Electronic Supplementary Material (ESI) for Chemical Communications

Exploiting Adamantane as a Versatile Organic Tecton: Multicomponent Catalytic Cascade Reactions.

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General technical data.

Thin layer chromatography (TLC) was carried out on a pre-coated aluminium plates with silica gel 60 F254 (Merck), and was visualised using ultraviolet light and/or aqueous $KMnO_4/I_2$. Flash column chromatography employed silica gel 60 (Merck, 230-400mesh). Meting points were determined on a Reichert hot-stage microscope and are uncorrected. Optical rotations were calculated using Polartronic H 532 (Schmidt + Haensch) instrument. Infrared spectra were recorded using a Perkin-Elmer Spectrum FT-IR spectrometer either as a thin film on sodium chloride discs or as a solid using golden gate apparatus. Proton nuclear magnetic resonance spectra were recorded at 500 and 300MHz on a Bruker DRX500 and DPX300 instruments, respectively. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane (δ = 0.00) and coupling constants are given in hertz (Hz). The following abbreviations are used: s = singlet, br = broad, d = doublet, dd = doublet of doublets, ddd = doublet of double doublets, dt = doublet of triplets, m = multiplet, t = triplet, td = triplet of doublets. ^{13}C-NMR spectra were recorded at 75 MHz on a Bruker DPX300 instrument and chemical shifts are reported in parts per million (ppm). Mass spectral data were determined at 70 eV on a Micromass ZMD 2000 electrospray (ES) machine. Accurate masses were obtained using a Bruker Daltonics micrOTOF spectrometer. The m/z data mentioned in case of 9-component cascades are the result of two runs using the auto sampler technique and by injecting the sample directly to the machine using a syringe pump.

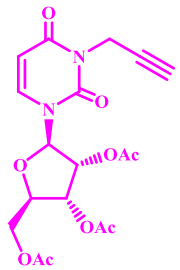
^{1}H-NMR peak assignments are mainly based on DEPT135, COSY, HMQC and HMBC spectral data.

All compounds were named according to the IUPAC system using the ACD/ILAB (ACD/IUPAC v.12.0 programme) web service (http:/www.acdlabs.com).

General Procedure A: N-propargylation.

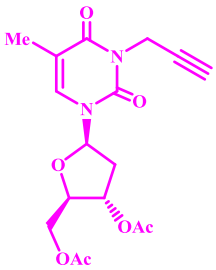
Propargyl bromide (80% solution in toluene, 2 equiv.) was added to a solution of the NH-heterocycle (1 equiv.) and K_2CO_3 in dry acetone and the mixture was stirred at room temperature for 16h. The mixture was filtered, the solvent removed under reduced pressure and the residue dissolved in $CHCl_3$ (20 mL). The organic layer was washed with water (2 × 10 mL), dried over anhydrous $MgSO_4$, filtered and the filtrate evaporated under *vacuo* to afford he product.

2',3',5'-Tri-*O*-acetyl-3-prop-2-yn-1-yluridine.[1]



Prepared by general procedure A from 2',3',5'-tri-*O*-acetyluridine. Flash column chromatography eluting with 7:3 v/v EtOAc/*n*-hexane afforded the product as a colourless gum (93%), $[\alpha]_D$ +17.1 (*c*, 35 mg/10 mL CH_2Cl_2); δ_H (500 MHz, $CDCl_3$); 7.41 (1H, d, *J* 8.2, pyrimidinyl 6-H), 6.02 (1H, d, *J* 4.7, ribosyl 1-H), 5.86 (1H, d, *J* 8.2, pyrimidinyl 5-H), 5.38 (1H, dd, *J* 5.9 and 4.7, ribosyl 2-H), 5.35-5.31 (1H, m, ribosyl 3-H), 4.71 (1H, dd, *J* 16.4 and 2.1, N*CH*$_A$CΞ), 4.65 (1H, dd, *J* 16.4 and 2.6, N*CH*$_B$CΞ), 4.36 (3H, br s, ribosyl 4-H and 5-CH_2), 2.18 (1H, dd, *J* 2.6 and 2.1, ΞCH), 2.14 (3H, s, OCOMe), 2.12 (3H, s, OCOMe), 2.11 (3H, s, OCOMe); δ_c (75 MHz, $CDCl_3$); 170.5, 170.1, 170.0, 163.3, 161.5, 150.5, 138.2, 103.1, 89.2, 80.1, 73.3, 71.3, 70.2, 63.2, 30.7, 21.2, 20.9, 20.8; υ_{max}/cm^{-1} (film); 2396, 2125, 1747, 1711, 1670, 1456, 1376, 1233; *m/z* (ES, %) 409 (MH^+, 65).

3',5'-Di-*O*-acetyl-3-prop-2-yn-1-ylthymidine.



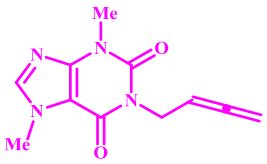
Prepared by general procedure A from 3',5'-di-*O*-acetylthymidine. Flash column chromatography eluting with 2:1 v/v EtOAc/*n*-hexane gave the product as a colourless gum (90%), $[\alpha]_D$ −3.2 (*c*, 10 mg/1 mL CH_2Cl_2); (Found: C, 55.90; H, 5.80; N, 7.45; $C_{17}H_{20}N_2O_7$ requires C, 56.04; H, 5.53; N, 7.69%); δ_H (500 MHz, $CDCl_3$); 7.29 (1H, br s, pyrimidinyl 6-H), 6.37 (1H, dd, *J* 9.1 and 5.9, deoxyribosyl 1-H), 5.22 (1H, dt, *J* 6.6 and 2.1, deoxyribosyl 3-H), 4.72 (2H, d, *J* 2.6, N*CH*$_2$CΞ), 4.38-4.34 (2H, m, deoxyribosyl 5-CH_2), 4.26 (1H, m, deoxyribosyl 4-H), 2.50 (1H, ddd, *J* 14.3, 5.9 and 2.1, deoxyribosyl 2-H_A), 2.18-2.15 (1H, m, deoxyribosyl 2-H_B), 2.16 (1H, m, ΞCH), 2.13 (3H, s, OCOMe), 2.11 (3H, s, OCOMe), 1.98 (3H, s, pyrimidinyl 5-Me); δ_c (75 MHz, $CDCl_3$); 170.7, 170.4, 162.3, 150.2, 147.5, 145.6,

132.9, 85.5, 82.0, 74.0, 70.6, 63.8, 37.6, 30.4, 20.9, 20.8, 13.3; υ_{max}/cm^{-1} (film); 3272, 2955, 1743, 1707, 1673, 1651, 1466, 1369, 1333, 1234; *m/z* (ES, %) 365 (MH^+, 100).

General Procedure B: Allene formation.[2]

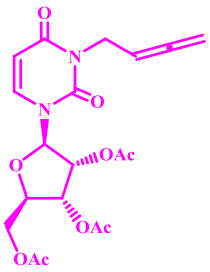
A mixture of alkyne (1 equiv.), dicyclohexylamine (1.8 equiv.), paraformaldehyde (2.5 equiv.) and CuI (0.5 equiv.) in dry dioxane was refluxed for 3h. The reaction mixture was cooled and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$ and the organic layer washed with (10%) NH_4OH three times then with water, dried over anhydrous $MgSO_4$, filtered and the filtrate evaporated under *vacuo* to give the crude allene which was purified by flash column chromatography.

1-(Buta-2,3-dien-1-yl)-3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (4a).[3]



Prepared by general procedure B from 3,7-dimethyl-1-(prop-2-yn-1-yl)-3,7-dihydro-1*H*-purine-2,6-dione.[4,5] Flash column chromatography eluting with EtOAc gave **4a** as a colourless fine needles (83%), mp. 128-130 °C; (Found: C, 56.70; H, 5.10; N, 24.15; $C_{11}H_{12}N_4O_2$ requires C, 56.89; H, 5.21; N, 24.12%); δ_H (300 MHz, $CDCl_3$); 7.53 (1H, s, purine 8-H), 5.36-5.27 (1H, m, CH_2CH=), 4.83-4.78 (2H, m, NCH_2CH=), 4.65-4.61 (2H, m, $=CH_2$), 4.00 (3H, s, NMe), 3.58 (3H, s, NMe); δ_c (75 MHz, $CDCl_3$); 208.8, 154.9, 151.2, 148.8, 141.5, 107.6, 86.3, 77.0, 39.5, 33.6, 29.7; υ_{max}/cm^{-1} (film); 3115, 2950, 1701, 1654, 1598, 1477, 1332; *m/z* (ES, %) 233 (MH^+, 100).

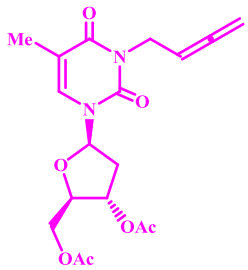
2',3',5'-Tri-*O*-acetyl-3-buta-2,3-dien-1-yluridine (4b).



Prepared by general procedure B from 2',3',5'-tri-*O*-acetyl-3-prop-2-yn-1-yluridine. Flash column chromatography eluting with 2:1 v/v EtOAc/*n*-hexane gave **4b** as a colourless gum

(80%), $[\alpha]_D$ + 30.6 (*c*, 4.2 mg/1 mL CH_2Cl_2); (Found: C, 53.85; H, 5.00; N, 6.45; $C_{19}H_{22}N_2O_9$ requires C, 54.03; H, 5.25; N, 6.63%); δ_H (500 MHz, $CDCl_3$); 7.37 (1H, d, *J* 8.1, pyrimidinyl 6-H), 6.01 (1H, d, *J* 4.3, ribosyl 1-H), 5.82 (1H, d, *J* 8.1, pyrimidinyl 5-H), 5.38 (1H, dd, *J* 5.9 and 4.3, ribosyl 2-H), 5.35-5.31 (1H, m, ribosyl 3-H), 5.29-5.23 (1H, m, CH_2CH=), 4.83-4.80 (2H, m, NCH_2CH=), 4.55-4.51 (2H, m, =CH_2), 4.36 (3H, br s, ribosyl 4-H and 5-CH_2), 2.15 (3H, s, OCOMe), 2.12 (3H, s, OCOMe), 2.11 (3H, s, OCOMe); δ_c (75 MHz, $CDCl_3$); 209.2, 170.6, 170.5, 169.9, 162.1, 150.8, 137.8, 103.1, 89.2, 86.0, 80.0, 77.6, 73.3, 71.3, 63.3, 39.6, 21.4, 21.1, 20.8 ; υ_{max}/cm^{-1} (film); 2107, 1960, 1746, 1666, 1457, 1423, 1388, 1229; *m/z* (ES, %) 423 (MH^+, 100).

3',5'-Di-*O*-acetyl-3-buta-2,3-dien-1-ylthymidine (4c).



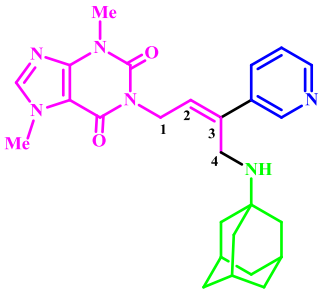
Prepared by general procedure B from 3',5'-di-*O*-acetyl-3-prop-2-yn-1-ylthymidine. Flash column chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave **4c** as a colourless gum (75%), $[\alpha]_D$ + 17.0 (*c*, 10 mg/1 mL CH_2Cl_2); (Found: C, 57.05; H, 5.85; N, 7.40; $C_{18}H_{22}N_2O_7$ requires C, 57.14; H, 5.86; N, 7.40%); δ_H (500 MHz, $CDCl_3$); 7.27 (1H, br s, pyrimidinyl 6-H), 6.35 (1H, dd, *J* 8.6 and 5.6, deoxyribosyl 1-H), 5.27 (1H, tt, *J* 12.8 1nd 6.4, CH_2CH=), 5.23-5.21 (1H, m, deoxyribosyl 3-H), 4.80 (2H, dt, *J* 6.4 and 3.0, NCH_2CH=), 4.56 (2H, dt, *J* 6.4 and 3.0, =CH_2), 4.36 (2H, d, *J* 3.9, deoxyribosyl 5-CH_2), 4.25 (1H, dt, *J* 5.9 and 3.9, deoxyribosyl 4-H), 2.49 (1H, ddd, *J* 14.1, 5.6 and 2.0, deoxyribosyl 2-H_A), 2.18-2.15 (1H, m, deoxyribosyl 2-H_B), 2.13 (3H, s, OCOMe), 2.11 (3H, s, OCOMe), 1.96 (3H, s, pyrimidinyl 5-Me); δ_c (75 MHz, $CDCl_3$); 209.5, 170.8, 170.5, 163.1, 150.9, 132.9, 111.0, 86.1, 85.8, 82.4, 77.3, 74.5, 64.2, 39.9, 38.0, 21.4, 21.2, 13.8; υ_{max}/cm^{-1} (film); 2954, 1957, 1744, 1703, 1671, 1647, 1466, 1367, 1232; *m/z* (ES, %) 379 (MH^+, 100).

General Procedure C: Pd catalysed 3-component cascades.

A mixture of substituted allene **4** (1 equiv.), aryl/heteroaryl iodide **5** (1.2 equiv.), 1-aminoadamantane **1** (1.2 equiv.), $Pd_2(dba)_3$ (2.5 mol%), TFP (tri-(2-furyl)phosphine) (10 mol%) and K_2CO_3 (3 equiv.) in MeCN was stirred and heated at 80 °C (oil bath temperature).

The mixture was cooled, filtered and the inorganic precipitate washed with MeCN. The filtrate was evaporated under reduced pressure and the resulting residue dissolved in $CHCl_3$ and washed with saturated NH_4Cl and then with saturated NaCl. The organic layer was dried with anhydrous $MgSO_4$, filtered, and the filtrate evaporated under reduced pressure. The residue was purified by flash chromatography.

1-[(2*Z*)-4-(Adamantan-1-ylamino)-3-(pyridin-3-yl)but-2-en-1-yl]-3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (6a).

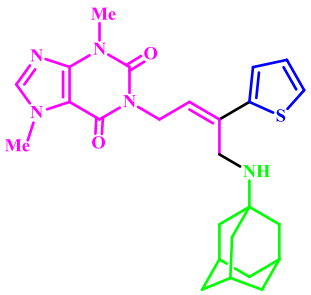


Prepared by general procedure C from **4a** and heating for 5h. Gradient elution chromatography with EtOAc and then 10:1 v/v EtOAc/MeOH gave the product **6a** (78%) as a colourless froth, mp 91-93°C; δ_H (300 MHz, $CDCl_3$); 8.77 (1H, d, *J* 1.5, pyridyl-H), 8.45 (1H, dd, *J* 4.9 and 1.5, pyridyl-H), 7. 87 (1H, dt, *J* 8.0 and 1.5, pyridyl-H), 7.55 (1H, s, purine-H), 7.21 (1H, ddd, *J* 8.0, 4.9 and 0.5, pyridinyl-H), 5.90 (1H, t, *J* 7.1, NCH_2CH=), 4.90 (2H, d, *J* 7.1, NCH_2CH=), 4.00 (3H, s, NMe), 3.82 (2H, s, =CCH_2N), 3.59 (3H, s, NMe), 2.10 (3H, br s, 3 × adamantyl-CH), 1.78 (6H, d, *J* 2.3, 3 × adamantyl-CH_2), 1.67 (6H, br s, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 155.4, 151.7, 149.3, 148.7, 148.1, 142.0, 139.6, 137.5, 134.1, 126.1, 123.4, 108.0, 51.4, 42.9, 39.9, 39.6, 37.2, 34.0, 30.2, 30.0; υ_{max}/cm^{-1} (film); 2906, 2848, 1704, 1661, 1550, 1455, 1358, 1310, 1234; *m/z* (ESI^+) 461.3 (100%, MH^+); (Found MH^+, 461.2675. $C_{26}H_{33}N_6O_2$ requires *MH*, 461.2660).

