IR,^{1}H-NMR and ^{13}C-NMR spectra of DTPA dianhydride were shown in Fig.2-3-01, 2-3-02 respectively. From the IR spectrum, we can find the peaks at 1820cm^{-1} (C=O stretch symmetric), 1774cm^{-1} (C=O asymmetric stretching) which are characteristics of cyclo-dianhydride. ^{1}H-NMR spectrum of DTPA dianhydride exhibited four different chemical shift values at 4.0ppm, 3.6ppm, 3.5ppm and 3.2ppm with expected coupling. ^{13}C-NMR spectrum of it showed distinct singlets at 171.65 and 165.67 also suggests the presence of dianhydride system. All the above furnished information has confirmed the structure of dianhydride system.

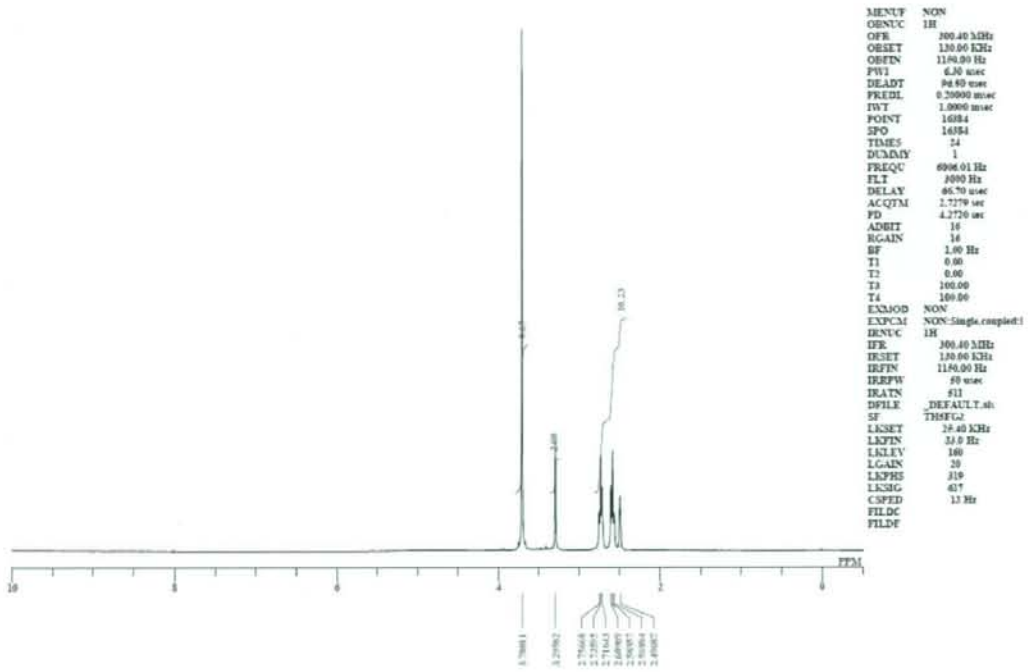


Fig. 2-3-01 ^{1}H-NMR of DTPA dianhydride

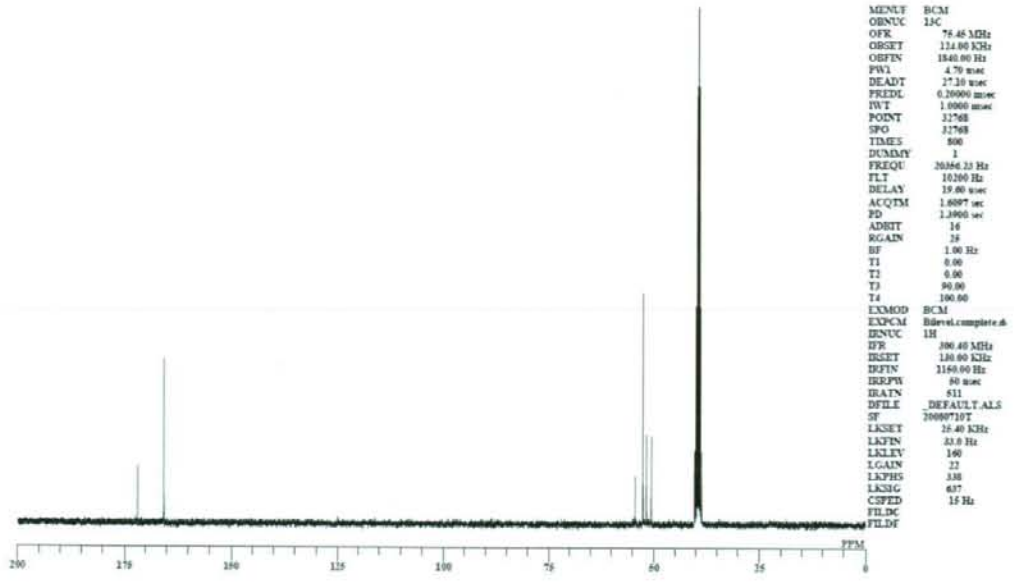
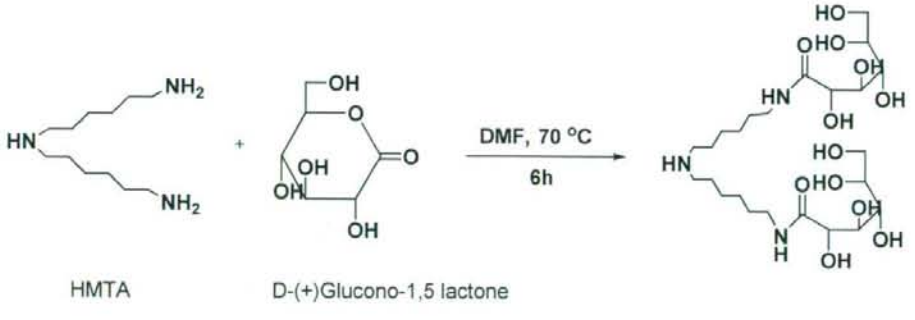


Fig. 2-3-02 ^{13}C-NMR of DTPA dianhydride

2-3-2 Synthesis of DTPA-HMTA-Glc(OAc)

2-3-2-1 Synthesis of HMTA-Glc(OH)

To a solution of D-(+)Glucono-1,5-lactone in adequate amount of DMF was added hexa-methylene triamine under inert conditions and the temperature of the reaction mixture was maintained at 70°C over a period of six hours. After ensuring the completion of reaction, product was left in refrigerator overnight and taken directly without further purification. Preparation of the title compound is depicted in Scheme 2-3-02

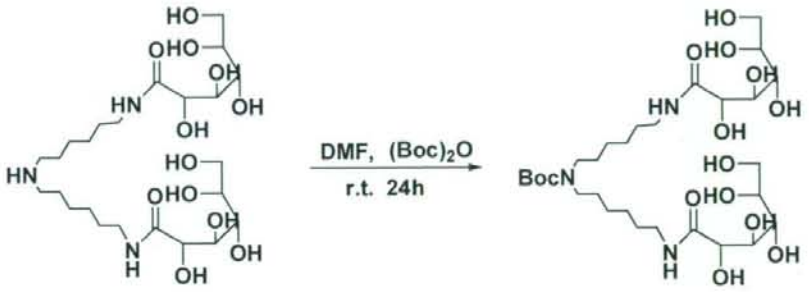


HMTA D-(+)Glucono-1,5 lactone

Scheme 2-3-02 Synthesis of HMTA-Glc(OH)

