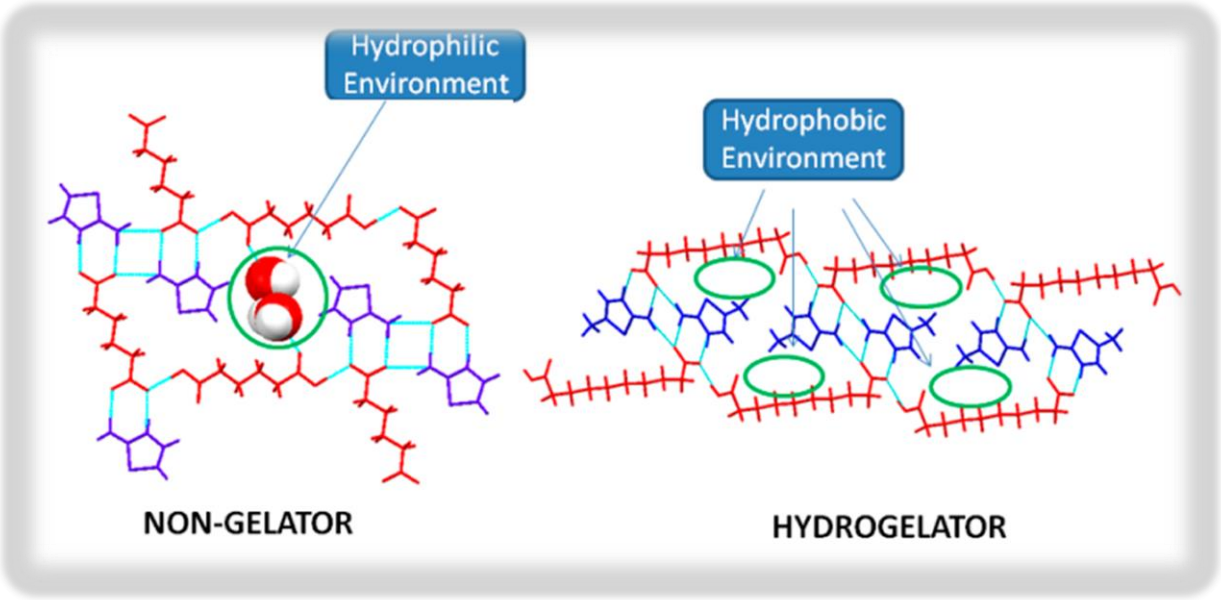
Chapter-3



Combinatorial library approach to realize 2-Aminothiazole based two-component Hydrogelator: A Structure–Property Correlation

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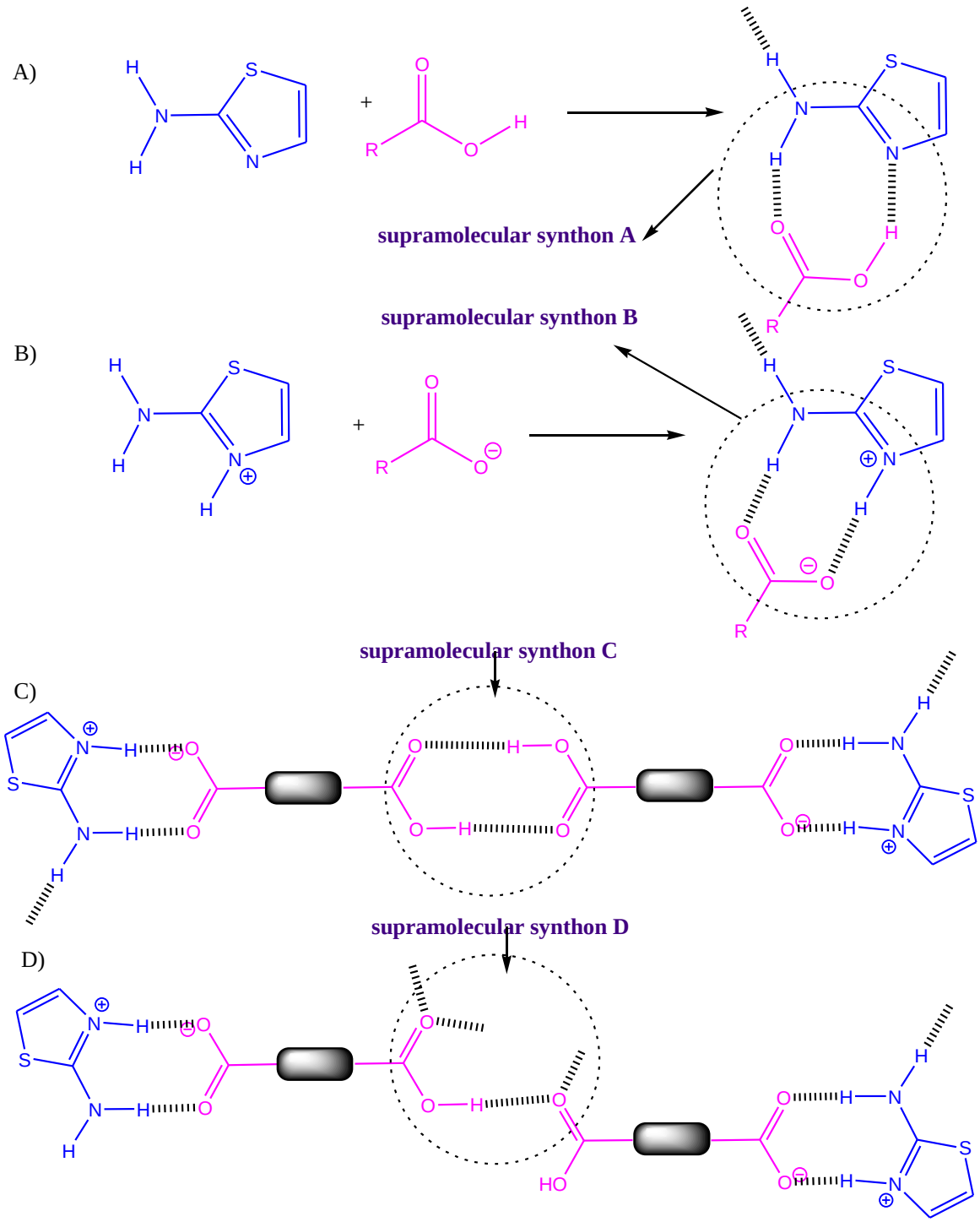
3.1 Introduction

Crystal engineering- a sub discipline of Supramolecular Chemistry- is the understanding of non-covalent interactions in the context of crystal packing, and exploiting those interactions for developing novel materials such as gas-storage materials, pharmaceutical active ingredient using the concept of polymorphism, magnetic materials, optical materials, etc.[1-4] Supramolecular Synthons,[5] are the structural units within supermolecules which assembled by intermolecular interactions, that convey the essential features of a crystal structure. Recently, crystal engineering and Supramolecular synthons are employed to design some physical gels or supramolecular gels.[6-11] Multicomponent gelator [12-15] give an edge over other class of single component gelators namely, a systematic change of one component to understand gelation/non-gelation property of a series of compounds, effect of functional groups (types and position), role of hydrophobic/ hydrophilic interaction by systematic change in alkyl chain or functional groups. Organic salts/cocrystals represent a special class of two component gelators. Organic salt/ cocrystals have distinguished advantage over other class of gelators such as ease of synthesis, almost quantitative yield, availability of carboxylic acids/amines with various backbones (aliphatic, aromatic and alicyclic) etc.

Herein, we present a combinatorial library approach to synthesize various 2-aminothiazole (and its methyl derivatives) based organic salts/cocrystals with potential application as gelling agent. 1, 3, 5-triazine moiety has been shown as a novel class of non-polymeric hydrogelator, which prompted us to explore other heterocyclic compounds as potent gelling agent. Moreover, predictable hydrogen bonded networks (HBN) or supramolecular assemblies of 2-aminothiazole moiety and carboxylic acid/ carboxylate ion provides an opportunity to design a new class of LMOGs (**Scheme 3.1)**. As it is evident from the **scheme 3.1** that thiazole moiety can form zero (0-D) dimensional networks with mono- and di- carboxylic acid when reacted in 1:1 molar ratio. The reliability of cyclic hydrogen bonded motif of graph set representation[16] $R_2^2(8)$ of 2-aminothiazoles (or its derivatives) was further supported by the CSD search of 2-aminothiazole based organic salts/ cocrystals(out of 20 hits 15 turned out to be 2-aminothiazole based salts/cocrystals) **(Table 3.1).**



Scheme 3.1 The probable supramolecular synthon in A) 2-aminothiazole-monocarboxylic acid cocrystals , B) 2-aminothiazolium-monocarboxylate salts, C) 2-aminothiazolium hydrogen-dicarboxylate (1:1 organic salts) having carboxylic dimer synthon; D) 2-aminothiazolium hydrogen-dicarboxylate (1:1 organic salts) having carboxylic catemer synthon.