NOE data ($CDCl_3$) for **6a**:

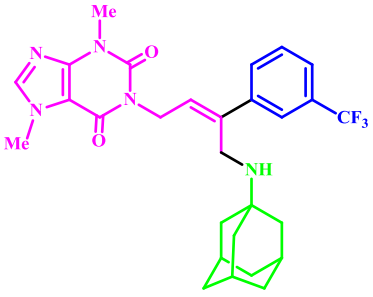
	% Enhancement				
Irradiated proton	1-H	2-H	4-H	Pyridyl-H	adamantyl-CH_2 (δ 1.74)
1-H		6.8	3.6	-	-
2-H	3.2		-	8.4 (δ 8.77) 6.1 (δ 7.87)	-
4-H	4.3	-		4.4 (δ 8.77) 3.6 (δ 7.87)	6.8

1-[(2*E*)-4-(Adamantan-1-ylamino)-3-(2-thienyl)but-2-en-1-yl]-3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (6b).



Prepared by general procedure C from **4a** and heating for 2h. Flash chromatography eluting with EtOAc gave the product **6b** (69%) as a colourless froth, mp 155-157°C; δ_H (300 MHz, $CDCl_3$); 7.50 (1H, s, purine-H), 7.17 (1H, dd, *J* 3.6 and 1.0, thienyl-H), 7.11 (1H, dd, *J* 5.1 and 1.0, thienyl-H), 6.93 (1H, dd, *J* 5.1 and 3.6, thienyl-H), 5.97 (1H, t, *J* 7.2, NCH_2CH=), 4.85 (2H, d, *J* 7.2, NCH_2CH=), 3.98 (3H, s, NMe), 3.81 (2H, s, =CCH_2N), 3.57 (3H, s, NMe), 2.11 (3H, br s, 3 × adamantyl-CH), 1.80 (6H, d, *J* 2.6, 3 × adamantyl-CH_2), 1.68 (6H, d, *J* 2.1, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 154.9, 151.2, 148.7, 145.3, 141.5, 136.4, 127.2, 124.1, 123.8, 122.1, 107.5, 50.9, 42.5, 39.7, 39.2, 36.8, 33.5, 29.7, 29.4; υ_{max}/cm^{-1} (film); 2903, 2846, 1702, 1660. 1549, 1454, 1361, 1310, 1233; *m/z* (ESI^+) 466.2 (100%, MH^+); (Found MH^+, 466.2289. $C_{25}H_{32}N_5O_2\ ^{32}S$ requires *MH*, 466.2271).

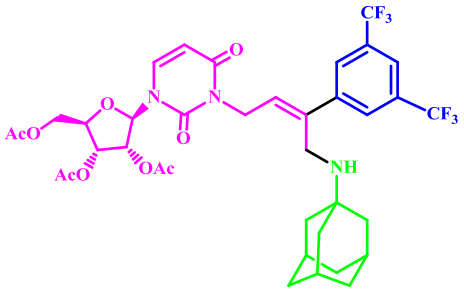
1-{(2*Z*)-4-(Adamantan-1-ylamino)-3-[3-(trifluoromethyl)phenyl]but-2-en-1-yl}-3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione (6c).



Prepared by general procedure C from **4a** and heating for 2h. Flash chromatography eluting with 30:1 v/v $CHCl_3$/MeOH gave the product **6c** (91%) as a colourless froth, mp 68-70°C; δ_H (300 MHz, $CDCl_3$); 7.86 (1H, s, phenyl-H), 7.75 (1H, d, *J* 7.7, phenyl-H), 7.52 (1H, s, purine-H), 7.47 (1H, d, *J* 7.7, phenyl-H), 7.39 (1H, t, *J* 7.7, phenyl-H), 5.90 (1H, t, *J* 7.1, NCH_2CH=), 4.90 (2H, d, *J* 7.1, NCH_2CH=), 3.99 (3H, s, NMe), 3.82 (2H, s, =CCH_2N), 3.59 (3H, s, NMe), 2.11 (3H, br s, 3 × adamantyl-CH), 1.79 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2),

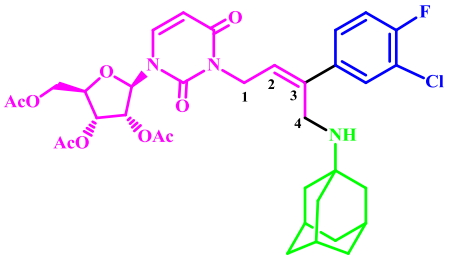
1.68 (6H, br d, *J* 1.6, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 155.0, 151.4, 148.9, 142.5, 141.6, 140.9, 130.4 (*J* 32.1), 129.6, 128.6, 125.5, 124.2 (*J* 272.0), 123.8 (*J* 4.4), 123.2 (*J* 4.4), 107.6, 50.9, 42.5, 39.6, 39.4, 36.8, 33.6, 29.8, 29.7; υ_{max}/cm^{-1} (film); 3310, 2907, 2849, 1702, 1661, 1604, 1550, 1487, 1455, 1415, 1334, 1258, 1234; *m/z* (ESI^+) 528.3 (100%, MH^+); (Found MH^+, 528.2575. $C_{28}H_{33}F_3N_5O_2$ requires *MH*, 528.2581).

2',3',5'-Tri-*O*-acetyl-3-{(2*Z*)-4-(adamantan-1-ylamino)-3-[3,5-bis(trifluoromethyl)phenyl]but-2-en-1-yl}uridine (6d).



Prepared by general procedure C from **4b** and heating for 5h. Flash column chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave the product **6d** (77%) as a pale yellow gum; $[\alpha]_D$ + 19.5 (*c*, 16 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 8.00 (2H, s, 2 × phenyl-H), 7.61 (1H, s, phenyl-H), 7.33 (1H, d, *J* 8.2, pyrimidinyl 6-H), 5.91 (1H, d, *J* 4.9, ribosyl 1-H), 5.78 (1H, t, *J* 7.1, NCH_2CH=), 5.74 (1H, d, *J* 8.2, pyrimidinyl 5-H), 5.28 (1H, dd, *J* 6.0 and 4.9, ribosyl 2-H), 5.23-5.19 (1H, m, ribosyl 3-H), 4.69 (2H, d, *J* 7.1, NCH_2CH=), 4.24 (3H, s, ribosyl 4-H and 5-CH_2), 3.62 (2H, s, =CCH_2N), 2.00 (9H, s, 2 × OCOMe and 3 × adamantyl-CH), 1.96 (3H, s, OCOMe), 1.64 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2), 1.56 (6H, br s, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 170.1 (CO), 169.5 (2 × CO), 161.9, 150.7, 144.0, 140.3, 137.5, 131.2 (q, *J* 33.2), 126.6 (brd, *J* 3.3), 125.9, 123.5 (q, *J* 237.1), 120.7 (q, *J* 3.9), 102.7, 88.7, 79.7, 73.0, 69.9, 62.8, 50.8, 42.5, 39.5, 39.4, 36.7, 29.6, 20.7, 20.4, 20.3; υ_{max}/cm^{-1} (film); 3313, 3023, 2908, 2850, 1755, 1713, 1668, 1455, 1383, 1310, 1280, 1227; *m/z* (ESI^+) 786.3 (100%, MH^+); (Found MH^+, 786.2941. $C_{37}H_{41}F_6N_3O_9$ requires *MH*, 786.2820).

2',3',5'-Tri-*O*-acetyl-3-[(2*Z*)-4-(adamantan-1-ylamino)-3-(3-chloro-4-fluorophenyl)but-2-en-1-yl]uridine (6e).

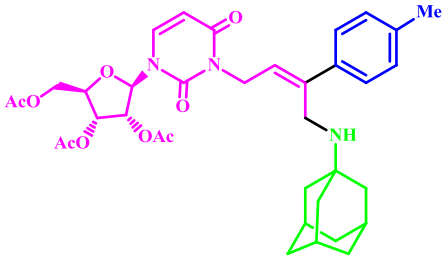


Prepared by general procedure C from **4b** and heating for 4h. Flash chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave the product **6e** (86%) as a pale yellow gum; $[\alpha]_D$ + 19.7 (*c*, 14 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 7.62 (1H, dd, *J* 7.1 and 2.2, phenyl-H), 7.44-7.39 (1H, m, phenyl-H), 7.40 (1H, d, *J* 8.2, pyrimidinyl 6-H), 7.05 (1H, t, *J* 8.5, phenyl-H), 6.00 (1H, d, *J* 4.4, ribosyl 1-H), 5.84 (1H, d, *J* 8.2, pyrimidinyl 5-H), 5.74 (1H, t, *J* 7.1, NCH_2CH=), 5.39 (1H, dd, *J* 5.5 and 4.4, ribosyl 2-H), 5.34-5.33 (1H, m, ribosyl 3-H), 4.75 (2H, d, *J* 7.1, NCH_2CH=), 4.35 (3H, s, ribosyl 4-H and 5-CH_2), 3.70 (2H, s, =CCH_2N), 2.13 (3H, s, OCOMe), 2.12 (3H, s, OCOMe), 2.10 (6H, s, OCOMe and 3 × adamantyl-CH), 1.74 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2), 1.67 (6H, br s, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 170.1 (CO), 169.6 (2 × CO), 162.0, 157.5 (*J* 248.8), 150.7, 140.8, 139 (*J* 4.4), 137.4, 128.6, 126.1 (*J* 6.6), 123.9, 120.5 (*J* 17.7), 116.1 (*J* 21.0), 102.8, 88.8, 79.7, 73.0, 69.9, 62.8, 50.8, 42.5, 39.54, 39.51, 36.8, 29.6, 20.8, 20.5, 20.4; υ_{max}/cm^{-1} (film); 3312, 2906, 2849, 1751, 1711, 1668, 1497, 1455, 1386, 1310, 1228; *m/z* (ESI^+) 702.3 (100%, MH^+); (Found MH^+, 702.2606. $C_{35}H_{42}ClFN_3O_9$ requires *MH*, 702.2588).

NOE data ($CDCl_3$) for **6e**:

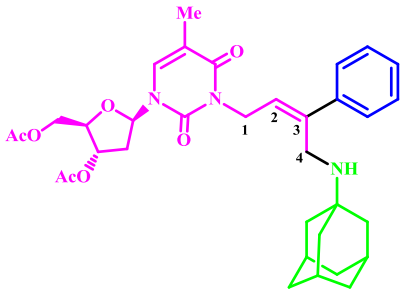
	% Enhancement				
Irradiated proton	1-H	2-H	4-H	phenyl-H	adamantyl-CH_2 (δ 1.74)
1-H		6.8	4.0	-	-
2-H	3.7		-	8.3 (δ 7.62) 6.6 (δ 7.41)	-
4-H	4.1	-		4.3 (δ 7.62) 3.3 (δ 7.41)	5.8

2',3',5'-Tri-*O*-acetyl-3-[(2*Z*)-4-(adamantan-1-ylamino)-3-(4-methylphenyl)but-2-en-1-yl]uridine (6f).



Prepared by general procedure C from **4b** and heating for 3h. Flash chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave the product **6f** (87%) as a pale yellow gum; $[\alpha]_D$ + 19.0 (*c*, 11 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 7.38 (2H, d, *J* 8.2, 2 × phenyl-H), 7.37 (1H, d, *J* 8.2, pyrimidinyl 6-H), 7.10 (2H, d, *J* 7.7, 2 × phenyl-H), 6.02 (1H, d, *J* 4.9, ribosyl 1-H), 5.82 (1H, d, *J* 8.2, pyrimidinyl 5-H), 5.76 (1H, t, *J* 7.1, NCH_2CH=), 5.37 (1H, dd, *J* 6.0 and 4.9, ribosyl 2-H), 5.35-5.31 (1H, m, ribosyl 3-H), 4.77 (2H, d, *J* 7.1, NCH_2CH=), 4.34 (3H, s, ribosyl 4-H and 5-CH_2), 3.79 (2H, s, =CCH_2N), 2.32 (3H, s, phenyl-Me), 2.13 (3H, s, OCOMe), 2.11 (3H, s, OCOMe), 2.08 (6H, s, OCOMe and 3 × adamantyl-CH), 1.73 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2), 1.66 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 170.1 (CO), 169.6 (2 × CO), 162.0, 150.7, 142.7, 138.4, 137.3, 137.1, 129.0, 126.2, 122.3, 102.9, 88.5, 79.6, 72.9, 69.9, 62.9, 50.8, 42.5, 39.8, 39.2, 36.8, 29.7, 21.1, 20.8, 20.5, 20.4; υ_{max}/cm^{-1} (film); 3313, 3022, 2906, 2849, 1748, 1712, 1668, 1511, 1455, 1371, 1310, 1228; *m/z* (ESI^+) 664.3 (100%, MH^+); (Found MH^+, 664.3252. $C_{36}H_{46}N_3O_9$ requires *MH*, 664.3229).

3',5'-Di-*O*-acetyl-3-[(2*Z*)-4-(adamantan-1-ylamino)-3-phenylbut-2-en-1-yl]thymidine (6g).



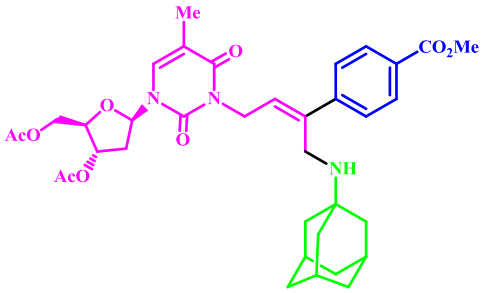
Prepared by general procedure C from **4c** and heating for 3h. Flash chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave the product **6g** (99%) as a pale yellow gum; $[\alpha]_D$ + 5.2 (*c*, 12 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 7.50 (2H, dd, *J* 8.0 and 1.4, 2 × phenyl-H), 7.31-7.22 (3H, m, 3 × phenyl-H and pyrimidinyl 6-H), 6.37 (1H, dd, *J* 8.5 and 5.8, deoxyribosyl 1-H), 5.82 (1H, t, *J* 7.1, NCH_2CH=), 5.21 (1H, dt, *J* 6.6 and 2.2, deoxyribosyl 3-H), 4.82 (2H,

d, *J* 7.1, NC*H*$_2$CH=), 4.38 (1H, dd, *J* 12.1 and 3.8, deoxyribosyl 5-H$_A$), 4.32 (1H, dd, *J* 12.1 and 3.8, deoxyribosyl 5-H$_B$), 4.24 (1H, dt, *J* 6.6 and 3.8, deoxyribosyl 4-H), 3.83 (2H, s, =C*H*$_2$N), 2.48 (1H, ddd, *J* 13.7, 5.5 and 1.6, deoxyribosyl 2-H$_A$), 2.20-2.08 (1H, ddd, *J* 13.7 ,5.5 and 1.6, deoxyribosyl 5-H$_B$), 2.12 (3H, s, OCOMe), 2.10 (3H, s, OCOMe), 2.09 (3H, s, 3 × adamantyl-CH), 1.95 (3H, s, pyrimidinyl 5-Me), 1.74 (6H, br d, *J* 2.2, 3 × adamantyl-CH$_2$), 1.66 (6H, br d, *J* 2.2, 3 × adamantyl-CH$_2$); δ_c (75 MHz, CDCl$_3$); 170.4, 170.2, 162.9, 150.7, 142.6, 141.4, 132.6, 128.3, 127.4, 126.3, 123.5, 110.8, 85.4, 82.0, 74.1, 63.9, 50.9, 42.6, 39.9, 39.3, 37.6, 36.8, 29.7, 20.9, 20.8, 13.5; υ_{max}/cm^{-1} (film); 3312, 3020, 2906, 2848, 1747, 1704, 1668, 1644, 1464, 1367, 1310, 1233; *m/z* (ESI$^+$) 606.3 (100%, MH$^+$); (Found MH$^+$, 606.3194. $C_{34}H_{44}N_3O_7$ requires *MH*, 606.3174).

NOE data (CDCl$_3$) for **6g**:

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	phenyl-H (δ 7.50)	adamantyl-CH$_2$ (δ 1.74)
1-H		5.8	3.6	-	-
2-H	4.3		-	11.9	-
4-H	4.3	-		6.8	7.0

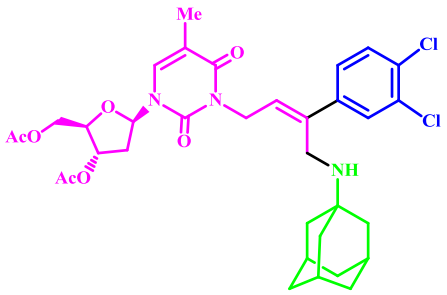
3',5'-Di-*O*-acetyl-3-{(2*Z*)-4-(adamantan-1-ylamino)-3-[4-(methoxycarbonyl)phenyl]but-2-en-1-yl}thymidine (6h).



