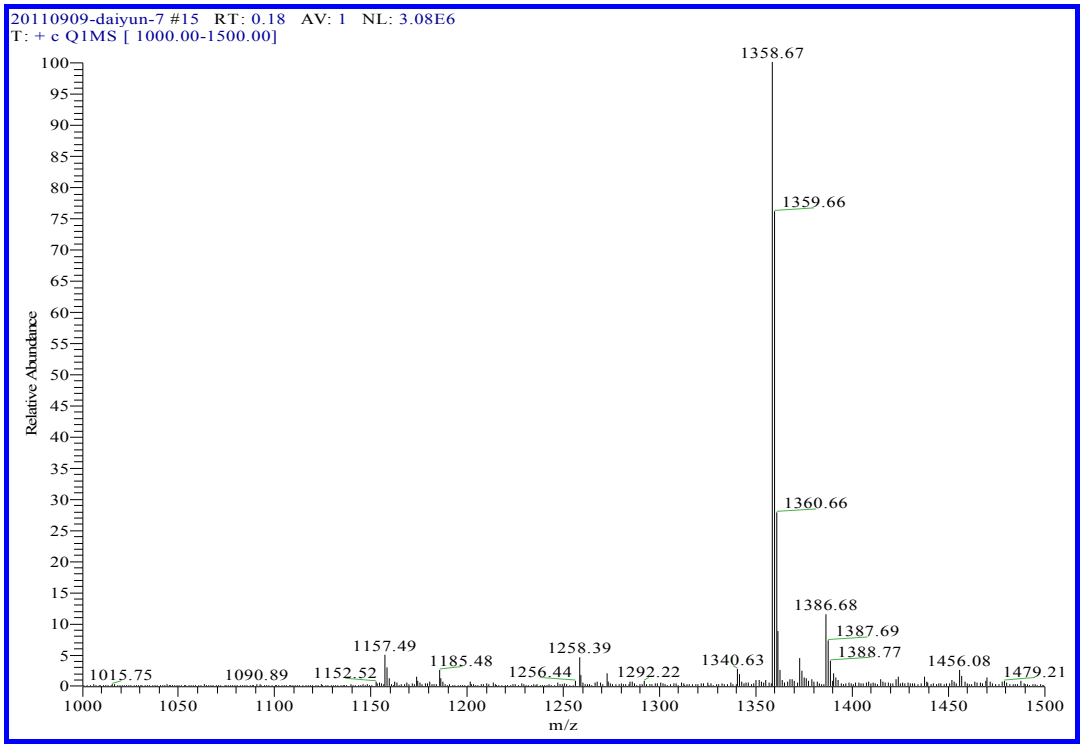
14. Mono-6^{A}-[3-(6-ammoniohexyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7d**



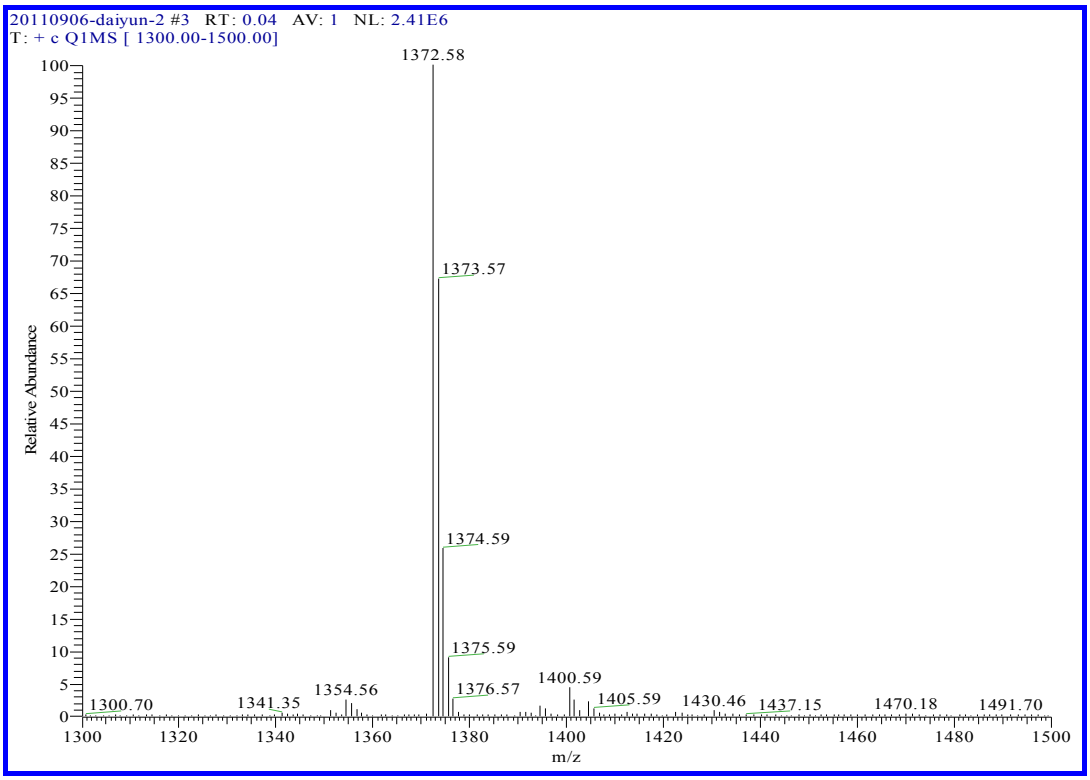


15. ESI-MS spectra

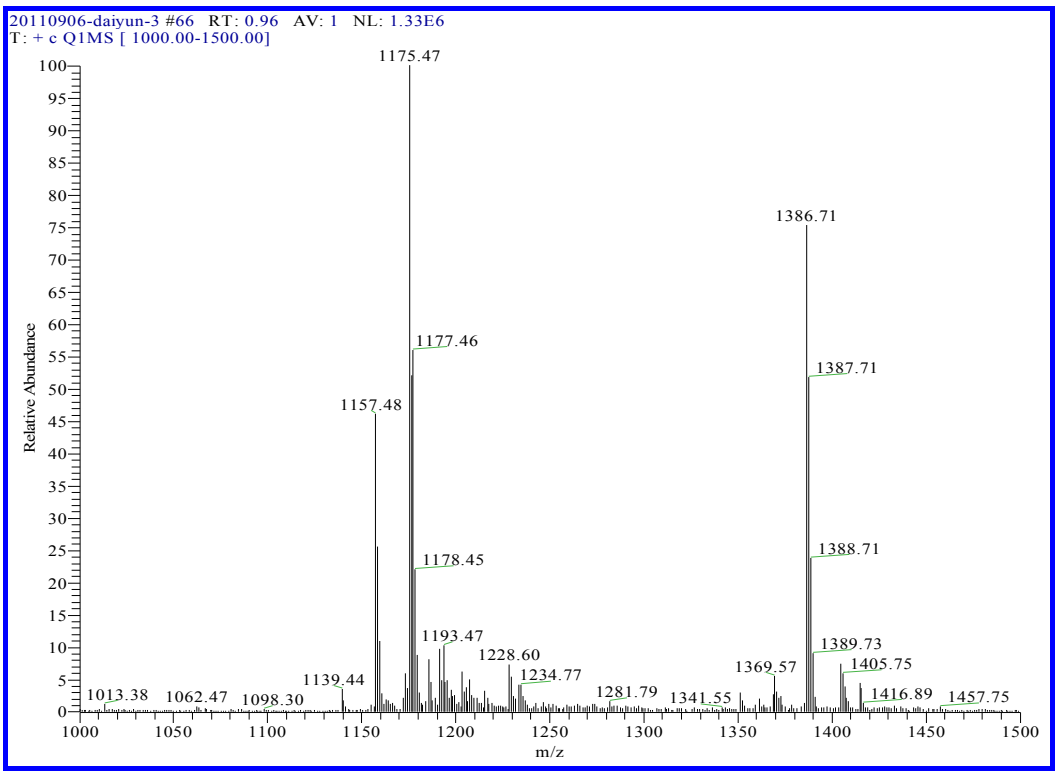