Table 3.1 List of compounds obtained after CSD search of 2-aminothiazole based organic salts/ cocrystals

S. No.	Name of the Compound CSD REFCODE	Supramolecular Synthon (graph set representation)	Weak secondary non-covalent interactions and overall Supramolecular assembly	References
I	2-Aminothiazolium 3,5-dinitrobenzoate JEFLEM	$R_2^2(8), R_4^2(8)$	(Nitro)O....S, 3D	17
II	2,2'-Diamino-4,4'-bi-1,3-thiazolium fumarate TADRUM	$R_2^2(8)$	(COOH)O...S(thiazole), N-H...O, 3D	18
III	2,2'-Diamino-4,4'-bi-1,3-thiazolium (2R,3R)-tartrate FIWJIF	$R_2^2(8)$	(COOH)O-H...O$^-$ (COO$^-$), (thiazole) S...O(COOH) ,3D	19
IV	2,2'-diamino-4,4'-bi-1,3-thiazol-3,3'-diium bis(2,2'-diamino-4,4'-bi-1,3-thiazol-3-ium) tetrakis(2-nitrobenzoate) VAYYIE	$R_2^2(8)$, $R_4^2(8)$, $S(6)$ Intramolecular interaction between (Nitro)O....O (carboxylate)	(Nitro)O...S, 3D	20
V	2,2'-Diamino-4,4'-bi-1,3-thiazolium bis(3-nitrobenzoate) EHACIA	$R_2^2(8), R_4^2(8)$	(Nitro)O...S, 3D	21
VI	bis(2-Aminothiazolium) succinate succinic acid MOSMIR	$R_2^2(8)$	(COOH)O-H...O$^-$(COO$^-$), (thiazole)S...O(COOH), 3D	22
VII	2-amino-1,3-thiazolium hydrogen maleate DUZPUK	$R_2^2(8), S(7)$	(thiazole)S...O(COOH), 3D	23
VIII	2-amino-1,3-thiazolium hydrogen fumarate DUZQAR	$R_2^2(8)$	(COOH)O-H...O$^-$ (COO$^-$), 3D	23
IX	2-Amino-4-phenylthiazolium hemikis(phthalate) ISIBUI	$R_2^2(8)$	N-H...O, (thiazole)S...O(COO$^-$), 3D	24
X	2-Amino-4-phenylthiazolium hydrogen maleate ISICIX	$R_2^2(8), S(7)$	(thiazole)S...O(COOH), 2D	24

XI	(-)-2,6-Diamino-4,5,6,7-tetrahydrobenzothiazole (L)-(+)-tartrate trihydrate FECZES	$R_2^2(8)$	(thiazole)S...O(COO^-), (hydroxyl)O-H...O(water), 3D	25
XII	2-Aminothiazolium trichloroacetate CUDREY	$R_2^2(8)$	Cl...π(thiazole), (thiazole)S...C(COO^-)	26
XIII	2-Amino-5-methyl-1,3-thiazolium-4-nitrobenzoate XUVPOU	$R_2^2(8)$	(thiazole)S...O(Nitro)	27
XIV	2-Amino-5-methyl-1,3-thiazolium 2-amino-5-methyl-1,3-thiazole 2-(2-(2,6-dichlorophenylamino) phenyl)acetic acid 2-(2-(2,6-dichlorophenylamino) phenyl)acetate XUVQEL	$R_2^2(8)$	(thiazole)S...N(amine), (amine)N-H....O^-(COO^-)	27

Surprisingly all the salts displayed cyclic heterosynthon of graph set representation $R_2^2(8)$ which matches well with the CSD search analysis carried out by Lynch et al.[28] on 2-aminoheterocylic-carboxylic acid. The consistent occurrence of cyclic heterosynthon of graph set $R_2^2(8)$ in 2-aminothiazole based salts/cocrystals and predictable hydrogen bonded network inspired us to design and synthesize a new series of 2-aminothiazole based organic salts/cocrystals. Moreover, the presence of additional hydrogen bonding site of amine functionality along with probable C-H…S/C-H….N interactions may lead to one dimensional (1D) or two dimensional (2D) hydrogen bonded network. In addition, a suitable position of the methyl group on thiazole moiety may provide an opportunity to understand the role of (methyl) C-H….S/N (thiazole) in gelation/non-gelation behavior of these salts/cocrystals.

It is well accepted that 1D HBN favors organogelation whereas 2D and 3D HBNs may lead to formation of a weak gel or non-gelation at all.[6, 29] Even though quite success is achieved in designing an organogelator based on crystal engineering approach; designating new hydrogelator is still a difficult task. Even though, there are few reports [30] suggesting that molecules forming porous supramolecular hydrogen bonded network with appropriate hydrophilic and hydrophobic balance may acts as a non-covalent hydrogelator. Furthermore studies are required to understand how water

gets immobilized in complex HBN. Other deriving force for the present study is availability of very few reports on organic salts/cocrystals of 2-aminothiazole and its derivatives, especially methyl derivatives of 2-aminothiazole which limits our understanding of weak of hydrogen bond such as (methyl)C-H…N or (methyl)C-H…S and its use as reliable supramolecular synthons.[22-23]

The combinatorial library was made by reacting seven aliphatic Dicarboxylic acids and three 2-aminothiazole darivatives **(Chart 3.1, Table 3.2)**.Out of 24 salts/ cocrystals synthesized in the present study, we are able to solve crystal structures of 11 salts/cocrystals to understand the role of various non-covalent interactions on gelation/ non-gelation behavior especially in bulk/xerogel state.

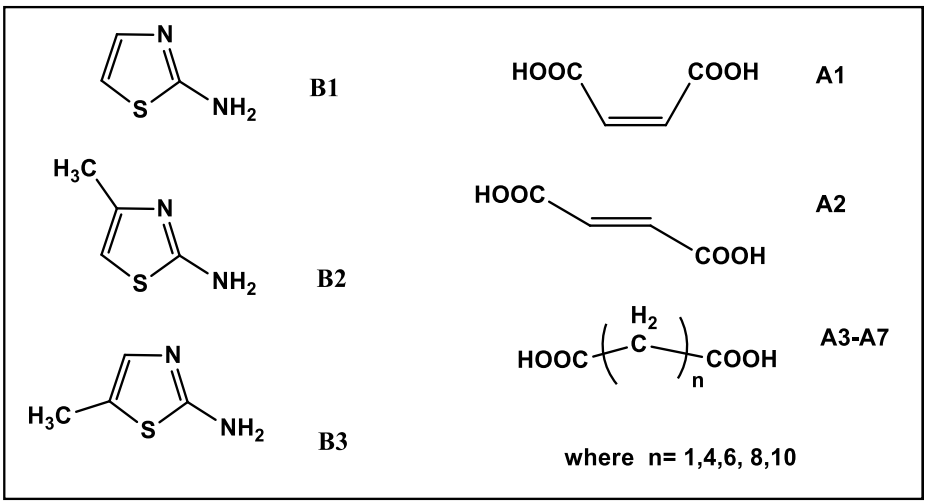


Chart 3.1 List of compounds employed to synthesize cocrystals/salts.

Table 3.2 Combinatorial library approach to synthesize series of cocrystals/salts

	A1 (1:1)	A2 (1:1)	A3 (1:1)	A4 (1:1)	A5 (1:1)	A6 (1:1)	A6 (1:2)	A7 (1:1)
B1	B1A1	B1A2	B1A3	B1A4	B1A5	B1A6	B1A6a	B1A7
B2	B2A1	B2A2	B2A3	B2A4	B2A5	B2A6	B2A6a	B2A7
B3	B3A1	B3A2	B3A3	B3A4	B3A5	B3A6	B3A6a	B3A7

Values in parenthesis i.e (1:1), (1:2) indicates the molar ratio of Acid/Amine

3.2 Experimental section

3.2.1 Materials and physical measurements

3.2.1.1 Materials

2-Amino thiazole, 2-Amino-4-methylethiazole, 2-Amino-5- methylethiazole, maleic acid, fumaric acid, malonic acid, adipic acid, suberic acid, sebacic acid and dodecanoic acid (All from Aldrich) were used as received. The other chemicals were of the highest commercial grade available and were used without further purification.

3.2.1.2 SEM measurement

Hot solution of a gelator was placed on a SEM sample holder and allowed to cool at room temperature to form gel, which is then dried under vacuum. The SEM image of xerogel was recorded on JEOL JSM5610 LV SEM instrument after carbon coating.

3.2.1.3 FT-IR measurement

FT-IR spectra were recorded on perkin elmer –RX FTIR. The solid sample was grinded together with anhydrous KBr using mortar pestle and a pallet was subjected to FT-IR analysis.

3.2.1.4 Powder X-ray diffraction study

Powder diffraction patterns of neat gelator (bulk) and xerogel (water slowly evaporated) were recorded on XPERT Philips (CuK_{α} radiation).

3.2.1.5 Single Crystal X-ray study

Crystals of B1A4, B1A5, B3A1, B3A2 and B1A6, B2A6, B3A6, B3A7 were obtained from 80/20 methanol/water mixture and methanol respectively in a slow evaporative condition at room temperature. Diffraction data for B1A6, B2A6, B3A2 and B3A6 was collected using SMART APEX diffractometer and B1A4, B1A5, B3A1, B3A7 were collected using Xcalibur, Eos, Gemini diffractometer. Structure solution/ refinement were carried out using the olex2 software. Graphics are generated using MERCURY 3.0.All structures are solved by direct methods and refined in a routine manner. In all cases, nonhydrogen atoms are treated anisotropically. Whenever possible, the hydrogen atoms are located on a difference Fourier map and refined. In other cases, the hydrogen atoms are geometrically fixed.

3.2.2 Synthesis

All the compounds were prepared by mixing the Dicarboxylic acids (A1-A7) with corresponding Amine (B1-B3) in hot methanolic solution in a 1:1/1:2 molar ratio. The mixtures were cooled slowly and kept at room temperature for drying. The brown/yellow solids obtained in quantitative yield were subjected to characterization by various physico-chemical techniques.

3.2.3 Analytical data

Compound-B1A1. m.p 146^{0}C,^{1}HNMR(400MHz, DMSO, TMS); δ7.792(s, 2H, NH_2), 7.075(d, 1H, CH), 6.692(d, 1H, CH), 6.170(d, 2H, CH=CH).

FT-IR(KBr);3239,3123,2311,1908,1701,1684,1616,1519,1355,1212,1168, 1036, 980, 788,711,611,499,415.

Compound-B1A2. m.p 174^{0}C, ^{1}HNMR (400MHz,DMSO, TMS); δ7.101(s, 2H,NH_2), 6.986(d, 1H, CH), 6.920(d, 1H, CH), 6.605(d, 2H, CH=CH).

FT-IR(KBr);3210,3165,2218,1928,1817,1704,1669,1613,1559,1372,1210,1143,1080, 1018,918,816,788,711,668,558,450,415.

Compound- B1A3. m.p 105^{0}C, ^{1}HNMR (400MHz,DMSO,TMS); δ7.197(s, 2H, NH_2), 6.942 (d, 1H, CH), 6.595(d, 1H, CH), 3.195(s, 2H, CH_2).

FT-IR(KBr); 3169,3086,2748,1908,1743,1685,1625,1580,1467,1410,1268 ,1220, 1168,987,866, 746,606,563,502,440.

Compound-B1A4. m.p 69^{0}C,^{1}HNMR (400MHz, DMSO, TMS); δ 6.898(s, 2H, NH_2), 6.833 (d, 1H, CH), 6.545(d, 1H, CH), 2.201(t, 4H, CH_2), 1.477-1.443(m, 4H, CH_2).