Prepared by general procedure C from **4c** and heating for 4h. Flash chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave the product **6h** (93%) as a pale yellow gum; [α]$_D$ + 7.6 (*c*, 13 mg/1 mL CHCl$_3$); δ_H (300 MHz, CDCl$_3$); 7.96 (2H, d, *J* 8.5, 2 × phenyl-H), 7.59 (2H, d, *J* 8.5, 2 × phenyl-H), 7.29 (1H, s, pyrimidinyl 6-H), 6.38 (1H, dd, *J* 5.8 and 8.5, deoxyribosyl 1-H), 5.90 (1H, t, *J* 7.1, NCH$_2$*CH*=), 5.22 (1H, dt, *J* 6.6 and 2.2, deoxyribosyl 3-H), 4.83 (2H, d, *J* 7.1, NC*H*$_2$CH=), 4.39 (1H, dd, *J* 4.4 and 12.1, deoxyribosyl 5-H$_A$), 4.33 (1H, dd, *J* 3.3 and 12.1, deoxyribosyl 5-H$_B$), 4.25 (1H, dt, *J* 3.6 and 6.3, deoxyribosyl 4-H), 3.89 (3H, s, CO$_2$Me), 3.81 (2H, s, =C*H*$_2$N), 2.49 (1H, ddd, *J* 1.6, 5.5 and 13.7, deoxyribosyl 2-H$_A$), 2.20

(1H, ddd, *J* 1.6, 6.6 and 13.7, deoxyribosyl 2-H_B), 2.12 (3H, s, OCOMe), 2.11 (3H, s, OCOMe), 2.10 (3H, s, 3 × adamantyl-CH), 1.96 (3H, s, pyrimidinyl 5-Me), 1.75 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2), 1.67 (6H, br s, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 170.3, 170.1, 166.9, 162.9, 150.6, 146.1, 141.8, 132.8, 129.6, 128.8, 126.3, 125.3, 110.8, 85.4, 82.0, 74.1, 63.8, 52.0, 50.8, 42.5, 39.8, 39.2, 37.5, 36.8, 29.6, 20.9, 20.8, 13.4; υ_{max}/cm^{-1} (film); 3311, 3018, 2906, 2848, 1746, 1704, 1669, 1645, 1606, 1465, 1366, 1278, 1233; *m/z* (ESI^+) 664.3 (100%, MH^+); (Found MH^+, 664.3239. $C_{36}H_{46}N_3O_9$ requires *MH*, 664.3229).

3',5'-Di-*O*-acetyl-3-[(2*Z*)-4-(adamantan-1-ylamino)-3-(3,4-dichlorophenyl)but-2-en-1-yl]thymidine (6i).

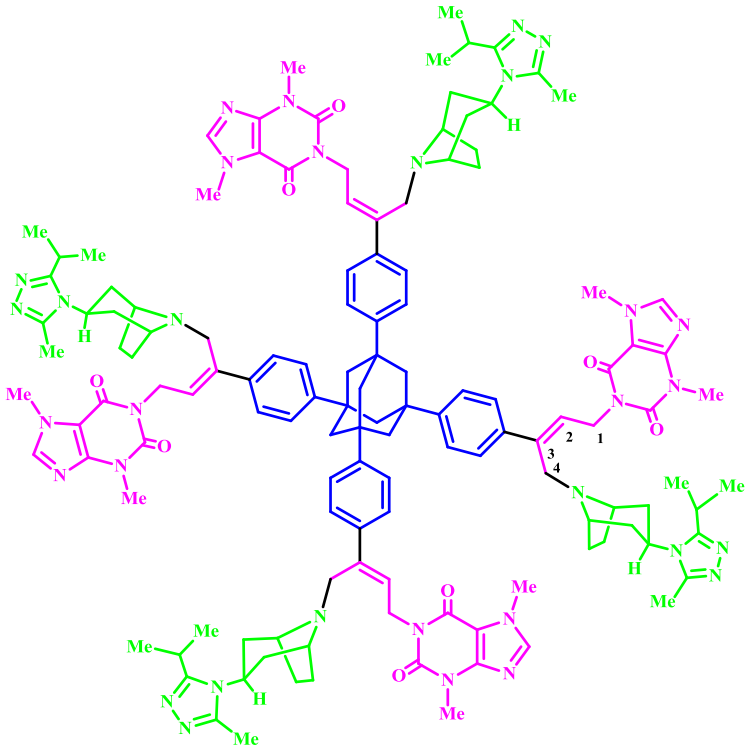


Prepared by general procedure C from **4c** and heating for 2h. Flash chromatography eluting with 1:1 v/v EtOAc/*n*-hexane gave the product **6i** (87%) as a pale yellow gum; $[\alpha]_D$ + 7.7 (*c*, 11 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 7.56 (1H, d, *J* 1.6, phenyl-H), 7.28 (1H, dd, *J* 8.2 and 1.6, 2 × phenyl-H), 7.19 (1H, d, *J* 8.2, phenyl-H), 7.18 (1H, s, pyrimidinyl 6-H), 6.27 (1H, dd, *J* 8.2 and 6.0, deoxyribosyl 1-H), 5.70 (1H, t, *J* 7.1, NCH_2CH=), 5.12 (1H, dt, *J* 6.6 and 2.2, deoxyribosyl 3-H), 4.68 (2H, d, *J* 7.1, NCH_2CH=), 4.28 (1H, dd, *J* 12.3 and 3.6, deoxyribosyl 5-H_A), 4.23 (1H, dd, *J* 12.3 and 3.6, deoxyribosyl 5-H_B), 4.15 (1H, dt, *J* 6.6 and 3.6, deoxyribosyl 4-H), 3.62 (2H, s, =CCH_2N), 2.38 (1H, ddd, *J* 14.3, 6.6 and 2.2, deoxyribosyl 2-H_A), 2.09 (1H, ddd, *J* 14.3, 8.2 and 1.6, deoxyribosyl 2-H_B), 2.02 (3H, s, OCOMe), 2.00 (6H, s, OCOMe and 3 × adamantyl-CH), 1.86 (3H, s, pyrimidinyl 5-Me), 1.64 (6H, br d, *J* 2.2, 3 × adamantyl-CH_2), 1.56 (6H, br s, 3 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 170.3, 170.1, 162.9, 150.6, 141.8, 140.5, 132.8, 132.2, 130.9, 130.0, 128.3, 125,7, 124.8, 110.8, 85.4, 82.0, 74.1, 63.8, 50.9, 42.5, 39.7, 39.3, 37.5, 36.8, 29.6, 20.9, 20.8, 13.4; υ_{max}/cm^{-1} (film); 3310, 3018, 2906, 2848, 1746, 1702, 1670, 1644, 1550, 1466, 1366, 1336, 1310, 1233; *m/z* (ESI^+) 674.2 (100%, MH^+); (Found MH^+, 674.2410. $C_{34}H_{42}Cl_2N_3O_7$ requires *MH*, 664.3229).

General Procedure D: Pd catalysed 9-component cascades.

A mixture of substituted allene **4** (4 equiv.), 1,3,5,7-tetrakis-(4-iodophenyl)adamantane **3** (1 equiv.), nucleophile **7** (4.4 equiv.), $Pd_2(dba)_3$ (2.5 mol%), TFP (tri-(2-furyl)phosphine) (10 mol%), and K_2CO_3 (6 equiv.) in MeCN or DMF was stirred and heated at 80 °C (oil bath temperature) for 3-32h. The mixture was filtered and the inorganic precipitate washed with MeCN. The solvent was removed under reduced pressure, the residue dissolved in $CHCl_3$ and washed with H_2O. The organic layer was dried over anhydrous $MgSO_4$, filtered, and the filtrate evaporated under reduced pressure. The residue was purified by flash chromatography.

1,1',1'',1'''-[Tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis(4,1-phenylene{(2*Z*)-4-[3-(3-isopropyl-5-methyl-4*H*-1,2,4-triazol-4-yl)-8-azabicyclo[3.2.1]-oct-8-yl]but-2-ene-3,1-diyl})]tetrakis(3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione) (8a).



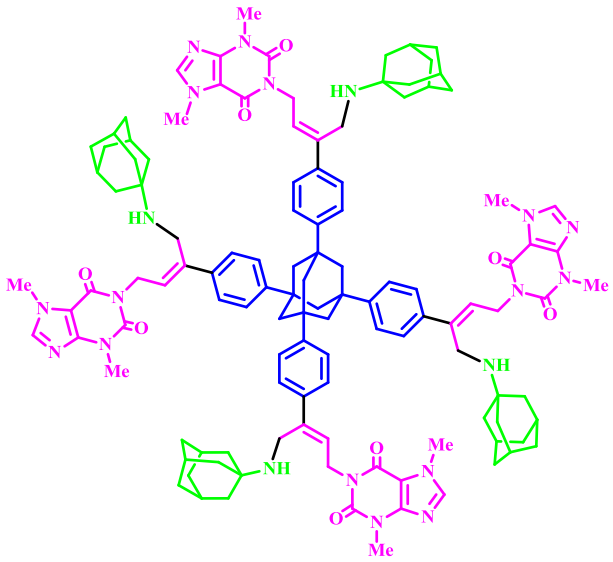
Prepared by general procedure D from **4a** in MeCN and heating for 24h. Flash chromatography gradient eluting with 20:1 v/v $CHCl_3$/MeOH then 15:1 v/v $CHCl_3$/MeOH gave the product **8a** (52%) as a colourless froth, mp 199-201°C; δ_H (300 MHz, $CDCl_3$); 7.54 (4H, s, 4 × purine-H), 7.46 (8H, d, *J* 8.2, 8 × phenyl-H), 7.37 (8H, d, *J* 8.2, 8 × phenyl-H), 5.88 (4H, t, *J* 6.2, 4 × NCH_2CH=), 4.93 (8H, d, *J* 6.2, 4 × NCH_2CH=), 4.24 (4H, m, 4 × azabicyclooctyl-H), 3.99 (12H, s, 4 × purine-NCH_3), 3.68 (8H, s, 4 × =CCH_2N), 3.58 (12H, s,

4 × purine-N*CH*$_3$), 3.46 (8H, br s, 8 × azabicyclooctyl-H), 2.96 (4H, m, 4 × triazolyl 3-*CH*(CH_3)$_2$), 2.37 (12H, s, 4 × triazolyl 5-CH_3), 2.21 (8H, br dd, *J* 8.7 and 3.6, 8 × azabicyclooctyl-H), 2.1 (20H, br s, 8 × azbicyclooctyl-H + 6 × adamantyl-CH_2), 1.66 (16H, br d, *J* 7.7, 16 × azabicyclooctyl-H), 1.32 (24H, d, *J* 6.7, 4 × triazolyl 3-CH(*CH*$_3$)$_2$); δ_c (75 MHz, $CDCl_3$);157.6, 153.5, 149.9, 149.3, 147.4, 146.7, 140.2, 138.9, 138.5, 125.3, 124.8, 123.0, 106.2, 57.2, 49.7, 45.8 (2 × C), 38.2, 37.5, 36.0, 32.2, 28.3, 25.2, 24.2, 20.2, 11.4; υ_{max}/cm^{-1} (film); 3384, 2935, 1704, 1661, 1603, 1549, 1513, 1455, 1415, 1357, 1314, 1286, 1234; *m/z* (ESI$^+$) 2321.3 (30%, $[M+Na]^+$); (Found $[M+Na]^+$, 2321.2911. $C_{130}H_{161}NaN_{32}O_8$ requires *[M+Na]*$^+$, 2321.3018); 2298.3 (28%, $[M+H]^+$); (Found $[M+H]^+$, 2298.3056. $C_{130}H_{161}N_{32}O_8$ requires *[M+H]*$^+$, 2298.3170); 1171.6 (34%, $[M+2Na]^{2+}$); (Found $[M+2Na]^{2+}$, 1171.6477. $C_{130}H_{160}Na_2N_{32}O_8$ requires *[M+2Na]*$^{2+}$, 1171.6441); 1160.7 (80%, $[M+H+Na]^{2+}$); (Found $[M+H+Na]^{2+}$, 1160.6560. $C_{130}H_{161}NaN_{32}O_8$ requires *[M+H+Na]*$^{2+}$, 1160.6531); 1150.2 (100%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1149.6660. $C_{130}H_{162}N_{32}O_8$ requires *[M+2H]*$^{2+}$, 1149.6621).

NOE data ($CDCl_3$) for **8a**.

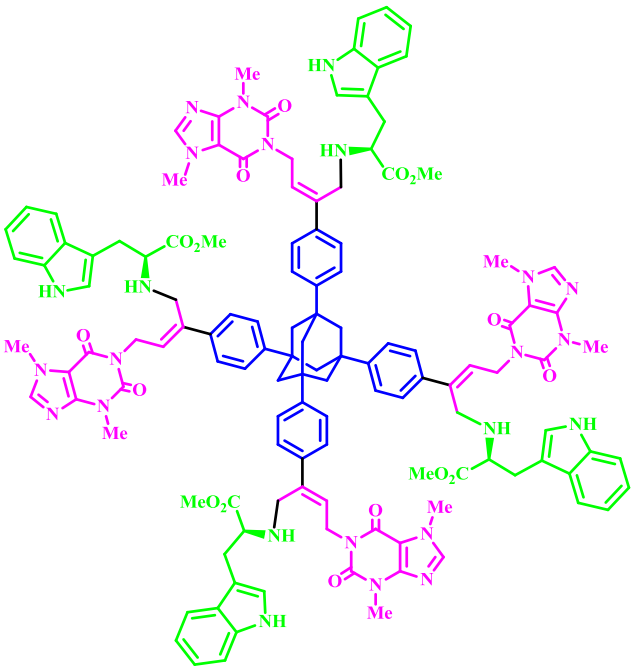
	% Enhancement				
Irradiated proton	1-H	2-H	4-H	Ph-H	Azabicyclooctyl-H
1-H		-8.7	-	-	-
2-H	-6.3		-	-	-
4-H	-1.0	-		-2.2 (δ 7.46)	-2.7 (δ 3.46)

1,1',1'',1'''-(Tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis{4,1-phenylene[(2*Z*)-4-(adamantan-1-ylamino)but-2-ene-3,1-diyl]})tetrakis(3,7-dimethyl-3,7-dihydro-1*H*-purine-2,6-dione) (8b).



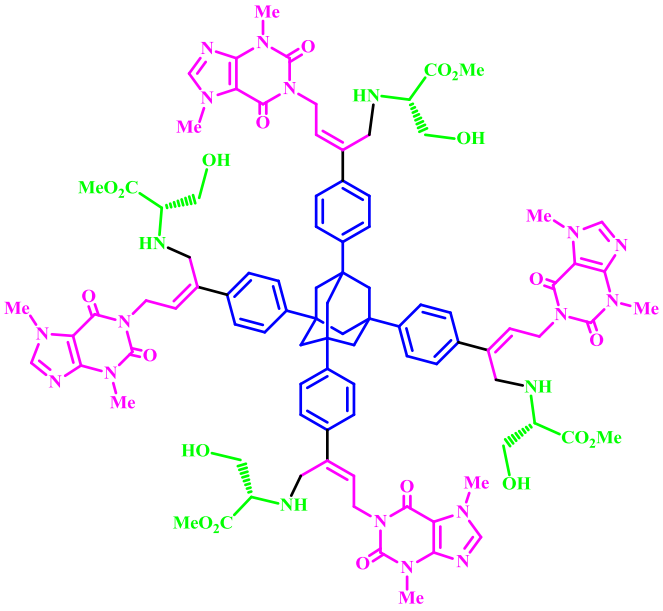
Prepared by general procedure D from **4a** in DMF and heating for 24h. Flash chromatography eluting with 10:1 v/v $CHCl_3$/MeOH gave the product **8b** (87%) as a colourless froth, mp 217-219°C; δ_H (300 MHz, $CDCl_3$); 7.50 (4H, s, 4 × purine-H), 7.49 (8 H, d, *J* 7.6, 8 × phenyl-H), 7.36 (8 H, d, *J* 7.6, 8 × phenyl-H), 5.85 (4H, t, *J* 7.2, 4 × NCH_2CH=), 4.87 (8H, d, *J* 7.2, 4 × NCH_2CH=), 3.98 (12H, s, 4 × NMe), 3.85 (8H, s, 4 × =CCH_2N), 3.57 (12H, s, 4 × NMe), 2.65 (4H, br s, 4 × NH), 2.08 (28H, br s, 12 × adamantyl-CH + 6 × adamantyl-CH_2 + 4 × NH), 1.77 (24H, br s, 12 × adamantyl-CH_2), 1.66 (24H, br s, 12 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 155.1, 151.4, 148.8, 148.6, 141.5, 141.2, 138.8, 126.3, 125.0, 124.1, 107.7, 51.3, 47.1, 42.2, 39.8, 39.0, 38.9, 36.8, 33.6, 29.8, 29.6; υ_{max}/cm^{-1} (film); 2903, 2847, 2366, 1704, 1660, 1604, 1549, 1486, 1454, 1413, 1357, 13101286, 1233; *m/z* (ESI^+) 1966.1097 (3%, $[M+H]^+$); (Found $[M+H]^+$, 1966.1097. $C_{118}H_{141}N_{20}O_8$ requires $[M+H]^+$, 1966.1236); 983.6 (93%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 983.5666. $C_{118}H_{142}N_{20}O_8$ requires $[M+2H]^{2+}$, 983.5654); 656.0 (100%, $[M+3H]^{3+}$); (Found $[M+3H]^{3+}$, 656.0474. $C_{118}H_{143}N_{20}O_8$ requires $[M+3H]^{3+}$, 656.0460).