2-3-2-2 Synthesis of Boc protected HMTA-Glc(OH)

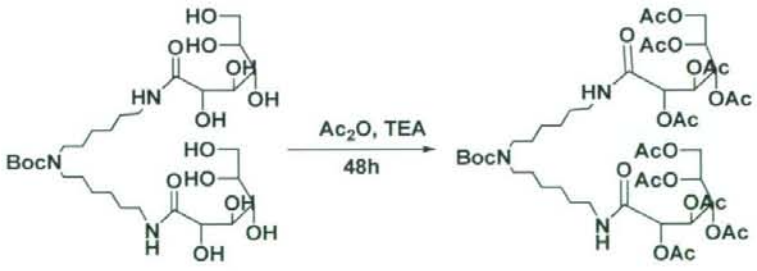
To a solution of DMF containing the above preparation was added Boc under cold conditions very carefully and the reaction mixture was subjected to through stirring under inert and dry condition then the reaction mixture was brought to room temperature and stirring was continued for a period of 24h. After completion of reaction the product was taken to next step without further purification.



Scheme 2-3-03 Synthesis of Boc protected HMTA-Glc(OH)

2-3-2-3 Synthesis of Boc protected HMTA-Glc(OAc)

To the above Boc protected compound under chilled condition triethyl amine and acetic anhydride was added carefully with continues stirring and after one hour the reaction mixture was brought to room temperature and stirred thoroughly for 48h. After the completion of reaction mixture was extracted in to ethylacetate and washed thoroughly with sat.$NaHCO_3$ and brine solution and the organic layer was rotaevaporated and purified by column chromatography by using step gradient mixtures of chloroform and methanol. Schematic procedure is summarized in Scheme 2-3-04.



Scheme 2-3-04 Synthesis of Boc-HMTA-Glc(OAc)

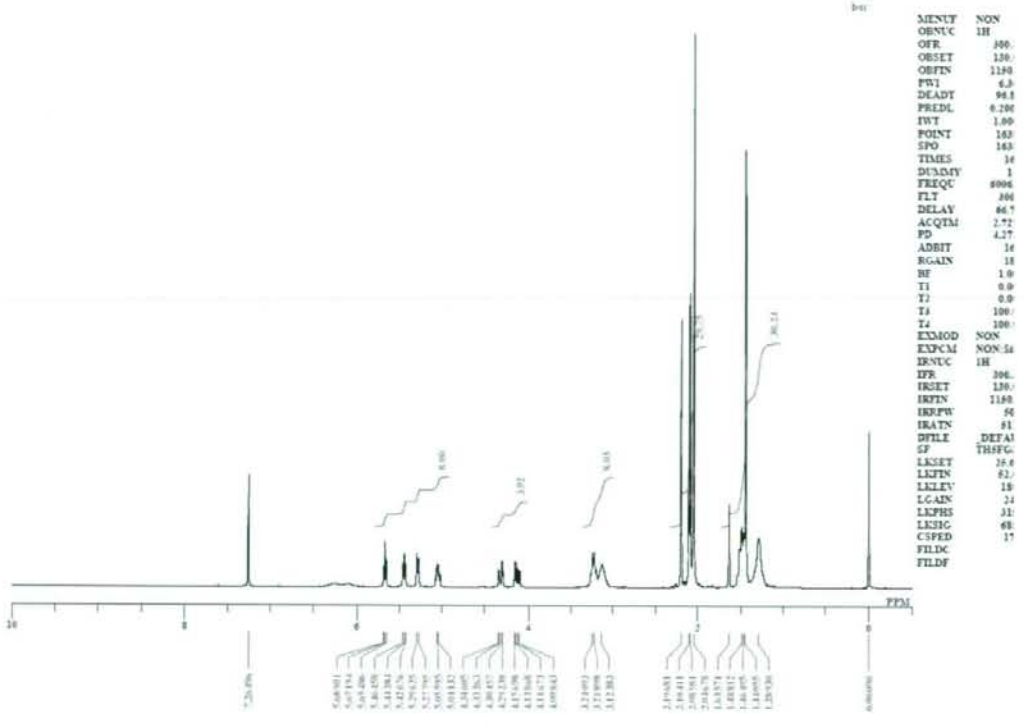
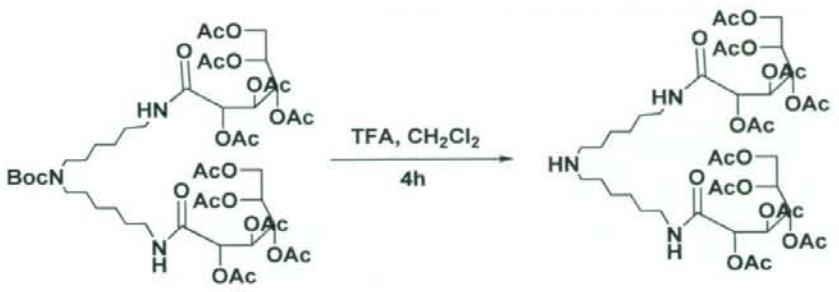


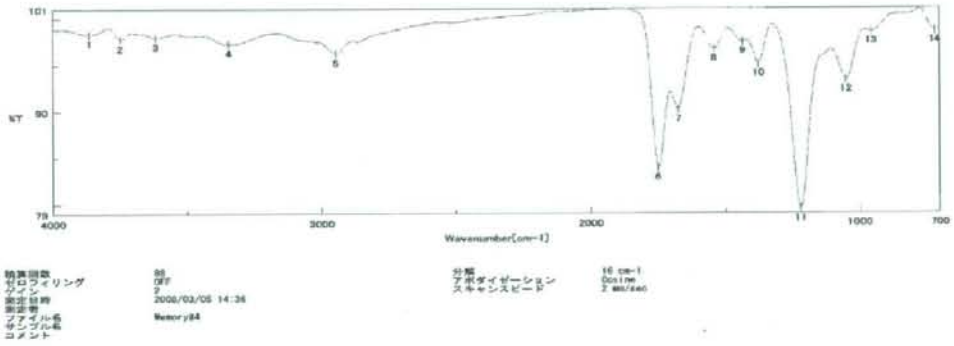
Fig. 2-3-03 ^{1}H-NMR spectrum of Boc-HMTA-Glc(OAc)

2-3-2-4 Synthesis of HMTA-Glc(OAc)

To a solution of above compound in dichloromethane was added triflouro acetic acid at 5° C carefully and the reaction was kept at room temperature for a period of 4h. After ensuring the completion of the reaction, reaction mixture was washed with and the organic phase was concentrated on rotaevaporation and this crude product was dissolved in ethyl acetate and washed successively with adequate amount of sat.$NaHCO_3$, water and finally with brine solution. Organic phase was concentrated under vacuum and the resulted crude product was purified by column chromatography using step gradient mixtures of chloroform and methanol as eluents.