FT-IR(KBr);3495,3366,3127,2484,1930,1699,1658,1634,1567,1519,1456,1327,1315, 1279,1198,1166,1014,925,901,793,710,563,538,485,418.

Compound-B1A5. m.p 78^{0}C, ^{1}HNMR (400MHz, MEOD, TMS); δ 6.971(d, 1H, CH), 6.576(d, 1H, CH), 2.332-2.285(t, 4H, CH_2), 1.663-1.590(m, 4H, CH_2),1.399-1.381 (m, 4H, CH_2).

FT-IR(KBr);3390,3197,2930,2355,1700,1632,1512,1467,1411,1349,1255,1191,1052, 930,795,726,684,560,499.

Compound-B1A6. m.p 104^{0}C,^{1}HNMR (400MHz, DMSO, TMS); δ6.947(s, 2H, NH_2), 6.887(d, 1H, CH), 6.543(d, 1H, CH), 2.111-2.150(t, 4H, CH_2), 1.490-1.456(m, 4H,CH_2), 1.291-1.240 (m, 8H, CH_2).

FT-IR(KBr);3381,3196,2936,2363,1699,1634,1509,1467,1408,1354,1299,1239,1187, 1051,931,860,723,680,543,415.

Compound-B1A6a. m.p 97^{0}C,^{1}HNMR (400MHz, DMSO, TMS); 6.914(d, 2H, CH), δ6.864(s, 4H, NH_2),6.527(d, 2H, CH), 2.196-2.160(t, 4H, CH_2), 1.493-1.458(m, 4H, CH_2), 1.296-1.243 (m, 8H, CH_2).

FT-IR(KBr);3270,3262,2389,1840,1714,1653,1619,1592,1484,1361,1301,1229,1132, 980,852,784,665,589,496,423

Compound-B1A7. m.p 88^{0}C, ^{1}HNMR (400MHz, MEOD, TMS); δ6.970 (d, 1H,CH), 6.574(d, 1H, CH), 2.311-2.274(t, 4H, CH_2), 1.631-1.577(m, 4H, CH_2), 1.355-1.308 (m, 12H, CH_2).

FT-IR(KBr);3390,3193,2852,2460,1913,1699,1628,1506,1467,1407,1342,1277,1185, 1060,931,902,864,722,686,532,474.

Compound-B2A1. m.p138^{0}C, ^{1}HNMR (400MHz, DMSO,TMS); δ8.088(s,2H, NH_2), 6.318(d, 1H, CH), 6.147(s, 2H, CH=CH), 2.107(d, 3H, CH_3).

FT-IR(KBr);3320,3103,2504,1880,1704,1655,1625,1584,1464,1355,1209,1072,982, 943,784,65,586,528,423

Compound-B2A2. m.p 148^{0}C,^{1}HNMR (400MHz, DMSO,TMS); δ6.859(s,2H,NH_2), 6.620(s, 2H, CH=CH), 6.085(d, 1H, CH), 2.049(d, 3H, CH_3).

FT-IR(KBr);3125,2328,1914,1792,1711,1667,1642,1562,1519,1429,1371,1275,1200, 1163,979,825,800,712,579,432.

Compound-B2A3. m.p133^{0}C, ^{1}HNMR (400MHz, DMSO, TMS); δ6.932(s,2H,NH_2), 6.105(d, 1H, CH), 3.208(s, 2H, CH2), 2.055(d, 3H, CH_3)

FT-IR(KBr);3296,3130,2488,1920,1714,1667,1606,1455,1361,1271,1189,1025,948, 891,824,750,504,539,456.

Compound-B2A4. m.p 103^{0}C,^{1}HNMR (400MHz,DMSO,TMS); δ6.787(s, 2H,NH_2), 6.076 (d, 1H, CH), 2.216-2.187(t, 4H, CH_2), 2.046(d, 3H, CH_3), 1.502-1.480(m, 4H, CH_2).

FT-IR(KBr);3234,2939,1793,1712,1639,1600,1536,1409,1350,1319,1250,1175,923, 888,728,620,591,523,439.

Compound-B2A5. m.p 99^{0}C, ^{1}HNMR (400MHz,DMSO,TMS); δ6.790 (d, 2H,NH_2), 6.076 (d, 1H, CH), 2.202-2.165(t, 4H, CH_2), 2.047(d, 3H, CH_3), 1.489-1.453(m, 4H, CH_2), 1.268-1.250(m, 4H, CH_2).

FT-IR(KBr);3427,3052,2936,2528,1932,1684,1614,1542,1465,1352,1253,1156,1102, 1007,932,725,684,565,491.

Compound-B2A6. m.p 89^{0}C, ^{1}HNMR (400MHz, DMSO,TMS); δ6.744 (s, 2H,NH_2), 6.086 (d, 1H, CH), 2.017(d, 3H, CH_3)2.178-2.142(t, 4H, CH_2), 1.455-1.421(m, 4H, CH_2), 1.220-1.196(m, 8H,CH_2).

FT-IR(KBr);3402,3296,2406,1937,1709,1622,1525,1469,1431,1366,1299,1237,1186, 1117,1045,985,898,768,676,543,426.

Compound-B2A6a. m.p 84^{0}C,^{1}HNMR(400MHz, DMSO,TMS);δ6.781(s, 4H, NH_2), 6.076 (d, 2H, CH),2.200(d, 6H, CH_3), 2.170-2.153(t, 4H, CH_2),1.420-1.409(m, 4H, CH_2) ,1.238-1.209(m, 8H, CH_2).

FT-IR(KBr);3306,2506,1897,1714,1632,1565,1453,1399,1366,1239,1217,1146,1107, 1023,965,802,752,626,523,465,436.

Compound-B2A7.m.p 92^{0}C, ^{1}HNMR (400MHz, DMSO, TMS); δ6.768 (s, 2H, NH_2), 6.074 (d,1H,CH), 2.049(d,3H,CH_3), 2.197-2.160(t,4H,CH_2),1.491-1.456(m,4H, CH_2), 1.220-1.196(m, 12H, CH_2).

FT-IR(KBr);3404,3114,2526,1942,1802,1712,1653,1522,1422,1302,1226,1116,925, 797,720,680,520,432.

Compound-B3A1. m.p 142^{0}C,^{1}HNMR (400MHz, $CDCl_3$, TMS); δ8.698(s,2H, NH_2), 6.689(d, 1H, CH), 6.343(s, 2H, CH=CH), 2.315(d, 3H, CH_3).

FT-IR(KBr);3423,3075,2719,1899,1704,1662,1616,1567,1470,1359,1256,1208,1180, 1041,923,877,819,753,638,600,504,421.

Compound-B3A2. m.p 182^{0}C, ^{1}HNMR (400MHz, DMSO, TMS); δ6.700(s, 2H, NH_2), 6.620(s, 2H, CH=CH), 6.577(d, 1H, CH), 2.172(d, 3H, CH_3).

FT-IR(KBr);3325,3031,1861,1712,1684,1646,1572,1532,1430,1355,1292,1171,1066, 996,922,824,752,705,630,560,506,413.

Compound-B2A3. m.p 116^{0}C,^{1}HNMR (400MHz, DMSO,TMS); δ6.874(s,2H, NH_2), 6.611(d, 1H, CH), 3.198(s, 2H, CH_2), 2.175(d, 3H, CH_3).

FT-IR(KBr);3285,3129,2460,1909,1726,1682,1592,1523,1463,1340,1267,1163,1106, 951,825,747,701,604,503,458.

Compound-B3A4. m.p 128^{0}C,^{1}HNMR(400MHz, DMSO, TMS); δ6.645(s, 2H, NH_2), 6.569(d, 1H, CH), 2.202(d, 3H, CH3), 2.184-2.166(t, 4H, CH_2), 1.490-1.436 (m, 4H, CH_2).

FT-IR(KBr);3400,3209,2947,2361,1946,1697,1634,1532,1462,1409,1357,1277,1201, 1064,910,823,735,660,575,452.

Compound-B3A5. m.p 138^{0}C, ^{1}HNMR (400MHz, DMSO,TMS); δ6.643(s,2H, NH_2), 6.569 (d, 1H, CH), 2.227-2.218(t, 4H, CH_2),2.203(d, 3H, CH_3), 1.523-1.505(m, 4H, CH_2), 1.268-1.250(m, 4H, CH_2).

FT-IR(KBr);3057,2354,1908,1699,1643,1550,1416,1333,1255,1178,1069,854,805, 704,642,526,442,413.

Compound-B3A6. m.p 83^{0}C,^{1}HNMR (400MHz,DMSO, TMS); δ6.631 (d, 2H, NH_2), 6.562 (d, 1H, CH), 2.169(d, 3H, CH_3), 2.160-2.152(t, 4H, CH_2), 1.468-1.455(m, 4H, CH_2), 1.236-1.220(m, 8H, CH_2).

FT-IR(KBr ;3247,2353,1888,1712,1657,1613,1536,1467,1415,1345,1308,1273,1152, 1210,1177,1064,963,874,824,755,701,643,502,427.

Compound-B3A6a. m.p 107^{0}C,^{1}HNMR(400MHz,DMSO,TMS); δ6.622(d, 4H,NH_2), 6.569 (d, 2H, CH),2.182(d, 6H, CH_3), 2.174-2.171(t, 4H, CH_2), 1.494-1.459(m, 4H, CH_2), 1.243-1.229(m, 8H, CH_2).

FT-IR(KBr);3353,3046,2917,2356,1909,1700,1667,1635,1575,1457,1371,1306,1234, 1187,859,732,689,547,436.

Compound-B3A7. m.p 110^{0}C,^{1}HNMR (400MHz,MEOD,TMS); δ6.612 (d,1H, CH), 2.307-2.269(t, 4H, CH_2), 2.255(s, 3H, CH_3), 1.631-1.595(m, 4H, CH_2),1.335-1.220 (m, 12H,CH_2).

FT-IR(KBr);3422,2921,1700,1613,1469,1433,1334,1281,1226,1186,1065,929,902, 822,723,679,524,474,411.