Tetramethyl (2*S*,2'*S*,2''*S*,2'''*S*)-2,2',2'',2'''-(tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis{4,1-phenylene[(2*Z*)-4-(3,7-dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-1-yl)but-2-ene-2,1-diyl]imino})tetrakis[3-(1*H*-indol-3-yl)propanoate] (8c).



Prepared by general procedure D from **4a** in MeCN and heating for 24h. Flash chromatography eluting with 9:1 v/v $CHCl_3$/MeOH gave the product **8c** (45%) as a colourless froth, mp 129-131°C; $[\alpha]_D$ + 9.1; δ_H (300 MHz, $CDCl_3$); 7.54 (4H, d, *J* 7.6, 4 × indolyl-H), 7.44 (4H, s, 4 × purine-H), 7.31 (8 H, d, *J* 8.6, 8 × phenyl-H), 7.24 (8 H, d, *J* 8.6, 8 × phenyl-H), 7.17 (4H, dd, *J* 8.6and 1.0, 4 × indolyl-H), 7.05 (8H, m, 8 × indolyl-H), 6.89 (4H, d, *J* 1.9, 4 × indolyl-H), 5.82 (4H, t, *J* 6.8, 4 × NCH_2CH=), 4.79 (8H, d, *J* 6.8, 4 × NCH_2CH=), 9.95-3.90 (4H, m, $CHCO_2Me$), 3.90 (12H, s, 4 × NMe), 3.75 (4H, d, *J* 6.7, 4 × =CCH_AN), 3.72 (4H, d, *J* 6.7, 4 × =CCH_BN), 3.65 (12H, s, CO_2Me), 3.52 (12H, s, 4 × NMe), 3.16 (4H, dd, *J* 14.3 and 6.6, 4 × CH_ACHCO_2Me), 3.05 (4H, dd, *J* 14.3 and 6.6, 4 × CH_BCHCO_2Me), 2.00 (16H, br s, 6 × adamantyl-CH_2 + 4 × NH); δ_c (75 MHz, $CDCl_3$); 175.4, 155.0, 151.4, 148.8, 148.4, 141.5, 140.5, 138.6, 136.1, 127.4, 126.3, 124.8 (2 x C), 123.0, 121.8, 119.3, 118.8, 111.3, 111.1, 107.6, 61.7, 51.8, 47.1, 46.6, 39.6, 38.9, 33.6, 32.0, 29.7; υ_{max}/cm^{-1} (film); 3330, 2926, 2853, 1701, 1659, 1549, 1456, 1355, 1233; *m/z* (ESI^+) 2234.0 (10%, $[M+H]^+$); (Found $[M+H]^+$, 2234.0270. $C_{126}H_{129}N_{24}O_{16}$ requires $[M+H]^+$, 2234.0013); 1117.5 (100%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1117.5083. $C_{126}H_{130}N_{24}O_{16}$ requires $[M+2H]^{2+}$, 1117.5043); 745.3 (40%, $[M+3H]^{3+}$); (Found $[M+3H]^{3+}$, 745.3410. $C_{126}H_{131}N_{24}O_{16}$ requires $[M+3H]^{3+}$, 745.3386).

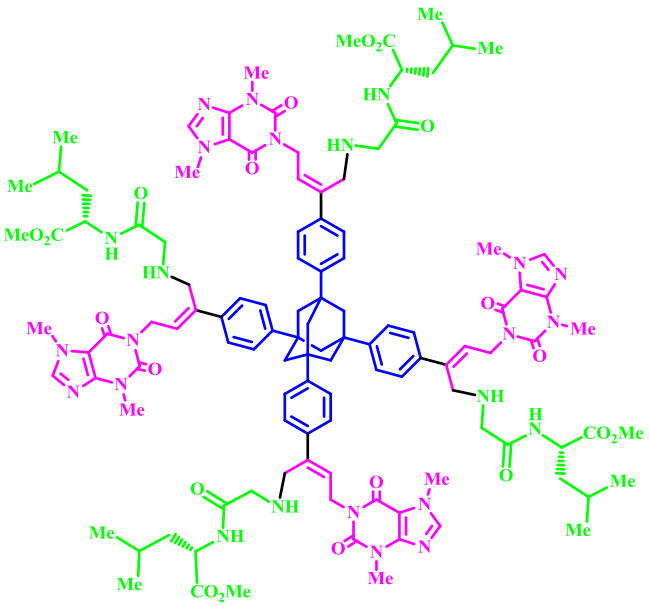
Tetramethyl (2*S*,2'*S*,2''*S*,2'''*S*)-2,2',2'',2'''-(tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis{4,1-phenylene[(2*Z*)-4-(3,7-dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-1-yl)but-2-ene-2,1-diyl]imino})tetrakis(3-hydroxypropanoate) (8d).



Prepared by general procedure D from **4a** in MeCN and heating for 32h. Flash chromatography eluting with 10:1 v/v $CHCl_3$/MeOH gave the product **8d** (49%) as a colourless froth, mp 136-138°C; $[\alpha]_D$ + 1.3; δ_H (300 MHz, $CDCl_3$); 7.50 (4H, s, 4 × purine-H), 7.44 (8H, d, *J* 8.5, 8 × phenyl-H), 7.38 (8H, d, *J* 8.5, 8 × phenyl-H), 5.91 (4H, t, *J* 7.1, 4 × NCH_2CH=), 4.95 (4H, dd, *J* 14.3 and 7.1, 4 × NCH_ACH=), 4.87 (4H, dd, *J* 14.3 and 7.1, 4 × NCH_BCH=), 3.98 (12H, s, 4 × NMe), 3.97 (4H, d, *J* 12.1, 4 × =CCH_AN), 3.87 (4H, dd, *J* 10.4 and 3.8, 4 × $CHCH_AOH$), 3.80 (4H, d, *J* 12.1, 4 × =CCH_BN), 3.75 (12H, s, 3 × CO_2Me), 3.63 (4H, dd, *J* 10.4 and 3.8, 4 × $CHCH_BOH$), 3.57 (12H, s, 4 × NMe), 3.58-3.51 (4H, m, 4 × $NHCHCH_2$), 2.07 (12H, br s, 6 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 173.2, 155.1, 151.4, 148.9, 148.7, 141.6, 140.4, 138.4, 126.2, 125.1, 124.8, 107.7, 62.7, 62.5, 52.1, 47.1, 46.3, 39.6, 39.0, 33.7, 29.8; υ_{max}/cm^{-1} (film); 3457, 2949, 1733, 1704, 1660, 1604, 1550, 1455, 1355, 1315, 1233; *m/z* (ESI$^+$) 1837.8 (14%, $[M+H]^+$); (Found $[M+H]^+$, 1837.8143. $C_{94}H_{109}N_{20}O_{20}$ requires *MH*, 1837.8122); 919.4 (100%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 919.4139. $C_{94}H_{110}N_{20}O_{20}$ requires $[M+2H]^{2+}$, 919.4097); 613 (23%, $[M+3H]^{3+}$); (Found $[M+3H]^{3+}$, 613.2781. $C_{94}H_{111}N_{20}O_{20}$ requires $[M+3H]^{3+}$, 613.2756).

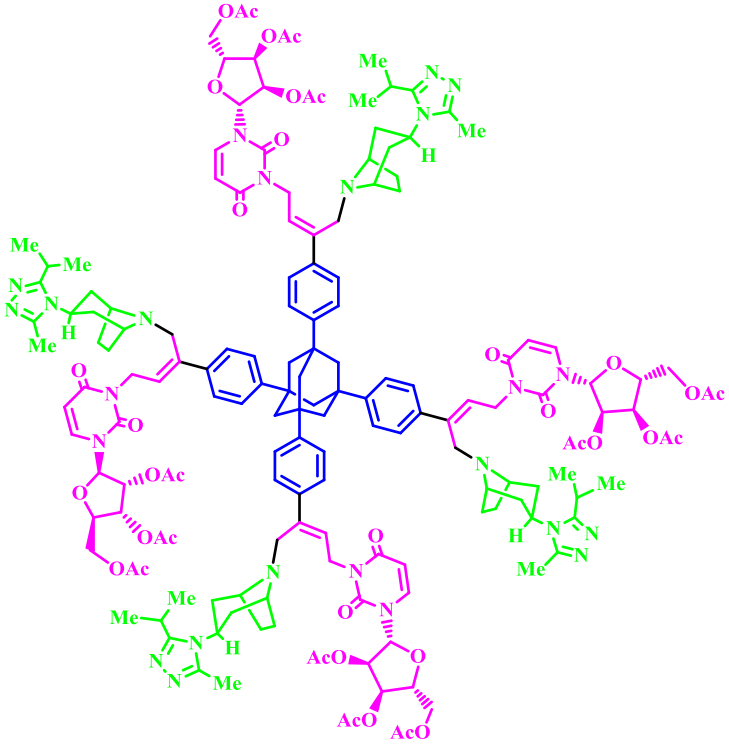
Tetramethyl (2*S*,2'*S*,2''*S*,2'''*S*)-2,2',2'',2'''-(tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis{4,1-phenylene[(2*Z*)-4-(3,7-dimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-

purin-1-yl)but-2-ene-2,1-diyl]imino(1-oxoethane-2,1-diyl)imino})tetrakis(4-methylpentanoate) (8e).



Prepared by general procedure D from **4a** in MeCN and heating for 26h. Flash chromatography eluting with 20:1 v/v $CHCl_3$/MeOH gave the product **8e** (55%) as a colourless froth, mp 106-108°C; $[\alpha]_D$ + 0.7; δ_H (300 MHz, $CDCl_3$); 7.66 (4H, d, *J* 8.2, 4 × CONH), 7.53 (4H, s, 4 × purine-H), 7.41 (8H, d, *J* 8.5, 8 × phenyl-H), 7.37 (8H, d, *J* 8.5, 8 × phenyl-H), 5.85 (4H, t, *J* 7.1, 4 × NCH_2CH=), 4.91 (4H, dd, *J* 14.3 and 7.1, 4 × NCH_ACH=), 4.83 (4H, dd, *J* 14.3 and 7.1, 4 × NCH_BCH=), 4.64 (4H, td, *J* 8.2 and 4.4, 4 × CONH*CH*), 3.99 (12H, s, 4 × purine 7-NMe), 3.93 (4H, d, *J* 12.9, 4 × =CCH_AN), 3.82 (4H, d, *J* 12.9, 4 × =CCH_BN), 3.68 (12H, s, 3 × CO_2Me), 3.58 (12H, s, 4 × purine 3-NMe), 3.35 (8H, br s, 4 × $NHCH_2CO$), 2.08 (12H, br s, 6 × adamantyl-CH_2), 2.04 (4H, br s, 4 × NH), 1.67-1.44 (12H, m, CH_2CHMe_2), 0.90 (12H, d, *J* 4.4, 4 × $CHMe_A$), 0.88 (12H, d, *J* 4.4, 4 × $CHMe_B$); δ_c (75 MHz, $CDCl_3$); 173.4, 171.9, 155.0, 151.4, 148.9, 148.6, 141.6, 140.7, 138.7, 126.5, 125.1, 125.0, 107.7, 52.2 (2C, Me and CH_2), 50.1, 47.9, 47.2, 41.2, 39.5, 39.0, 33.7, 29.8, 24.9, 23.0, 21.8; υ_{max}/cm^{-1} (film); 3334, 3008, 2955, 1742, 1705, 1660, 1604, 1549, 1512, 1452, 1355, 1315, 1234; *m/z* (ESI^+) 2170.1 (6%, $[M+H]^+$); (Found $[M+H]^+$, 2170.1061. $C_{114}H_{145}N_{24}O_{20}$ requires *MH*, 2170.0946); 1085.6 (100%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1085.5578. $C_{114}H_{146}N_{24}O_{20}$ requires $[M+2H]^{2+}$, 1085.5567); 724.0 (63%, $[M+3H]^{3+}$); (Found $[M+3H]^{3+}$, 724.0418. $C_{114}H_{147}N_{24}O_{20}$ requires $[M+3H]^{3+}$, 724.0402).

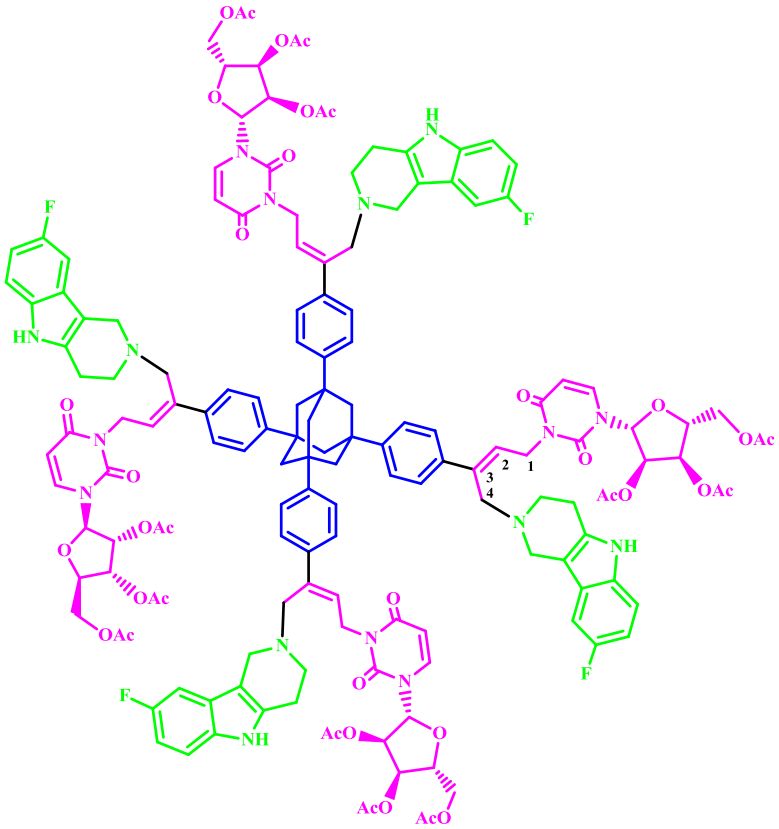
1,1',1'',1'''-[Tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis(4,1-phenylene{(2*Z*)-4-[3-(3-isopropyl-5-methyl-4*H*-1,2,4-triazol-4-yl)-8-azabicyclo[3.2.1]oct -8-yl]but-2-ene-3,1-diyl})]tetrakis(2', 3', 5'-tri-*O*-acetyluridine) (8f).



