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Tweaking of supramoleculargelation properties of a dipeptide based ambidextrous organogelator through a cooperative influence of hydrophobicity, steric bulk and conformational flexibility of side chain residue of a single hydrophobic α-amino acid encrypted on a designed molecular frame

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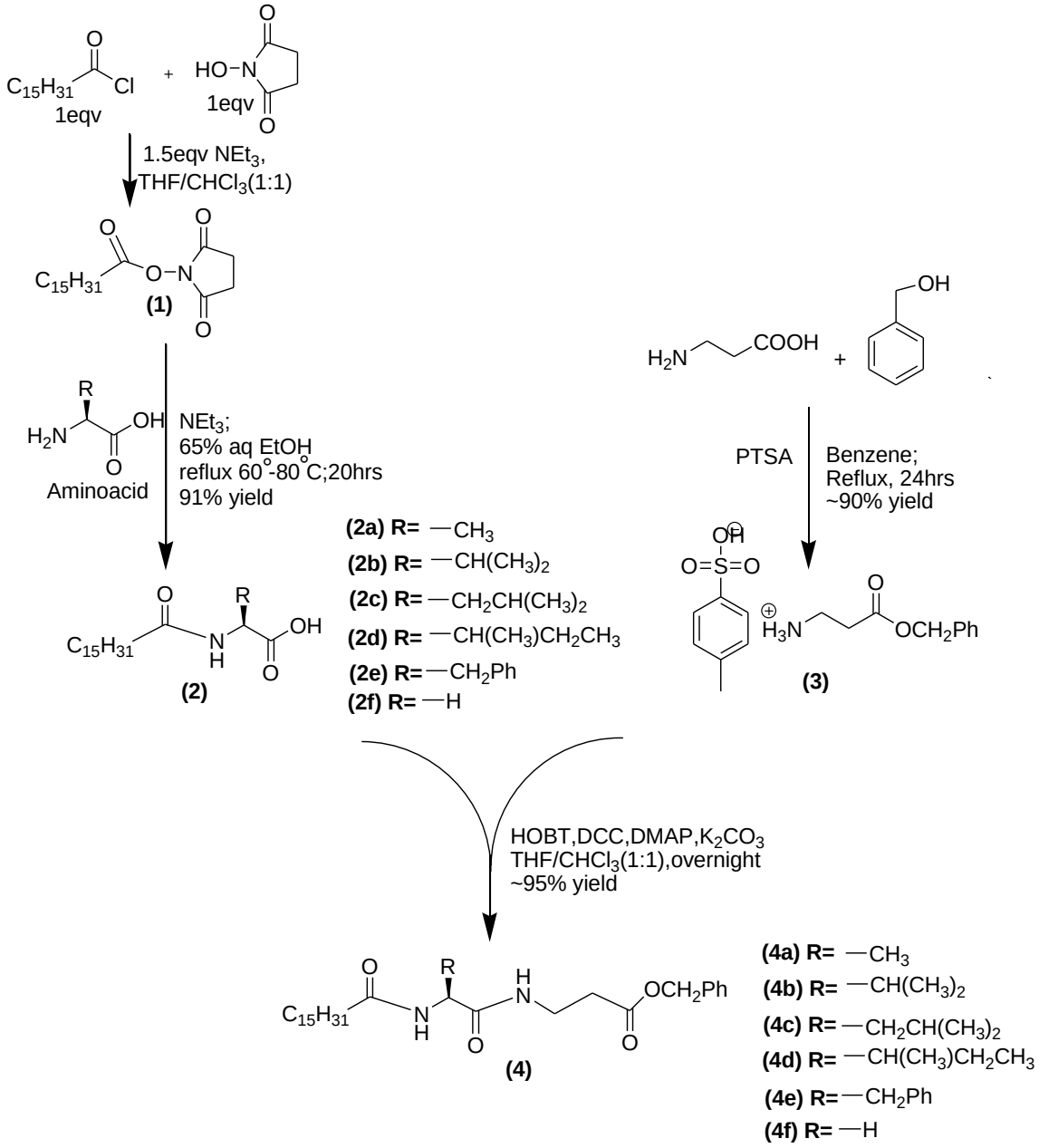
Scheme 1:


1eqv
1eqv
1.5eqv NEt3,
THF/CHCl3(1:1)
(1)
Aminoacid
NEt3;
65% aq EtOH
reflux 60°-80°C;20hrs
91% yield
(2)
(2a) R= —CH3
(2b) R= —CH(CH3)2
(2c) R= —CH2CH(CH3)2
(2d) R= —CH(CH3)CH2CH3
(2e) R= —CH2Ph
(2f) R= —H
PTSA
Benzene;
Reflux, 24hrs
~90% yield
(3)
HOBT,DCC,DMAP,K2CO3
THF/CHCl3(1:1),overnight
~95% yield
(4)
(4a) R= —CH3
(4b) R= —CH(CH3)2
(4c) R= —CH2CH(CH3)2
(4d) R= —CH(CH3)CH2CH3
(4e) R= —CH2Ph
(4f) R= —H

Synthesis of N-Succinimidylpalmitate (1): To stirred suspension of N-Hydroxysuccinimide (5.0 g, 43mmole, 1eqv) in 40 ml of THF:$CHCl_3$mixture (1:1) and Triethylamine (9 ml, 64.6mmole, 1.5eqv); was added drop wise a solution of Palmitoyl Chloride (12.5 ml, 43mmole, 1eqv) in 20 ml of THF:$CHCl_3$ mixture (1:1) and stirred for overnight at room temperature. Solid precipitate was filtered and the filtrate was diluted with 25 ml of $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml×2), saturated brine solution (25 ml × 2).Organic layer was collected and dried over anhyd. Na_2SO_4 and evaporated under reduced pressure which was then recrystallized from 25mlofisopropanol to get the desired product (13.8 g;90.8% yield). This compound was used for the next step without any further purification.

Synthesis of N-hexadecanoyl-alanine (2a): To a solution of N-Succinimidylpalmitate (3.0 g, 8.4mmole, 1eqv.), Alanine (0.897 g, 10.08mmole, 1.2eqv.) in 40 ml of 65% Ethanol; Triethylamine (2.5 ml, 17.9mmole, 2.1eqv.) was added and put to reflux (60-80^{0}C) for 20hrs. Then the reaction mixture was concentrated under reduced pressure and taken up in 25 ml Ethyl acetate and washed sequentially with ice cold 1 (N) HCl (30 ml× 2), saturated brine solution (25 ml×2).Organic layer was collected and dried over anhyd. Na_2SO_4 and evaporated under reduced pressure to give the desired product (2.6 g;94.5% yield; m.p=94^{0}C). This compound was used for the next step without any further purification.

Synthesis of N-hexadecanoyl-valine (2b): To a solution of N-Succinimidylpalmitate (3.0 g, 8.4mmole, 1eqv.), Valine (1.2 g, 10.08mmole, 1.2eqv.) in 40 ml of 65% Ethanol; Triethylamine (3 ml, 21.56mmole, 2.5eqv.) was added and put to reflux (60-80^{0}C) for 20hrs. Then the reaction mixture was concentrated under reduced pressure and taken up in 25 ml Ethyl acetate and washed sequentially with ice cold 1 (N) HCl (30 ml×2), saturated brine solution (25 ml× 2).Organic layer was collected and dried over anhyd. Na_2SO_4 and evaporated under reduced pressure to give the desired product (2.867 g;95.95% yield; m.p=98^{0}C). This compound was used for the next step without any further purification.

Synthesis of N-hexadecanoyl-isoleucine (2c): To a solution ofN-Succinimidylpalmitate (1.6 g, 4.526mmole, 1eqv.), Isoleucine (0.713 g, 5.44 mmole,1.2eqv.) in 25 ml of 65% Ethanol; Triethylamine (1.3 ml, 9.34mmole, 2.1eqv.) was added and put to reflux (60-80^{0}C) for 20hrs. Then the reaction mixture was concentrated under reduced pressure and taken up in 25 ml Ethyl acetate and washed sequentially with ice cold 1 (N) HCl (30 ml×2), saturated brine solution (25 ml× 2).Organic layer was collected and dried over anhyd. Na_2SO_4 and evaporated under reduced pressure to give the desired product (1.572 g;94% yield). This compound was used for the next step without any further purification.

4.63Synthesis of N-hexadecanoyl-leucine (2d): To a solution of N-Succinimidylpalmitate (2.0 g, 5.6mmole, 1eqv.), Leucine (0.885 g, 6.7mmole, 1.2eqv.) in 25 ml of 65% Ethanol; Triethylamine (1.6 ml, 11.5mmole, 2.05eqv.) was added and put to reflux (60-80°C) for 20hrs. Then the reaction mixture was concentrated under reduced pressure and taken up in 25 ml Ethyl acetate and washed sequentially with ice cold 1 (N) HCl (30 ml× 2), saturated brine solution (25 ml×2).Organic layer was collected and dried over anhyd. Na_2SO_4 and evaporated under reduced pressure to give the desired product (1.48 g;71.4% yield). This compound was used for the next step without any further purification.

Synthesis of N-hexadecanoyl-phenylalanine (2e): To a solution ofN-Succinimidylpalmitate (2.0 g, 5.5mmole, 1eqv.), Phenyl alanine (1.11 g, 6.7mmole, 1.2eqv.) in 30 ml of 65% Ethanol; Triethylamine (1.6 ml, 11.5mmole, 2.05eqv.) was added and put to reflux (60-80°C) for °20hrs. Then the reaction mixture was concentrated under reduced pressure and taken up in 25 ml Ethyl acetate and washed sequentially with ice cold 1 (N) HCl (30 ml×2) , saturated brine solution (25 ml× 2).Organic layer was collected and dried over anhyd Na_2SO_4 and evaporated under reduced pressure to give the desired product (1.6 g; 70.35% yield). This compound was used for the next step without any further purification.

Synthesis of N-hexadecanoyl-glycine (2f): To a solution of N-Succinimidylpalmitate (0.6 g, 1.7 mmole, 1 eqv.), glycine (1.0 g, 2.1 mmole, 1.2eqv.) in 30 ml of 65% Ethanol; Triethylamine (0.6 ml, 4.2 mmole, 2.05 eqv.) was added and put to reflux (60-80°C) for °20hrs. Then the reaction mixture was concentrated under reduced pressure and taken up in 25 ml Ethyl acetate and washed sequentially with ice cold 1 (N) HCl (30 ml×2) , saturated brine solution (25 ml× 2).Organic layer was collected and dried over anhyd Na_2SO_4 and evaporated under reduced pressure to give the desired product (0.5 g; 75% yield). This compound was used for the next step without any further purification.

Synthesis of PTSA-salt of β-Alanine benzyl ester (3): In 100 ml of benzene a mixture ofβ-Alanine (5 g, 56.12mmol), PTSA.H2O (11.7419 g, 64.36mmol) and benzyl alcohol (11.642ml, 112.29mmol) was taken. After refluxing in Dean-Stark apparatus for 24hrs, 40 ml of diethyl ether was added to it with immediate precipitation of PTSA-salt ofβ-Alanine benzyl ester. The salt was then filtered, washed with 10 ml of diethyl ether and was dried under reduced pressure. This compound was used for the next step without any further purification.

Synthesis of 4 (a): To a solution of N-hexadecanoyl-alanine (0.500 g, 1.5mmole, 1eqv.) in 5 ml of THF, HOBt (0.304 g, 2.2mmole, 1.5eqv.) was added and kept on stirring in ice water bath at 0°C.After 10mins of stirring, DMAP (0.018 g, 0.15mmole, 0.093eqv.) and solution of DCC (0.618 g, 2.9mmole,1.93eqv.) in 5 ml of $CHCl_3$ was added to it and kept stirring. Finally, after 15mins, K_2CO_3 (0.311 g, 2.2mmole, 1.47eqv) and PTSA-salt of β-Alanine benzyl ester (0.632 g, 1.8mmole, 1.2eqv.) was added and kept on stirringovernight. The reaction mixture was then concentrated under reduced pressure and taken up in 30 ml $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml×2), saturated brine (25 ml×2).The organic layer was collected and dried over anhyd. $Na_2SO_4$and then purified by silica column chromatography (60%EtOAc/Petroleum ether) to get the desired product. (0.532 g, 72% yield).

^{1}HNMR (300MHz, $CDCl_3$) : δ ::0.85-0.87 (t, -NHCOCH$_2$CH$_2$ (CH$_2$)$_{12}$C$\underline{H}_3$, 3H), 1.24-1.32 (t, -NHCOCH$_2$CH$_2$(C$\underline{H}_2$)$_{12}$CH$_3$,24H), 1.59-1.65 (s, -NHCOCH(C$\underline{H}_3$)NHCOCH$_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 3H), 1.90 (s, - NHCOC$\underline{H}_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 2H), 2.1-2.2 (t, -NHCOCH$_2$C$\underline{H}_2$ (CH$_2$)$_{12}$CH$_3$, 2H), 2.5-2.6 (t, -CONHCH$_2$C$\underline{H}_2$COOCH$_2$Ph, 2H), 3.50-3.54 (t, -CONHC$\underline{H}_2$CH$_2$COOCH$_2$Ph, 2H), 4.35-4.43 (q, -NHCOC$\underline{H}$(CH$_3$)NHCOCH$_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 1H), 5.13 (s, -CONHCH$_2$CH$_2$COOC$\underline{H}_2$Ph, 2H), 6.11-6.13 (d, -CON$\underline{H}$CH$_2$CH$_2$COOCH$_2$Ph, 1H), 6.59-6.62 (s, -N$\underline{H}$COCH$_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 1H), 7.26-7.38 (bs, aromatic, 5H).^{13}C NMR(75 MHz, $CDCl_3$) :δ_C : 173.27, 172.93, 171.407, 135.6, 128.62, 128.4, 128.28, 77.46, 77.041, 76.61, 66.59, 49.23, 36.7, 34.976, 33.99, 33.69, 31.9, 31.2, 29.63, 29.49, 29.33, 29.28, 25.75, 25.54, 25.544, 24.865, 24.77, 22.67, 19.13, 18.22, 14.09.IR (KBr) ν: 3849.86, 3685.76, 3304.68, 2918.91, 2850.13, 1732.23,

1633.84, 1538.08, 1454.64, 1244.43, 1044.03, 882.92, 695.39.ESI-MS (m/z) $C_{29}H_{48}N_2O_4$ (EXACT MASS=488.36)511.34 (100%, $[M + Na]^+$), 527.31(12%, $[M + K]^+$).