Mono-6^{A}-[3-(2-(1,3-dioxoisoindolin-2-yl)ethyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **5a**



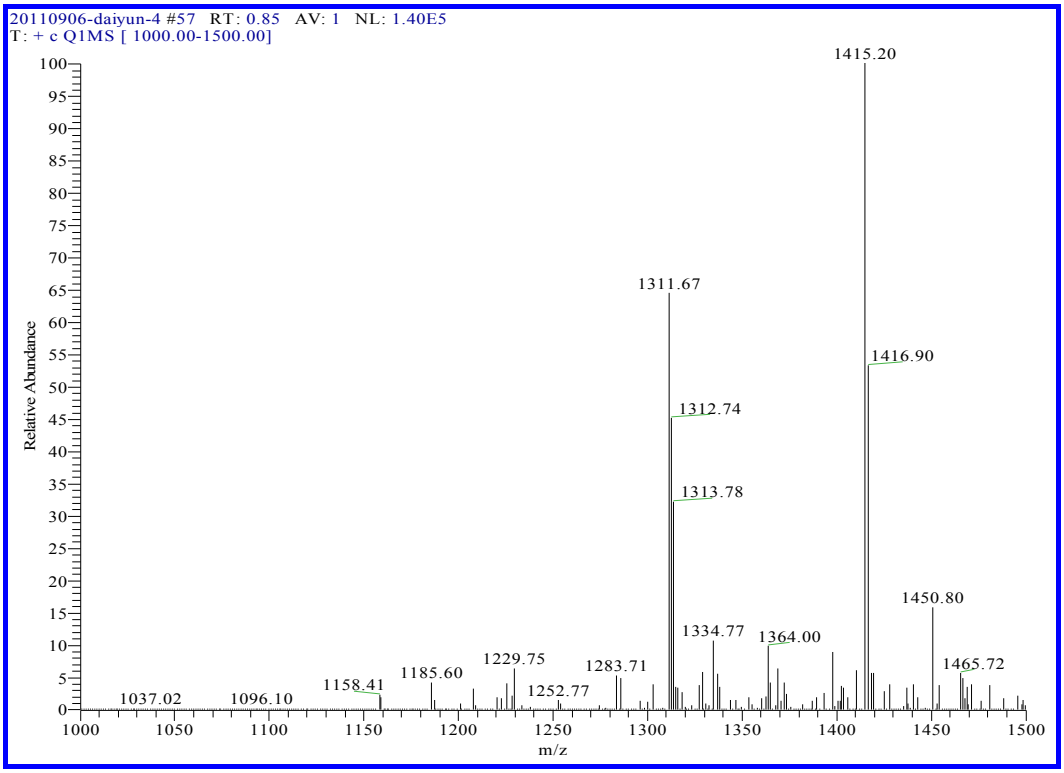
Mono-6^{A}-[3-(3-(1,3-dioxoisoindolin-2-yl)propyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodext-rin tosylate, **5b**



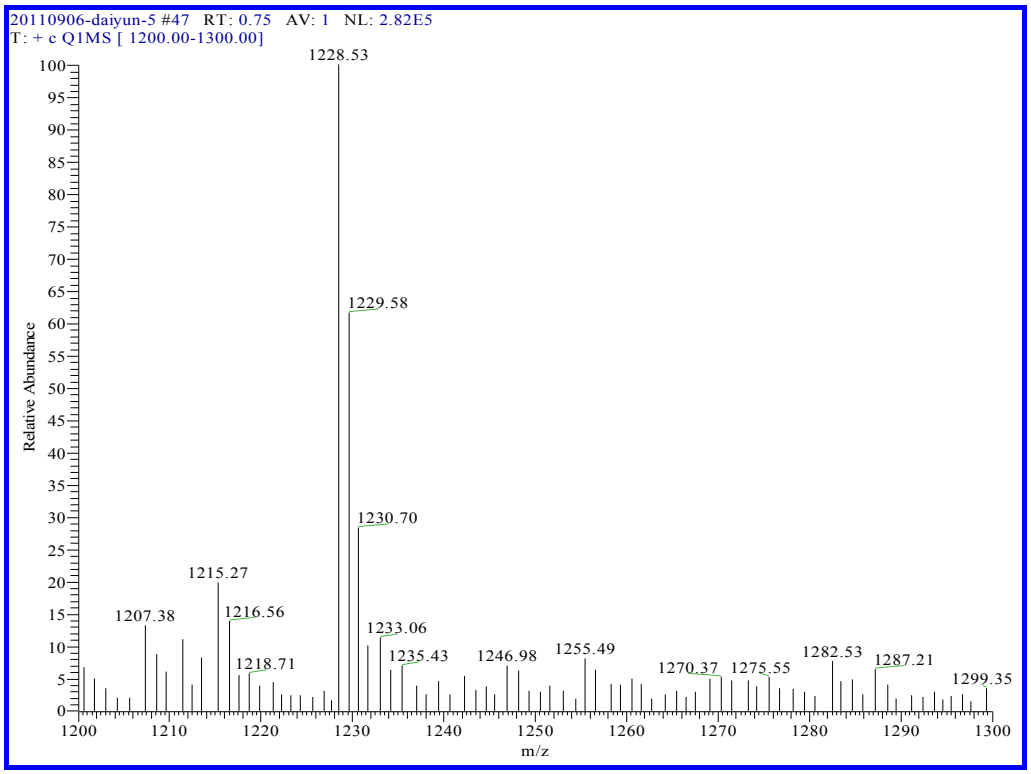
Mono-6^{A}-[3-(4-(1,3-dioxoisoindolin-2-yl)butyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextr-in tosylate, **5c**



