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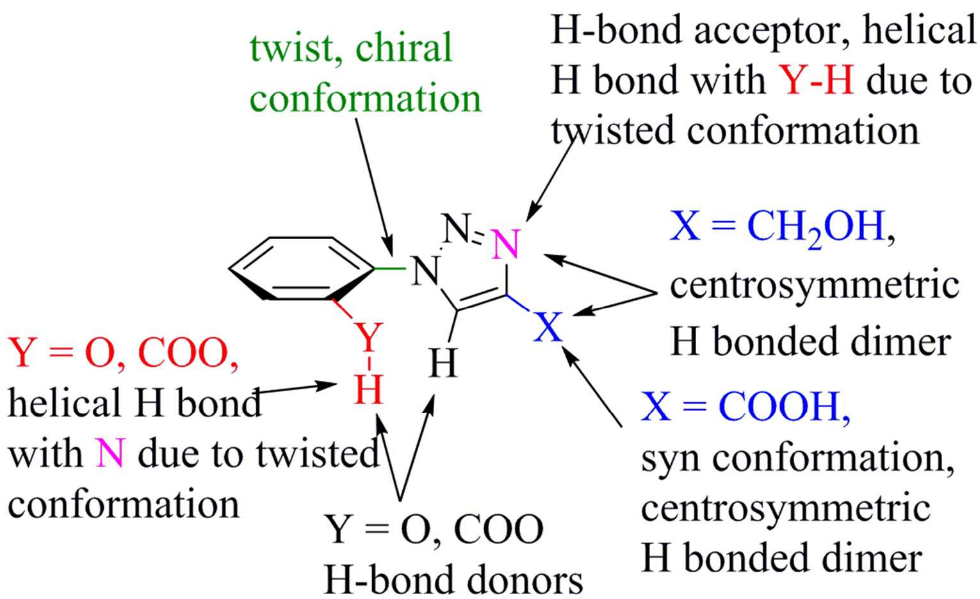

Interplay of twisted conformations and O-H…N and O-H…O hydrogen bond synthons on supramolecular chirality in OH and COOH substituted 1-aryl-1H-1,2,3-triazoles
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ARTICLE TYPE

Substituent effect on the formation of helical to layered hydrogen bond network in hydroxyl and carboxyl substituted 1-aryl-1*H*-1,2,3-triazoles.

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Six structurally related 1-aryl-1*H*-1,2,3-triazoles substituted with hydroxyl and carboxyl groups have been studied by single crystal X-ray crystallography. O-H…N and O-H…O hydrogen bond synthons play a predominant role in the crystal engineering of these derivatives. The positions of the hydroxyl and carboxyl groups are important and decide on the dihedral angle of the twisted conformations of these molecules in the solid state which in turn dictates the formation of helical or layered hydrogen bond motifs and the chirality of the crystals.

Introduction

Chirality is a fascinating and ever-green topic in chemistry.[1,2] Molecules that are inherently achiral in the solution phase can crystallize in specific conformations that are chiral in the solid state.[3-6] While doing so they can crystallize either as racemic modification (racemic conglomerate) consisting of only one enantiomeric form in the crystal lattice or as a racemic compound consisting of a 1:1 mixture of both the enantiomeric forms in the crystal lattice. The former leads to the formation of chiral crystals. Chiral crystals are important and they are useful in enantioselective catalysis, sensing and chromatography as mentioned in a recent article by Avnir.[7] In addition to molecular chirality of small achiral molecules in the solid state, chiral supramolecular structures can be formed by supramolecular assembly, typically through hydrogen bond and other weak intermolecular interactions.[8-12] One such supramolecular system is the formation of hydrogen bonded helical assembly. Hydrogen bonded supramolecular helical assembly is common in biological molecules such as peptides and oligonucleotides and occur both in solution phase and solid state. Solid state supramolecular chemistry is a contemporary topic and study of organic solid state supramolecular structures is actively pursued.[13-20] Formation of enantio pure helical supramolecular solid state structure from a small achiral molecule is a very intriguing phenomenon. Formation of chiral crystals from small achiral organic molecules is a challenge in crystal engineering and the outcome is still often unpredictable.[21-25] Recently Hu and Cao have reported generation of chiral crystals from achiral 2-aminothiazole derivatives.[26] Herein we report a systematic investigation of effect of molecular twist on the molecular chirality in the solid state of otherwise achiral 1-aryl-1*H*-1,2,3-triazoles, the effect of hydroxyl and carboxyl groups on helical hydrogen bond synthon to form supramolecular hydrogen bond network and finally the role of the position of hydroxyl and carboxyl groups on the formation chiral or racemic crystals. An attempt is made to correlate the structural features of six 1-aryl-1*H*-1,2,3-triazoles to the chirality of the crystals and the formation of either enantiopure or racemic helical hydrogen bonded network.