Synthesis of 4 (b): To a solution of N-hexadecanoyl-valine (0.500 g, 1.41mmole, 1eqv.) in 5 ml of THF, HOBt (0.285 g, 2.11mmole, 1.5 eqv) was added and kept on stirring in ice water bath at 0^0C.After 10mins of stirring, DMAP (0.017 g, 0.14mmole, 0.1eqv.) and solution of DCC (0.561 g, 2.72mmole, 1.93 eqv) in 5 ml of $CHCl_3$ was added to it and kept stirring. Finally, after 15mins, K_2CO_3 (0.286 g, 2.07mmole, 1.47eqv.) and PTSA-salt of β-Alanine benzyl ester (0.595 g, 1.69mmole, 1.2eqv.) was added and kept on stirringovernight. Thereaction mixture was then concentrated under reduced pressure and taken up in 30 ml $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml× 2), saturated brine (25 ml × 2).The organic layer was collected and dried over anhyd. $Na_2SO_4$and then purified by silica column chromatography (40%EtOAc/Petroleum ether) to get the desired product. (0.525 g, 72% yield).
^{1}HNMR (300 MHz, $CDCl_3$) : δ:: 0.875-0.918 (m, -NHCOCH$_2$CH$_2$ $(CH_2)_{12}C\underline{H_3}$ and >CHCH $(C\underline{H_3})_2$, 9H), 1.27 (bs, -NHCOCH$_2$CH$_2$$(C\underline{H_2})_{12}CH_3$, 24H), 1.58-1.65 (m, -NHCOCH$_2$C$\underline{H_2}$ $(CH_2)_{12}CH_3$, >CHC$\underline{H}$ $(CH_3)_2$, 3H), 2.11-2.24 (t, -NHCOC$\underline{H_2}$CH$_2$$(CH_2)_{12}CH_3$, 2H), 2.59-2.62 (t, -CONHCH$_2$C$\underline{H_2}$COOCH$_2$Ph, 2H), 3.5-3.6 (m, CONHC$\underline{H_2}$CH$_2$COOCH$_2$Ph, 2H), 4.17-4.2 (t, >C$\underline{H}$CH $(CH_3)_2$, 1H), 5.09-5.1 (s, -CONHCH$_2$CH$_2$COOC$\underline{H_2}$Ph, 2H), 6.11-6.13 (d, - N$\underline{H}$COCH$_2$CH$_2$ $(CH_2)_{12}CH_3$), 1H), 6.52 (s, -CON$\underline{H}$CH$_2$CH$_2$COOCH$_2$Ph, 1H), 7.26-7.35 (bs, aromatic, 5H). ^{13}C NMR(75 MHz, $CDCl_3$) :δ_C : 173.6, 172.4, 171.8, 135.64, 128.6, 128.34, 128.18, 77.47, 77.05, 76.62, 66.53, 57.53, 41.35, 36.53, 35.02, 33.9, 33.47, 31.9, 29.67, 29.64, 29.61, 29.5, 29.33, 29.26, 25.64, 24.81, 22.82, 22.66, 22.20, 14.08. IR (KBr) ν: 3295.17, 2918.06, 2849.75, 1737.69, 1637.40, 1557.89, 1461.89, 1271.73, 1187.97, 1098.5, 1007.4, 940.48, 885.17, 697.04.ESI-MS (m/z) $C_{31}H_{52}N_2O_4$ (EXACT MASS=516.37) 517.379 (100%, $[M + H]^+$), 539.37 (20%, $[M + Na]^+$).

Synthesis of 4 (c): To a solution of N-hexadecanoyl-isoleucine (1.5 g, 4.06mmole, 1eqv.) in 5 ml of THF,HOBt (0.822 g,6.09 mmole,1.5eqv.) was added and kept on stirring in ice water bath at 0^0C.After 10mins of stirring, DMAP (0.045 g,0.373mmole, 0.092eqv.) and solution of DCC (1.7 g 8.241mmole, 2.03 eqv.) in 5 ml of $CHCl_3$ was added to it and kept stirring. Finally, after 15mins, K_2CO_3 (0.823 g, 5.968mmole, 1.47eqv.) and PTSA-salt of β-Alanine benzyl ester (1.7 g, 4.87mmole, 1.2eqv.) was added and kept on stirringovernight. The reaction mixture was then concentrated under reduced pressure and taken up in 30 ml $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml× 2), saturated brine (25 ml × 2).The organic layer was collected and dried over anhyd. $Na_2SO_4$and then purified by silica column chromatography (45%EtOAc/Petroleum ether) to get the desired product. (0.532 g, 72% yield).
^{1}HNMR (300MHz, $CDCl_3$) : δ ::0.84-0.895 (m, -NHCOCH$_2$CH$_2$ $(CH_2)_{12}C\underline{H_3}$and >CHCH $(C\underline{H_3})$CH$_2$C$\underline{H_3}$, 9H), 1.2-1.38 (bs, -NHCOCH$_2$CH$_2$ $(C\underline{H_2})_{12}$CH$_3$) and >CHCH $(CH_3)C\underline{H_2}CH_3$, 26H), 1.55-1.61 (s, -NHCOCH$_2$C$\underline{H_2}$ $(CH_2)_{12}CH_3$ and >CHC$\underline{H}$ $(CH_3)CH_2CH_3$, 3H), 2.09-2.3 (m, -NHCOC$\underline{H_2}$CH$_2$ $(CH_2)_{12}CH_3$, 2H), 2.56-2.60 (t, -CONHCH$_2$C$\underline{H_2}$COOCH$_2$Ph, 2H), 3.4-3.58 (q, CONHC$\underline{H_2}$CH$_2$COOCH$_2$Ph, 2H), 4.17-4.22 (t, >C$\underline{H}$CH $(CH_3)CH_2CH_3$, 1H), 5.09-5.13 (bs, -CONHCH$_2$CH$_2$COOC$\underline{H_2}$Ph, 2H), 5.9-6.15 (d, -N$\underline{H}$COCH$_2$CH$_2$ $(CH_2)_{12}CH_3$, 1H), 6.3-6.35 (s, CON$\underline{H}$CH$_2$CH$_2$COOCH$_2$Ph, 1H), 7.3-7.35 (bs, aromatic, 5H). ^{13}C NMR(75 MHz, $CDCl_3$) :δ_C : 173.1, 171.9, 171.4, 135.5, 128.6, 128.4, 128.3, 128.2, 128.18, 77.46, 77.05, 76.62, 66.59, 66.5, 57.47, 49.45, 37.37, 36.68, 34.96, 33.9, 33.66, 31.9, 29.67, 29.64, 29.5, 29.33, 29.27, 25.71, 25.02, 24.84, 22.67, 15.33, 14.08, 11.22.IR (KBr) ν: 3291, 2918.06,

2849.88, 1732.99, 1633.86, 1556.75,1463.94, 1170.12,1018.61, 952.44, 883, 697.02.ESI-MS (m/z) $C_{32}H_{54}N_2O_4$ (EXACT MASS= 530.40)553.4 (100%, $[M + Na]^+$).

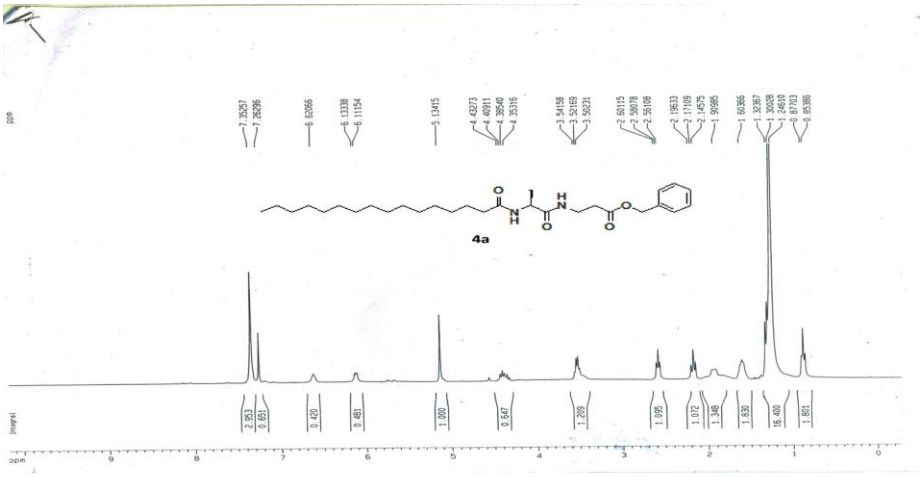
Synthesis of 4 (d): To a solution of N-hexadecanoyl-leucine (1.38 g, 3.7mmole, 1eqv.) in 5 ml of THF, HOBt (0.749 g, 5.55mmole, 1.5 eqv.) was added and kept on stirring in ice water bath at 0^0C.After 10mins of stirring, DMAP (0.042 g, 0.34mmole, 0.092eqv.) and solution ofDCC (1.54 g, 7.511mmole, 2.03 eqv) in 5 ml of $CHCl_3$ was added to it and kept stirring. Finally, after 15mins, K_2CO_3 (1.751 g, 5.439mmole, 1.47eqv.) and PTSA-salt of β-Alanine benzyl ester (1.57 g, 4.44mmole, 1.2eqv.) was added and kept on stirringovernight. The reaction mixture was then concentrated under reduced pressure and taken up in 30 ml $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml × 2), saturated brine (25 ml × 2).The organic layer was collected and dried over anhyd. $Na_2SO_4$and then purified by silica column chromatography (55%EtOAc/Petroleum ether) to get the desired product. (1.378 g, 70% yield).
^{1}HNMR (300MHz, $CDCl_3$) : δ ::0.85-0.911 (q, -NHCOCH$_2$CH$_2$ $(CH_2)_{12}C\underline{H_3}$and >CHCH$_2$CH $(C\underline{H_3})_2$, 9H), 1.15-1.25 (bs, -NHCOCH$_2$CH$_2$ $(C\underline{H_2})_{12}CH_3$, 24H), 1.55-1.65 (d, -NHCOCH$_2C\underline{H_2}$ $(CH_2)_{12}CH_3$and >CH$C\underline{H_2}C\underline{H}$ $(CH_3)_2$, 5H), 2.08-2.1 (t, -NHCO$C\underline{H_2}CH_2$ $(CH_2)_{12}CH_3$, 2H), 2.55-2.6 (q, -CONHCH$_2C\underline{H_2}$COOCH$_2$Ph, 2H), 3.49-3.55 (q, -CONH$C\underline{H_2}$CH$_2$COOCH$_2$Ph, 2H), 4.37-4.4 (t, >$C\underline{H}$CH$_2$CH $(CH_3)_2$, 1H), 5.1-5.15 (bs, -CONHCH$_2$CH$_2$COO$C\underline{H_2}$Ph, 2H), 5.8-5.89 (s, -$N\underline{H}$COCH$_2$CH$_2$ $(CH_2)_{12}CH_3$, 1H), 6.5-6.58 (s, CO$N\underline{H}$CH$_2$CH$_2$COOCH$_2$Ph, 1H), 7.3-7.73 (bs, aromatic, .5H).^{13}C NMR(75 MHz, $CDCl_3$) :δ_C : 173.2, 172.3, 171.8, 135.5, 128.59, 128.38, 128.43, 128.23, 128.18, 77.47, 77.05, 76.62, 66.53, 51.53, 41.35, 36.53, 35.01, 33.9, 33.47, 31.9, 29.67, 29.64, 29.61, 29.5, 29.33, 29.26, 25.64, 24.81, 24.77, 22.82, 22.66, 22.2, 14.08. IR (KBr) ν: 3296.52, 2917.83, 2849.96, 1737.71, 1635.24, 1540.04, 1464.26, 1387.95, 1171.89, 1071.86, 960.70, 696.15.ESI-MS (m/z) $C_{32}H_{54}N_2O_4$ (EXACT MASS= 530.40) 531.4 (100%, $[M + H]^+$).

Synthesis of 4 (e): To a solution of N-hexadecanoyl-phenylalanine (1.58 g, 3.9mmole, 1eqv) in 5 ml of THF, HOBt (0.790 g, 5.85mmole, 1.5 eqv.) was added and kept on stirring in ice water bath at 0^0C.After 10mins of stirring, DMAP (0.043 g, 0.358mmole, 0.092eqv.) and solution of DCC (`1.631 g, 7.917mmole, 1.93 eqv) in 5 ml of $CHCl_3$ was added to it and kept stirring. Finally, after 15mins, K_2CO_3 (0.792 g, 5.73mmole, 1.47eqv.) and PTSA-salt of β-Alanine benzyl ester (1.64 g, 4.68mmole, 1.2eqv.) was added and kept on stirringovernight. The reaction mixture was then concentrated under reduced pressure and taken up in 30 ml $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml × 2), saturated brine (25 ml × 2).The organic layer was collected and dried over anhyd $Na_2SO_4$and then purified by silica column chromatography (30%EtOAc/Petroleum ether) to get the desired product. (1.24 g, 56.4% yield).
^{1}HNMR (300MHz, $CDCl_3$) : δ ::0.89-.0.95 (t, -NHCOCH$_2$CH$_2$ $(CH_2)_{12}C\underline{H_3}$, 3H), 1.15-1.35 (bs, -NHCOCH$_2$CH$_2$$(C\underline{H_2})_{12}CH_3$, 24H), 1.51-1.6 (d, -NHCOCH$_2C\underline{H_2}$ $(CH_2)_{12}CH_3$, 2H), 2.1-2.28 (t, -NHCO$C\underline{H_2}CH_2$ $(CH_2)_{12}CH_3$, 2H), 2.3-2.55 (m, -CONHCH$_2C\underline{H_2}$COOCH$_2$Ph, 2H), 2.99-3.15 (dd, >CH$C\underline{H_2}$Ph, 2H), 3.37-3.49 (m, -CONHC$\underline{H_2}$CH$_2$COOCH$_2$Ph, 2H), 4.5-4.59 (d, >C$\underline{H}$CH$_2$Ph, 1H), 5.07-5.14 (bs, -CONHCH$_2$CH$_2$COO$C\underline{H_2}$Ph, 2H), 6.07-6.14 (d and s, -$N\underline{H}$COCH$_2$CH$_2$ $(CH_2)_{12}CH_3$and -CON$\underline{H}$CH$_2$CH$_2$COOCH$_2$Ph, 2H), 7.16-7.35 (m, >CHCH$_2\underline{Ph}$ and-CONHCH$_2$CH$_2$COOCH$_2\underline{Ph}$, 10H).^{13}C NMR(75 MHz, $CDCl_3$) :δ_C : 173.095, 171.805, 170.956, 136.626, 135. 56, 129.22, 128.63, 128.60, 128.41, 128.27, 126.942, 77.79, 77.05, 76.63, 66.52, 54.45, 49.51, 38.72, 36.55, 34.76, 33.79, 33.51, 31.92, 29.69, 29.66, 29.48, 29.35, 29.21, 25.57, 25.463, 24.78, 22.69, 14.12.IR (solid)

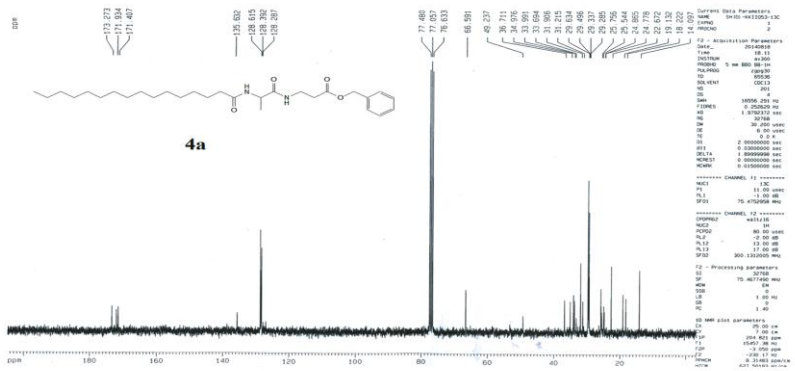
ν: 3583, 3512, 3130, 2989, 2905, 2274, 2239, 1698, 1634, 1574, 1539, 1428, 1369, 1023, 905, 786. ESI-MS (m/z) $C_{35}H_{52}N_2O_4$ (EXACT MASS= 564.4) 565.42 (100%, $[M + H]^+$).