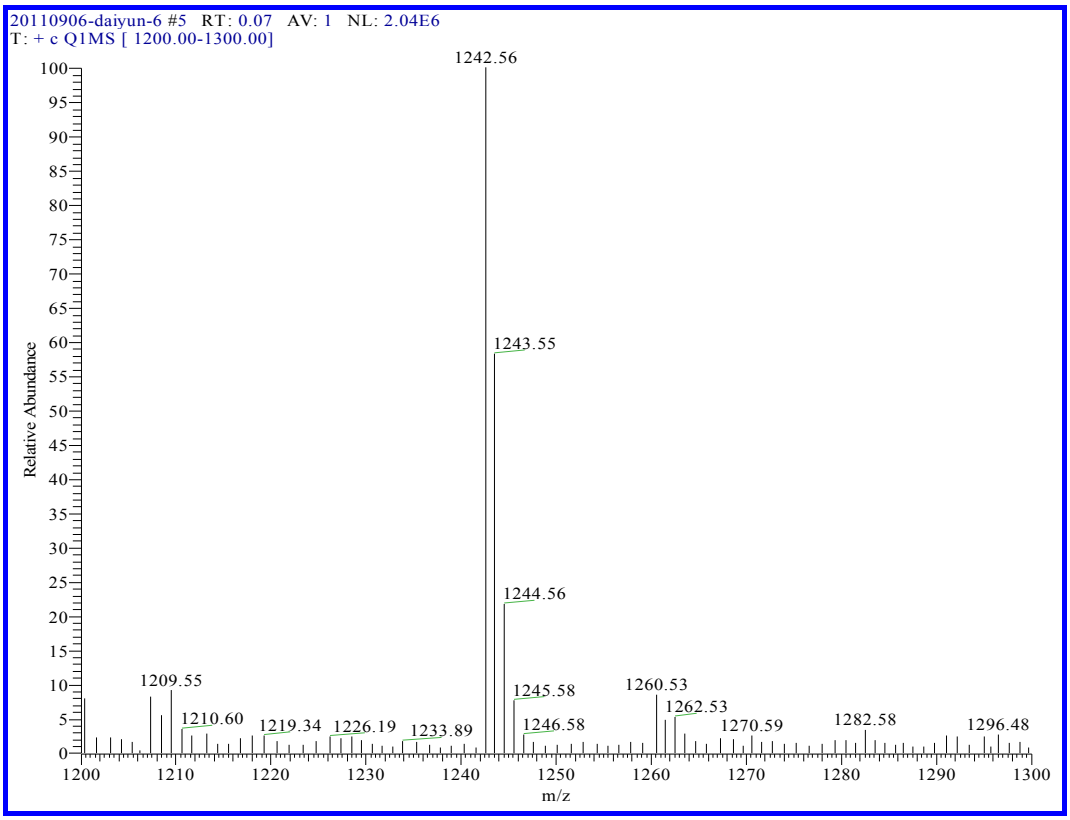
Mono-6^{A}-[3-(6-(1,3-dioxoisoindolin-2-yl)hexyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclod-extr in tosylate, **5d**



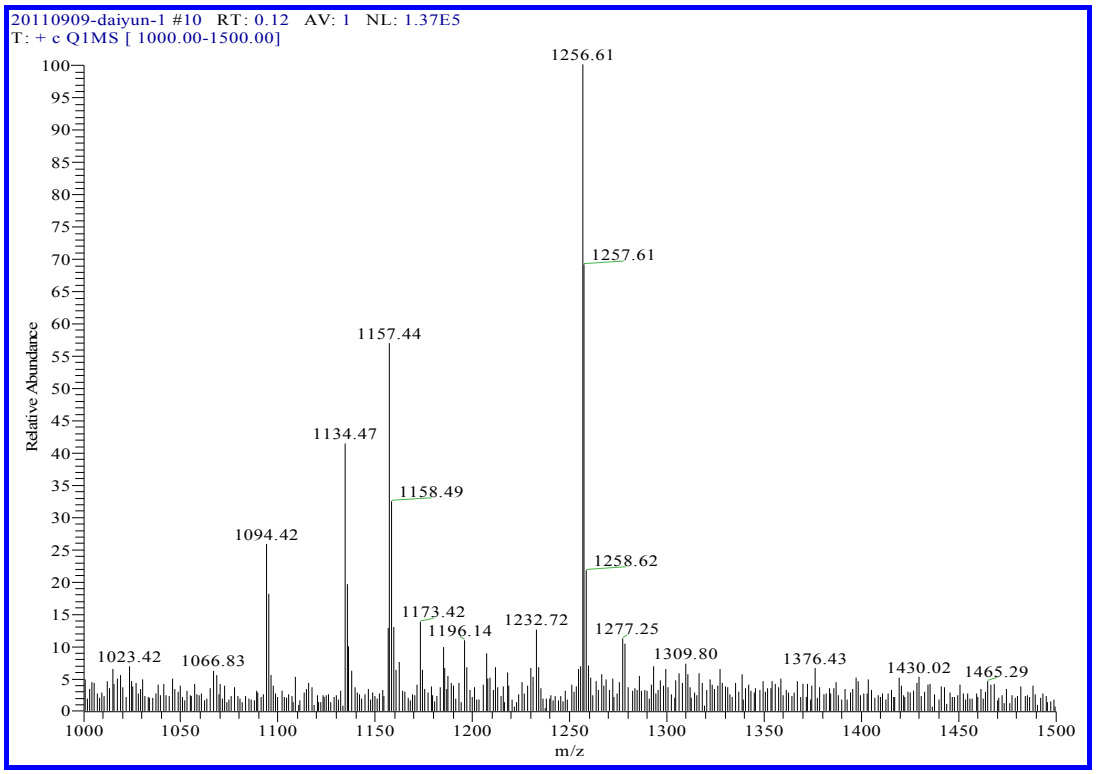