Scheme 2-3-05 Synthesis of HMTA-Glc(OAc)



Terminal IR 8/03. (Neat - put as capillary film on CH_2Cl_2)

Fig.2-3-04 IR spectrum of HMTA-Glc(OAc)

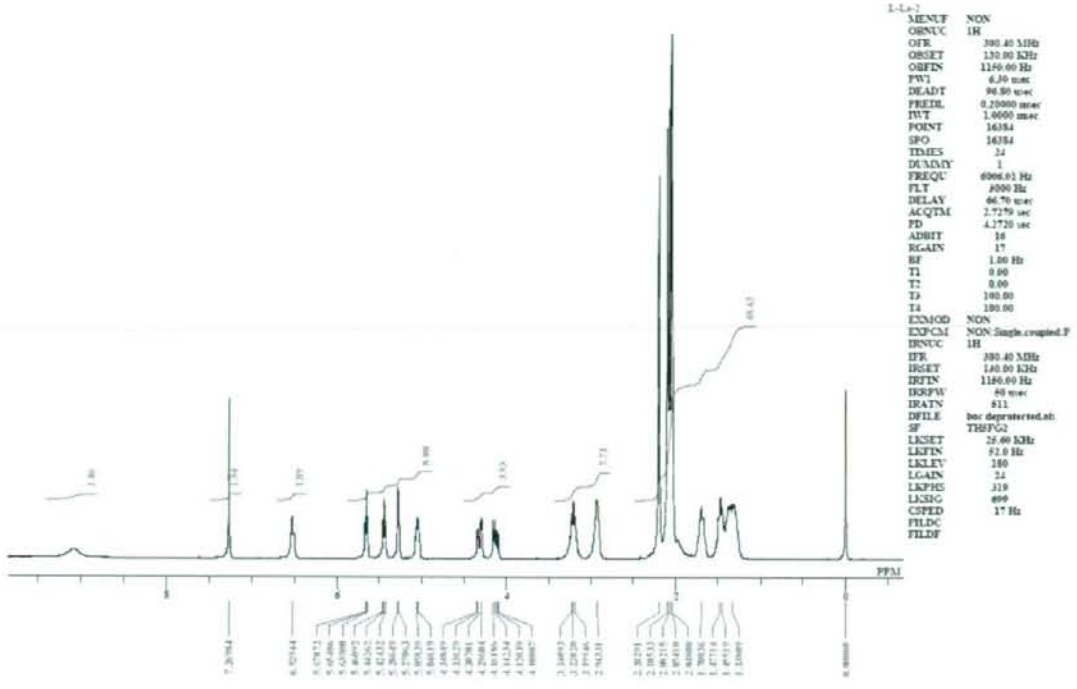


Fig. 2-3-05 ^{1}H-NMR Spectrum of HMTA-Glc(OAc)

IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral analysis of the above compound has confirmed its structure. ^{1}H-NMR spectrum of it showed different chemical shift values at exhibited regions 5.67-5.06ppm, 4.34-4.10ppm, 3.22ppm, 2.94ppm, 2.20-204ppm and 1.70-1.33ppm with expected multiplicity.

^{13}C-NMR of it showed distinctive singlets at 170.65-166.26 indicates the presence of amide C=O group all other aliphatic carbons observed between 71.78-20.48ppm. In addition to these data mass peak at m/z 998 suggests the formation of expected compound.

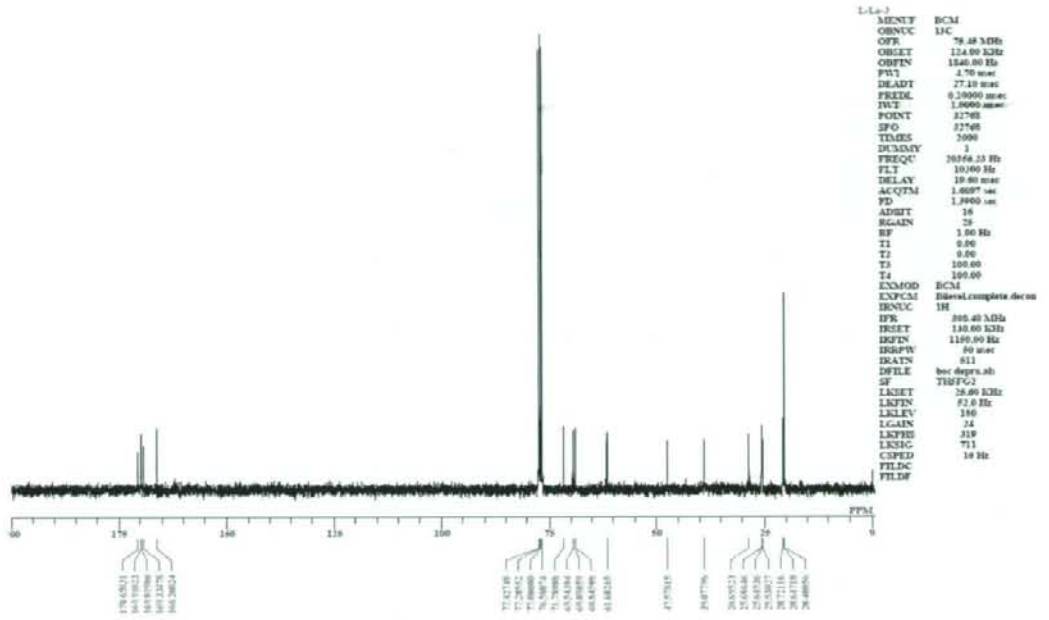
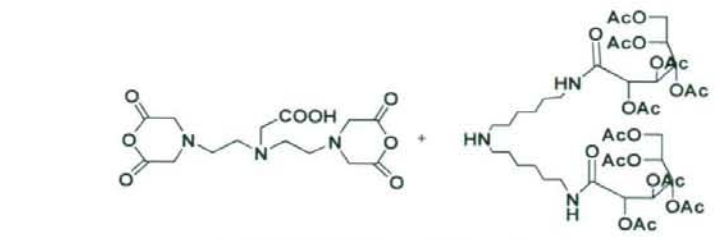


Fig. 2-3-06 ^{13}C-NMR Spectrum of HMTA-Glc(OAc)

2-3-2-5 Synthesis of DTPA-HMTA-Glc(OAc)

To a solution of DTPA di-anhydride in DMF was added terminal in quantitative ratio and the mixture was refluxed for 24h at 60°C and after the completion of the reaction DMF was removed under vacuum and the crude product was extracted into ethyl acetate and washed with water thoroughly to remove the traces of DMF and finally dried to get the pure compound. During treatment with excess of water the second unreacted anhydride ring was opened in to a dicarboxylic system.