Prepared by general procedure D from **4b** in MeCN and heating for 5h. Flash column chromatography gradient eluting with EtOAc and then 2:1 v/v EtOAc/MeOH gave the product **8f** (56%) as a colourless froth, mp 134-136°C; $[\alpha]_D$ + 18.9 (*c*, 10 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 7.45 (8H, d, *J* 8.4, 8 × phenyl-H), 7.40 (8H, d, *J* 8.4, 8 × phenyl-H), 7.38 (4H, s, 4 × pyrimidinyl 6-H), 6.00 (4H, d, *J* 4.6, 4 × ribosyl 1-H), 5.83 (4H, s, 4 × pyrimidinyl 5-H), 5.82 (4H, t, *J* 7.0, 4 × NCH_2CH=), 5.40-5.32 (8H, m, 4 × ribosyl 2-H + 4 × ribosyl 3-H), 4.86 (4H, dd, *J* 14.8 and 7.0, 4 × NCH_ACH=), 4.82 (4H, dd, *J* 14.8 and 7.0, 4 × NCH_BCH=), 4.35 (12H, s, 4 × ribosyl 4-H + 4 × ribosyl 5-CH_2), 4.26-4.21 (4H, m, 4 × azabicyclooctyl-H), 3.62 (8H, s, 4 × =CCH_2N), 3.43 (8H, br s, 8 × azabicyclooctyl-H), 2.98-2.90 (4H, m, 4 × triazolyl 3-$CH(CH_3)_2$), 2.37 (12H, s, 4 × triazolyl 5-CH_3), 2.18-2.02 (28H, m, 16 × azabicyclooctyl-H + 6 × adamantyl-CH_2), 2.13 (12H, s, 4 × ribosyl OMe), 2.12 (12H, s, 4 × ribosyl OMe), 2.09 (12H, s, 4 × ribosyl OMe), 1.65 (16H, br d, *J* 7.7, 16 × azabicyclooctyl-H), 1.32 (24H, d, *J* 6.7, 4 × triazolyl 3-$CH(CH_3)_2$); δ_c (75 MHz, $CDCl_3$); 170.1 (CO), 169.6 (2 × CO), 162.0, 159.1, 150.7, 150.67, 148.2, 141.0, 139.9, 137.5, 126.8, 125.2, 124.5, 102.8, 88.8, 79.6, 72.9, 69.9, 62.9, 58.7, 51.2, 47.3 (2 x C), 39.6, 39.0, 37.4, 26.6, 25.7, 21.6, 20.8, 20.5, 12.9 (One aliphatic carbon could not be located due to peak

overlaps); υ_{max}/cm^{-1} (film); 2934, 1750, 1711, 1669, 1512, 1455, 1386, 1228; *m/z* (ESI^+) 3058.5 (2%, $[M+H]^+$); (Found $[M+H]^+$, 3058.4522. $C_{162}H_{201}N_{24}O_{36}$ requires *MH*, 3058.4630); 1551.7 (100%, $[M+2Na]^{2+}$); (Found $[M+2Na]^{2+}$, 1551.7152. $C_{162}H_{200}Na_2N_{24}O_{36}$ requires $[M+2Na]^{2+}$, 1551.7171); 1529.7 (61%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1529.7358. $C_{162}H_{202}N_{24}O_{36}$ requires $[M+2H]^{2+}$, 1529.7351).

1,1',1'',1'''-(Tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis{4,1-phenylene[(2*Z*)-4-(8-fluoro-1,3,4,5-tetrahydro-2*H*-pyrido[4,3-*b*]indol-2-yl)but-2-ene-3,1-diyl]})tetrakis(2', 3', 5'-tri-*O*-acetyluridine) (8g).



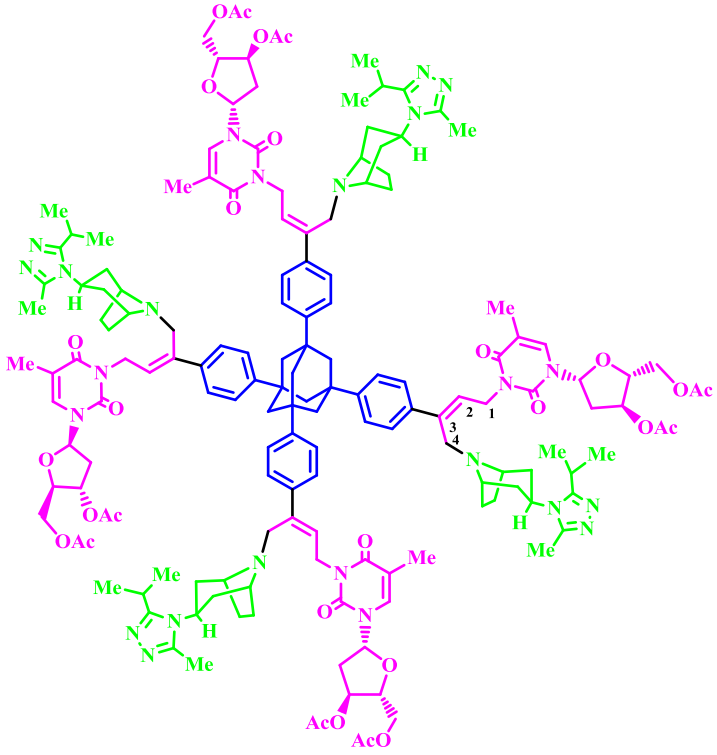
Prepared by general procedure D from **4b** in MeCN and heating for 3h. Flash column chromatography eluting with 30:1 v/v EtOAc/MeOH gave the product **8g** (62 %) as a colourless froth, mp 144-146°C; $[\alpha]_D$ + 24.7 (*c*, 12 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 8.02 (4H, br s, 4 × NH), 7.38 (8H, d, *J* 7.9, 8 × phenyl-H), 7.36 (4H, d, *J* 8.2, 4 × pyrimidinyl 6-H), 6.98 (8H, d, *J* 7.9, 8 × phenyl-H), 7.07 (4H, dd, *J* 8.6 and 4.5, 4 × pyridoindolyl-H), 6.98 (4H, dd, *J* 9.5 and 1.8, 4 × pyridoindolyl-H), 6.76 (4H, dt, *J* 9.1 and 2.3, 4 × pyridoindolyl-H), 6.04 (4H, d, *J* 4.4, 4 × ribosyl 1-H), 5.85 (4H, t, *J* 6.4, 4 × NCH_2CH=), 5.82 (4H, d, *J* 8.2, 4 × pyrimidinyl 5-H), 5.34 (8H, dd, *J* 8.7 and 6.1, 4 × ribosyl 2-H + 4 ×

ribosyl 3-H), 4.81 (8H, d, *J* 6.4, 4 × N*CH*$_2$CH=), 4.33 (12H, s, 4 × ribosyl 4-H + 4 × ribosyl 5-CH_2), 3.76 (8H, br s, 4 × =C*CH*$_2$N), 3.64 (8H, br s, 4 × pyridoindolyl 1-CH_2), 2.81 (8H, br s, 4 × pyridoindolyl-CH_2), 2.60 (8H, br s, 4 × pyridoindolyl-CH_2), 2.12 (12H, s, 4 × ribosyl OMe), 2.11 (12H, s, 4 × ribosyl OMe), 2.05 (12H, s, 4 × ribosyl OMe), 1.85 (12H, br s, 6 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 170.4 (CO), 169.8 (2 x CO), 162.2, 157.7 (*J* 232.2), 150.9, 148.6, 140.3, 139.6, 137.4, 134.6, 132.5, 126.6 (*J* 9.2), 126.57, 125.9, 125.0, 111.2 (*J* 9.2), 109.0 (*J* 4.5), 108.8 (*J* 25.3), 103.8, 102.9 (*J* 25.3), 88.5, 79.9, 73.1, 70.2, 63.2, 49.8, 49.3, 47.1, 40.0, 39.0, 29.9, 23.8, 21.0, 20.7, 20.6; υ_{max}/cm^{-1} (film); 3373, 3023, 2929, 1748, 1712, 1667, 1483, 1455, 1372, 1325, 1229; *m/z* (ESI^+) 2882.1 (10%, $[M+H]^+$); (Found $[M+H]^+$, 2882.0786. $C_{154}H_{157}F_4N_{16}O_{36}$ requires *MH*, 2882.0877); 1441.5 (100%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1441.5480. $C_{154}H_{158}F_4N_{16}O_{36}$ requires $[M+2H]^{2+}$, 1441.5475); *m/z* (ESI^+) 961.4 (100%, $[M+3H]^{3+}$); (Found $[M+3H]^{3+}$, 961.4. $C_{154}H_{159}F_4N_{16}O_{36}$ requires $[M+3H]^{3+}$, 961.3674).

NOE data ($CDCl_3$) for **8g**.

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	Ph-H	pyridoindolyl-H
1-H		-11.4	-4.6	-	-1.7 (δ 3.64)
2-H	-7.3		-	-6.5 (δ 7.38)	-
4-H	-7.0	-		-7.9 (δ 7.38)	-4.9 (δ 3.64) -5.8 (δ 2.81) -2.1 (δ 2.60)

1,1',1'',1'''-[Tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis(4,1-phenylene{(2*Z*)-4-[3-(3-isopropyl-5-methyl-4*H*-1,2,4-triazol-4-yl)-8-azabicyclo[3.2.1]oct-8-yl]but-2-ene-3,1-diyl})]tetrakis(3', 5'-di-*O*-acetylthymidine) (8h).



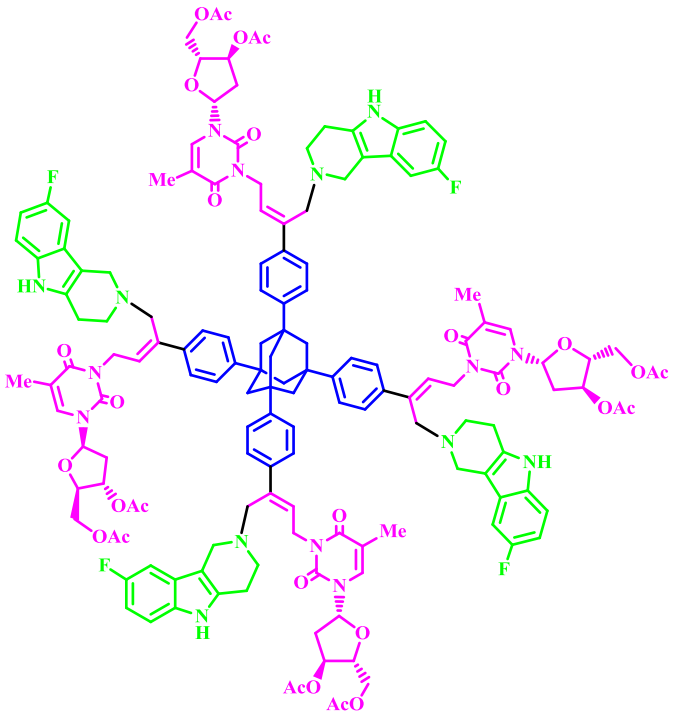
Prepared by general procedure D from **4c** in MeCN and heating for 4h. Flash chromatography gradient eluting with 4:1 v/v EtOAc/MeOH and then 1:1 v/v EtOAc/MeOH gave the product **8h** (69%) as a colourless froth, mp 146-148°C; $[\alpha]_D$ + 2.6 (*c*, 11 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 7.46 (8H, d, *J* 8.6, 8 × phenyl-H), 7.37 (8H, d, *J* 8.6, 8 × phenyl-H), 7.29 (4H, s, 4 × pyrimidinyl 6-H), 6.37 (4H, dd, *J* 5.6 and 8.4, 4 × deoxyribosyl 1-H), 5.85 (4H, t, *J* 6.7, 4 × NCH_2CH=), 5.22 (4H, dd, *J* 4.5and 2.1, 4 × deoxyribosyl 3-H), 4.87 (8H, d, *J* 6.7, 4 × NCH_2CH=), 4.37 (4H, dd, *J* 12.2 and 3.6, 4 × deoxyribosyl 5-H_A), 4.35 (4H, dd, *J* 12.2 and 3.6, 4 × deoxyribosyl 5-H_B), 4.27-4.24 (8H, m, 4 × azabicyclooctyl-H + 4 × deoxyribosyl 4-H), 3.67 (8H, s, 4 × =CCH_2N), 3.44 (8H, br s, 8 × azabicyclooctyl-H), 2.98-2.93 (4H, m, 4 × triazolyl 3-$CH(CH_3)_2$), 2.51 (4H, dd, *J* 5.6 and 1.5, 4 × deoxyribosyl 2-H_A), 2.46 (4H, dd, *J* 5.6 and 1.5, 4 × deoxyribosyl 2-H_B), 2.37 (12H, s, 4 × triazolyl 5-CH_3), 2.23-2.05 (28H, m, 16 × azabicyclooctyl-H + 6 × adamantyl-CH_2), 2.14 (12H, s, 4 × deoxyribosyl OMe), 2.12 (12H, s, 4 × deoxyribosyl OMe), 1.96 (12H, s, 4 × pyrimidinyl 5-Me), 1.66 (16H, br d, *J* 7.9, 16 × azabicyclooctyl-H), 1.32 (24H, d, *J* 6.9, 4 × triazolyl 3-CH(CH_3)$_2$); δ_c (75 MHz, $CDCl_3$); 170.8, 170.6, 163.4, 159.5, 151.1, 151.0, 148.6, 141.2, 140.3, 133.2, 127.1, 125.9, 124.9, 111.2, 85.9, 82.5, 74.5, 64.3, 59.1, 51.6, 47.7 (2 x C), 40.2, 39.4, 37.9, 37.8, 27.1, 26.1, 22.0, 21.3, 21.2, 13.9, 13.3 ; υ_{max}/cm^{-1} (film); 3333, 2932, 1746, 1703, 1668, 1645, 1513, 1467, 1366, 1235; *m/z* (ESI^+) 2904.5 (8%, $[M+Na]^+$); (Found $[M+Na]^+$, 2904.4779. $C_{158}H_{200}NaN_{24}O_{28}$ requires *MNa*, 2904.4856); 2882.5 (15%,

$[M+H]^+$); (Found $[M+H]^+$, 2882.4986. $C_{158}H_{201}N_{24}O_{28}$ requires *MH*, 2882.5037); 1493.7 (68%, $[M+2Na]^{2+}$); (Found $[M+2Na]^{2+}$, 1463.7397. $C_{158}H_{200}NaN_{24}O_{28}$ requires $[M+2Na]^{2+}$, 1463.7374); 1441.8 (100%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1441.7615. $C_{158}H_{202}N_{24}O_{28}$ requires $[M+2H]^{2+}$, 1441.7555).

NOE data ($CDCl_3$) for **8h**.

	% Enhancement				
Irradiated proton	1-H	2-H	4-H	Ph-H	Azabicyclooctyl-H
1-H		-9.5	-1.1	-	-
2-H	-5.1		-	-	-
4-H	-2.1	-		-1.9 (δ 7.46)	-4.3 (δ 3.44)

1,1',1'',1'''-(Tricyclo[3.3.1.1^{3,7}]decane-1,3,5,7-tetrayltetrakis{4,1-phenylene[(2*Z*)-4-(8-fluoro-1,3,4,5-tetrahydro-2*H*-pyrido[4,3-*b*]indol-2-yl)but-2-ene-3,1-diyl]})tetrakis(3', 5'-di-*O*-acetylthymidine) (8i).