3.3 Results and Discussion

A simple mixing of amine with dicarboxylic acids (1:1 and 1:2) in a suitable solvent resulted in the formation of cocrystals/salts, depending upon the pK_a difference of bases, 2-aminothiazole (B1), 4-methyl-2-aminothiazole (B2) and 5-methyl-2-aminothiazole (B3) and various dicarboxylic acids. In the present study, 24 salts were synthesized out of which 21 compounds were reacted in the molar ratio 1:1 (acid: amine) and three compounds in the molar ratio 1:2 (acid: amine). The formations of cocrystals/salts were established by FT-IR and ^{1}HNMR.Maleic acid (A1) when reacted with amines B1, B2 and B3 in the molar ratio (1:1) resulted in the formation of mono-carboxylate salts (B1A1, B2A1 and B3A1), which was confirmed by the

presence of parent maleic acid strong C=O asymmetric stretching peak in the range of 1701-1704 cm^{-1} along with presence of additional peak characteristic of carboxylate (asymmetric C=O stretching) in the range of 1650-1550 cm^{-1}. The formation of monocarboxylate salt was further confirmed by the ^{1}H-NMR and single crystal x-ray studies.

Similarly, fumaric acid (A2) and malonic acid (A3) also showed the formation of mono carboxylate salt (one carboxylic acid C=O asymmetric i.e 1667-1669 cm^{-1} and one carboxylate C=O stretching i.e 1616cm^{-1}) with B1, B2 and B3. Understandably, due to very low pK_1 values of fumaric acid, maleic acid, and malonic acid as compared with 2-aminothiazole base leads to the formation of mono-carboxylate salts of these acids (difference between pK of acid and amine (ΔpK) =3 or more leads to the formation of salt),[31] whereas other aliphatic dicarboxylic acids resulted in the formation of cocrystals except decanedioic acid (A6) formed mono-carboxylate (B3A6) as well as dicarboxylate salts (B3A6a). The formations of cocrystals/salts were confirmed by single crystal X-ray studies in most of the cases.

3.3.1 Gelation studies

All the newly synthesized compounds were subjected to gelation test in various solvents with varying degree of polarity including highly polar solvent i.e. water **(Table 3.3)**. Most of salts/cocrystals showed fewer tendencies to immobilize the solvents used in the present study except 2-amino-5-methylthiazolium hydrogen 1, 8-decanedicarboxylate (B3A6) which displayed excellent capability to harden water. In order to establish the role of free carboxylic acid in gelation process, a series of 1:2 salts of sebacic acids and 2-aminothiazole derivatives were synthesized. Interestingly, the salt B3A6a turned out to be non-gelator. It establishes the role of free -COOH in generating 1D hydrogen bonded chain as one of the requirement of gelation. As gelation was not shown by 1,6-octanedioic acid and 1,10-dodecanedioic acid recommend a critical chain length is required to impart the gelation behaviour in these series of compounds i.e. methylene group (n= 8). In order to explore the strength of hydrogel formed by **B3A6** salt a graph of T_{gel} verses concentration of gelator molecules in wt% (w/v) is plotted. The plot showed a gradual increase in T_{gel} up to a certain concentration of gelator (8 wt %) afterward T_{gel} values were found to be independent of gelator concentration **(Figure 3.1)**. Understandably, the increase in gelator concentration improves the self-aggregation and stability of supramolecular

assembly not beyond certain critical concentration. The nature of graph for T_{gel} versus concentration of gelator is very frequent observed for supramolecular gelators .

Table 3.3 Gelation Behaviour of B1A1-B3A7

Solvent	B1A1	B1A2	B1A3	B1A4	B1A5	B1A6	B1A6a	B1A7	B2A1	B2A2	B2A3	B2A4
Water	S	S	S	S	S	S	S	S	S	S	S	S
Methanol	S	S	S	S	S	S	S	S	S	S	S	S
Ethanol	S	S	S	S	S	S	S	S	S	S	S	S
1-pentanol	C	C	S	S	P	P	P	P	S	S	S	S
1-Heptanol	S	S	S	S	S	S	S	S	S	S	S	S
Iso-octane	S	S	P	P	P	P	P	P	S	S	P	P
n-octadecane	S	S	S	S	S	S	S	S	S	S	S	S
Toluene	P	P	S	S	S	S	S	S	P	P	S	S
Xylene	C	C	C	C	C	S	S	S	C	C	C	S

Solvent	B2A5	B2A6	B2A6a	B2A7	B3A1	B3A2	B3A3	B3A4	B3A5	B3A6	B3A6a	B3A7
Water	S	S	S	S	S	S	S	S	S	**G (4.34)**	S	S
Methanol	S	S	S	S	S	S	S	S	S	S	S	S
Ethanol	S	S	S	S	S	S	S	S	S	S	S	S
1-pentanol	P	P	P	P	S	S	S	S	P	P	P	P
1-Heptanol	S	S	S	S	S	S	S	S	S	S	S	S
Iso-octane	P	P	P	P	S	S	P	P	P	P	P	P
n-octadecane	S	S	S	S	S	S	S	S	S	S	S	S
Toluene	S	S	S	P	P	P	P	P	P	P	P	P
Xylene	C	S	S	C	C	C	C	C	C	S	S	S

C=crystal, p=ppt,G=gel, s=solution, the values within the bracket represents MGC (in wt %).

To get an insight into the gelator morphology SEM studies were carried out on xerogel (dried gel) of B3A6. Xerogel gelators showed entangled fibrous network of molecules which might have immobilized the solvent through various non-covalent interactions **(Figure 3.2)**.

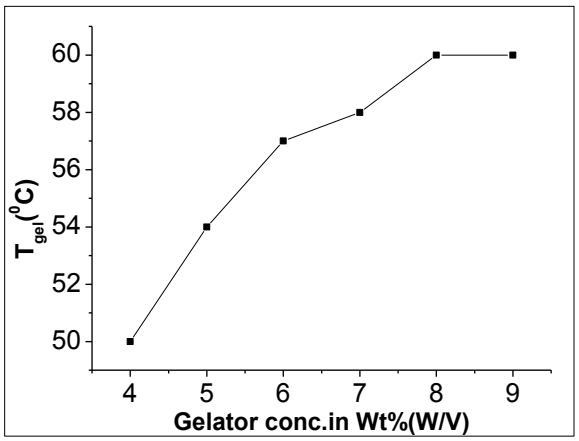


Figure 3.1 Effect of gelators B3A6 concentration (in wt %) on sol-to-gel

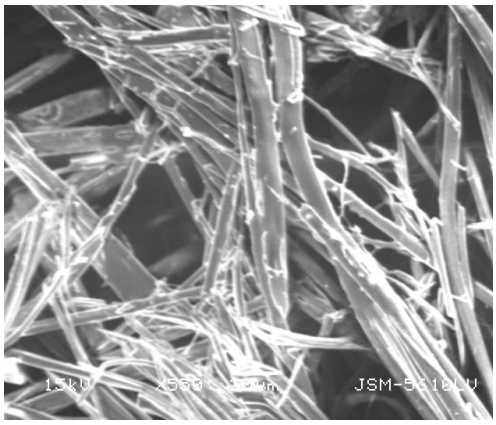


Figure 3.2 SEM images of xerogel of B3A6 in water at 4 wt% (w/v).

3.3.2 Single Crystal X-ray Studies

To understand the probable cause of hydrogelation/non-gelation of thiazole based salts/cocrystals with dicarboxylic acid, single crystal x-ray studies of synthesized compound were carried out. Single crystal studies of gelling/non-gelling compounds provide an opportunity to look inside the packing pattern of molecules to ascertain the probable cause of gelation at least to xerogel (dried gel) state. Fortunately, we are able to obtain the x-ray structure of gelator molecules (B3A6) along with structures of 10 non-gelator molecules **(Table 3.4)**.

1. 2-aminothiazolium-hydrogen propanedioate (B1A3): B1A3 crystallizes out in the non-centrosymmetric monoclinic space group $P2_1$ **(Figure 3.3)**. The asymmetric unit consists of one molecules of malonic acid and one molecule of 2-aminothiazole. Propanedioic acid was found in mono-carboxylate form containing intramolecular hydrogen bonding i.e. O-H…O (O…O= 2.481Å, ∠O-H…O= 150.81^0).Components were found to be strongly hydrogen bonded with each other through cyclic N-H.....O interactions forming R_2^2 (8) graph set. Interestingly, the 0D hydrogen bonded network is extended to 1D network through unusual non-covalent interaction (carbonyl) O…S (thiazole) (O…S = 3.033Å).

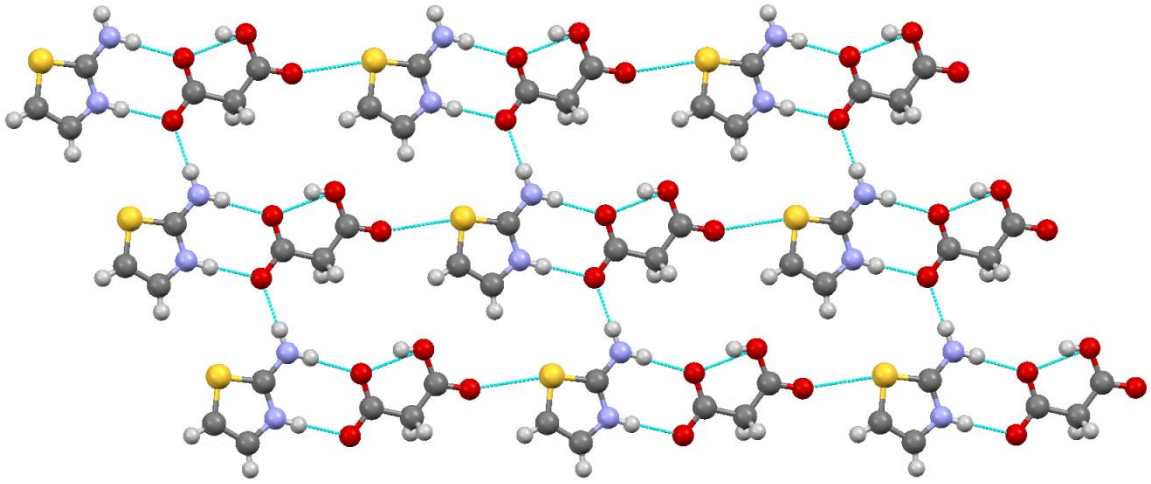


Figure 3.3 View of **B1A3**: 2D network of N-H…O and O….S interactions.

2. Bis(2-aminothiazolium)-hexanedioate-hexanedioic acid monohydrate (B1A4.H_2O): B1A4.H_2O salt crystallizes out in a Triclinic space group P-1. The asymmetric unit found to contain half of hexanedioic acid and half of hexanedioate moiety along with one molecule of 2-aminothiazole and water.