特許出願の関係で

ここでは開示できない

DMF, R.T. 24h

Excess water

Scheme 2-3-06 Synthesis of DTPA-HTMA-Glc(OAc)

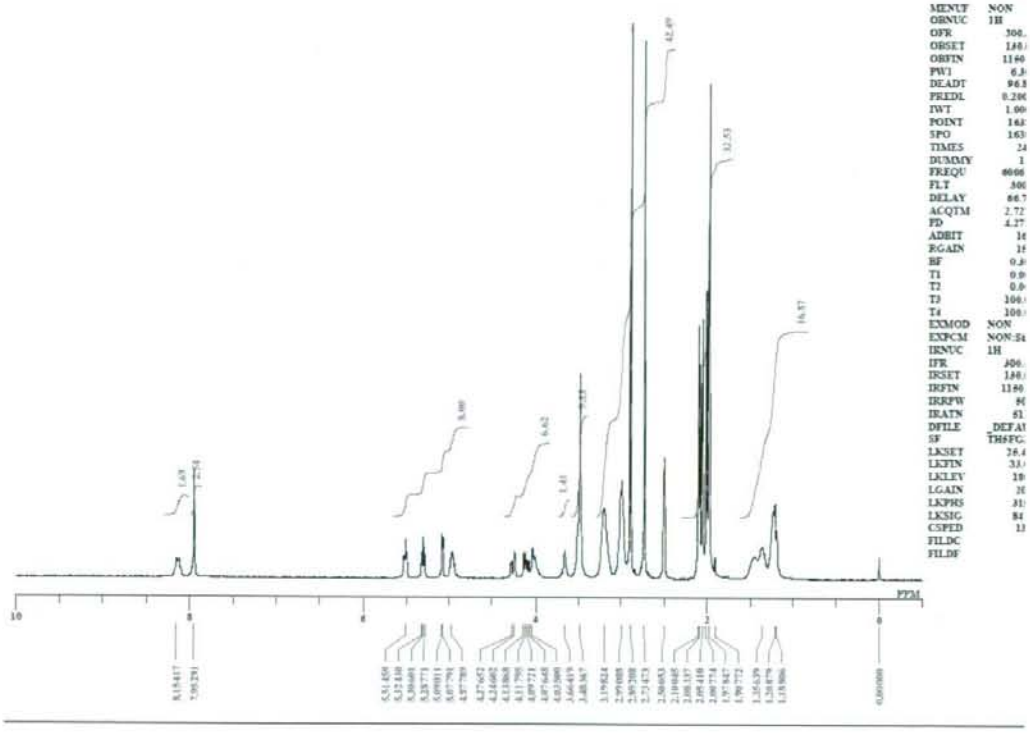


Fig. 2-3-07 ^{1}H-NMR of DTPA-HMTA-Glc(OAc)

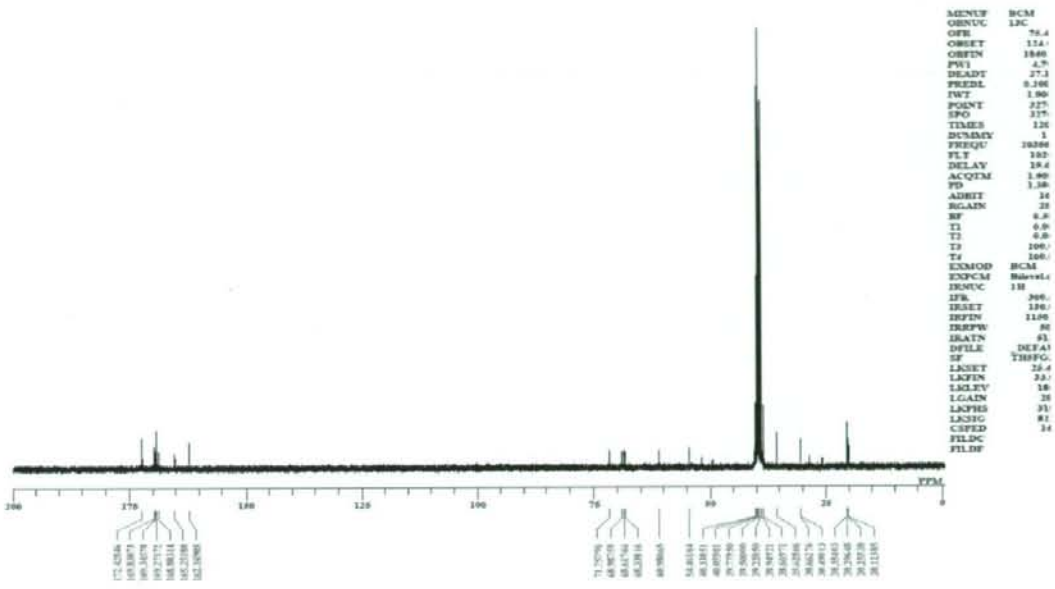


Fig. 2-3-08 ^{13}C-NMR of DTPA-HMTA-Glc(OAc)

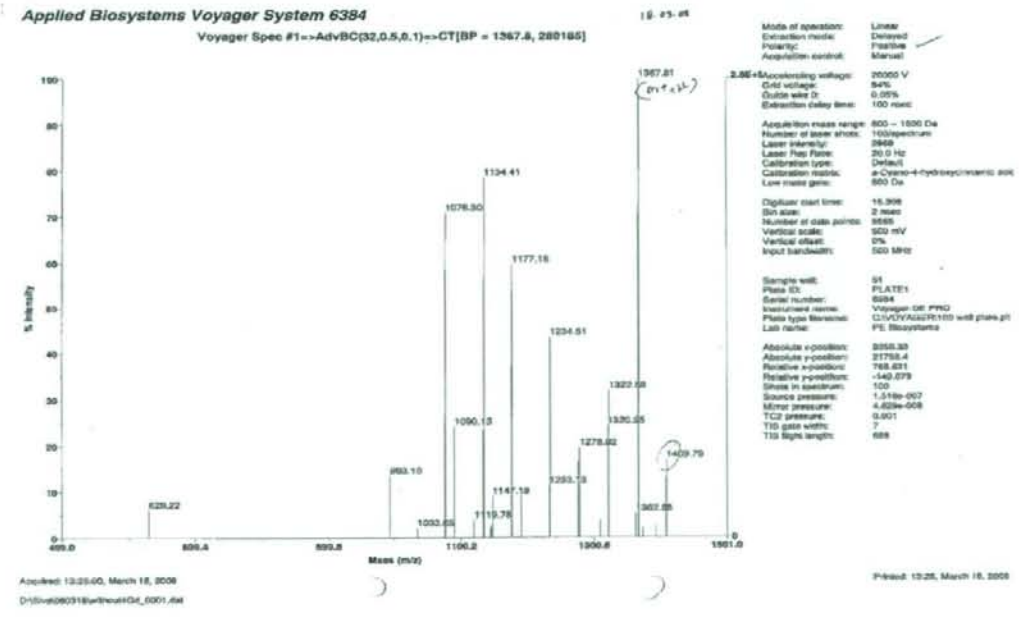
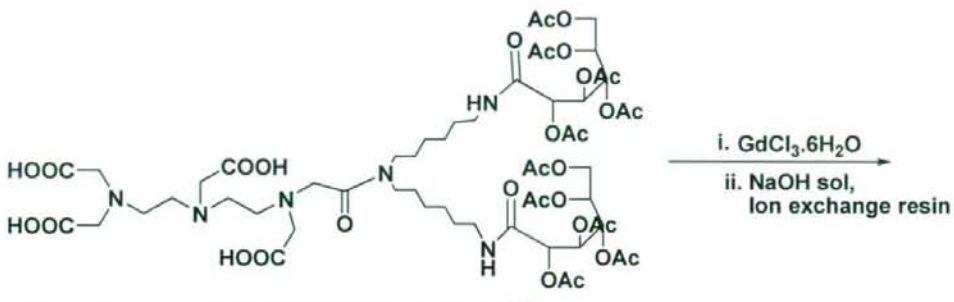