Synthesis of 4 (f): To a solution of N-hexadecanoyl-glycine (0.500 g, 1.59mmole, 1eqv.) in 5 ml of THF, HOBt (0.322 g, 2.39mmole, 1.5eqv.) was added and kept on stirring in ice water bath at 0°C.After 10mins of stirring, DMAP (0.019 g, 0.159mmole, 0.1eqv.) and solution of DCC (0.633 g, 3 mmole,1.93eqv.) in 5 ml of $CHCl_3$ was added to it and kept stirring. Finally, after 15mins, K_2CO_3 (0.322 g, 2.33mmole, 1.47eqv) and PTSA-salt of β-Alanine benzyl ester(0.65 g, 1.9mmole, 1.2eqv.) was added and kept on stirringovernight. The reaction mixture was then concentrated under reduced pressure and taken up in 30 ml $CHCl_3$ and washed sequentially with ice cold 1 (N) HCl (25 ml×2), saturated brine (25 ml×2).The organic layer was collected and dried over anhyd. $Na_2SO_4$and then purified by silica column chromatography (60%EtOAc/Petroleum ether) to get the desired product. (0.62 g, 82% yield).

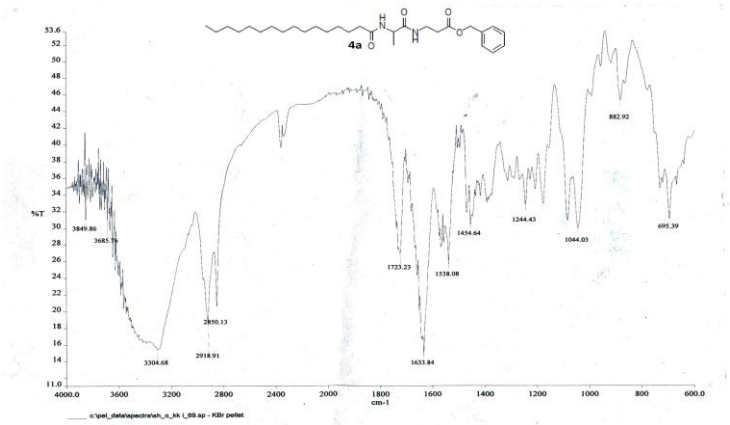
^{1}HNMR (300MHz, $CDCl_3$) : δ ::0.85-0.90 (t, -NHCOCH$_2$CH$_2$ (CH$_2$)$_{12}$C<u>*H*</u>$_3$, 3H), 1.24-1.25 (t, -NHCOCH$_2$CH$_2$(C<u>*H*</u>$_2$)$_{12}$CH$_3$, 24H), 1.5-1.66 (s, - NHCOC<u>*H*</u>$_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 2H), 2.0-2.2 (t, -NHCOCH$_2$C<u>*H*</u>$_2$ (CH$_2$)$_{12}$CH$_3$, 2H), 2.5-2.6 (s, -CONHCH$_2$C<u>*H*</u>$_2$COOCH$_2$Ph, 2H), 3.54-3.6(s, -CONHC<u>*H*</u>$_2$CH$_2$COOCH$_2$Ph, 2H), 4.20-4.24 (s, -NHCOC<u>*H*</u>(CH$_3$)NHCOCH$_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 1H), 5.2 (s, -CONHCH$_2$CH$_2$COOC<u>*H*</u>$_2$Ph, 2H), 6.11-6.13 00-6.1(d, -CON<u>*H*</u>CH$_2$CH$_2$COOCH$_2$Ph, 1H), 6.60-6.62 (s, -N<u>*H*</u>COCH$_2$CH$_2$ (CH$_2$)$_{12}$CH$_3$, 1H), 7.3-7.38 (bs, aromatic, 5H).^{13}C NMR(75 MHz, $CDCl_3$) :δ_C : 173.27, 172.93, 171.407, 135.6, 128.62, 128.4, 128.28, 77.46, 77.041, 76.61, 66.59, 49.23, 36.7, 34.976, 33.99, 33.69, 31.9, 31.2, 29.49, 29.33, 29.28, 25.75, 25.54, 25.54, 24.86, 24.77, 22.67, 19.13, 18.22, 14.09.IR (KBr) ν: 3321, 2914, 2849, 1725, 1667, 1520, 1422, 1214, 1077, 898, 719, 647.ESI-MS (m/z) $C_{29}H_{48}N_2O_4$ (EXACT MASS=474.36) 475.369 (12%, $[M + H]^+$), 497.244 (100%, $[M + Na]^+$).



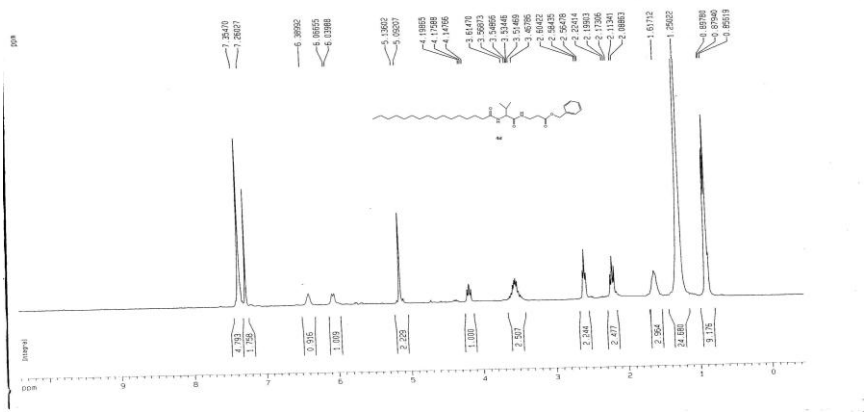
^{1}H-NMR SPECTRA OF **4a.**



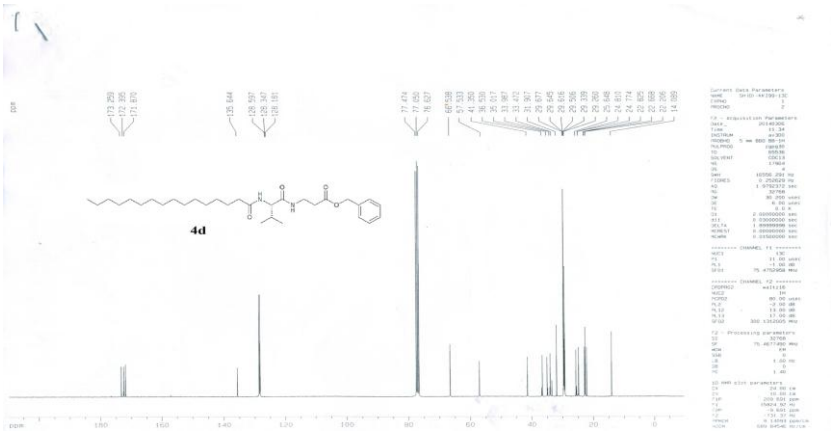
^{13}C-NMR SPECTRA OF **4a.**



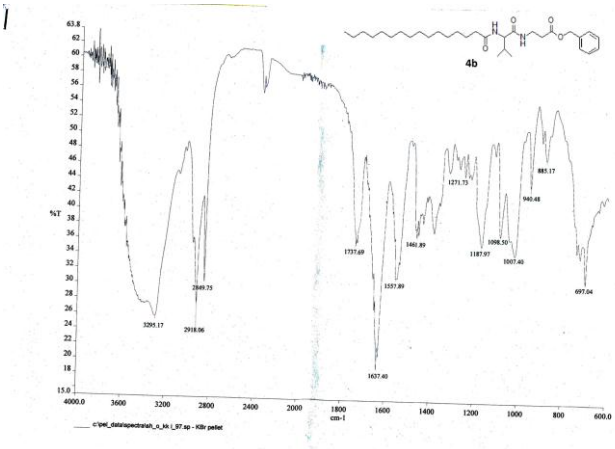
IR (in KBr) SPECTREA OF **4a**



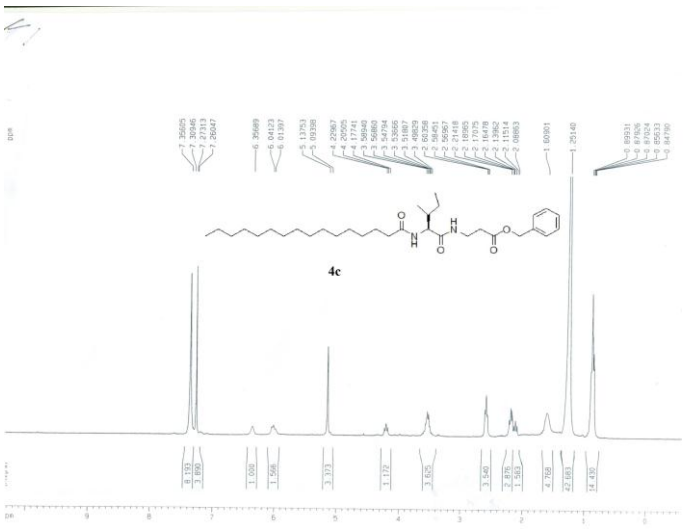
^{1}H-NMR of **4b**.



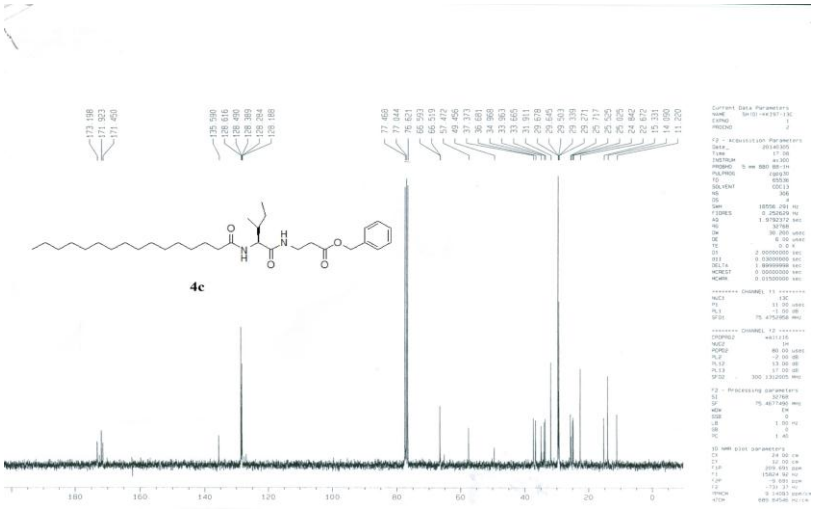
^{13}C-NMR SPECTRA OF **4b.**



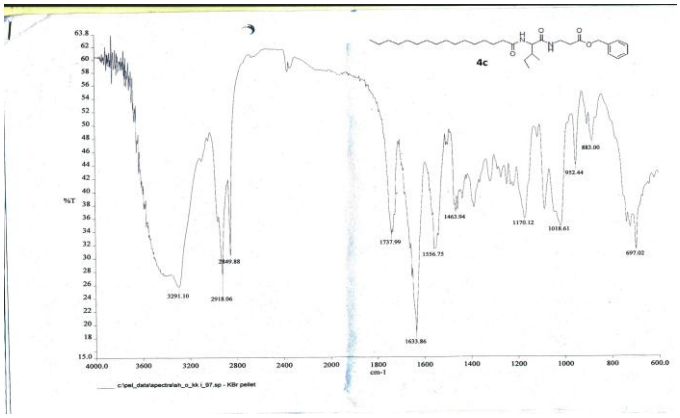
IR (in KBr) SPECTREA OF **4b**



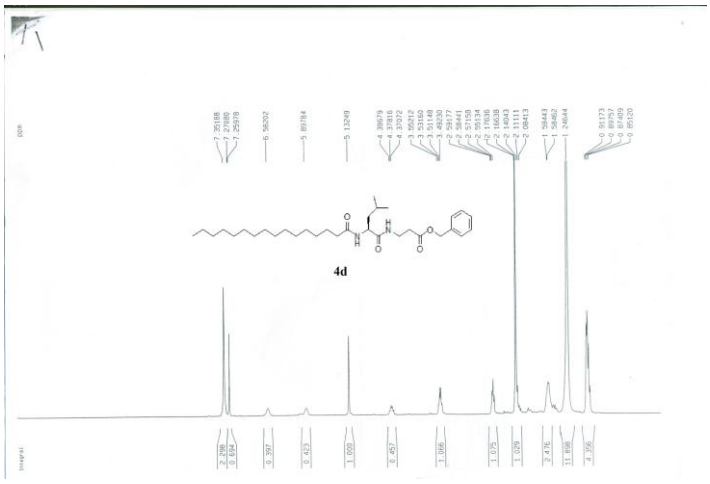
^{1}H-NMR of **4c**.