Mono-6^{A}-[3-(2-aminoethyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6a**



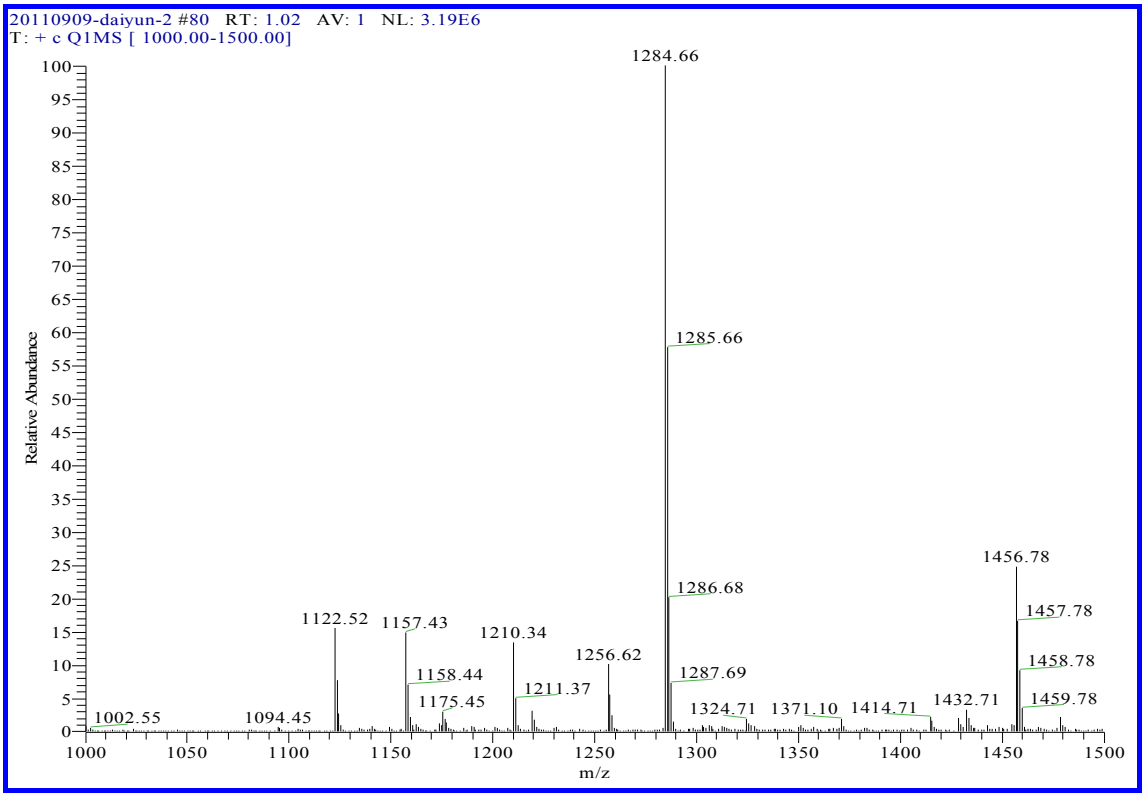
Mono-6^{A}-[3-(3-aminopropyl)-imidazolium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6b**