Fig. 2-3-09 Mass spectrum of DTPA-HMTA-Glc(OAc)

2-3-2-6 Synthesis of Gd-DTPA-HMTA-Glc(OAc)

To a solution of above prepared ligand in water was added triethylamine and pyridine and the mixture was stirred thoroughly. To this $GdCl_3.6H_2O$ was added slowly and the reaction was kept at 90°C and stirred for 24h. After completion of the reaction water was removed under vacuum and the crude product was dissolved in water and the excess of Gd was removed by using Chelex resign and after removal of excess Gd resin was filtered off and then the protected glycoside hydroxyl groups were deprotected under alkaline condition. After completion of hydrolysis it was treated with DOWEX 50W-X8 ion exchange resin and after completion of ion exchange resin was filtered and the filtrate was concentrated under vacuum.



特許出願の関係で

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Scheme 2-3-07 Synthesis of Gd-DTPA-HMTA-Glc(OAc)

2-3-3 Experimental

D-(+) Glucono-1,5 lactone, DMF, DTPA were procured from Wako Pure Chemical Industries, LTD. HETA was procured from Aldrich chemicals LTD. IR spectra were recorded on FTIR-spectrometer, using reflection on silicon. ^{1}H and ^{13}C NMR spectra were recorded on JEOL EX300 (300 MHz). Mass measurements were performed on VOYAGER-Deporimerix.

2-3-3-1 Synthesis of DTPA dianhydride

DTPA (3.0g, 7.6 mmol) was added to a mixture of acetic anhydride (3.0 ml, 31.8 mmol) and pyridine (4.5 ml, 53.6 mmol) and the reaction mixture was thoroughly stirred for 24h at 65° C. After that reaction mixture was washed repeatedly with acetic anhydride (20ml) and acetonitrile (20ml). White solid obtained was dried strongly to get 2.45g (6.94 mmol), 90%.

IR (KBr): ν (cm^{-1}); 3445(O=C<u>OH</u>), 1816 (O=COC=O), 1761 (<u>O=C</u>OH)

^{1}H-NMR

δ (ppm) = 3.70 (s, -CO-<u>CH_2</u>-CO- X 4)

=3.29 (s, -<u>CH_2</u>COOH)

=2.73 (t, $COCH_2N\underline{CH_2}CH_2N$ X 2)

=2.58 (t, $COCH_2NCH_2\underline{CH_2}N$ X2)

^{13}C-NMR

δ (ppm)= 171.9 (<u>O=C</u>OH)

=165.7 (<u>O=C</u>OC=O)

=54.5 (N<u>C</u>H_2COOH)

=52.1 (<u>C</u>H_2O=COC=O)

=50.7, 51.7 (NCH_2CH_2 X 2)

2-3-3-2 Synthesis of HMTA-Glc(OH)

To 3.26 g of D-(+)Glucono-1,5- lactone in 20ml of dimethyle formamide (DMF) was added 2.0g (9.2 mmol) of hexamethylene triamine under nitrogen atmosphere. Temperature of the reaction mixture was maintained at 70° C and after completion of the reaction compound was kept in refrigerator overnight and used for next step without further purification.

2-3-3-3 Synthesis of Boc-HMTA-Glc(OAc)

To 5.26 g (9.20 mmol) of HMTA-Glc(OH) in 10ml of DMF was added 2.0 g (9.20 mmol) of $(Boc)_2O$ under cold conditions. Reaction mixture was thoroughly stirred for 24 which will leave a clear solution. To this clear solution under cold conditions 9.40 g (92.1 mmol) of acetic anhydride and 10ml of triethyamine were added slowly and the effective stirring was continued for 48h at room temperature. To this reaction mixture adequate amount of ethylacetate was added and washed thoroughly with Sat. $NaHCO_3$ and then with brine solution to remove the DMF. Organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. This crude compound was purified by column chromatography using chloroform and methanol as step gradients as eluents. Removal of solvent yields 9.26g (92%) of brown colored compound.

^{1}H-NMR

δ (ppm) = 8.12 (m, <u>NH</u>C=O X 2)

= 5.66 (t, C=OCH(OAc)<u>CH</u>(OAc) X 2)

= 5.43 (t, C=OCH(OAc)CH(OAc)<u>CH</u>(OAc) X 2)

= 5.27 (d, C=O<u>CH</u>(OAc) X 2)

= 5.05 (m, C=OCH(OAc)CH(OAc)CH(OAc)<u>CH</u>(OAc) X 2)

= 4.32 (dd, C=OCH(OAc)CH(OAc)CH(OAc)CH(OAc)CH_aH_b(OAc) X 2)
= 4.10 (dd, C=OCH(OAc)CH(OAc)CH(OAc)CH(OAc)CH_aH_b(OAc) X 2)
= 3.22 (m, -NH$CH_2$$CH_2$ X 2)
= 2.93 (t, N(Boc)$CH_2$$CH_2$ X 2)
= 2.20-2.04 (m, CH(OAc) X 10)
= 1.71-1.41 (m, $NHCH_2(CH_2)_4CH_2NH$ X 4)
= 1.25 (s, $OCOC(CH_3)_3$)

2-3-3-4 Synthesis of HMTA-Glu(OAc)

To 10.43 g (9.56 mmol) of completely protected ligand in dichloromethane was added 8.52 ml (114.72 mmol) of trifluoroacetic acid(TFA) at 5°C carefully with constant stirring. Reaction mixture was allowed to stir over a period of 4h. After the completion of the reaction excess of TFA was quenched by washing the organic layer with water. Then the organic layer is evaporated under vacuum. This resulted crude product was dissolve in ethyl acetate and washed with Sat. $NaHCO_3$ to neutralize the organic layer (tested with pH paper). Later organic layer was concentrated under vacuum and finally crude product so obtained was purified by column chromatography by using chloroform and methanol step gradient mixtures as eluents. By removing the organic solvent under reduced pressure pale brown crystals was obtained in 86% (8.23g) of yield.