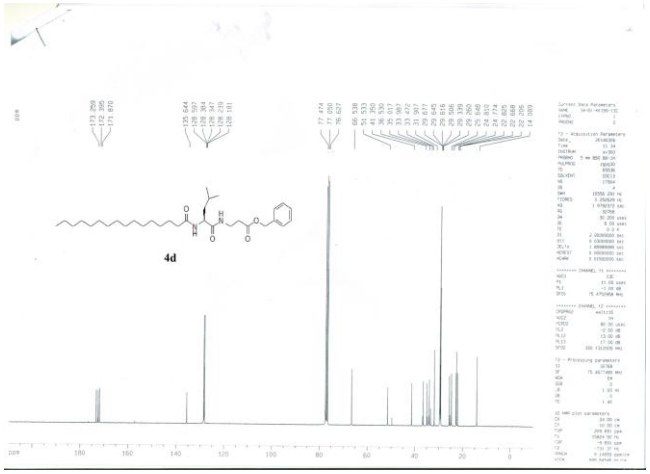
^{13}C-NMR SPECTRA OF **4c.**



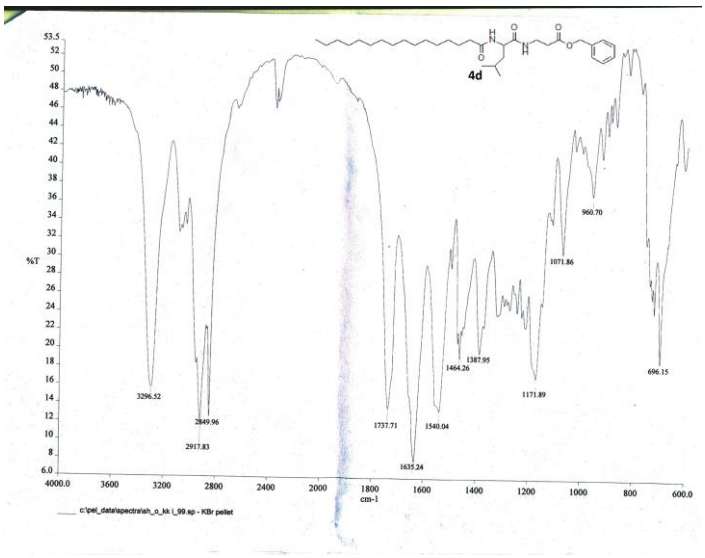
IR (in KBr) SPECTREA OF **4c**



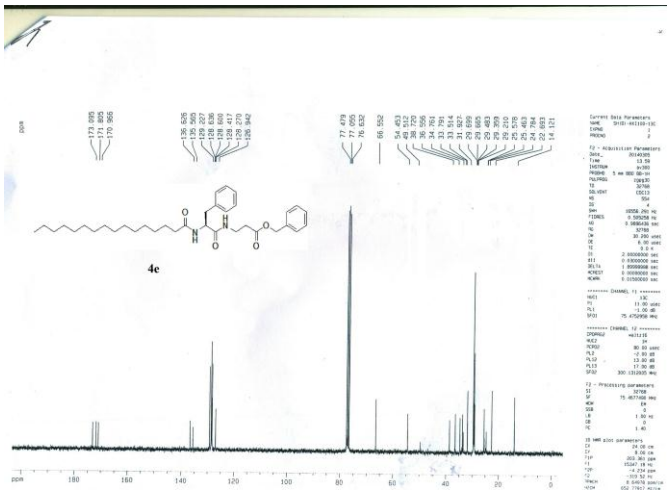
^{1}H-NMR of **4d**.



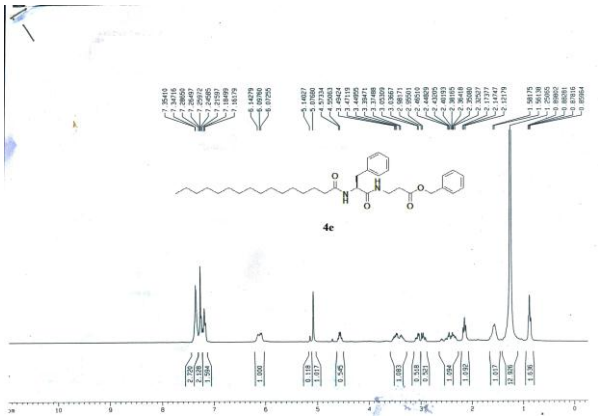
^{13}C-NMR SPECTRA OF **4d.**



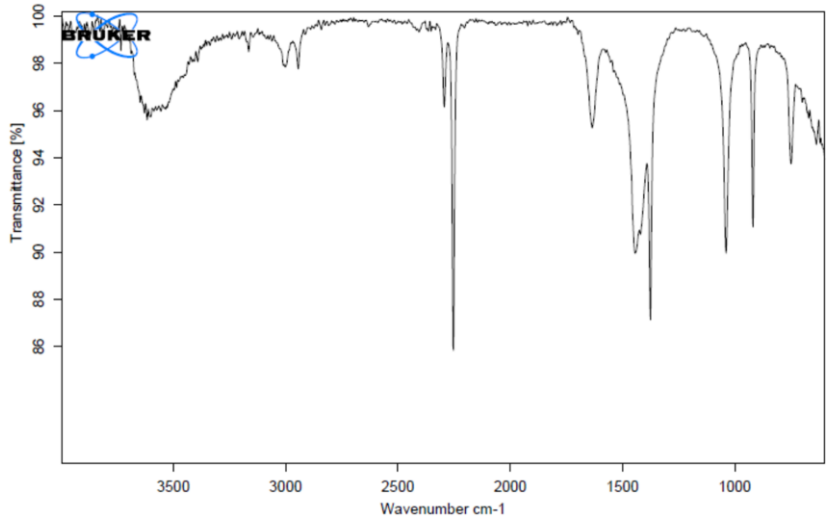
IR (in KBr) SPECTRA OF **4d**



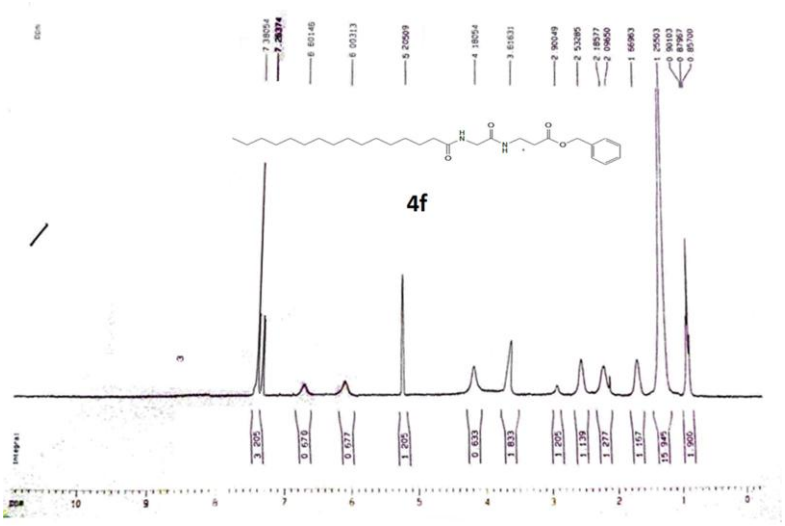
^{1}H-NMR of **4e**.



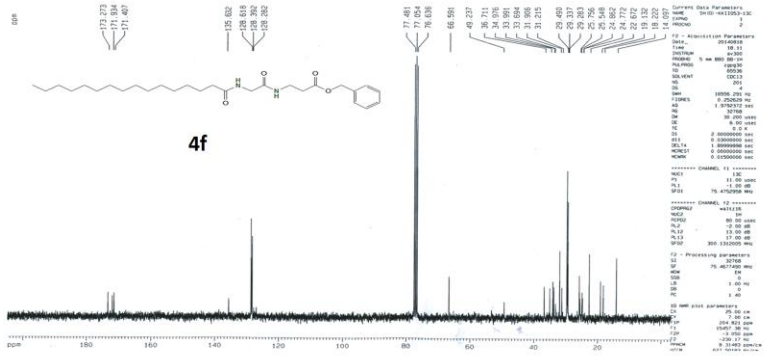
^{13}C-NMR SPECTRA OF **4e.**



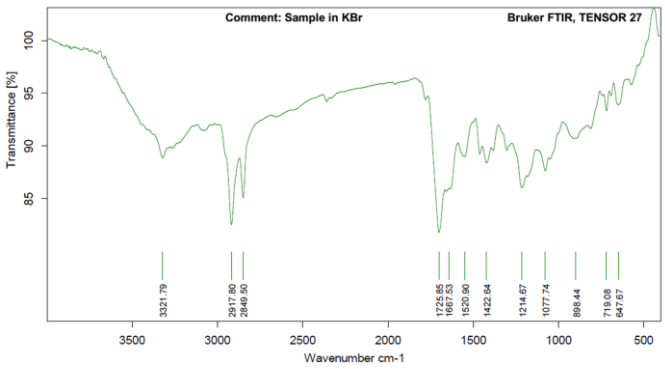
IR (solid) SPECTRA OF **4e.**



^{1}H-NMR of **4f**.

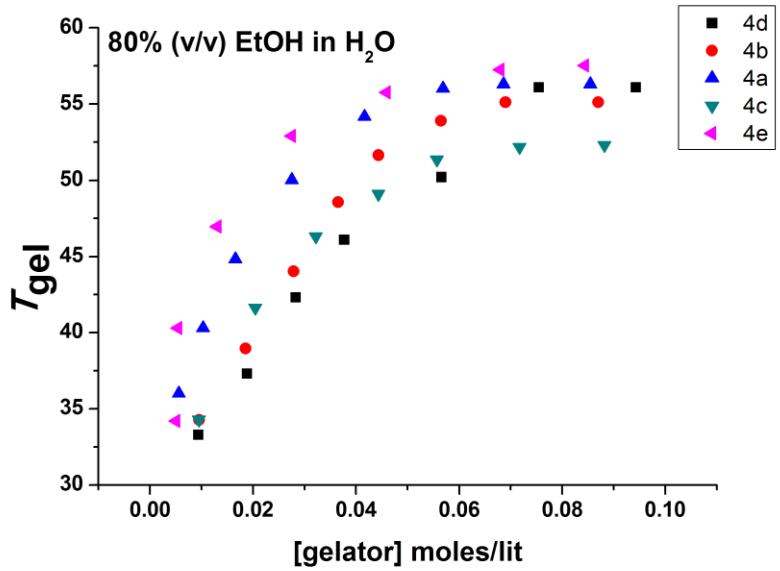


^{13}C-NMR SPECTRA OF **4f**.

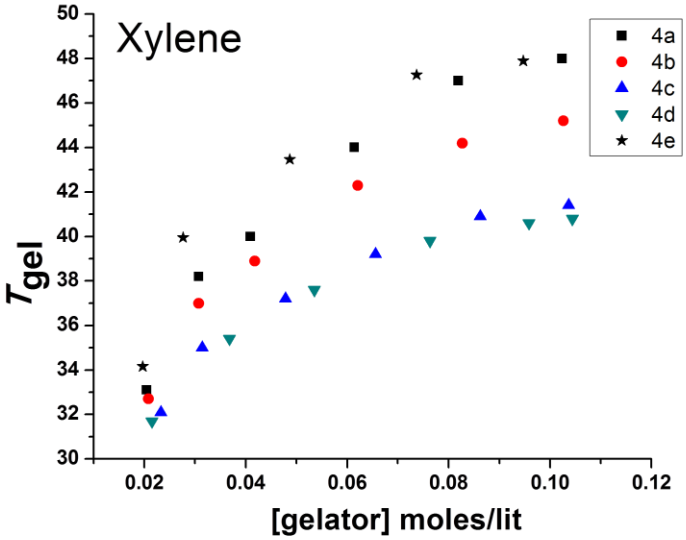


IR SPECTRA OF **4f**.

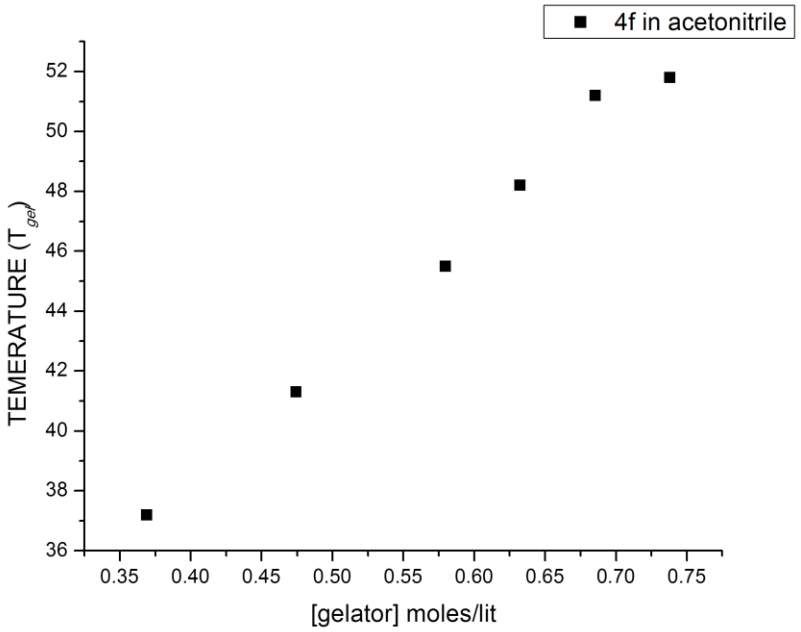
THERMAL STABILITY:



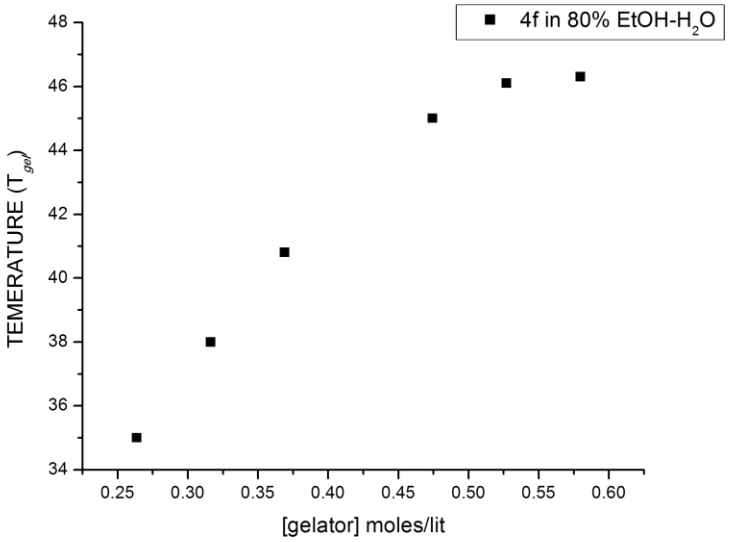
FigureS1. T_{gel}(°C) versus concentration (moles/lit) plot of different gelator in 80%(v/v) EtOH in H_2O.