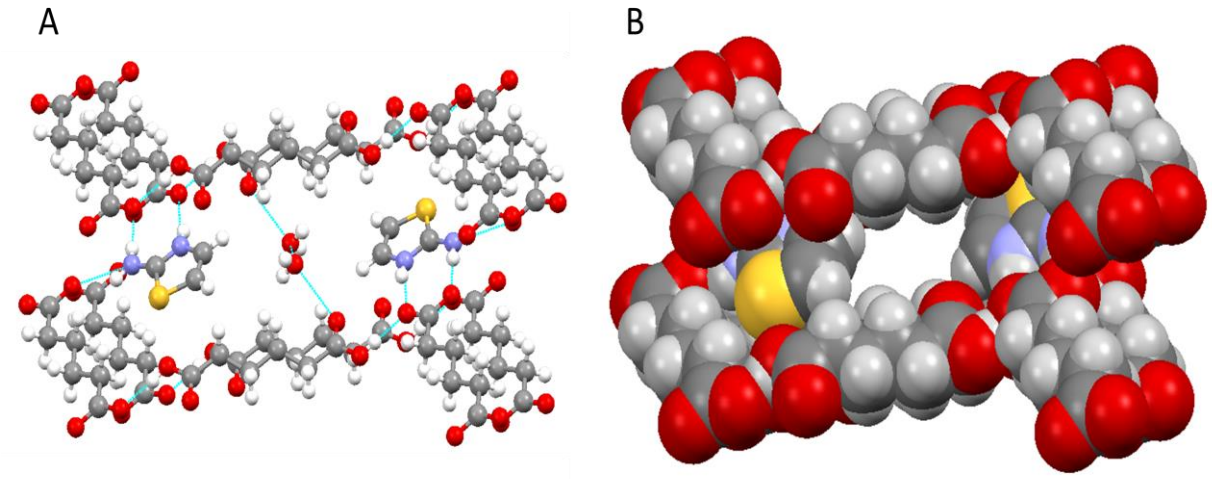


Figure 3.4 View of B1A4.H_2O: A) 2D hydrogen bonded network containing water molecules B) Hydrogen bonded network after removal of water molecules (space fill model).

The structure contains well defined 1D hydrogen bonded network of COOH…COO^- which is extended to other direction by dicarboxylate species hydrogen bonded to two thiazole moieties($^+$N-H…O^- and .N-H…O interaction). Supramolecular assembly of B1A4.H_2O is found to be containing well defined void occupied by water molecules (**Figure 3. 4** A and B). Water molecules found to be hydrogen bonded with carbonyl oxygen of adipic acid moiety.

3. 2-aminothiazole/octanedioic acid cocrystal (B1A5): B1A5 crystallized out in the Monoclinic P $2_1/n$ space group. The asymmetry unit contain one 2-aminothiazole molecules and half octanedioic acid molecules sitting at a special position. The two species were found to be strongly hydrogen-bonded through N-H.....O (N....O =2.873 Å, ∠ N-H…O= 171.5°) and O-H…N (O…N= 2.641Å, ∠ O-H…N = 153.18 °) cyclic supramolecular synthons **(Scheme 3.1)**. The overall assembly is found to be 2D through the amine proton non-covalent interaction to neighbouring carbonyl oxygen of A5 molecules (N-H…O= 2.873, ∠ N-H…O = 149.70°). A weak rarely observed C-H…S[32] interaction is also observed in the B1A5 crystal structure leading to 3D network (C-H…S = 3.809Å, ∠ C-H…S= 154.42°) (**Figure 3.5)**, which may be due to packing forces in crystalline phase.

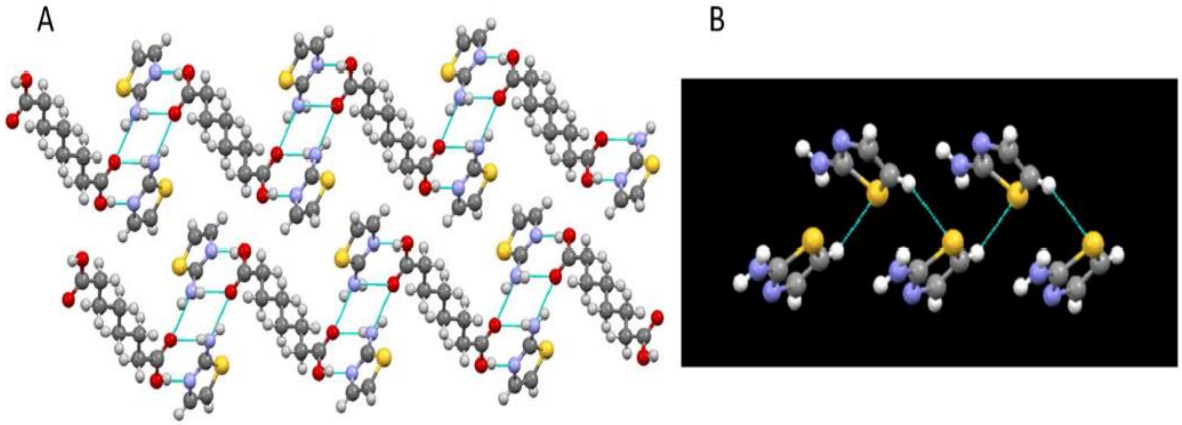


Figure 3.5 View of B1A5: A) 2D hydrogen bonded network of N-H…O, O-H…N; B) a weak non-covalent interaction C-H…S (thiazole) present in the structure.

4. 2-Aminothiazole/decanedioic acid cocrystal (B1A6). B1A6 crystallizes in a monoclinic space group P $2_1/c$ **(Figure 3.6)**. The asymmetry unit contains one molecule of 2-aminothiazole and a half molecule of decanedioic acid sitting at a special position. The B1 and A6 molecules are joined through cyclic supramolecular

synthon of $R_2^2(8)$ graph set (O-H…N = 2.636 Å, angle O-H…N = 170.68°, N-H…O = 2.949Å, ∠ N-H…O=163.2°) forming 0D HBN. The supramolecular assembly is extended to 2D due to presence of hydrogen bond between one of the amine hydrogen and carbonyl oxygen of acid moiety. A critical examination of the structure showed C-H…π interaction between thiazole ring hydrogen and neighbouring thiazole moiety π electrons (C-H…..thiazole$_{centroide}$ = 3.772, β ∠C-H…thiazole$_{centroide}$= 133.9°, α ∠Thiazole$_{centroide}$-C…H(thiazole ring) = 12.44°).

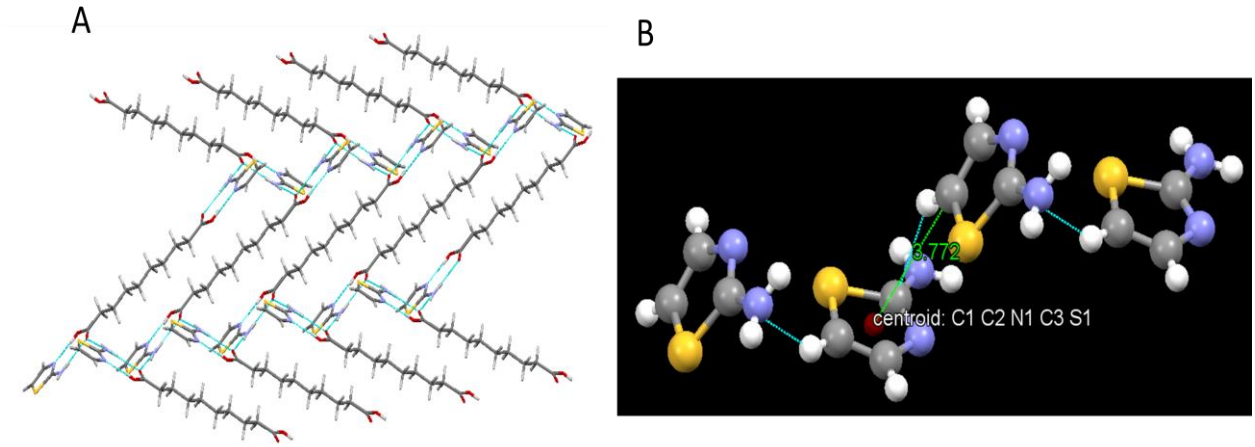


Figure 3.6 View of B1A6: A) 2D hydrogen bonded network mediated by N-H…O and O-H…N interaction B) weak C-H…π interaction between neighbouring 2-aminothiazole moiety.

5. 2-amino-4-methylthiazole/octanedioic acid cocrystal (B2A5): B2A5 crystallizes out in centrosymmetric monoclinic space group $P2_1/c$. The asymmetric unit contains one molecule of 2-amino-4-methylthiazole and half molecules of octanedioic acid sitting at a special position. 1D hydrogen bonded network is formed by strong O-H…N and N-H…O cyclic supramolecular synthon as shown in **scheme 3.1**. The supramolecular assembly extends to 2D sheet like structure through the formation of C-H…O (C…O = 3.465Å, ∠ C-H…O= 164.71°) interactions between the thiazole ring hydrogen and hydroxyl oxygen of acid. Interestingly, the methyl proton of 2-amino-4-methylthiazole is found not interacting with any neighbouring atoms **(Figure 3.7)**.

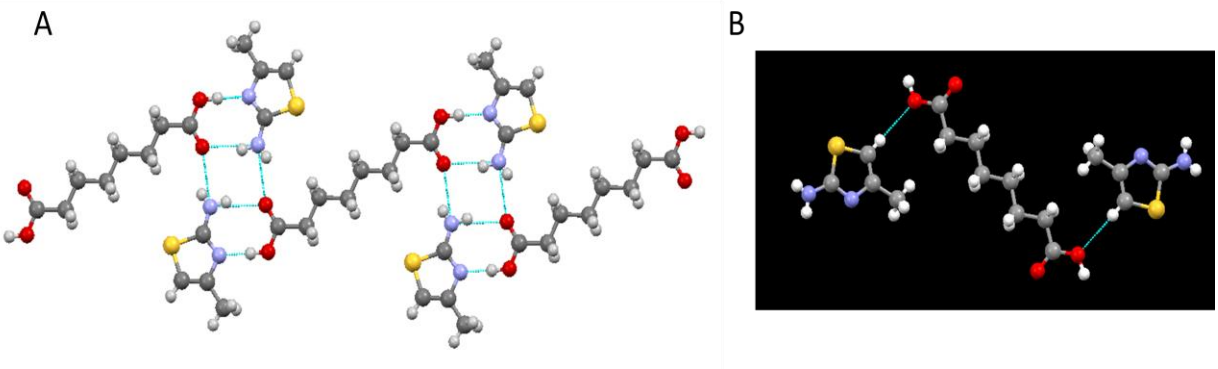


Figure 3.7 View B2A5: A) 1D hydrogen bonded network through cyclic N-H…O and O-H…N non-covalent interactions B) weak C-H…O interaction between neighbouring acid and amine.