^{1}H-NMR
δ (ppm) = 6.52 (m, NHC=O X 2)
= 5.65 (t, C=OCH(OAc)CH(OAc) X 2)
= 5.44 (t, C=OCH(OAc)CH(OAc)CH(OAc) X 2)
= 5.27 (d, C=OCH(OAc) X 2)
= 5.05 (m, C=OCH(OAc)CH(OAc)CH(OAc)CH(OAc) X 2)
= 4.30 (dd, C=OCH(OAc)CH(OAc)CH(OAc)CH(OAc)CH_aH_b(OAc) X 2)
= 4.10 (dd, C=OCH(OAc)CH(OAc)CH(OAc)CH(OAc)CH_aH_b(OAc) X 2)
= 3.22 (m, -NH$CH_2$$CH_2$ X 2)
= 2.94 (m, NH$CH_2$$CH_2$ X 2)
= 2.20-2.04 (m, CH(OAc) X 10)
= 1.71-1.33 (m, $NHCH_2(CH_2)_4CH_2NH$ X 4)
^{13}C-NMR
δ (ppm) = 170.69 (s, C=ONH)
= 71.78 (s, C=OCH(OAc) X 2)
= 69.54 (s, C=OCH(OAc)CH(OAc) X 2)
= 69.05 (s, C=OCH(OAc)CH(OAc)CH(OAc) X 2)
= 68.84 (s, C=OCH(OAc)CH(OAc)CH(OAc) CH(OAc) X 2)
= 61.60 (s, C=OCH(OAc)CH(OAc)CH(OAc) CH(OAc)CH_2(OAc) X 2)
= 47.57 (s, C=ONHCH_2 X 2)
= 39.07 (s, NH$CH_2$$CH_2$ X 2)

= 28.69 (s, C=ONHCH$_2$<u>CH$_2$</u> X 2)
= 25.68 (s, NHCH$_2$<u>CH$_2$</u> X 2)
= 25.64 (s, C=ONHCH$_2$CH$_2$<u>CH$_2$</u> X 2)
= 25.53 (s, NHCH$_2$CH$_2$<u>CH$_2$</u> X 2)
= 20.72, 20.64, 20.40 (s, (OC=O<u>CH$_3$</u>)$_3$ X 10)

2-3-3-5 Synthesis of DTPA-HMTA-Glc(OAc)

To a solution of 0.5 g (1.40 mmol) of DTPA dianhydride in DMF was added 1.39 g (1.40 mmol) of HMTA-Glc(OAc) and the reaction mixture was stirred vigorously over a period of 24h under nitrogen atmosphere. After completion of the reaction solvent was removed under vacuum and washed with chloroform and then to that excess of water was added to initiate the opening of the second anhydride system. After completion of hydrolysis water was evaporated to get pale brown colour compound 1.65g (86%).

^{1}H-NMR
δ (ppm) = 8.15 (m, <u>NH</u>C=O X 2)
= 5.51 (t, C=OCH(OAc)<u>CH</u>(OAc) X 2)
= 5.30 (t, C=OCH(OAc)CH(OAc)<u>CH</u>(OAc) X 2)
= 5.08 (d, C=O<u>CH</u>(OAc) X 2)
= 4.97 (m, C=OCH(OAc)CH(OAc)CH(OAc)<u>CH</u>(OAc) X 2)
= 4.25 (dd, C=OCH(OAc)CH(OAc)CH(OAc)<u>CH</u>(OAc)C<u>H$_a$H$_b$</u>(OAc) X 2)
= 4.10 (dd, C=OCH(OAc)CH(OAc)CH(OAc)<u>CH</u>(OAc)CH$_a$<u>H$_b$</u>(OAc) X 2)
= 3.66 (s, N<u>CH$_2$</u>C=ON)
= 3.48 (s, N<u>CH$_2$</u>COOH X 4)
= 3.19 (m, -C=ON<u>CH$_2$</u>CH$_2$ X 4)
= 2.89 (m, NH<u>CH$_2$</u>CH$_2$ X 2)
= 2.50 (m, NHCH$_2$<u>CH$_2$</u> X 2)
= 2.10-1.90 (m, CH(O<u>Ac</u>) X 10)
= 1.35-1.18 (m, NHCH$_2$(<u>CH$_2$</u>)$_4$CH$_2$NH X 4)
^{13}C-NMR
δ (ppm) = 169.80 (s, <u>C=O</u>NH)
= 71.78 (s, C=O<u>CH</u>(OAc) X 2)
= 68.98 (s, C=OCH(OAc)<u>CH</u>(OAc) X 2)
= 68.61 (s, C=OCH(OAc)CH(OAc)<u>CH</u>(OAc) X 2)
= 68.33 (s, C=OCH(OAc)CH(OAc)CH(OAc) <u>CH</u>(OAc) X 2)
= 63.20 (s, N<u>CH$_2$</u>C=O)
= 60.98 (s, C=OCH(OAc)CH(OAc)CH(OAc) CH(OAc)<u>CH$_2$</u>(OAc) X 2)
= 54.46 (N<u>CH$_2$CH$_2$</u>N X 2)
= 52.40 (C=ON<u>CH$_2$</u> X 4)
= 35.62 (s, C=ONHCH$_2$<u>CH$_2$</u> X 4)
= 30.66 (s, C=ONHCH$_2$CH$_2$<u>CH$_2$</u> X 2)

= 20.35, 20.29, 20.25, 20.13 (s, $(OC=OCH_3)_3$ X 10)

2-3-3-6 Synthesis of Gd-DTPA-HMTA-Glc(OAc)

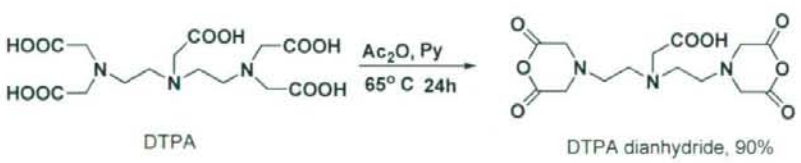
To a solution of DTPA-HMTA-Glc(OAc) (1.30g, 0.95 mmol) in water was added 0.75g (9.5 mmol) of pyridine was added and stirred thoroughly. To this well stirred solution 0.353g (0.95 mmol) of gadolinium chloride was added and the temperature of the reaction was kept constant at 65°C and refluxed for 24h. After completion of the reaction excess gadolinium was removed by treating with Chelex 100 resin (Na form 100-200, 2.8 g). After removal of excess gadolinium water was removed under reduced pressure and the resulted dried compound was dissolved in 30 ml of ion exchange water and to this 20 ml of 1N NaOH solution was added and stirred for 2 h at room temperature to hydrolyse the protected acetyl groups. The resulted solution was then treated with DOWEX 50W-X8 ion exchange resin(H form 100-200, 2.5 g). After completion of treatment, resin was filtered off and filtrate was evaporated to give the Gd-DTPA-HMTA-Glc(OH) in 0.85g (80%) of yield.

2-3-4 Synthesis of Gd-DTPA-E complex

In my experiment, the new Gd-DTPA-E was synthesized by the reaction of DTPA-E with equimolar amount of gadolinium in water which was in turn prepared from DTPA di anhydride and ethylene diamine.

2-3-4-1 Synthesis of DTPA dianhydride

DTPA dianhydride was prepared according to the previously established procedure (1). DTPA was added to a mixture of acetic anhydride and pyridine and stirred thoroughly over a period of 24h at 65°C under inert conditions. After the completion of reaction mixture was filtered and washed thoroughly with acetic anhydride and acetonitrile. This was dride over suffident peiod of time under vacuum and the yield of the product was 90%. Scheme 2-3-08 depicted the preparation route of DTPA dianhydride.