FigureS2. T_{gel}(°C) versus concentration (moles/lit) plot of different gelator in Xylene

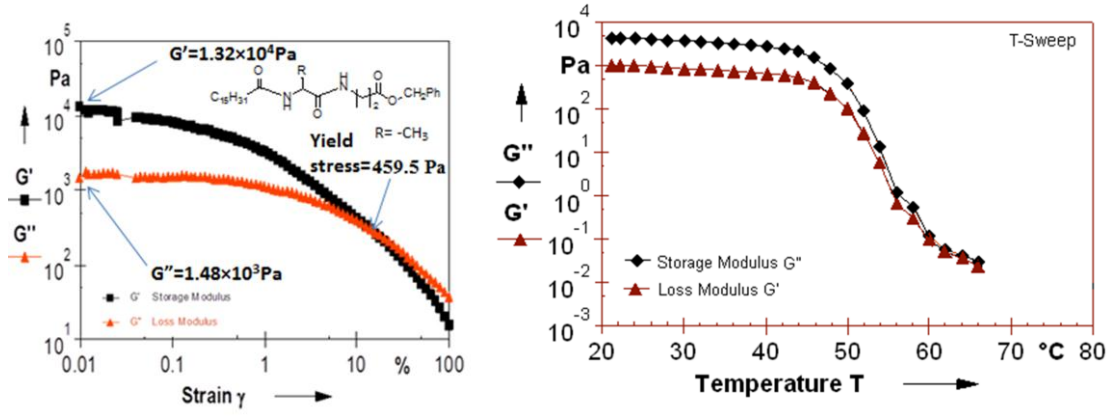


FigureS3.T_{gel}(°C) versus concentration (moles/lit) plot of **4f**gelator in acetonitrile

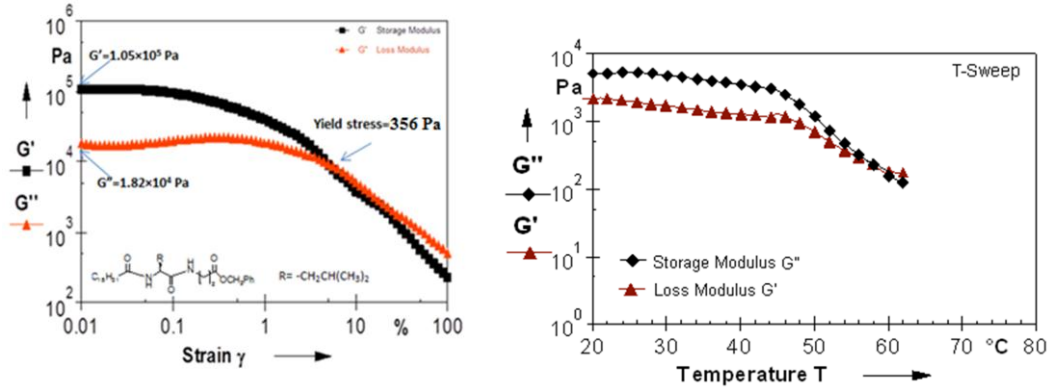


FigureS4. T_{gel}(°C) versus concentration (moles/lit) plot of **4f**gelator in 80%(v/v) EtOH in H_2O.

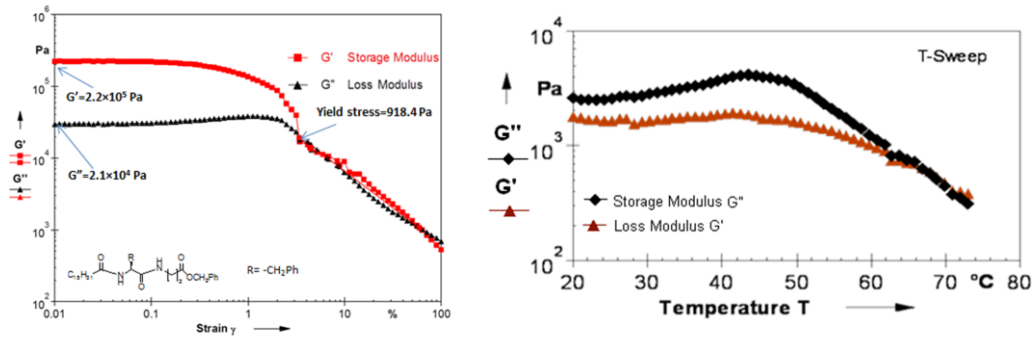
RHEOLOGY:



FigureS5. Strain amplitude sweep experiment (at 10rads/sec)andTemperature sweep experiment at constant frequency of 2Hz and heating rate 2°C/min for (**4a**) in acetonitrile.

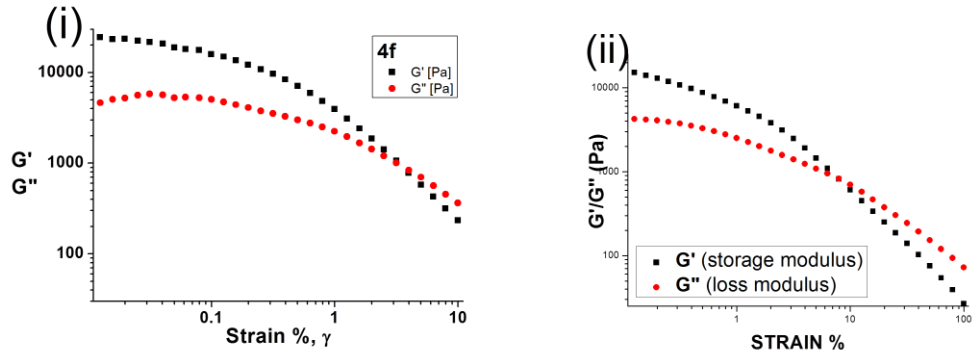


FigureS6. Strain amplitude sweep experiment (at 10rads/sec) andTemperature sweep experiment at constant frequency of 2Hz and heating rate 2°C/min for (**4c**) in acetonitrile.



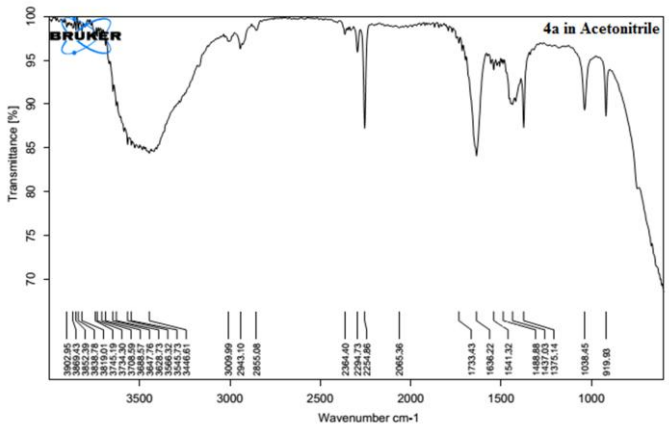
FigureS7. Strain amplitude sweep experiment (at 10rads/sec)andTemperature sweep experiment at constant frequency of 2Hz and heating rate 2°C/min for (**4e**) in acetonitrile.

RHEOLOGY:

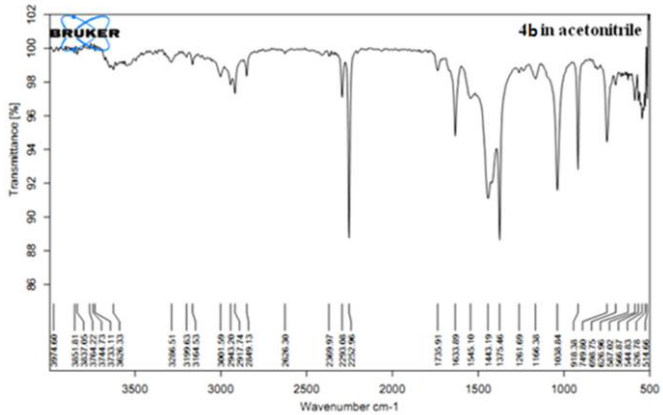


FigureS8. Strain amplitude sweep experiment (at 10rads/sec)for(i) **4f** in acetonitrile and (ii) **4c** in EtOH.