Prepared by general procedure D from **4c** in MeCN and heating for 6h. Flash column chromatography eluting with 20:1 v/v EtOAc/MeOH gave the product **8i** (74%) as a colourless froth, mp 155-157°C; $[\alpha]_D$ + 6.2 (*c*, 11 mg/1 mL $CHCl_3$); δ_H (300 MHz, $CDCl_3$); 8.18 (4H, br s, 4 × NH), 7.36 (8H, d, *J* 8.1, 8 × phenyl-H), 7.26 (4H, s, 4 × pyrimidinyl 6-H), 7.13 (8H, d, *J* 8.1, 8 × phenyl-H), 7.02 (4H, dd, *J* 8.5 and 4.4, 4 × pyridoindolyl-H), 6.95 (4H,

dd, *J* 9.6 and 1.9, 4 × pyridoindolyl-H), 6.73 (4H, dt, *J* 9.2 and 2.4, 4 × pyridoindolyl-H), 6.36 (4H, dd, *J* 7.9 and 5.9, 4 × deoxyribosyl 1-H), 5.85 (4H, t, *J* 6.5, 4 × NCH_2CH=), 5.20 (4H, dd, *J* 4.4 and 1.8, 4 × deoxyribosyl 3-H), 4.82 (8H, d, *J* 6.5, 4 × NCH_2CH=), 4.38 (4H, dd, *J* 12.2 and 3.7, 4 × deoxyribosyl 5-H_A), 4.30 (4H, dd, *J* 12.2 and 3.7, 4 × deoxyribosyl 5-H_B), 4.23 (4H, dd, *J* 5.8 and 3.2, 4 × deoxyribosyl 4-H), 3.76 (8H, br s, 4 × =CCH_2N), 3.61 (8H, br s, 4 × pyridoindolyl 1-CH_2), 2.77 (8H, br s, 4 × pyridoindolyl-CH_2), 2.50-2.43 (16H, br m, 4 × pyridoindolyl-CH_2 + 4 × deoxyribosyl 2-CH_2), 2.12 (12H, s, 4 × deoxyribosyl OMe), 2.10 (12H, s, 4 × deoxyribosyl OMe), 1.95 (12H, s, 4 × pyrimidinyl 5-Me), 1.77 (12H, br s, 6 × adamantyl-CH_2); δ_c (75 MHz, $CDCl_3$); 169.3, 169.1, 161.8, 156.3 (*J* 232.2), 149.5, 147.2, 138.9, 138.3, 133.2, 131.5, 131.2, 125.2 (*J* 9.2), 125.15, 124.7, 123.6, 109.7 (*J* 9.2), 109.5, 107.4 (*J* 4.5), 107.3 (*J* 25.2), 101.4 (*J* 23.0), 84.3, 80.9, 73.0, 62.7, 54.5, 48.6, 47.9, 45.7, 38.8, 37.5, 36.4, 22.3, 19.7, 19.66, 12.3; υ_{max}/cm^{-1} (film); 3346, 2927, 1744, 1702, 1643, 1465, 1366, 1325, 1232; *m/z* (ESI^+) 2706.1 (2%, $[M+H]^+$); (Found $[M+H]^+$, 2706.1237. $C_{150}H_{157}F_4N_{16}O_{28}$ requires *MH*, 2705.1284); *m/z* (ESI^+) 1353.6 (59%, $[M+2H]^{2+}$); (Found $[M+2H]^{2+}$, 1353.5679. $C_{150}H_{158}F_4N_{16}O_{28}$ requires $[M+2H]^{2+}$, 1353.5678); 902.7 (100%, $[M+3H]^{3+}$); (Found $[M+3H]^{3+}$, 902.7141. $C_{150}H_{159}F_4N_{16}O_{28}$ requires $[M+3H]^{3+}$, 902.7143).

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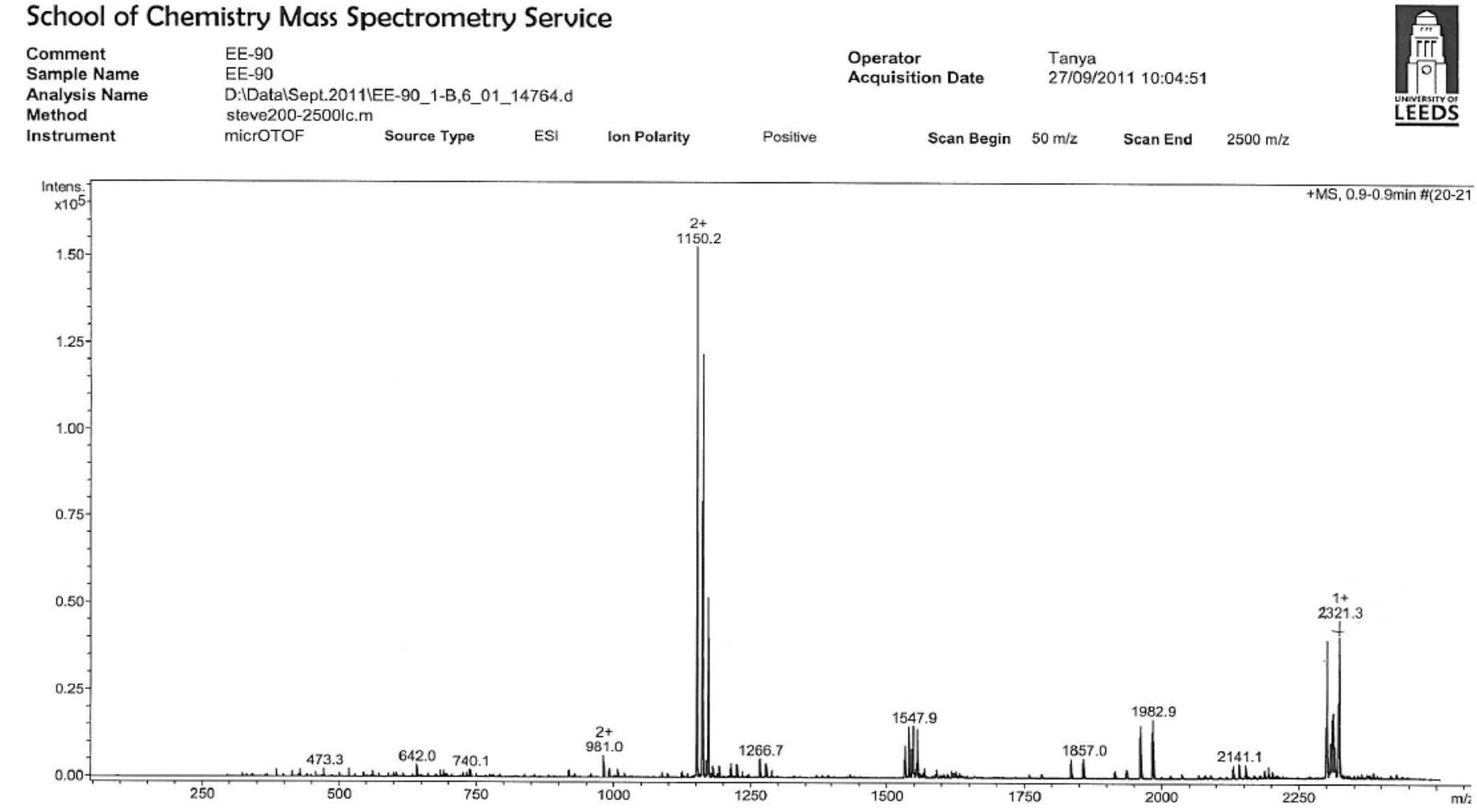

Fig. (1): HRMS of **8a** using autosampler technique.

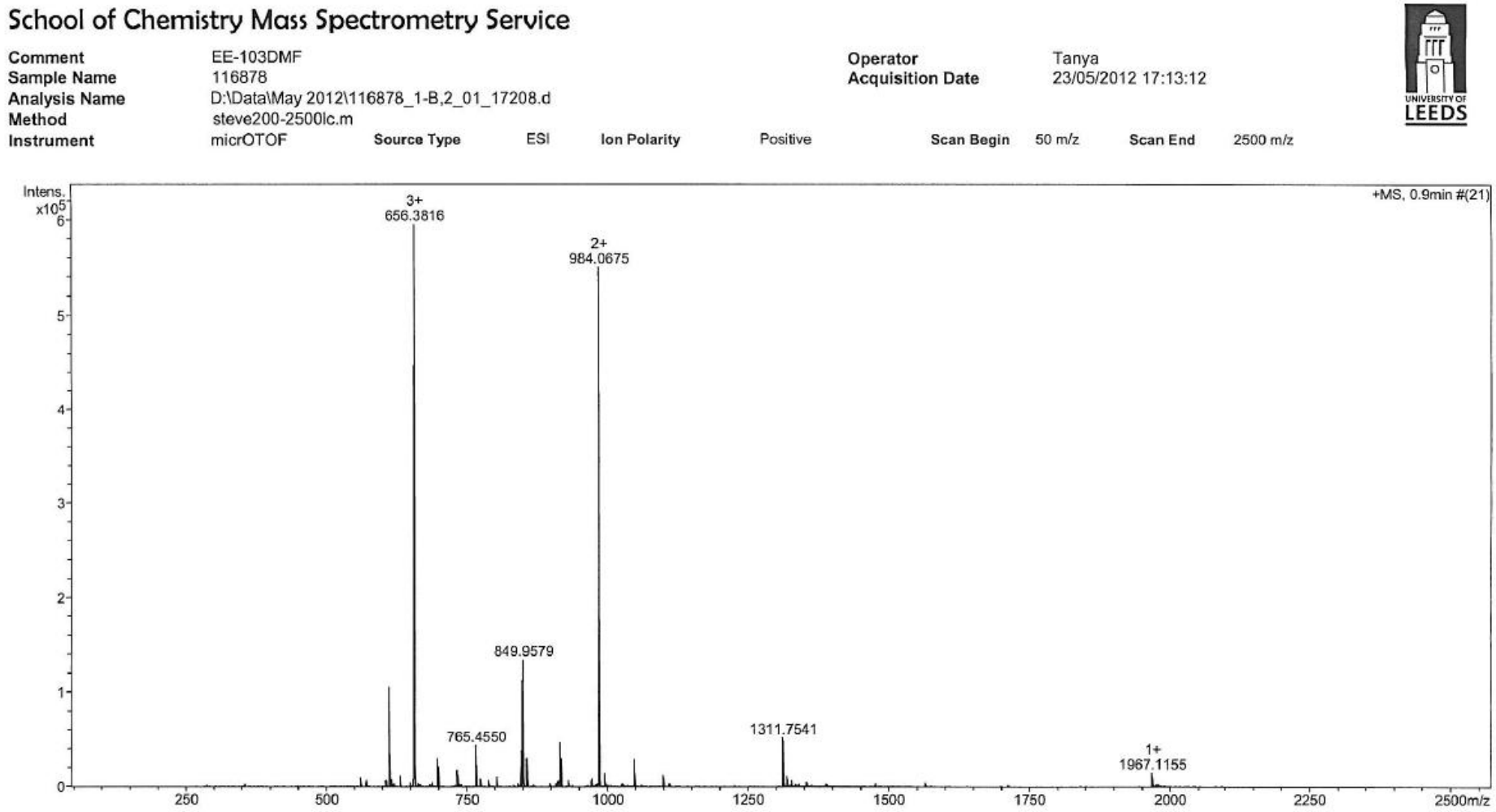

Fig. (2): HRMS of **8b** using autosampler technique.

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Comment	EE-104					**Operator**	Tanya		
Sample Name	116851					**Acquisition Date**	23/05/2012 16:43:39		
Analysis Name	D:\Data\May 2012\116851_1-B,1_01_17207.d								
Method	steve200-2500lc.m								
Instrument	micrOTOF	**Source Type**	ESI	**Ion Polarity**	Positive	**Scan Begin**	50 m/z	**Scan End**	2500 m/z

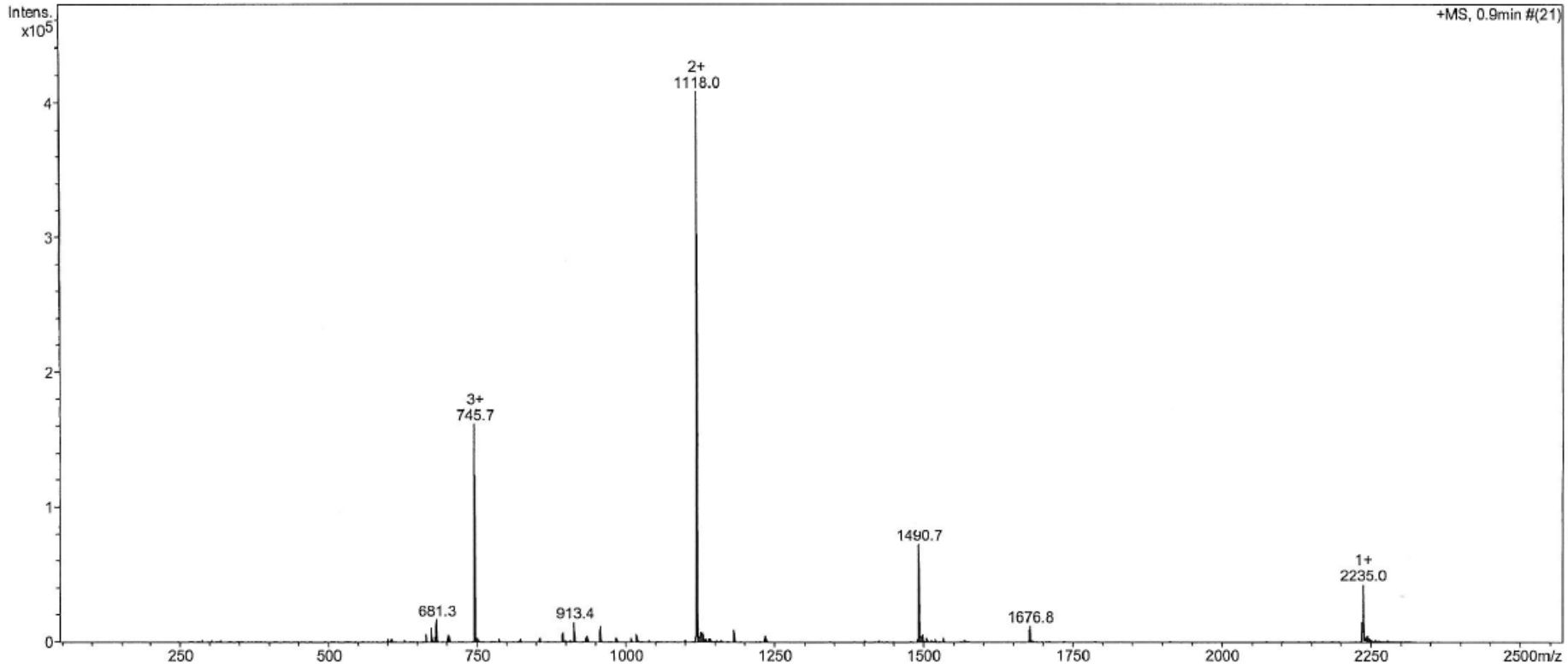

Fig. (3): HRMS of **8c** using autosampler technique.

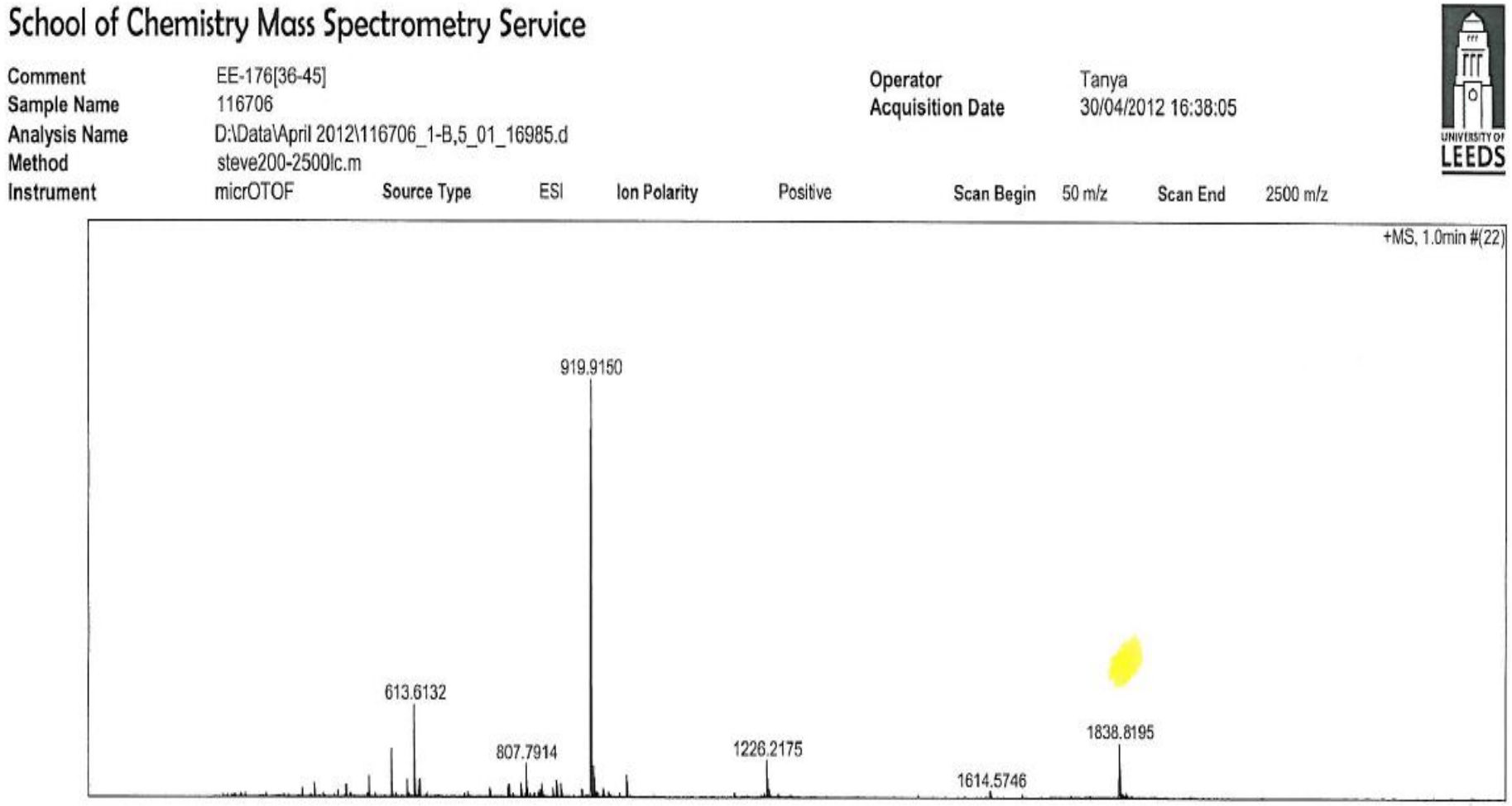

Fig. (4): HRMS of **8d** using autosampler technique.