6. 2-amino-4-methyl thiazole/decanedioic acid cocrystal (B2A6). B2A6 also crystallizes out in one of the most common space group i.e. P 2_1/c. The two components of cocrystals are found in the asymmetric unit having one molecule of 2-amino-4-methylthiazole and half molecule of decanedioic acid. The cyclic supramolecular synthon with R_2^2 graphic set is observed in the crystal structure leading to 0-D network, which is extended to 2D network through the strong H-bond between carbonyl oxygen and free amine N-H proton i.e. N-H…O (N…O =2.979 Å, ∠N-H…O= 161.31°) **(Figure 3.8)**.

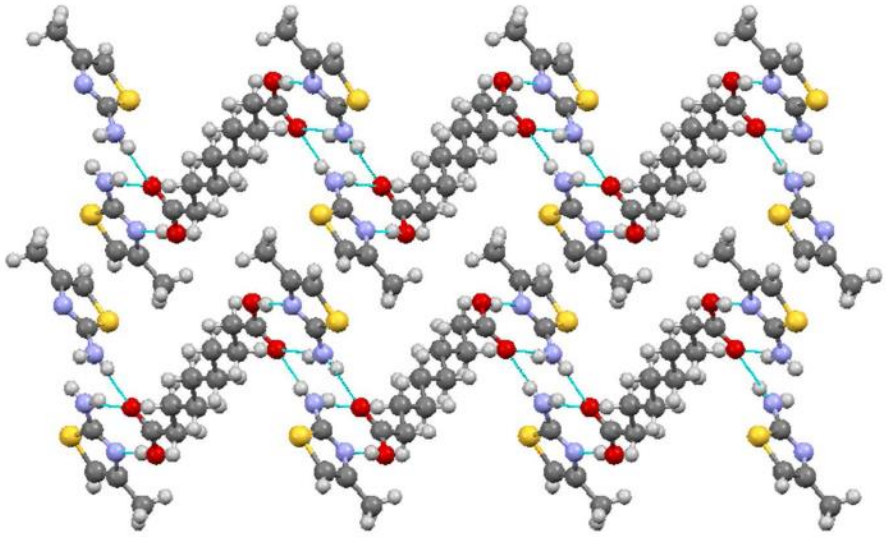


Figure 3.8 View B2A6: 2-D sheet like supramolecular assembly containing N-H…O and O-H...N interactions.

Crystal structure of B2A6 does not show any other significant weak non-covalent interactions as observed in the other crystal structures.

7. 2-amino-5-methylthiazolium hydrogen maleate (B3A1). The reaction of B3 with A1 resulted in molar ratio 1:1 resulted into the formation of monocarboxylate salt (B3A1) **(Figure 3.9)**. B3A1 crystals were found to be in monoclinic P 2_1/n space group. The asymmetric unit of B3A1 contains one molecule of 2-amino-5-methylthiazolium and maleic acid. The one hydrogen of carboxylic acid is found to be intramolecular hydrogen bonded between two carboxylic acid groups. The robust cyclic supramolecular synthons between thiazole ring nitrogen, amine hydrogen and charged oxygen atoms is also observed in B3A1. 0-D network of acid/amine extend into twisted 1D HBN through the additional amine hydrogen with the carbonyl oxygen. Furthermore, 1D chain extend to more complex assembly through the weak (thiazole)C-H…O (C…O= 3.727Å, ∠ C-H…O= 162.18°) and (methyl)C-H…O (C…O= 3.409Å, ∠ C-H…O= 154.99°).

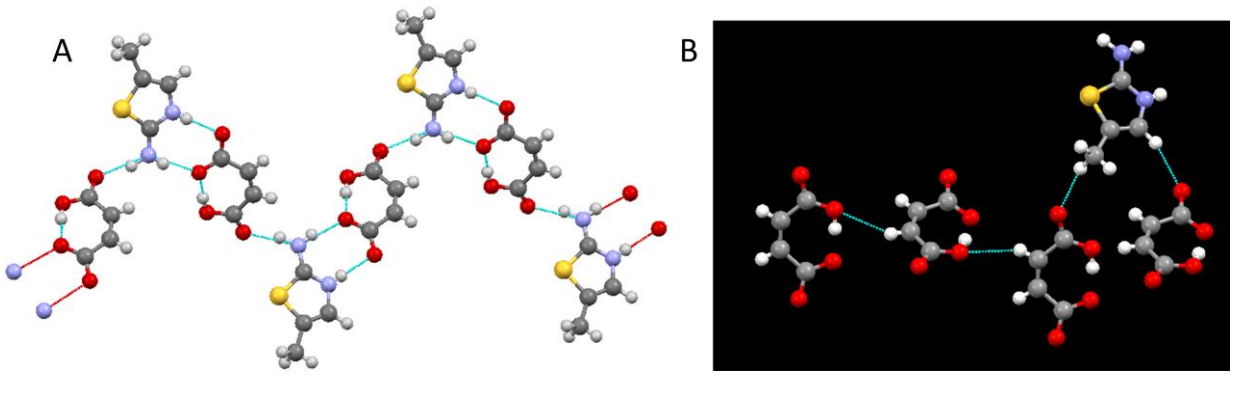


Figure 3.9 View B3A1: A) 1D hydrogen bonded zig-zag structure through N^+-H…O^- and N-H…O ; B) presentation of weak interaction such as (thiazole)C-H…O, (methyl)C-H…O,(alkene)C-H…O.

8. Crystal Structure of 2-Amino-5-methylthiazolium fumarate: fumaric acid (B3A2). The asymmetric unit of salt B3A2 (Monoclinic, C 2/c) contains a half molecule of fumaric acid and a half molecule of fumarate ion along with one molecule of 2-amino-5-methylthiazolium cation. The fumarate ion was H-bonded with other fumaric acid molecules leading to 1D chain along with interacting with 2-amino-5-methylthiazolium ion resulting into 2D network **(Figure 3.10A)**.

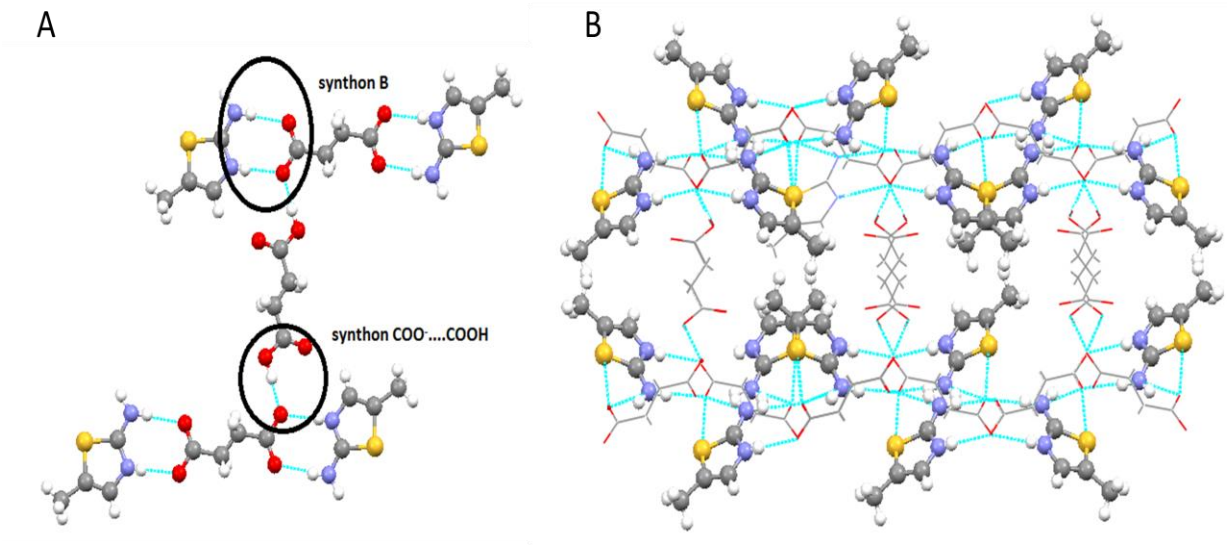


Figure 3.10: A) Supramolecular synthons observed in B3A2**;** B) 3D hydrogen bonded network of B3A2.

Interestingly, the 2D network of salt B3A2 extends to 3D through the unusual H-bond, C=O...S (thiazole). The carbonyl oxygen of carboxylate group, not the carbonyl group of carboxylic acid, is interacting with the thiazole sulphur (O...S= 3.194Å). The other secondary force observed in the crystal structure is C-H...S(C-H...S=2.791Å, ∠C-H..S= 144.35°) leads to complex hydrogen bonded network **(Figure 3.10B)**.

9. Crystal Structure of 2-Amino-5-methylthiazolium hydrogen 1,10-decanedioate (B3A6): B3A6 crystallizes in the space group monoclinic P $2_1/n$ space group. The asymmetric unit contains monocarboxylate salt of A6 and B3. The robust 1D hydrogen bonded network of COOH...COO^- is observed along with N-H...O and O-H...N(thiazole) cyclic supramolecular synthons. The additional Hydrogen bonding sites of amines leads to the 2-D network through the bifurcated H-bond with C=O. The overall supramolecular assembly found to have well defined void **(Figure 3.11)**. These space or opening seen in the space fill model of B3A6 suggests probable sites where solvents get entrapped or weakly H-bonded.