DTPA

DTPA dianhydride, 90%

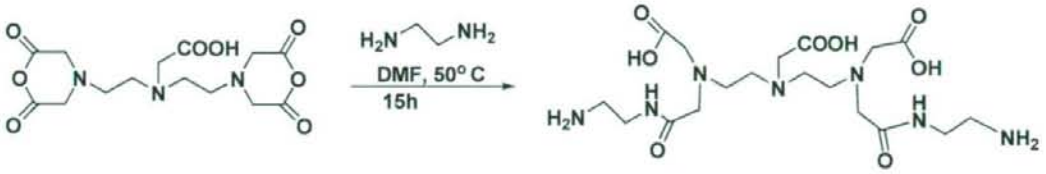
Scheme 2-3-08 Synthesis of DTPA dianhydride

^{1}H-NMR and ^{13}C-NMR spectra of DTPA dianhydride were shown in Fig.2-3-10, 2-3-11 respectively. From the IR spectrum, we can find the peakes at 1820cm^{-1} (C=O stretch symmetric), 1774cm^{-1} (C=O asymmetric stetching) which are charecteristics of cyclo-dianhydride. ^{1}H-NMR spectrum of DTPA dianhydride exhibited four different chemical shift values at 4.0ppm, 3.6ppm,

3.5ppm and 3.2ppm with expected coupling. ^{13}C-NMR spectrum of it showed distinct singlets at 171.65 and 165.67 also suggests the presence of di-anhydride system. All the above furnished information has confirmed the structure of dianhydride system.

2-3-4-2 Synthesis of DTPA-E

To a solution of DTPA di anhydride in DMF was added excess amount of ethylene diamine and the reaction mixture was thoroughly stirred at 50°C for a period of 15h. After completion of the reaction DMF was removed under reduced pressure and the excess of E was removed by washing repeatedly with chloroform.



Scheme 2-3-09 Synthesis of DTPA-E

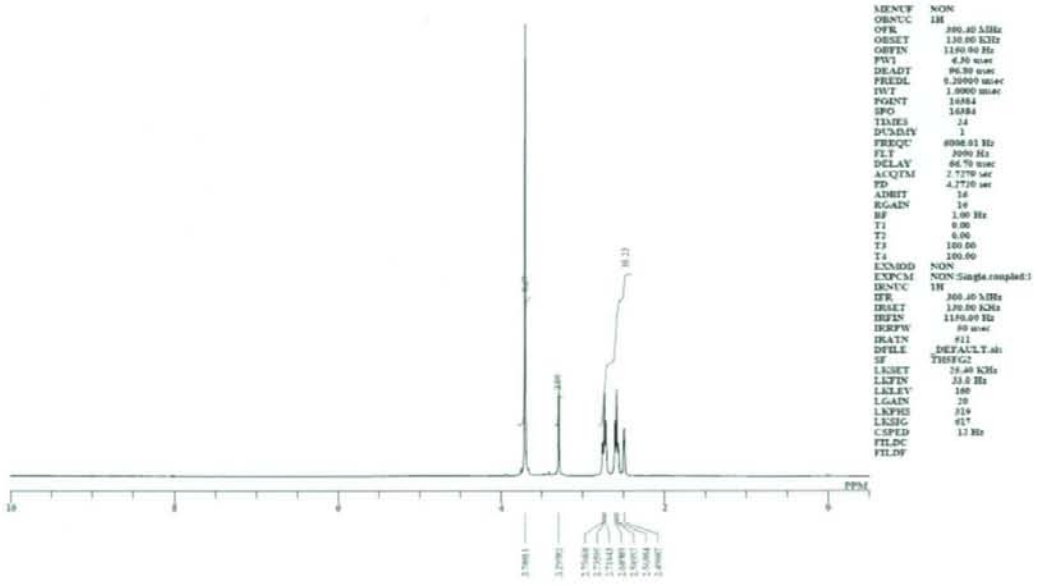


Fig. 2-3-10 ^{1}H-NMR of DTPA di-anhydride

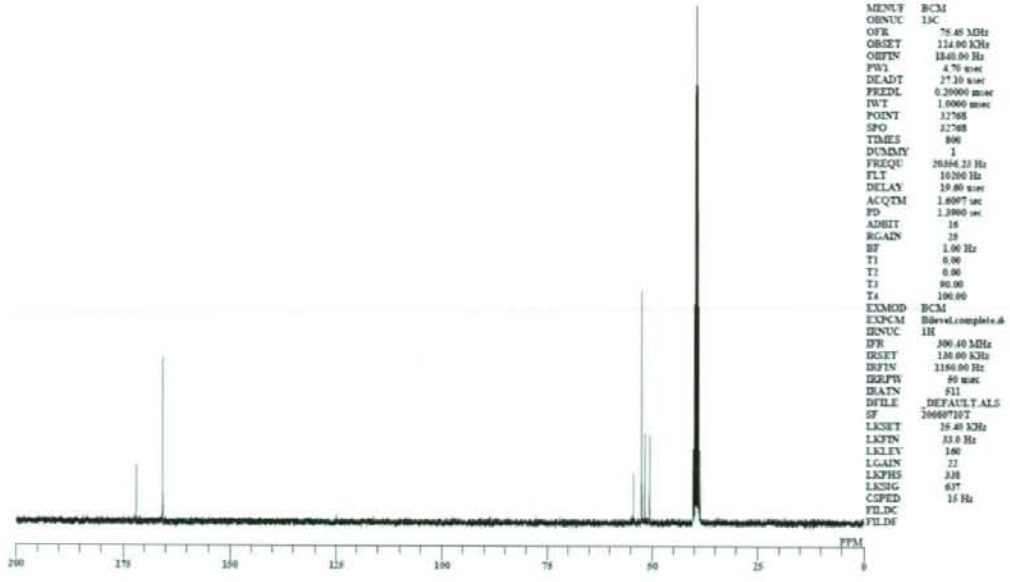


Fig. 2-3-11 ^{13}C-NMR of DTPA di-anhydride

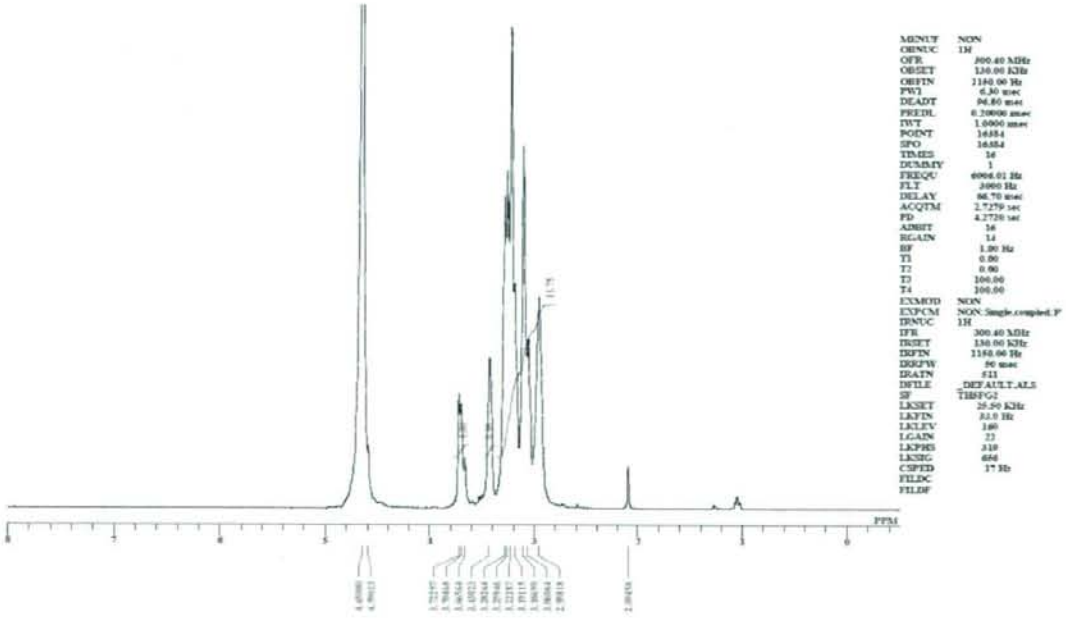
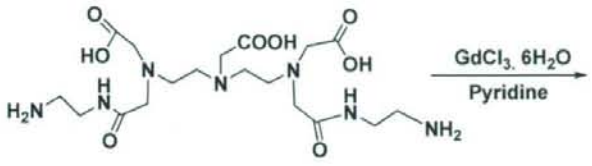