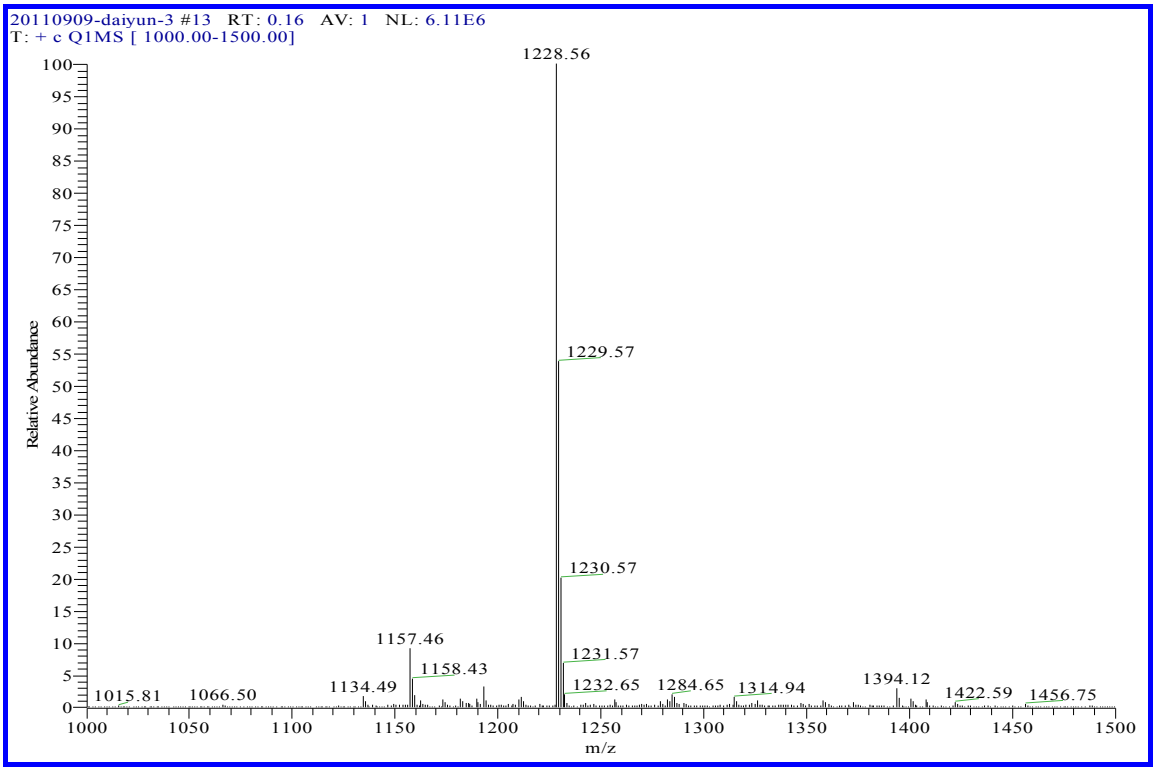
Mono-6^{A}-[3-(4-aminobutyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6c**



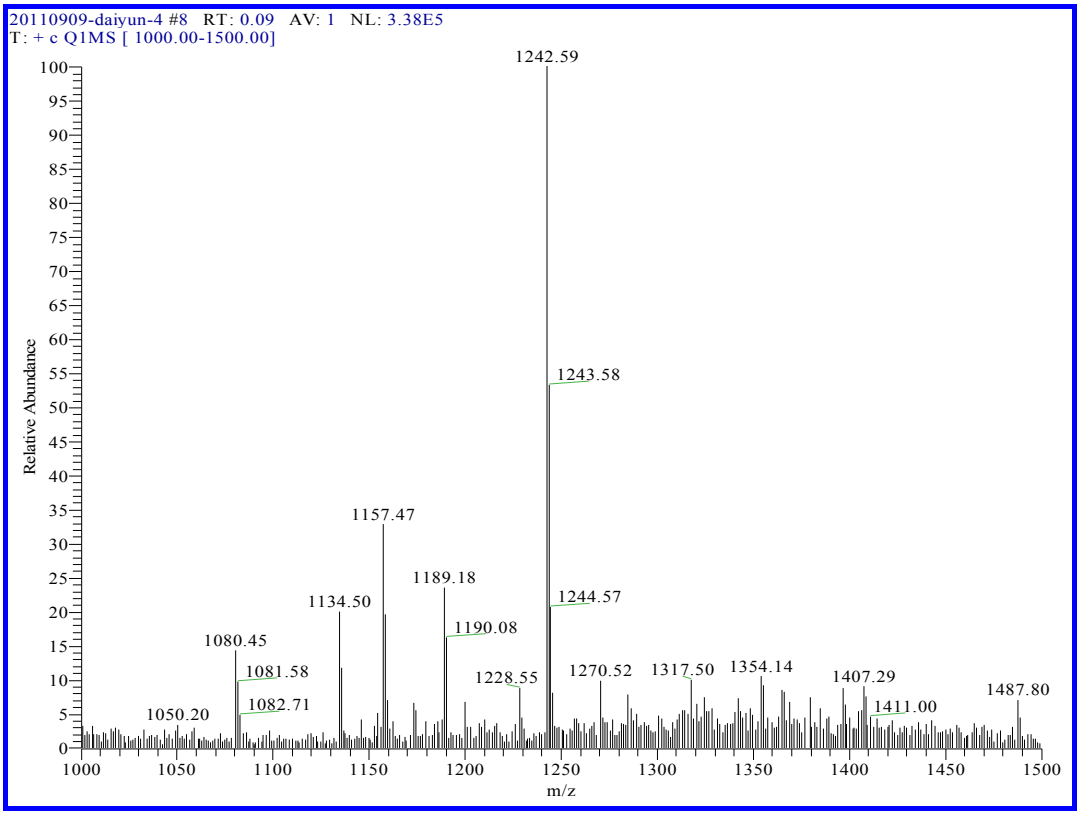
Mono-6^{A}-[3-(6-aminohexyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin tosylate, **6d**



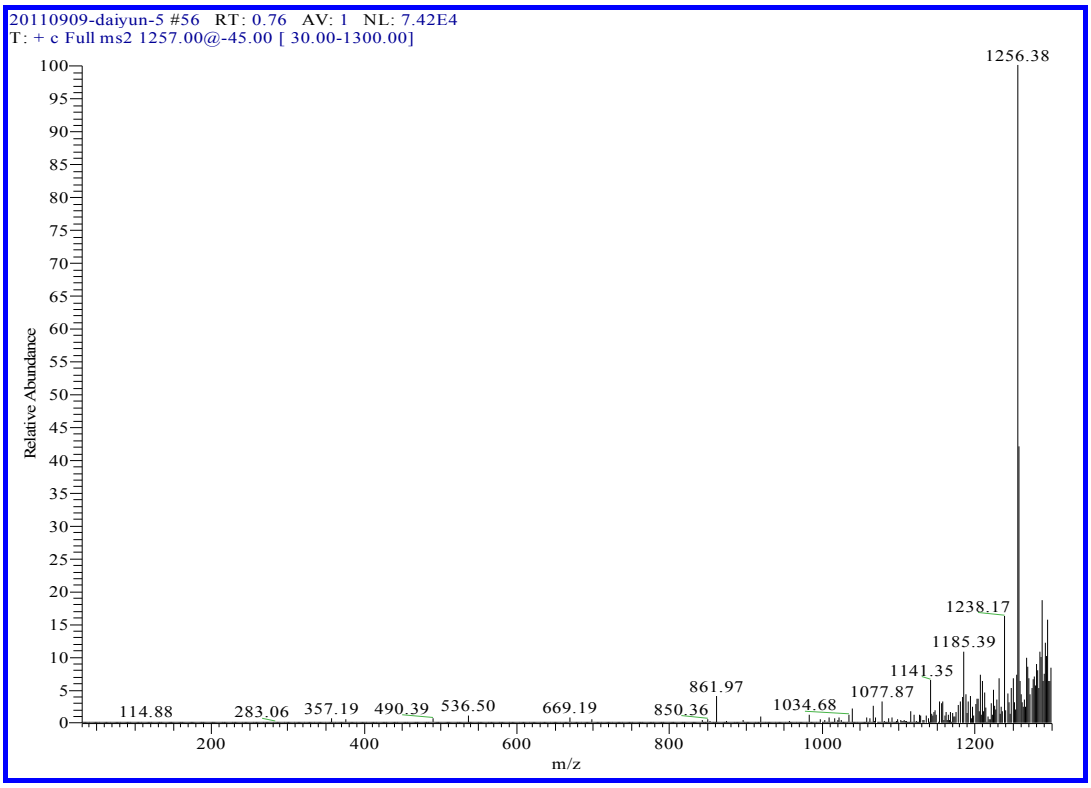
Mono-6^{A}-[3-(2-ammonioethyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7a**



Mono-6^{A}-[3-(3-ammoniopropyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7b**



Mono-6^{A}-[3-(4-ammoniobutyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7c**



Mono-6^{A}-[3-(6-ammoniohexyl)-imidazol-1-ium]-6^{A}-deoxy-β-cyclodextrin chloride, **7d**