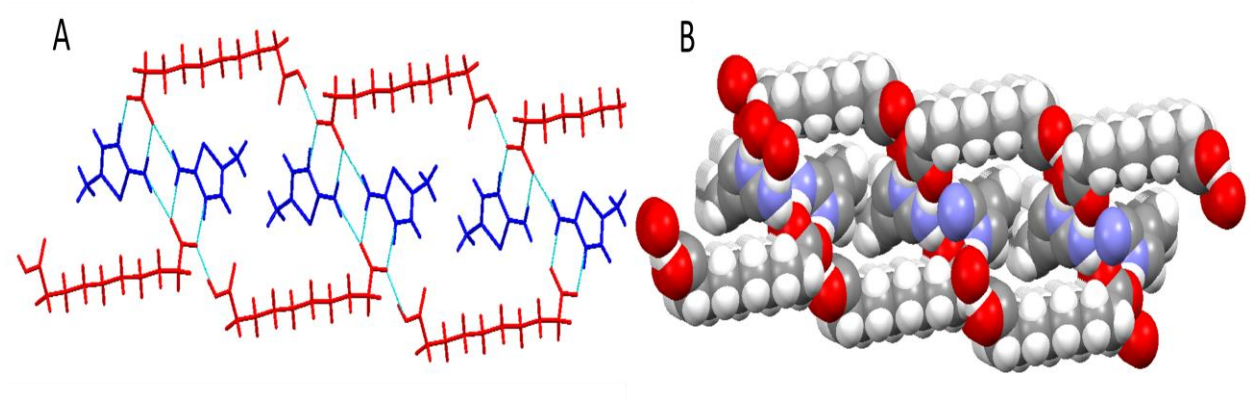


Figure 3.11 A) 3D network of B3A6 in capped sticks model (red coloured and blue colored capped sticks represents dicarboxylic acids and thiazole amines, respectively) and B) Space fill model.

10. Crystal Structure of bis(2-Amino-5-methylthiazolium) 1,10-decanedioate (B3A6a): to establish the role of free carboxylic acid in gelation, Acid and amine are reacted in 1:2 molar ratio. The salt B3A6a crystallizes out in monoclinic crystal system with space group P 2_1/n. The asymmetric unit of crystalline phase contains 2 molecules of 2-amino-5-methylthiazole and one molecule of 1,10-decanedioic acid. 1D hydrogen bonded network of B3A6a comprise of two different hydrogen bond motifs namely, $R_2^2(8)$ [(thiazole) N-H...O(N...O=2.609Å, ∠N-H...O= 165.13°), (amine) N-H...O (N...O= 2.772 Å, ∠ N-H...O= 166.61°)] and $R_4^2(8)$ [N...O =2.817Å, ∠N-H...O= 148.63°; N...O=2.834Å, ∠ N-H...O= 142.97°; N...O=2.762Å, ∠N-H...O = 169.56°; N...O= 2.772Å, ∠ N-H...O = 166.61°) **(Figure 3.12A).** The 1D hydrogen-bonded networks extends to 2D through the presence of multiple weak C-H...O interaction [(thiazole)C...O = 3.373Å, C-H...O= 169.32°] **(Figure 3.12B)**. The space fill model of the structure of B3A6A depicts no void as seen in the structure of mono carboxylate salt (B3A6) compounds.

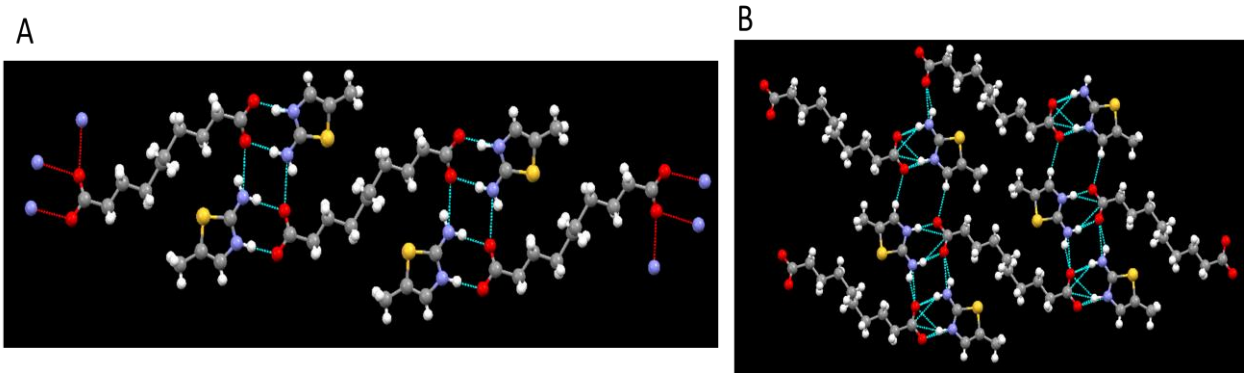


Figure 3.12 A) 1D hydrogen bonded network of B3A6A B) 2D hydrogen bonded network mediate by C-H...O interactions.

11. **Crystal Structure of 2-Amino-5-methylthiazolium/1, 12-dodecanedioic acid cocrystal (B3A7):** The non-gelator structure B3A7 crystallizes out in a triclinic (P-1) with one molecule of acid and amine in the asymmetric unit. 1D hydrogen bonded network of B3A7 is created by the combination of two hydrogen bonded motifs, i.e. $R_2^2(8)$ and $R_4^2(8)$ graph set. No significant secondary interaction is observed in the structure **(Figure 3.13)**.

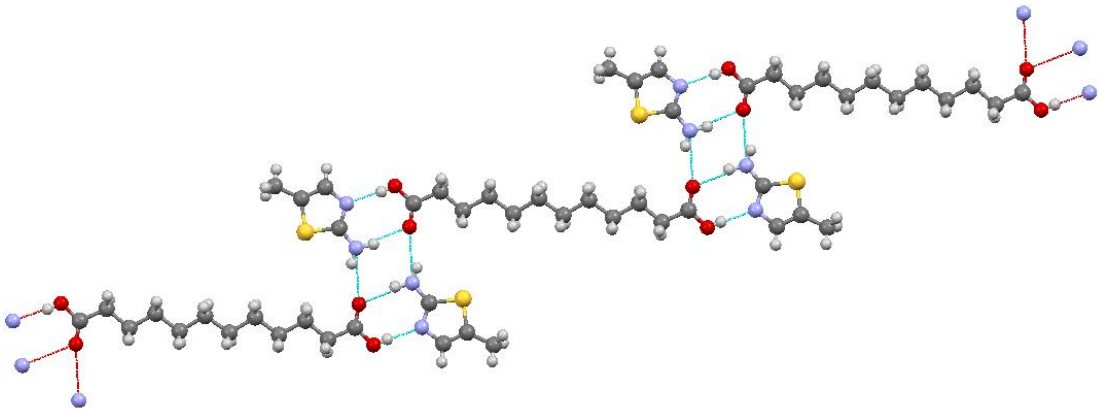


Figure 3.13 1D hydrogen bonded network of B3A7.

Table 3.4 Crystallographic information of salt/ cocrystals

	B1A3	**B1A4**	**B1A5**	**B1A6**	**B2A5**	**B2A6**
Empirical Formula	$C_6 H_8 N_2O_4S_1$	$C_9H_{16}N_2O_5S_1$	$C_7H_{11}N_2O_2S_1$	$C_{16}H_{26}N_4O_4S_2$	$C_{16} H_{26} N_4 O_4 S_2$	$C_{18}H_{30}N_4O_4S_2$
Fw	204.21	264.30	187.24	402.55	402.54	430.60
Crystal size (mm^3)	0.27×0.21× 0.18	0.60×0.59× 0.15	0.85×0.65× 0.18	0.48×0.13× 0.12	0.32×0.27× 0.18	0.42×0.21× 0.20
Crystal system	monoclinic	Triclinic	Monoclinic	Monoclinic	monoclinic	Monoclinic
Space group	P 2_1	P-1	$P2_1/n$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a/A^0	6.3856(5)	4.95459(19)	9.0290(3)	8.4023(6)	5.2800(2)	8.702(6)
b/A^0	6.6445(5)	7.5581(3)	5.75526(18)	7.5547(5)	22.5958(11)	7.721(5)
c/A^0	10.5589(8)	17.8016(6)	18.2666(6)	17.3163(12)	8.6882(4)	17.891(13)
α/deg	90	92.253(3)	90.00	90.00	90.00	90.00
β/deg	91.304(7)	90.649(3)	98.566(3)	103.335(2)	97.883(4)	95.326(14)
γ/deg	90	109.029(4)	90.00	90.00	90.00	90.00
Volume $(A^0)^{-3}$	447.76(6)	629.50(4)	938.62(6)	1069.55(13)	1026.76(8)	1196.9(14)
Z	2	1	2	2	2	2
$D_{calc.}$	1.514	1.394	1.325	1.250	1.302	1.195
F(000)	212	280	396	428	428	460
μ(MoKα) (mm^{-1})	3.161	2.432	2.796	0.275	2.591	0.250
Temperature(K)	293(2)	298	298(2)	298(2)	293	293(2)
obsd reflns [$I > 2\sigma(I)$]	1477	2290	1763	1872	1452	2090
params refined	126	188	120	127	131	138
goodness of fit	1.645	0.991	1.201	1.136	0.840	0.902
final R1 on obsd data	0.0645	0.0526	0.0494	0.0478	0.0546	0.0424
final wR2 on obsd data	0.2109	0.1553	0.1547	0.1174	0.1828	0.1167
CCDC No.	989348	964477	964476	930266	989346	949111