Fig. 2-3-12 ^{1}H-NMR of DTPA-E

2-3-4-3 Synthesis of Gd-DTPA-E

To a solution of DTPA-E in ion exchange water was added pyridine, gadolinium chloride and stirred the reaction at 50°C for 24h. After completion of the reaction water was removed and the resulted crude product was washed with ether repeatedly and dried.



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Scheme 2-3-10 Synthesis of Gd-DTPA-E

2-3-4-4 Synthesis of DTPA dianhydride

DTPA (3.0g, 7.6 mmol) was added to a mixture of acetic anhydride (3.0 ml, 31.8 mmol) and pyridine (4.5 ml, 53.6 mmol) and the reaction mixture was thoroughly stirred for 24h at 65° C. After that reaction mixture was washed repeatedly with acetic anhydride (20ml) and acetonitrile (20ml). White solid obtained was dried strongly to get 2.45g (6.94 mmol), 90%.

IR (KBr): ν (cm^{-1}) ; 3445(O=C<u>OH</u>), 1816 (O=COC=O), 1761 (<u>O=C</u>OH)

^{1}H-NMR

δ (ppm) = 3.70 (s, -CO-<u>CH_2</u>-CO- X 4)

=3.29 (s, -<u>CH_2</u>COOH)

=2.73 (t, $COCH_2N\underline{CH_2}CH_2N$ X 2)

=2.58 (t, $COCH_2NCH_2\underline{CH_2}N$ X2)

^{13}C-NMR

δ (ppm)= 171.9 (<u>O=C</u>OH)

=165.7 (<u>O=C</u>OC=O)

=54.5 (N<u>C</u>H_2COOH)

=52.1 (<u>C</u>H_2O=COC=O)

=50.7, 51.7 (NCH_2CH_2 X 2)

2-3-4-5 Synthesis of DTPA-E

To a solution of DTPA dianhydride 1.0g (2.8 mmol) in DMF was added 0.94g (14.0 mmol) of ethylene diamine and the reaction mixture was stirred at 50°C over a period of 15h. After completion of reaction DMF was removed under reduced pressure and the crude product was

washed with chloroform to remove the excess of E. This was recrystallised from *i*-propanol to yield 1.02g (78%) as pale while compound.

^{1}H-NMR

δ (ppm) = 3.71 (s, $N\underline{CH_2}C{=}ONH$ X 2)

= 3.43 (s, NCH_2COOH X 3)

= 3.39-2.90 (m)

2-3-4-6 Synthesis of Gd-DTPA-E

To a solution of DTPA-E 0.8g (1.60 mmol) in ion exchange water was added 1.30g (16.0 mmol) of pyridine was added and stirred thoroughly. To this solution 0.62g (1.60 mmol) of gadolinium chloride was added and the temperature of the reaction was kept constant at 50°C and refluxed for 24h. After completion of the reaction excess gadolinium was removed by treating with Chelex 100 resin (Na form 100-200, 2.8 g). After removal of excess gadolinium resin was filtered off and the filtrate was rota- evaporated under reduced pressure and the crude complex was washed with 2-propanol to get 0.82g (75%) of pale yellow compound.

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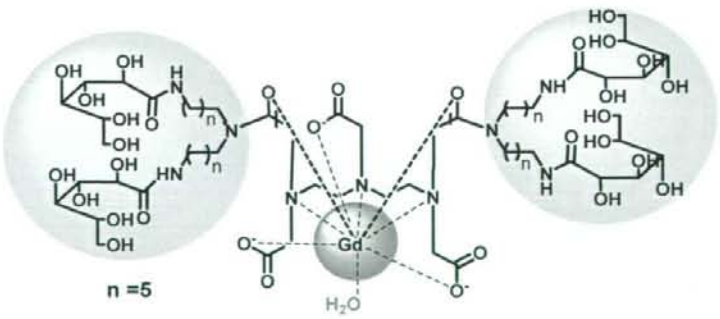
2-4 Synthesis of New -Symmetric Gd-DTPA-Sugar Frame Work

2-4-1 Introduction

Over the past two decades Magnetic Resonance Image (MRI) has become a very powerful tool of diagnostic medicine. The use of paramagnetic metal complexes as image enhancement agent aloe imaging that, for several important applications, is otherwise unobtainable.[1,2] Since the Gd(III) ion, with a $4f^7$ electronic configuration has a S= 7/2 ground state ,it is particularly attractive as a imaging agent. Paramagnetic materials have been investigated as MRI contrast agents (CAs). These materials enhance the contrast of the image indirectly by lowering the magnetic relaxation time of water protons in the surrounding tissues.[3] The most frequently used CAs are stable gadolinium (III) complexes with hydrophilic poly(aminicarboxylate) ligands resulting in rapid extracellular distribution and renal elimination. Gd (III) is preferred because of its favorable magnetic properties. Depending on the density of the ligand one or more water molecules might be directly coordinated to the paramagnetic center. Gd complexes with amphiphilic properties have previously been prepared and evaluated as blood-pool and liver imaging agents. Long chain amides and esters of Gd DTPA are the most common.[4] As we now, the glycoside groups have a specific target and combine with asialoglycoprotein receptor (ASGPR) on the surface of hepatocyte. Also, the glycoside groups, which were introduced into DTPA, can improve the water –solubility of contrast agent. So in this work, DTPA was used as a core and glycoside was used as a biofunctional group to prepare a series of dendritic Gd-complexes for novel MRI contrast agents. To overcome the defects of MRI contrast agents. I have been synthesized a novel complexes containing four sugar and two sugar groups for MR image by using different linker to connect the MR imaging moiety with biofunctional group by sugars.



Scheme 2-4-01 Synthesis of Target molecule

特許出願の関係で

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Scheme 2-4-02 Synthesis of Target molecule

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Scheme 2-4-03 Synthesis of Target molecule

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Scheme 2-4-04 Synthesis of Target molecule