FT-IR

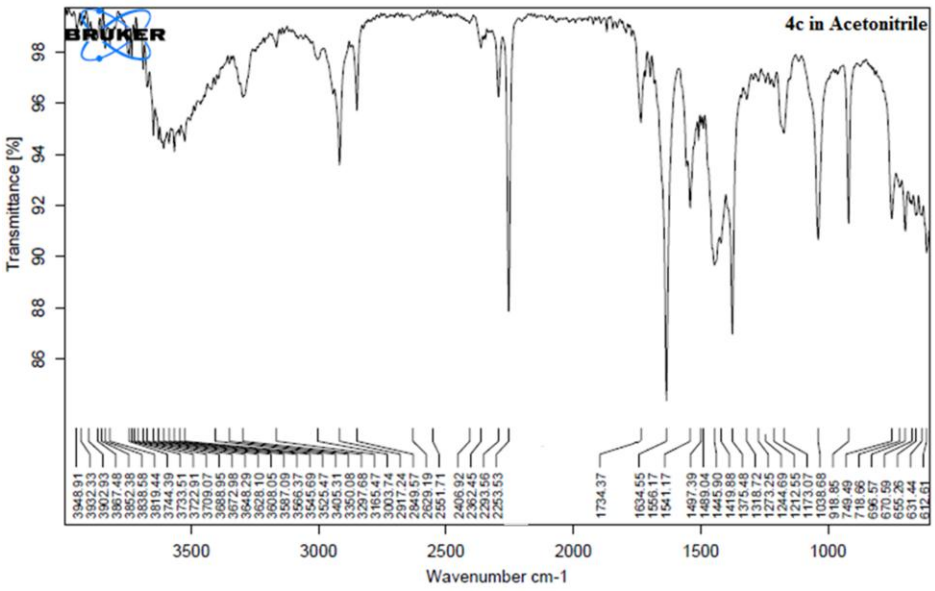


FigureS9. FT-IR spectra of **4a** in acetonitrile

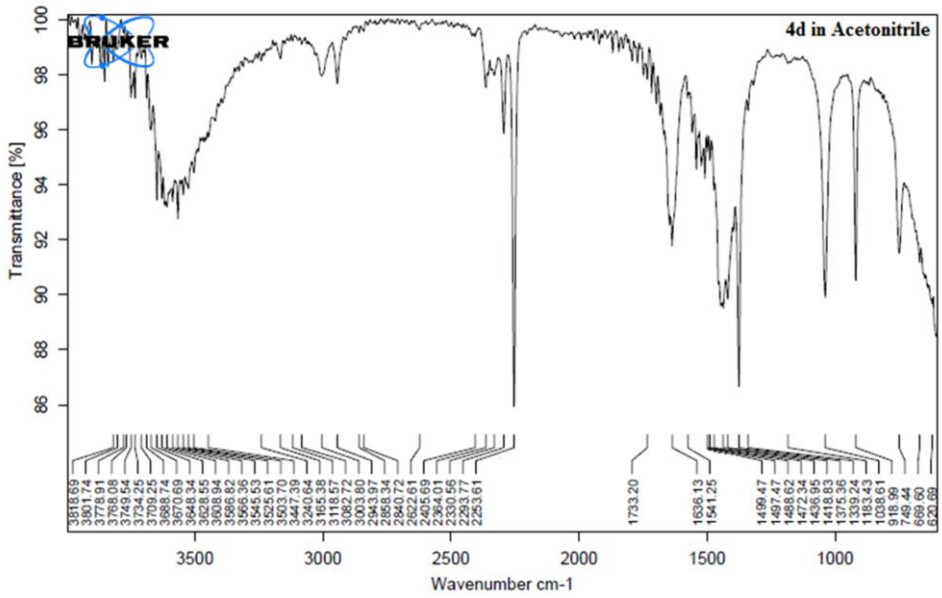


FigureS10. FT-IR spectra of **4b** in acetonitrile

FT-IR

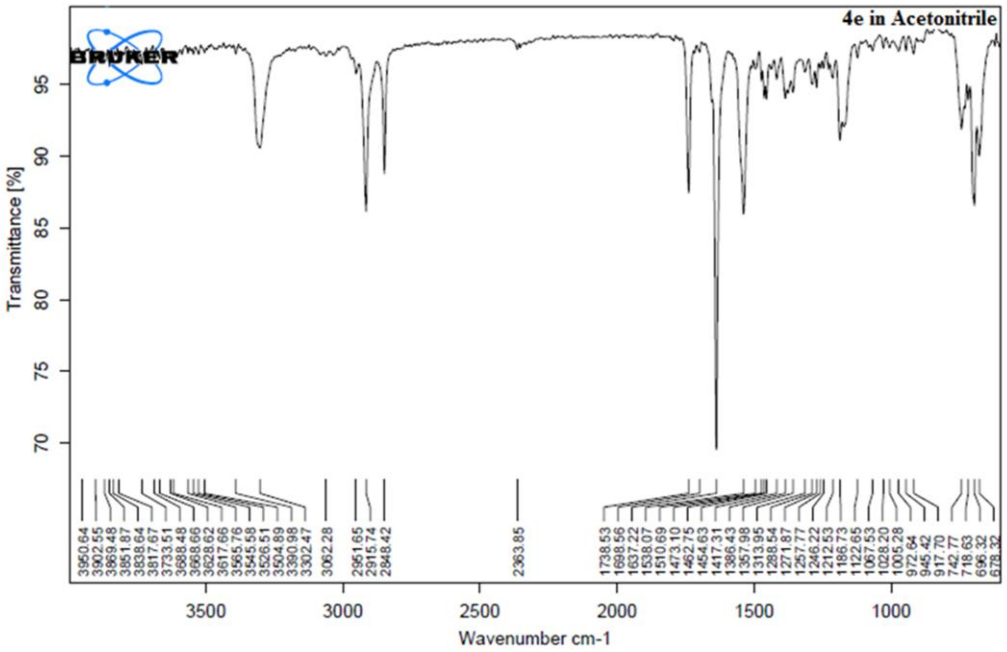


FigureS11. FT-IR spectra of **4c** in acetonitrile

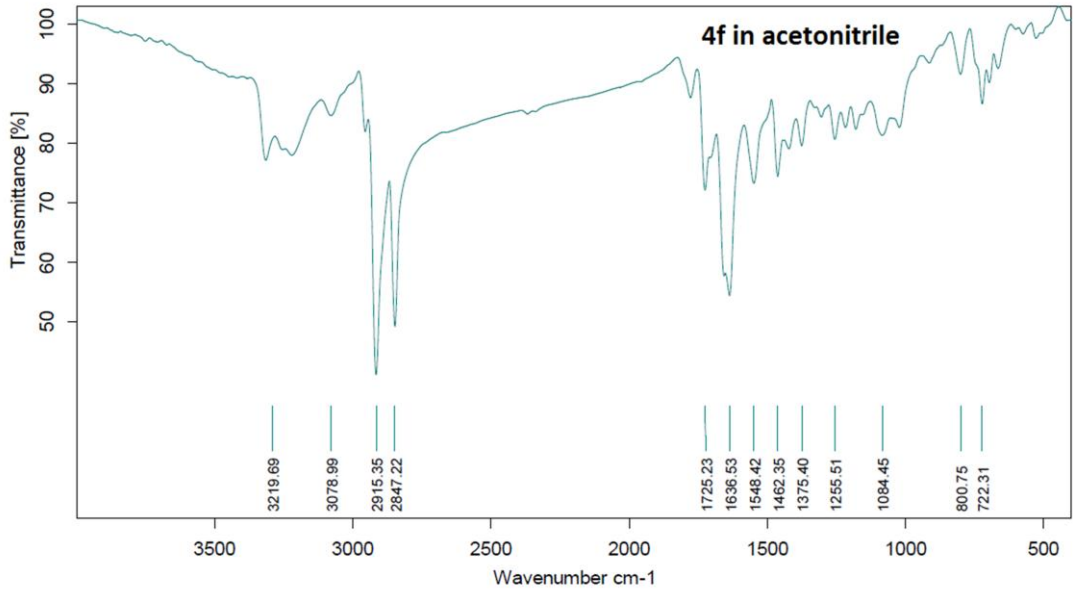


FigureS12. FT-IR spectra of **4d** in acetonitrile

FT-IR

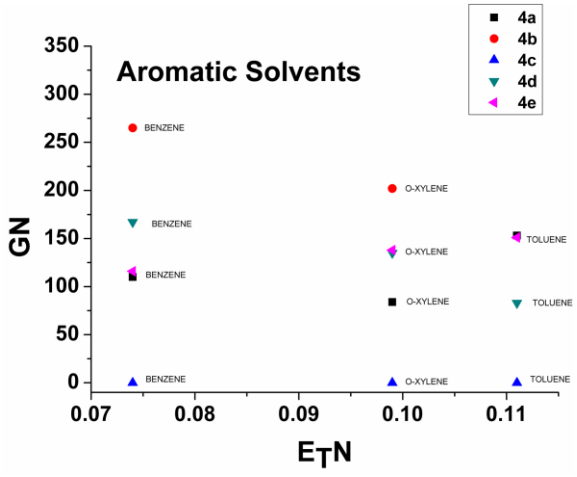


FigureS13. FT-IR spectra of **4e** in acetonitrile.

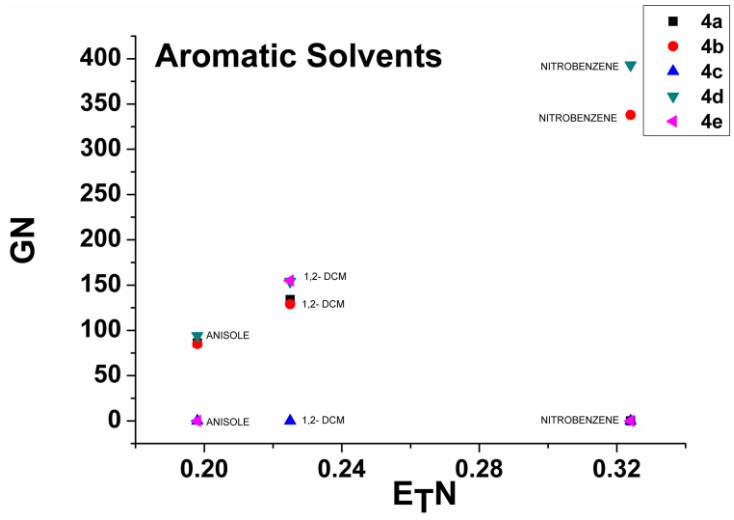


FigureS14. FT-IR spectra of **4e** in acetonitrile.

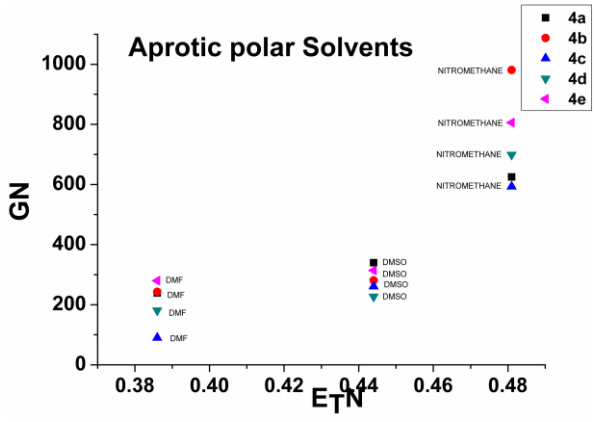
SOLVENT- EFFECT:



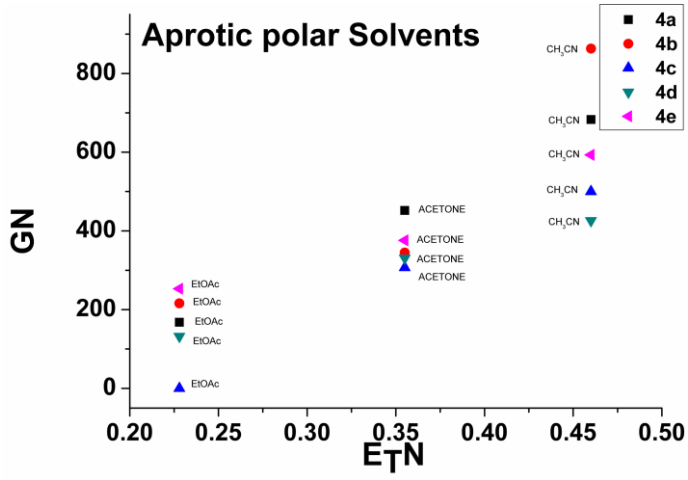
FigureS15. Plot of GN versus E_TN of the gelators in aromatic solvents.



FigureS16. Plot of GN versus E_TN of the gelators in aromatic solvents.

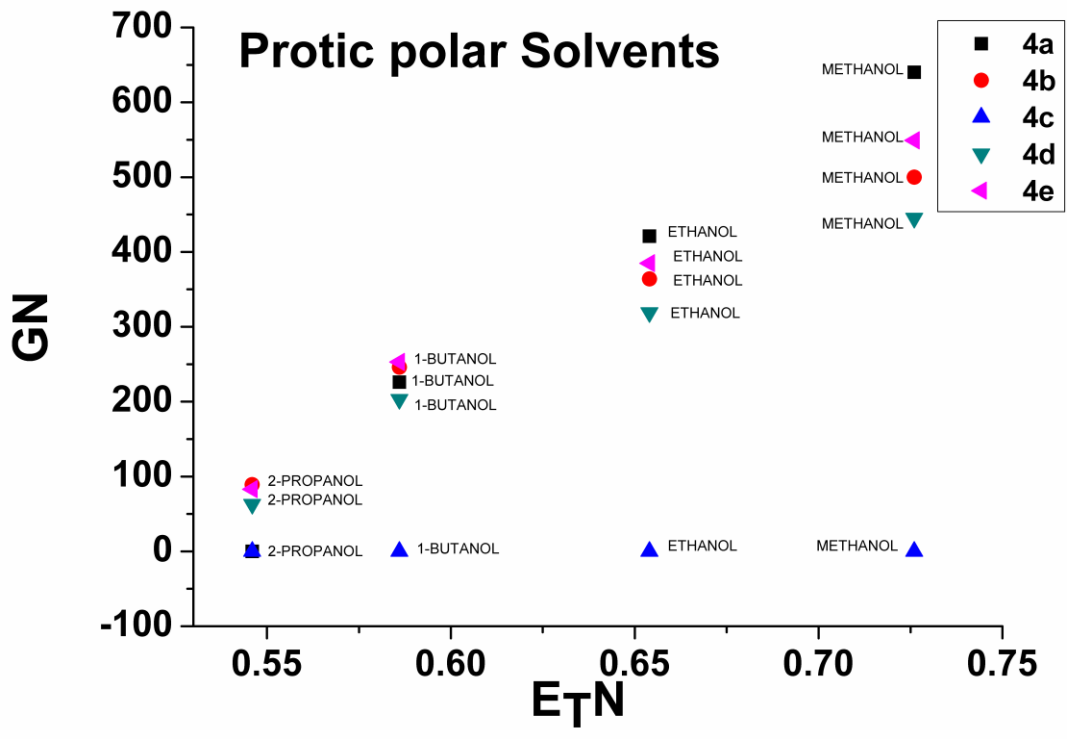


FigureS17. Plot of GN versus E_TN of the gelators in aprotic polar solvents.



FigureS18. Plot of GN versus E_TN of the gelators in aprotic polar solvents.

SOLVENT-EFFECT



FigureS19. Plot of GN versus E_T30 of the gelators in protic polar solvents.

SOLVENT-EFFECT

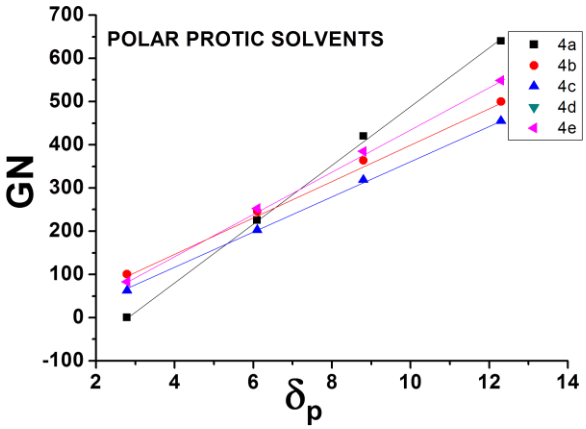


Figure S20. GN versus δ_p plot of gelators in polar protic solvents.

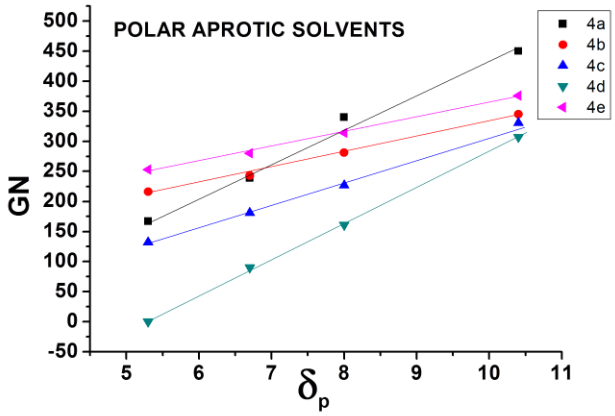


Figure S21. GN versus δ_p plot of gelators in polar aprotic solvents.

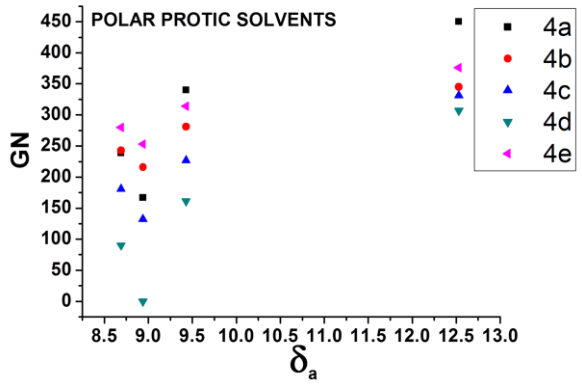


Figure S22. GN versus δ_a plot of gelators in polar protic solvents.

SOLVENT-EFFECT

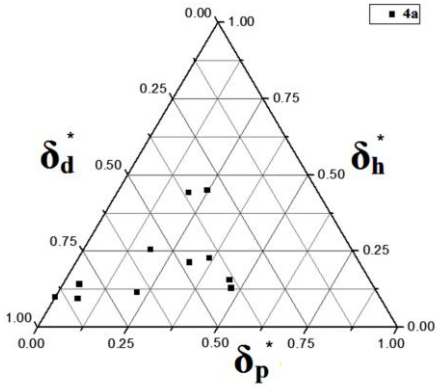


Figure S23. Teas plot of Hansen Parameters for **4a** in solvents of gelation

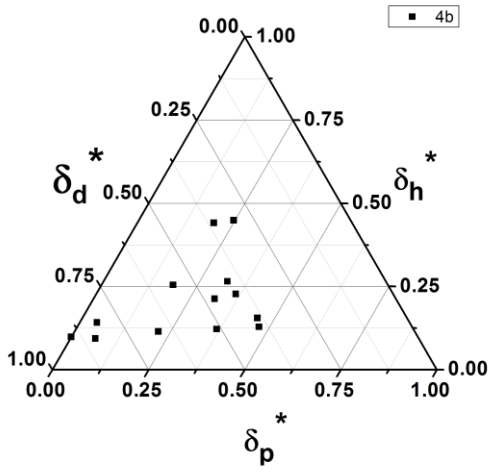


Figure S24. Teas plot of Hansen Parameters for **4b** in solvents of gelation

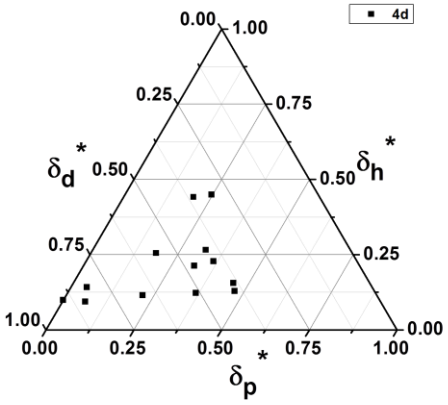
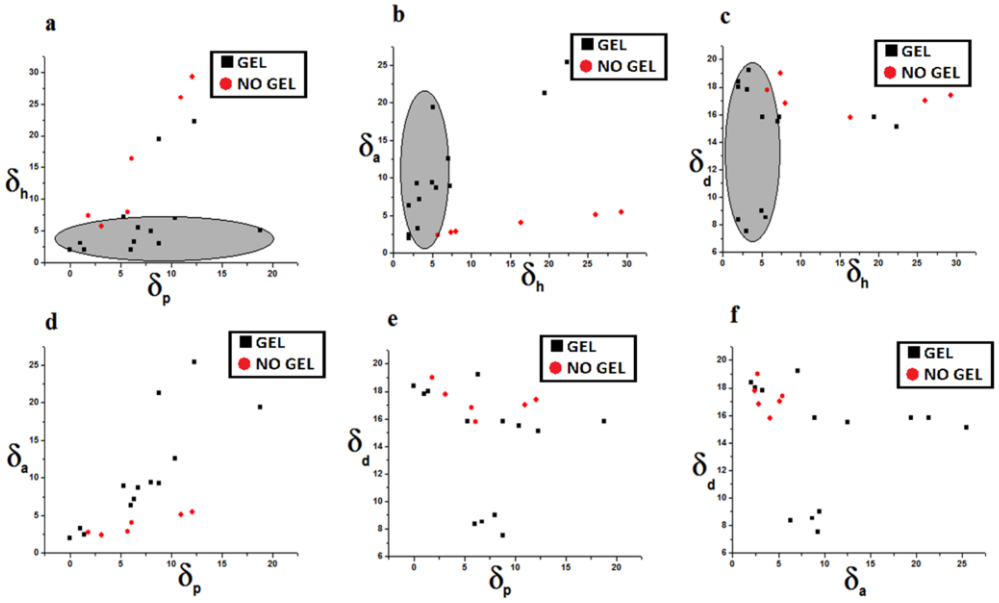