	B3A1	**B3A2**	**B3A6**	**B3A7**	**B3A6a**
Empirical formula	$C_{32}H_{40}N_8O_{16}S_4$	$C_8H_{10}N_2O_4S_1$	$C_{14}H_{24}N_2O_4S_1$	$C_{20}H_{34}N_4O_4S_2$	$C_{36}H_{60}N_8O_8S_4$
Fw	920.98	230.25	316.42	458.65	861.19
Crystal size (mm^3)	0.98×0.60 ×0.15	0.42×0.21× 0.20	0.42×0.21× 0.21	0.90×0.58× 0.16	0.29×0.25× 0.18
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic	monoclinic
Space group	$P2_1/n$	C 2/c	$P2_1/n$	P-1	$P2_1/n$
a/A^0	4.16465(11)	20.921(6)	12.800(17)	7.8169(4)	11.3596(3)
b/A^0	22.5580(7)	9.511(3)	4.945(7)	7.8365(6)	14.6265(7)
c/A^0	10.8698(3)	10.886(3)	27.64(4)	11.4009(8)	13.1548(4)
α/deg	90.00	90.00	90.00	73.310(6)	90.00
β/deg	93.487(2)	103.274(4)	94.730(19)	82.018(5)	91.993(3)
γ/deg	90.00	90.00	90.00	65.685(6)	90.00
Volume $(A^0)^{-3}$	1019.29(5)	2108.2(11)	1744(4)	609.17(7)	2184.36(14)
Z	4	4	4	1	4
$D_{calc.}$	1.500	1.464	1.205	1.250	1.309
F(000)	480	976	680	246	920
μ(MoKα) (mm^{-1})	2.848	0.301	0.201	2.243	2.470
Temperature(K)	298	298(2)	298(2)	298	293
obsd reflns [$I > 2\sigma(I)$]	3429	3590	2443	2326	4188
params refined	176	142	193	145	271
goodness of fit	1.493	1.284	0.986	0.761	1.622
final R1 on obsd data	0.0473	0.0540	0.0756	0.0459	0.0722
final wR2 on obsd data	0.1684	0.1581	0.1981	0.1558	0.2265
CCDC No.	958280	949112	930265	958299	989347

3.3.3 Powder X-ray Diffraction study

One of the commonly followed method to ascertain the packing of molecules inside the gelator fibers is comparing the powder X-ray Diffraction (PXRD) patterns of bulk Solid, Simulated Single crystal structure(if any), xerogel(dried gel) and gel network containing solvent.[33] This method is useful in determining the gelator fibers structure in xerogel state with certainty, if single crystal structure of gelator is known, but lack the concrete evidence to propose packing inside the gelator fibres in the gelled state, due to strong scattering by the solvents. The simulated and xerogel PXRD of the salt B3A6 were found nearly superimposable, while PXRD patterns of the bulk did not match well with that of the simulated or xerogel PXRDs **(Figure 3.14)**. This means that the single crystal structures of the salt concerned represent the Xerogel whereas the corresponding bulk material contains different crystalline phases. We are not in position to comment on the packing of B3A6 molecules in gelator fibres in the gel state due to strong masking of diffraction peaks by the solvent.

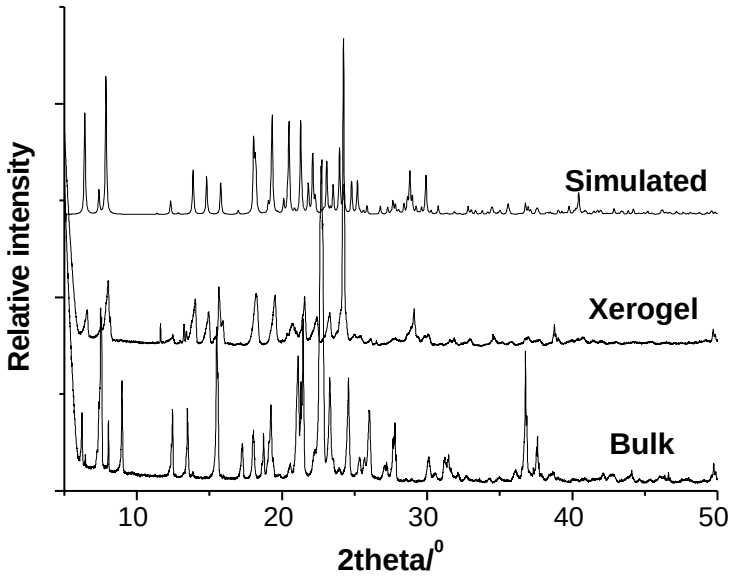
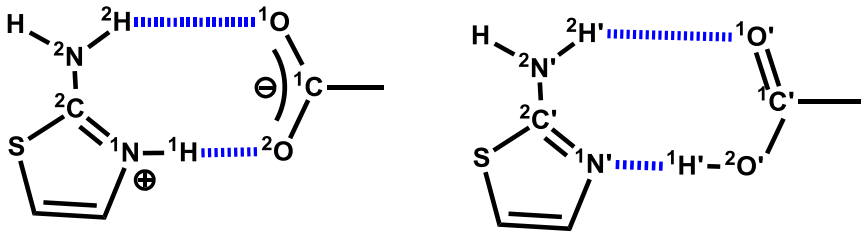


Figure 3.14 Powder X-ray Diffraction pattern of B3A6 in Bulk, xerogel and simulated (Single crystal X-ray structure).

The single crystal structures of 11 salts/cocrystals displayed robust supramolecular synthon (A and B), **(Scheme 3.2)** cyclic N-H...O/ $^{+}$N-H...O^{-} with graph set $R_2^2(8)$, between 2-aminothiazole and carboxylic/carboxylate functional group. A detailed list

of bond distances and bond angle of atoms involved in the formation of heterosynthon R_2^2 (8) obtained from the single crystal studies are tabulated in **Table 3.5**.



Scheme 3.2 The naming scheme adopted for study of R_2^2 (8) graph set representation of Supramolecular synthons A and B observed in the crystal structures.

Table 3.5 Distances (Å) and angle (°) for the geometrical features in the hetero-synthon R_2^2 (8) in various salts and cocrystals

	Name of compound	Type of synthon	Bond distances (in Å)				Bond Angles (in°) (^{2}N-^{2}C-^{1}N)
			^{2}O'....^{1}N'	^{1}O'... ^{2}N'	^{1}N'...^{2}C,	^{2}N'... ^{2}C'	
Co-crystals	B1A5	B	2.641	2.884	1.316	1.329	123.98
	B1A6	B	2.636	2.949	1.309	1.326	123.28
	B2A5	B	2.587	2.914	1.303	1.333	123.52
	B2A6	B	2.664	2.951	1.313	1.339	123.97
	B3A7	B	2.614	2.953	1.308	1.339	123.45

	Name of compound	Type of synthon	Bond distances (in Å)				Bond Angles (in°) (^{2}N-^{2}C-^{1}N)
			^{2}O....^{1}N	^{1}O... ^{2}N	^{1}N...^{2}C	^{2}N... ^{2}C	
Salts	B1A3	A	2.778	2.765	1.33	1.295	125.25
	B1A4.H_2O	A	2.689	2.767	1.325	1.312	123.02
	B3A1	A	2.733	2.812	1.327	1.311	125.50
	B3A2	A	2.697	2.862	1.320	1.323	125.13
	B3A6	A	2.694	2.790	1.322	1.331	122.98
	B3A6a	A	2.609	2.772	1.318	1.326	123.54

The difference between the distance of ^{2}O…^{1}N and ^{1}O…^{2}N in supramolecular synthon A in the reported salt crystal structures were found to well below 0.2Å in agreement with the earlier analysis.[34] However, the hydrogen bond distance (^{2}O'…^{1}N' and ^{1}O'…^{2}N') in supramolecular synthon B was found to well above 0.2 Å matching well for the formation of adducts or cocrystals. The bond angle between ^{2}N-^{2}C-^{1}N (or ^{2}N'-^{2}C'-^{1}N') of 2-aminothiazole moiety was found to lie between 122.98° to 125.50° suggested the role of substitution on thiazole moiety irrespective of formation of salts or cocrystals.

Our study support the formation of the 2-aminothiazole/carboxylic acid heterosynthon R_2^2 (8) as a reliable supramolecular motif despite the change in environment (carboxylic acid backbone and substitution on 2-aminothiazole). The another important supramolecular synthon observed in this series of salt/cocrystal is the cyclic bifurcated H-bond between carbonyl oxygen and amino group hydrogen, i.e. heterosynthon with graph set $R_4^2(8)$. Interestingly, the sulphur atom of thiazole moiety is found to be involved in many secondary interaction such as S...O and C-H...S interaction, which is less known supramolecular synthons.[24-26] We believe that the presence of the bunch of weak interactions such as C-H...O, C-H...S, S...O, etc. provide the extra stability of supramolecular assembly and play a decisive role in the formation of gel/crystalline phase.

Fortunately, we have the crystals in the series of compounds (B1A6, B2A6 and B3A6) with same alkyl chain length (hydrophobic forces) with structural variation only on thiazole moiety. Single crystal packing of structurally similar gelling compound (B3A6) and non-gelling compounds (B1A6 and B2A6) brought the striking fact that B1A6 and B2A6 both formed hydrogen bonded 2D sheets whereas gelling compound B3A6 formed 3D network with a void. Moreover, B3A6 hydrogen bonded network is stabilized by the presence of weak (thiazole)C-H...O bond, which is absent in the case of non-gelling compounds. Evidently, the role of position of methyl group on the thiazole moiety in the series of organic salts/ cocrystals (B1A6, B2A6 and B3A6) is to provide the steric hindrance in the packing of overall supramolecular assemblies leading to distorted H-bond network with a cavity, where solvent may get immobilized. We would like to stress that very few examples are reported in the literature where gelator molecules were found to be interacting with their gelling solvent, based on single crystal and computational studies,[30,38-41] having

well-defined void to accommodate the solvent molecules. In an elegantly designed experiment, Uday maitra and his group were able to establish the formation of hydrophobic void during hydrogelation.[42] Interestingly, the salt **B1A4**, a non-gelator, also displayed the formation of well-defined void having two molecules of water occupy the empty space **(Figure 3.4B)**. The single crystal data collected at 25°C showed the water molecules strongly hydrogen bonded without any distortion in thermal ellipsoid. Understandably, strong held water molecules in the guest molecule support the crystalline phase instead of metastable gel phase. The observation makes us to believe that hydrophobic forces due to alkyl chain are critical for inducing gelation of water. Many more such examples need to be discovered to support the hypothesis that hydrogelation is favoured by small molecules capable of formation of 3D network with appropriate cavity to immobilize water.

3.4 Conclusions

A new series of 2-aminothiazole based salts were synthesized and characterized for their gelation behaviour. 11 single crystals of gelator and non-gelling compounds were solved to understand the probable cause of gelation of water by these series of compounds. It is very clear from our study that formation of void along with sufficient hydrophobic interaction may help in hydrogelation. Single crystal of two compounds namely B1A4 (non-gelator) and B3A6 (gelator) showed the supramolecular assembly leading to the formation of void suggested the crucial role of hydrophobic carbon chain in inducing the immobilization of solvent in these void. We believe more such studies need to be undertaken so that the hypothesis that 3D supramolecular assembly having hydrophobic pockets supports hydrogelation will be established.

3.5 References

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