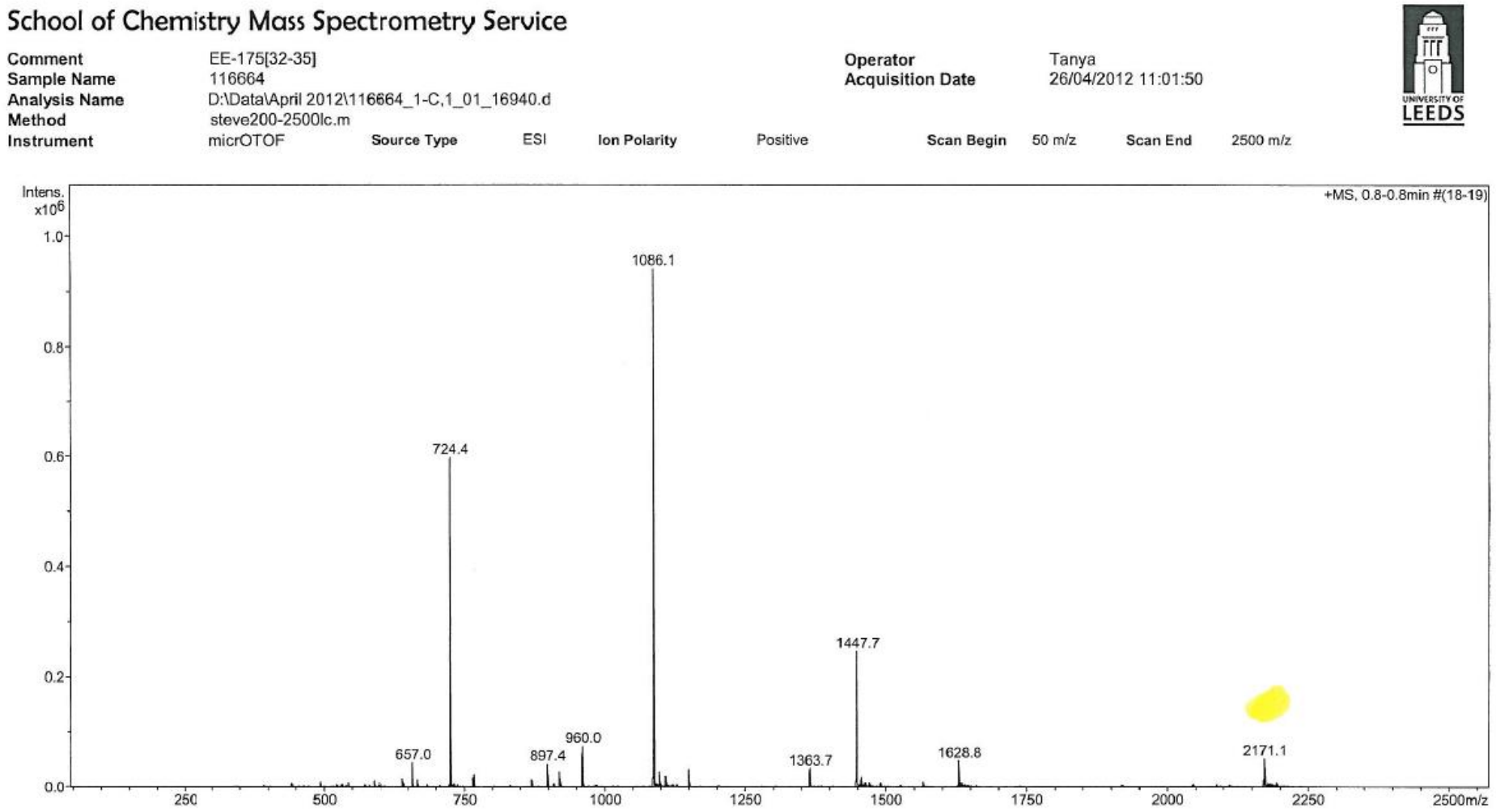

Fig. (5): HRMS of **8e** using autosampler technique.

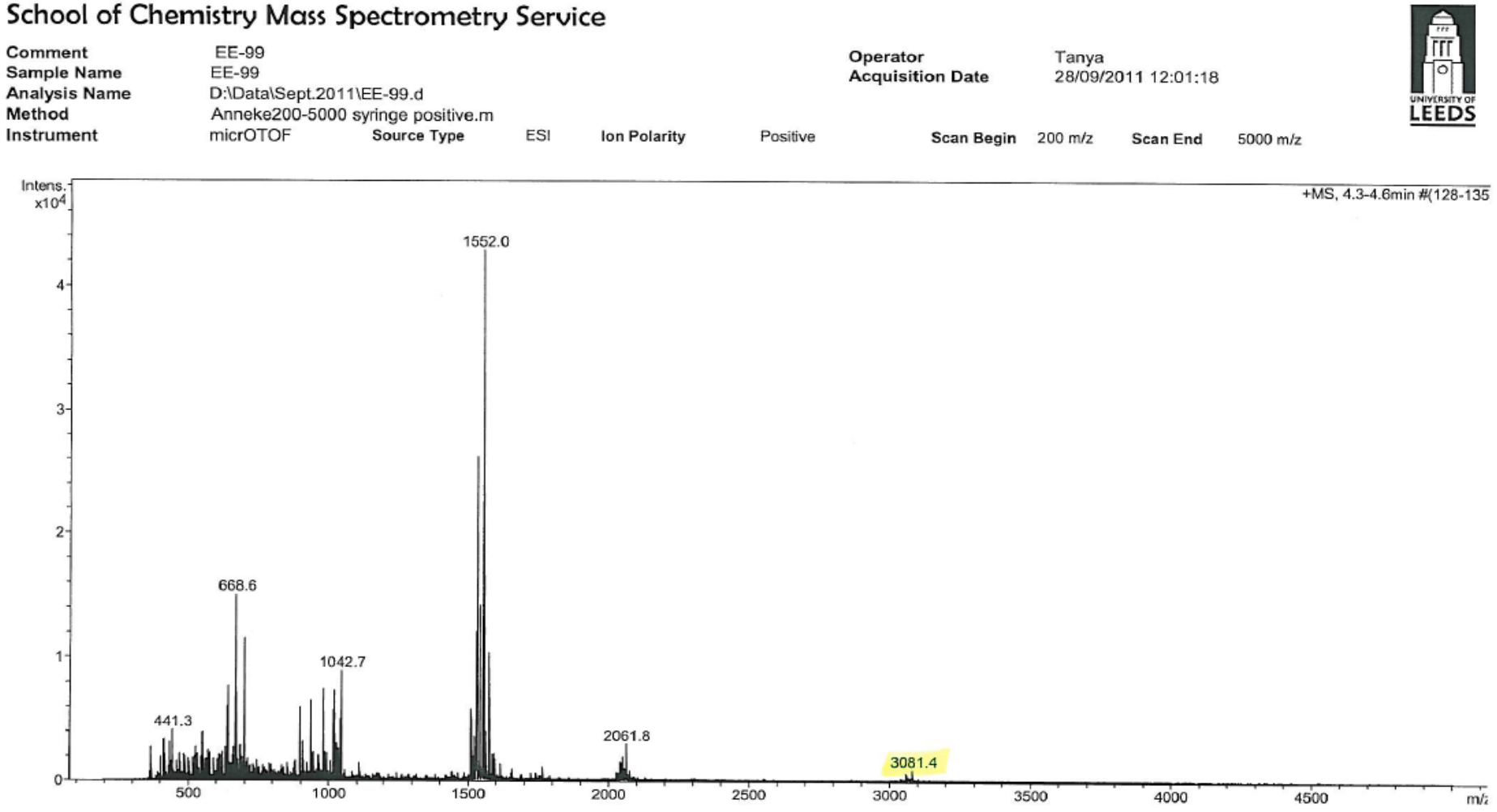

Fig. (6): HRMS of **8f** using syringe pump technique.

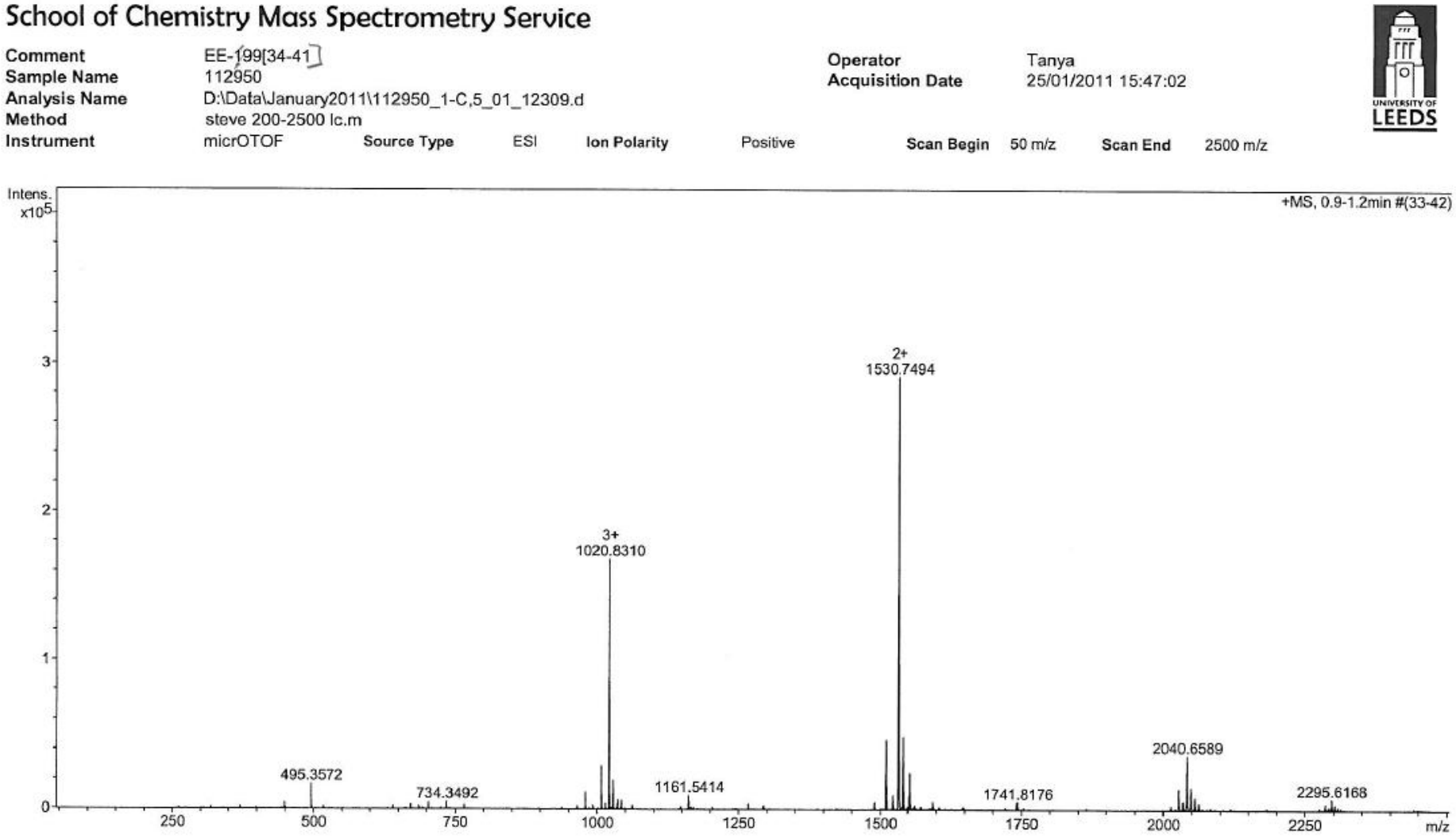

Fig. (7): HRMS of **8f** using autosamplar technique.

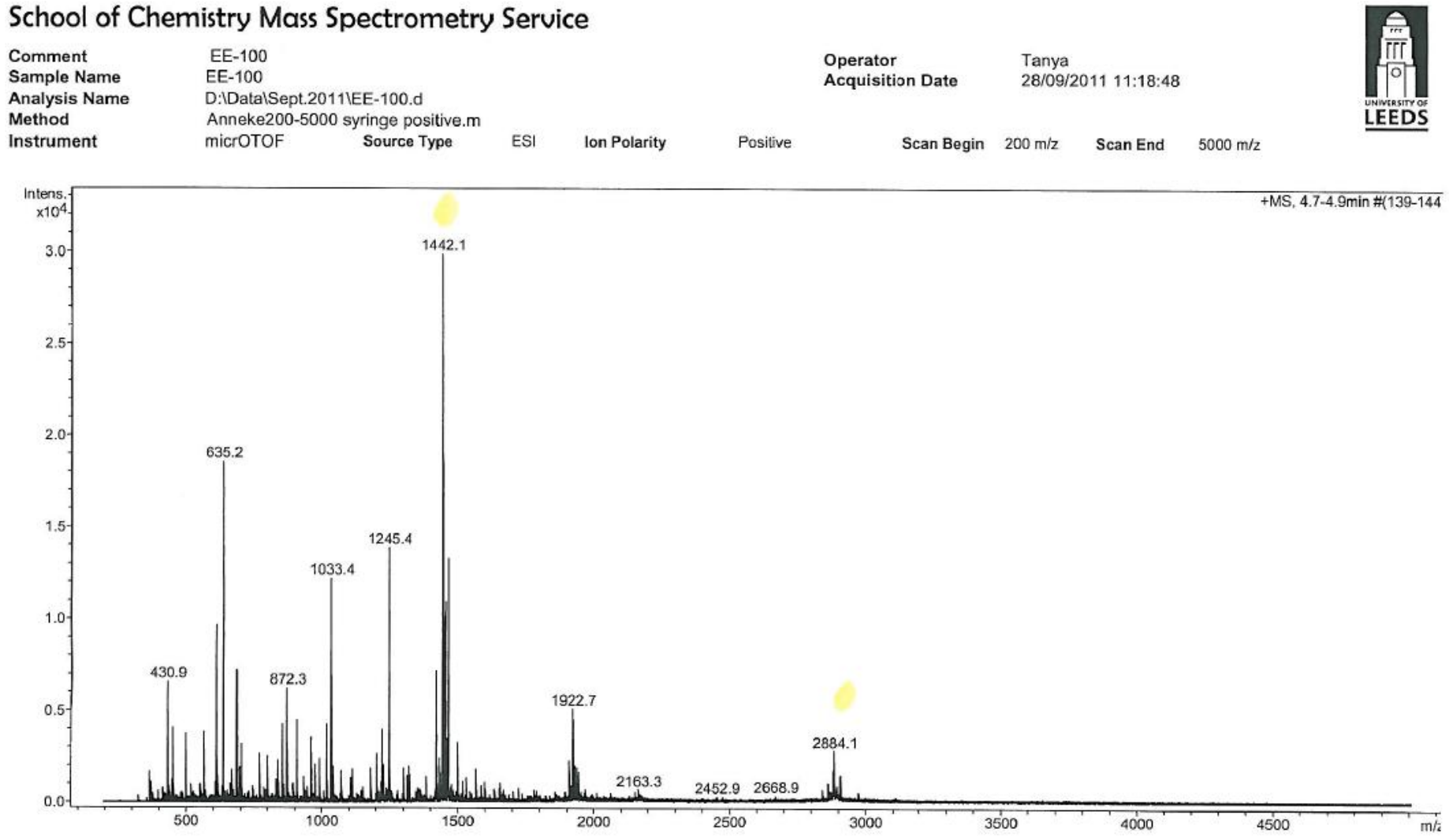

Fig. (8): HRMS of **8g** using syringe pump technique.