Figure S25. Teas plot of Hansen Parameters for **4d** in solvents of gelation

Panel–I



Panel-II

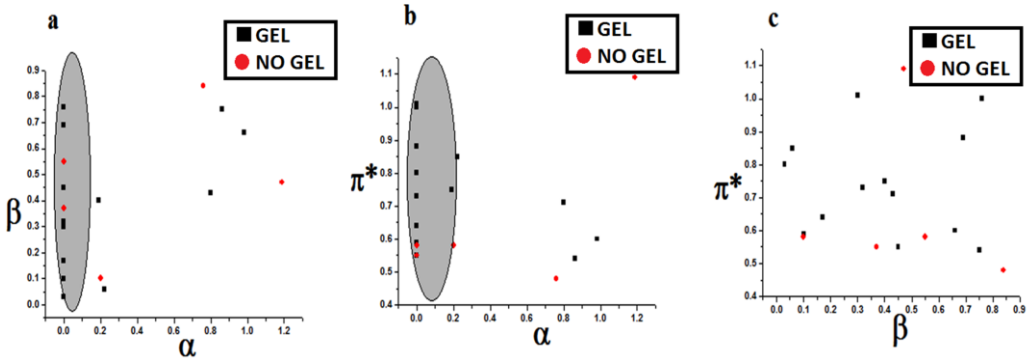


Figure S26.Plotsof, (a)$\delta_h$vsδ_p(b)$\delta_a$vsδ_h, (c) $\delta_d$vsδ_h and(d)$\delta_a$vsδ_p(e) $\delta_d$vsδ_p (f) δ_d vsδ_a(HSP)[panel I]and(a) βvs.α, (b)π^* vs.αand(c) π^*vs.β (KT)[panel II]of gelators**4a-4e**[shaded zones are prevailin g area of gelation]**.**

XRD:

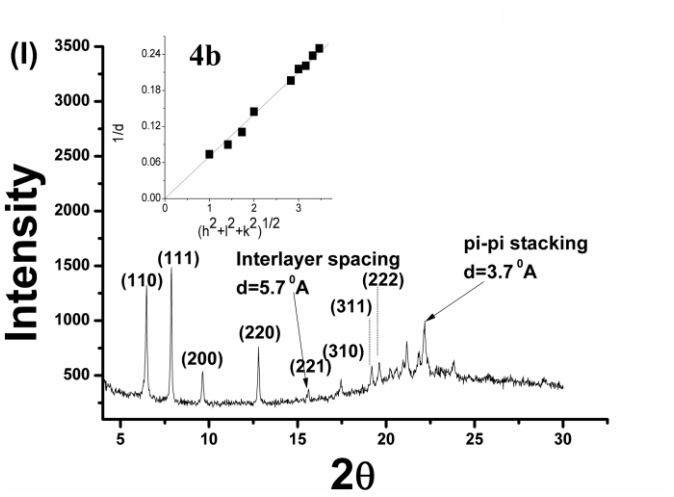


Figure S27XRD profile of xero-gels (intensity vs. 2θ) for**4b**in acetonitrile [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

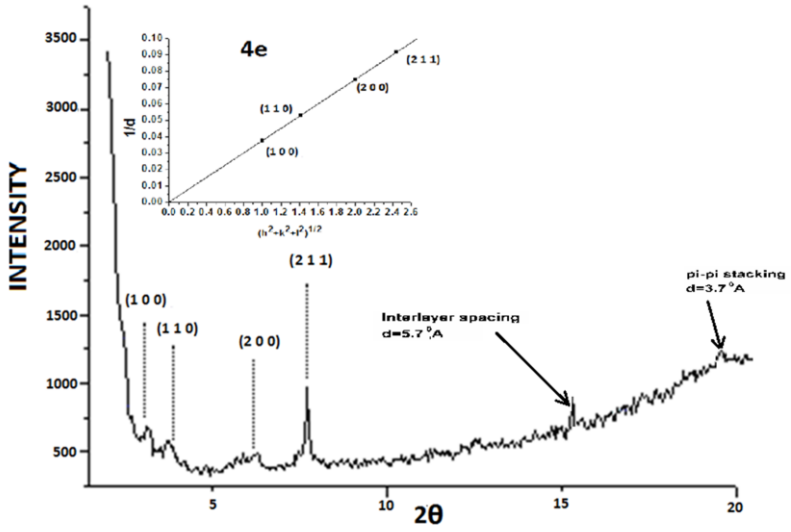


Figure S28XRD profile of xero-gels (intensity vs. 2θ) for **4e** in acetonitrile [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

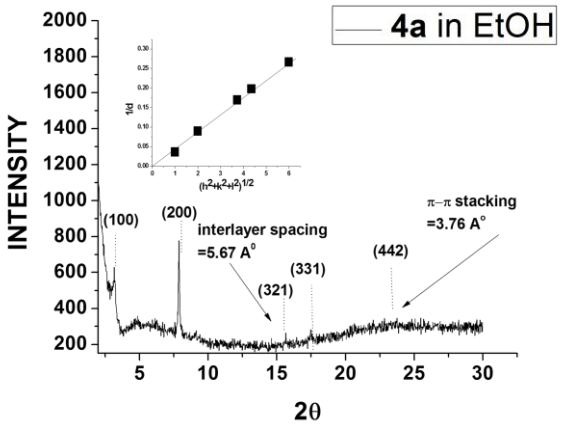


Figure S29XRD profile of xero-gels (intensity vs. 2θ) for **4a** in EtOH [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

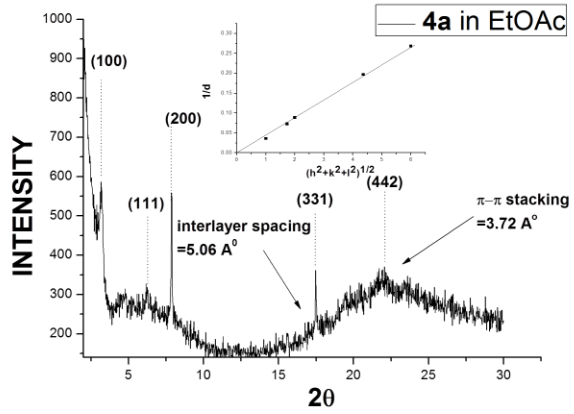


Figure S30XRD profile of xero-gels (intensity vs. 2θ) for **4a** in EtOAc [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

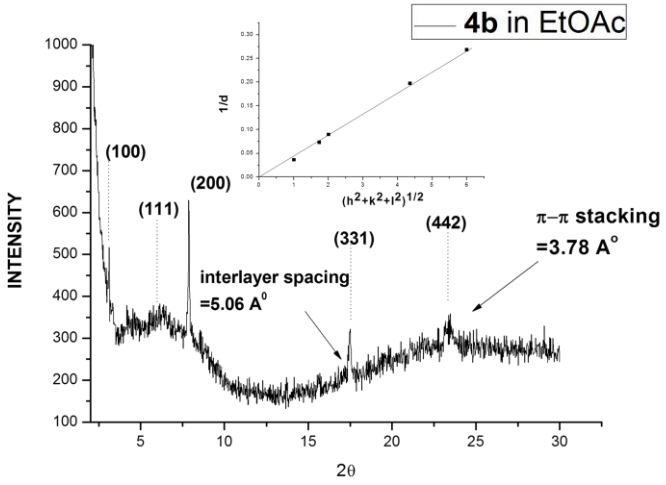


Figure S31XRD profile of xero-gels (intensity vs. 2θ) for **4b** in EtOAc [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

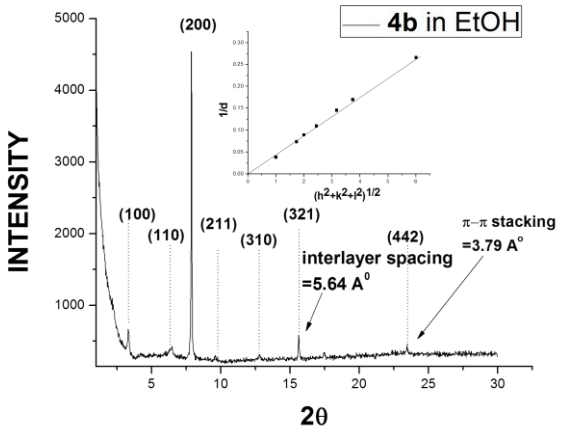


Figure S32XRD profile of xero-gels (intensity vs. 2θ) for **4b** in EtOH [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

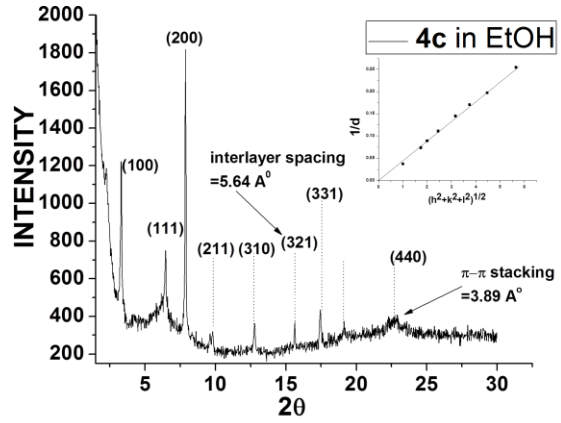


Figure S33XRD profile of xero-gels (intensity vs. 2θ) for **4c** in EtOH [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

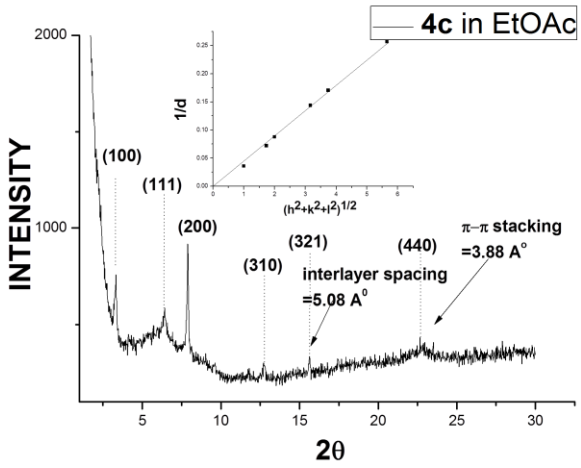


Figure S34XRD profile of xero-gels (intensity vs. 2θ) for **4c** in EtOAc [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

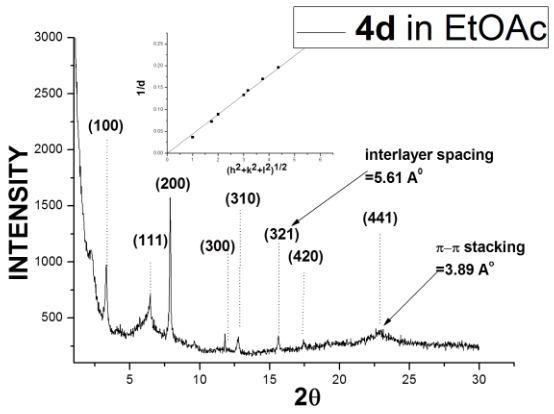


Figure S35XRD profile of xero-gels (intensity vs. 2θ) for **4d** in EtOAc [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

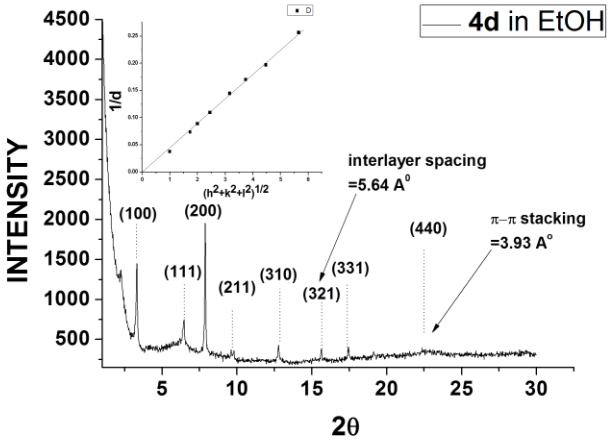


Figure S36XRD profile of xero-gels (intensity vs. 2θ) for **4d** in EtOH [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

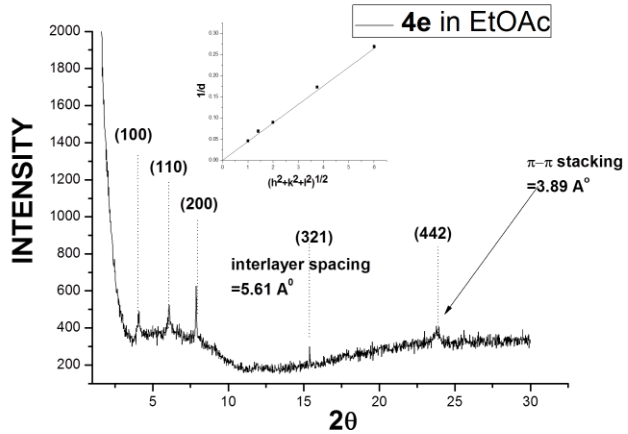


Figure S37XRD profile of xero-gels (intensity vs. 2θ) for **4e**in EtOAc [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

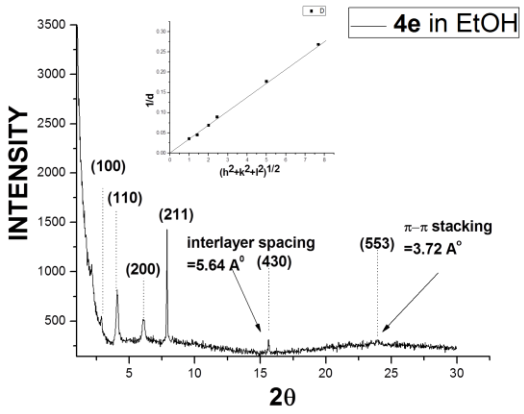


Figure S38XRD profile of xero-gels (intensity vs. 2θ) for **4e** in EtOH [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

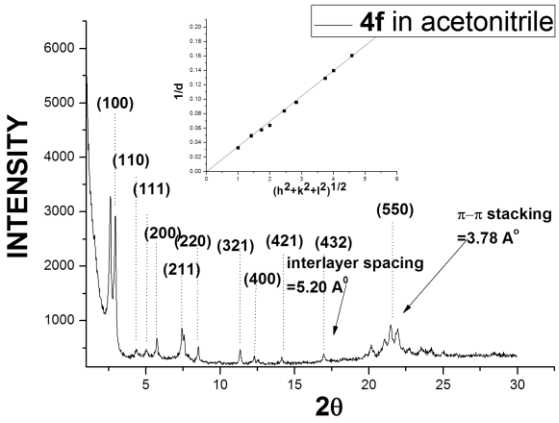


Figure S39XRD profile of xero-gels (intensity vs. 2θ) for **4f** in acetonitrile [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

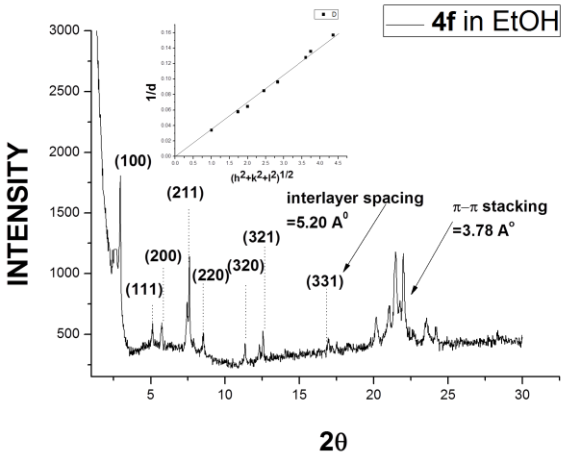


Figure S40XRD profile of xero-gels (intensity vs. 2θ) for **4f** in EtOH [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

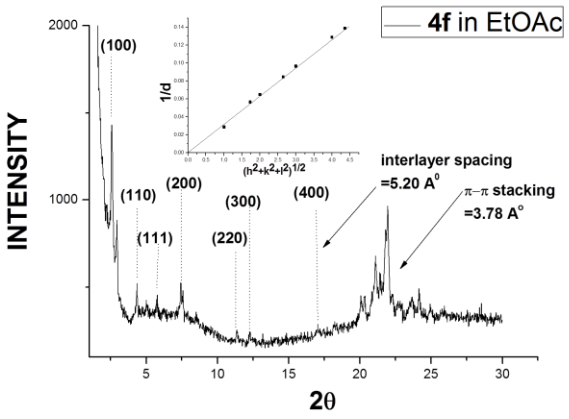


Figure S41XRD profile of xero-gels (intensity vs. 2θ) for **4f**in EtOAc [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

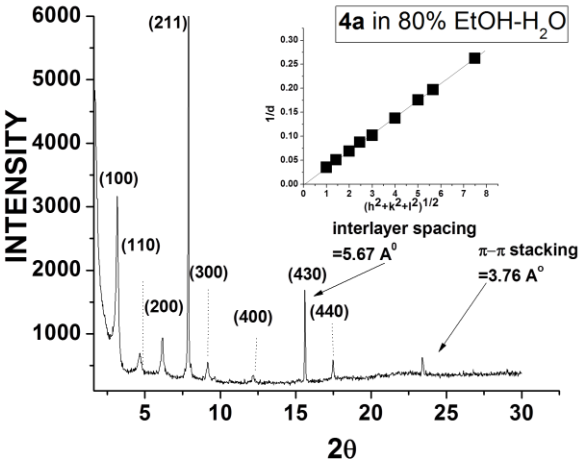


Figure S42XRD profile of xero-gels (intensity vs. 2θ) for **4a** in 80% EtOH-Water [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

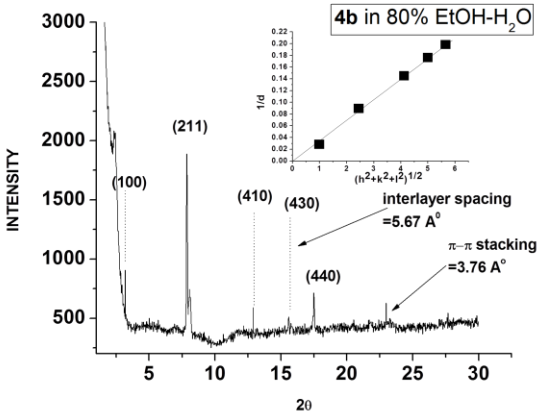


Figure S43XRD profile of xero-gels (intensity vs. 2θ) for **4b** in 80% EtOH-Water [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

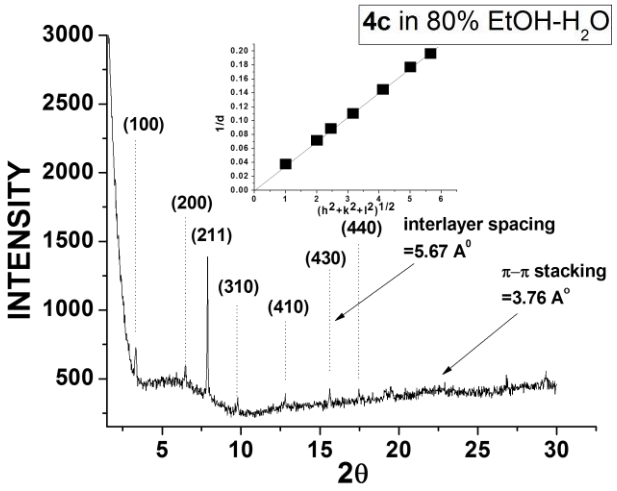


Figure S44XRD profile of xero-gels (intensity vs. 2θ) for **4c** in 80% EtOH-Water [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

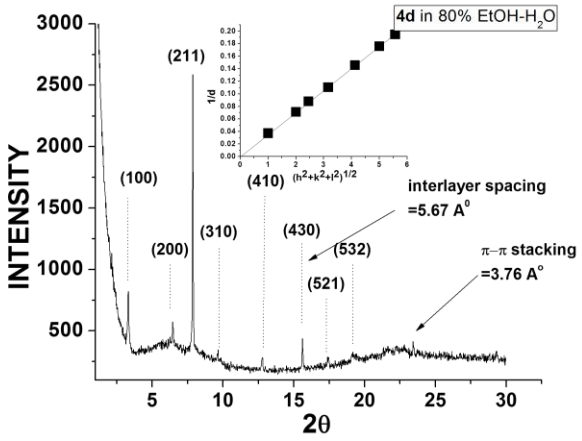


Figure S45XRD profile of xero-gels (intensity vs. 2θ) for **4d** in 80% EtOH-Water [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

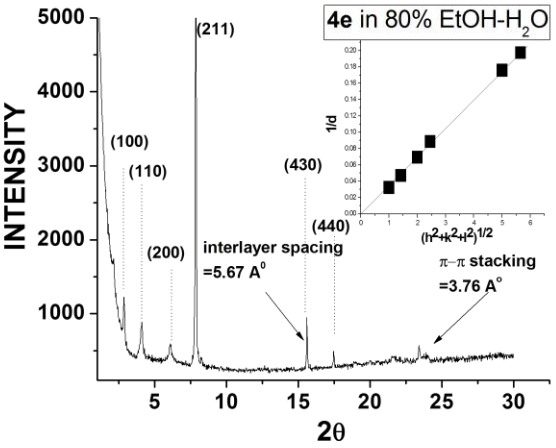


Figure S46XRD profile of xero-gels (intensity vs. 2θ) for **4e** in 80% EtOH-Water [inset represent s respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

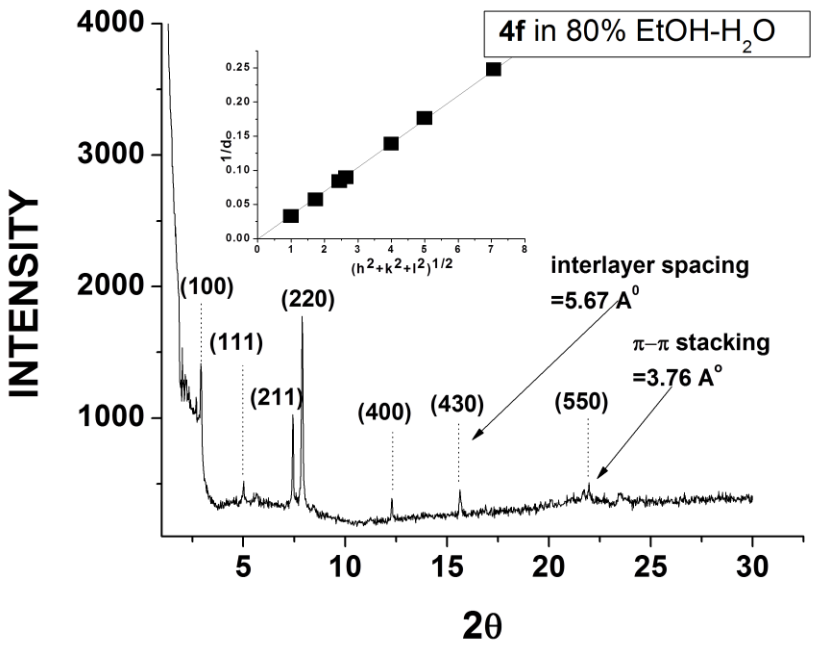


Figure S47XRD profile of xero-gels (intensity vs. 2θ) for **4f** in 80% EtOH-Water [inset represents respective plots of d^{-1} vs. $\sqrt{(h^2+l^2+k^2)}$]

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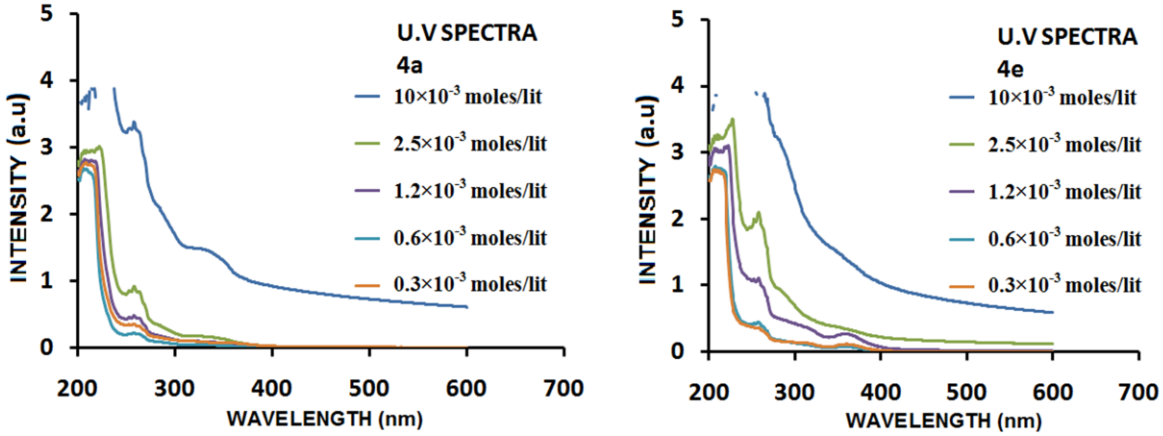

Figure S48U.V spectra of gelator **4a** and **4e** in acetonitrile at different concentrations.

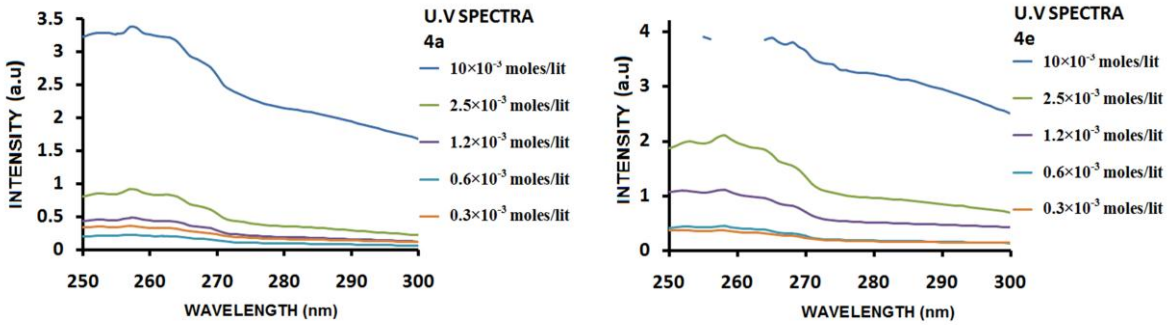

Figure S49U.V spectra of gelator **4a** and **4e** in acetonitrile at different concentrations.

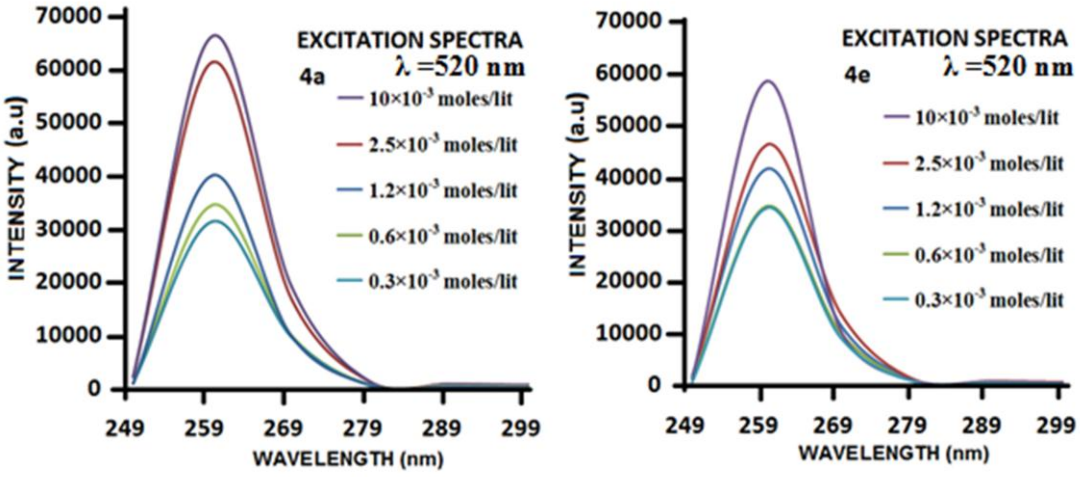

Figure S50Fluorescence excitation spectra of gelator **4a** and **4e** in acetonitrile at different concentrations.