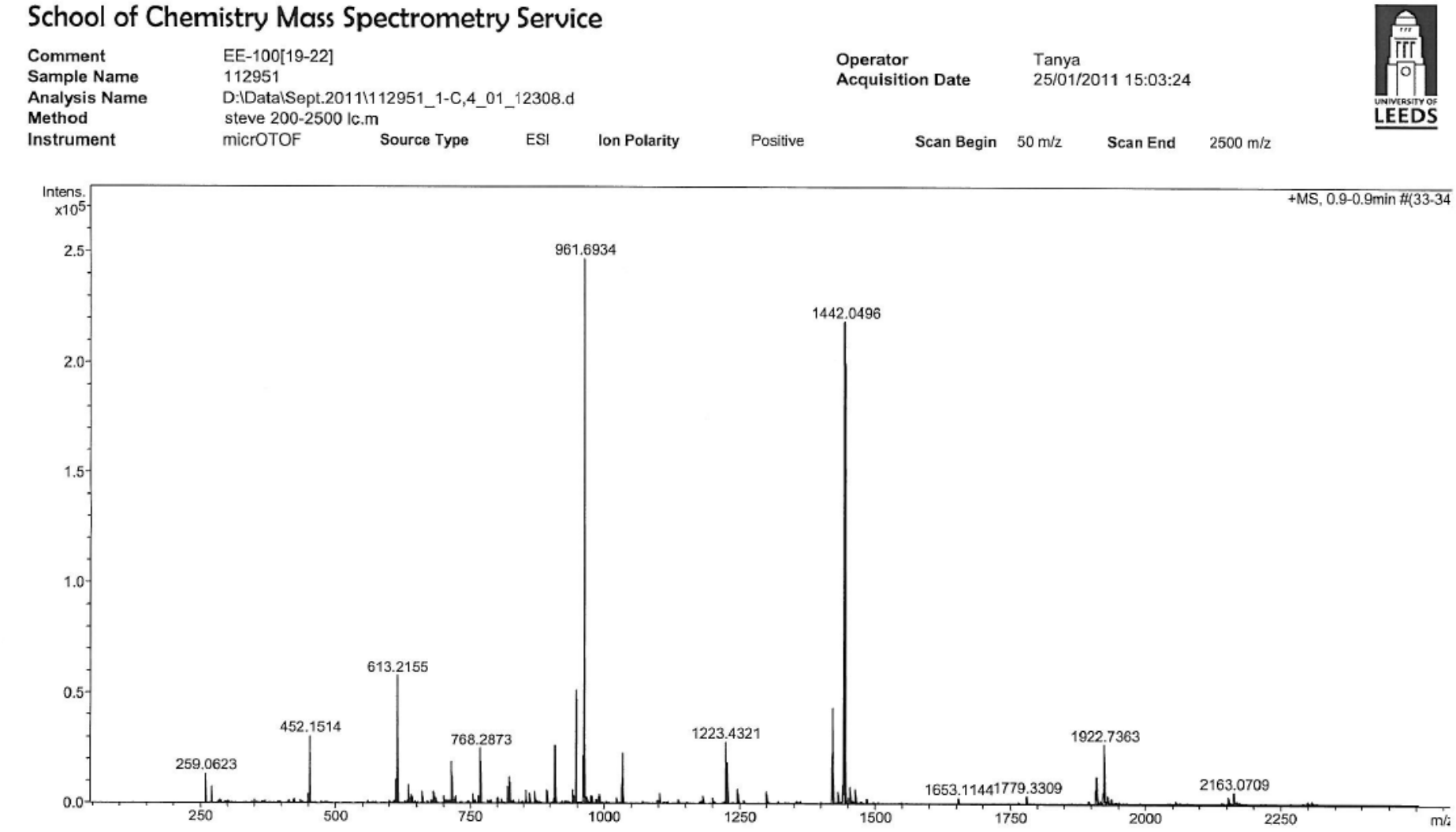

Fig. (9): HRMS of **8g** using autosamplar technique.

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Comment	EE-93					**Operator**	Tanya		
Sample Name	EE-93					**Acquisition Date**	28/09/2011 10:23:27		
Analysis Name	D:\Data\Sept.2011\EE-93.d								
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Instrument	micrOTOF	**Source Type**	ESI	**Ion Polarity**	Positive	**Scan Begin**	200 m/z	**Scan End**	5000 m/z

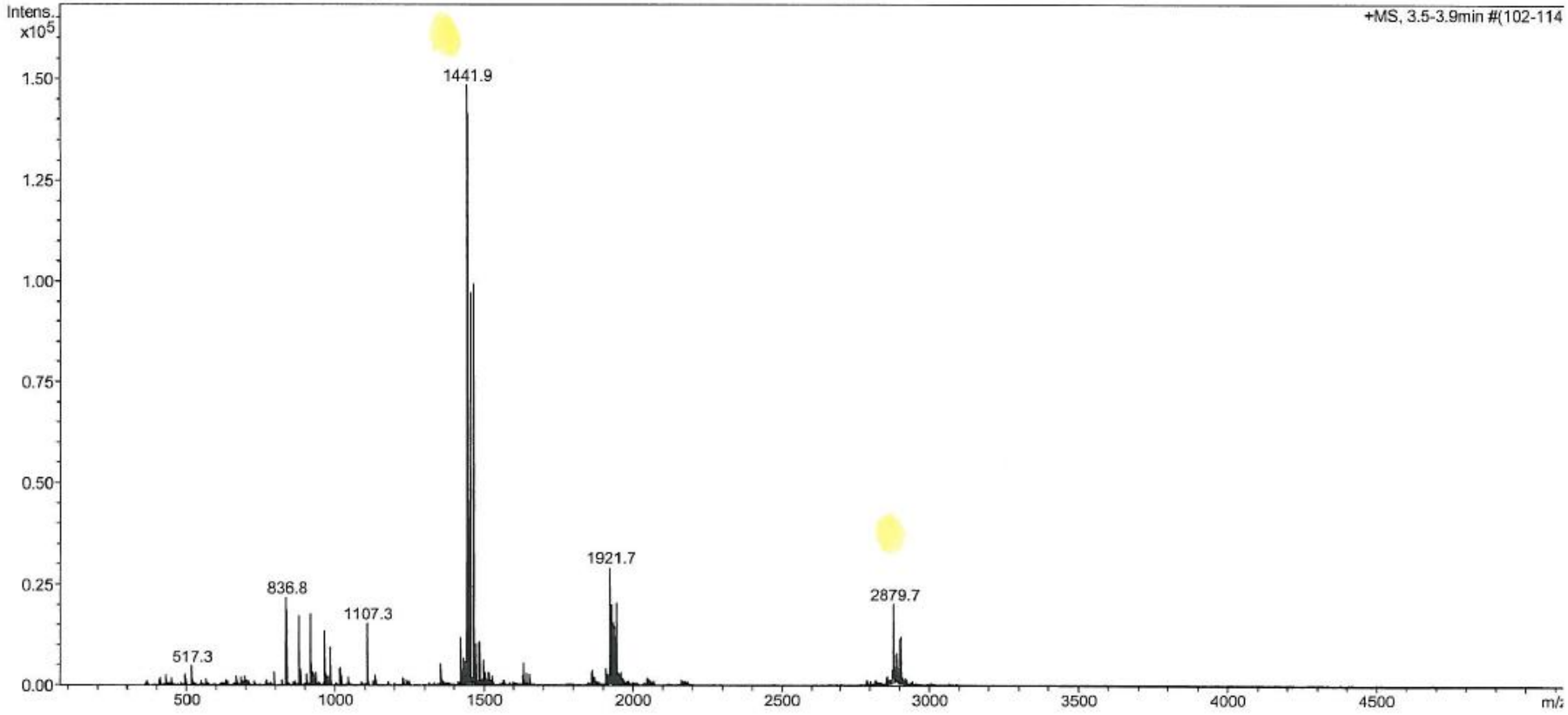

Fig. (10): HRMS of **8h** using syringe pump technique.

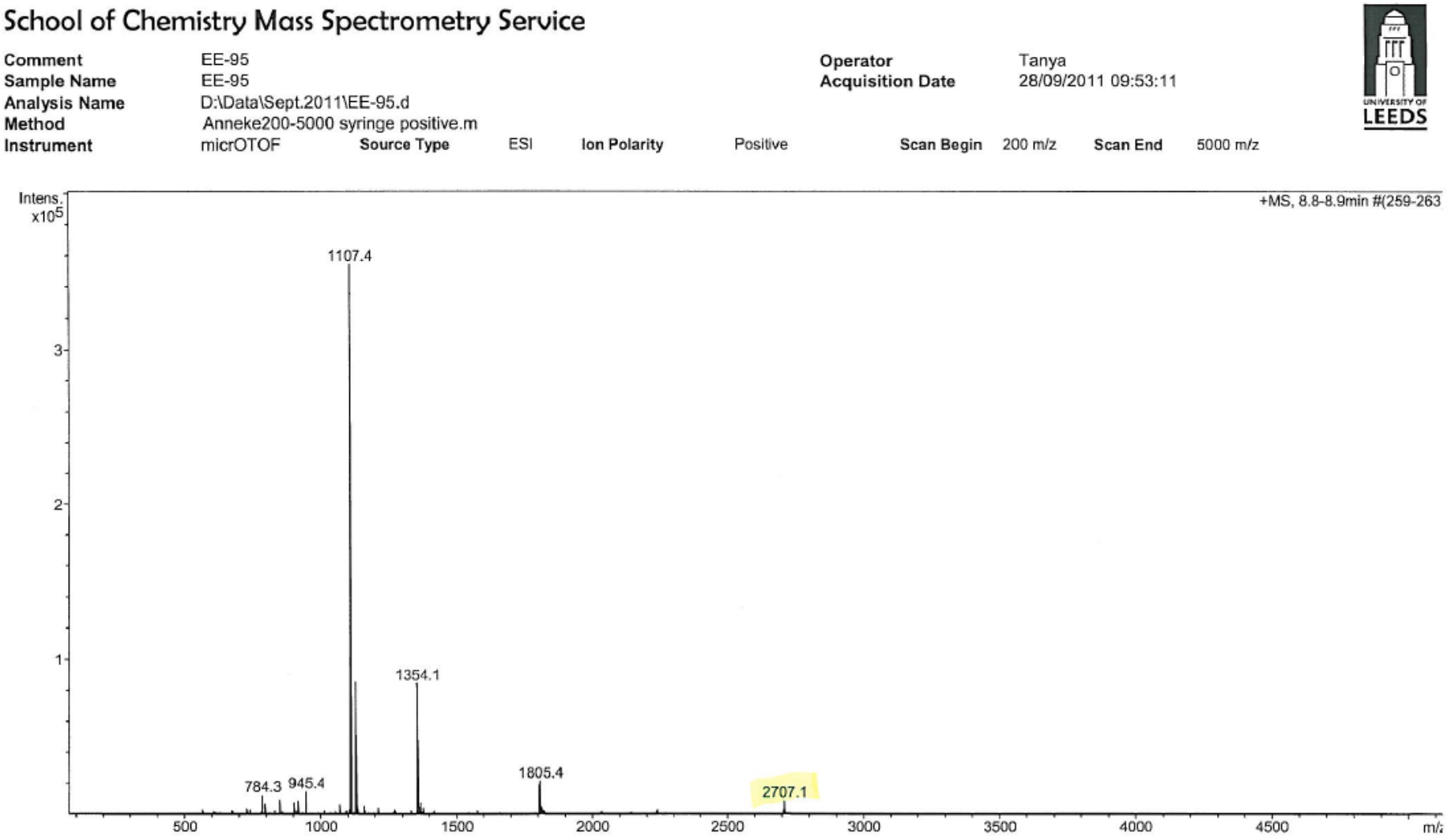

Fig. (11): HRMS of **8i** using syringe pump technique.

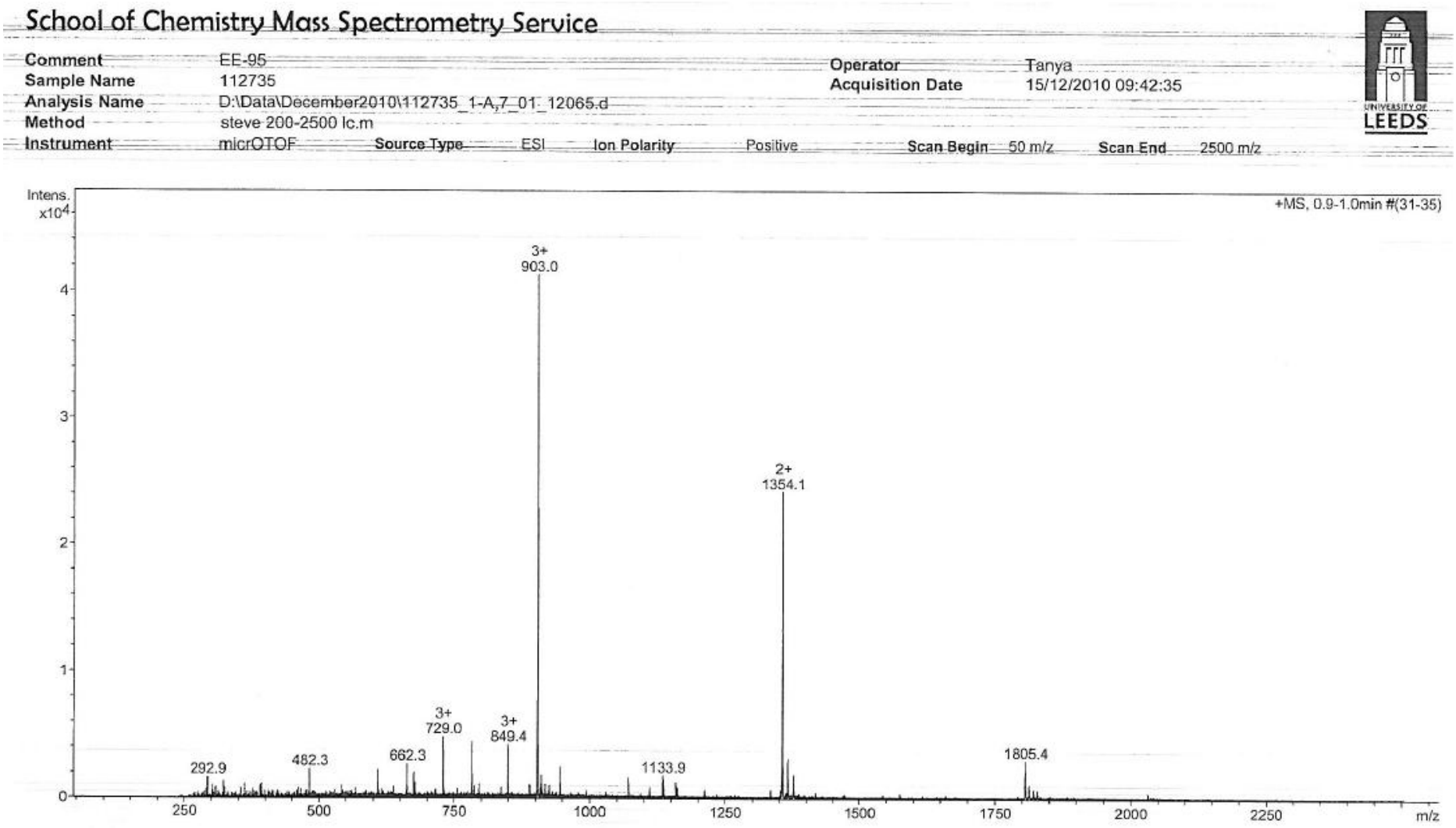

Fig. (12): HRMS of **8i** using autosamplar technique.