Results and discussion

The structures of the triazole derivatives, namely 2-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)benzoic acid (**1**), 2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)benzoic acid (**2**), 1-(2-carboxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid (**3**), 1-(2-hydroxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid (**4**), 2-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)phenol (**5**) and 4-(4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)benzoic acid (**6**), along with their structures in the crystals with contact points for non-covalent interactions, are shown in Figure 1.

There are several reasons why these 1-aryltriazole derivatives (**1-6**) (Figure 1) are chosen for this study. They are that (a) the triazole ring is endowed with hydrogen bond donor (acidic C-H bond) and hydrogen bond acceptors (N atoms) that can promote hydrogen bond network, (b) the *ortho* substituted aryl ring and the triazole ring are expected to be twisted that would render chirality in the solid state, (c) the carboxylic acid and hydroxyl groups endow the structures with multiple hydrogen bond contacts and hence would enable extended hydrogen bond network facilitating the formation of supramolecular structures in the solid state. Derivatives **1**, **2** and **3** were synthesized by the cycloaddition reaction of 2-azidobenzoic acid to propargyl alcohol, phenylacetylene and propiolic acid, respectively. Derivatives **4** and **5** were synthesized by the cycloaddition reaction of 2-azidophenol to propargyl alcohol and propiolic acid, respectively. Derivative **6** was synthesized by the cycloaddition addition of 4-azidobenzoic acid with propargyl alcohol (Scheme 1).

All these derivatives were thoroughly characterized by spectroscopic methods. First we briefly describe the crystal structure of each of the derivatives and then discuss the crystal engineering aspects, namely, the effect of twisted conformation, position and orientation of hydrogen bond donor/acceptor groups on the formation of hydrogen bond synthons leading to chiral crystals or otherwise.

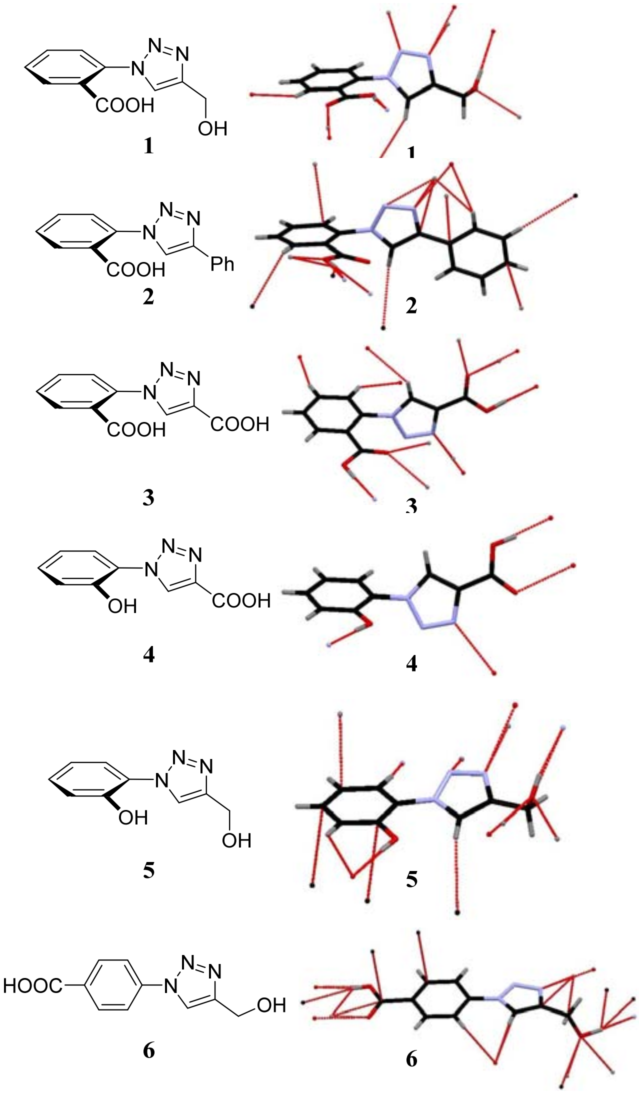
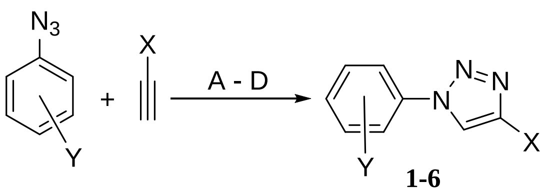


Fig.1 Chemical structures of 1-aryl-1*H*-triazole derivatives (**1-6**) (left) and their structures in the crystal (right) with multiple contact points for non-covalent interactions in red.

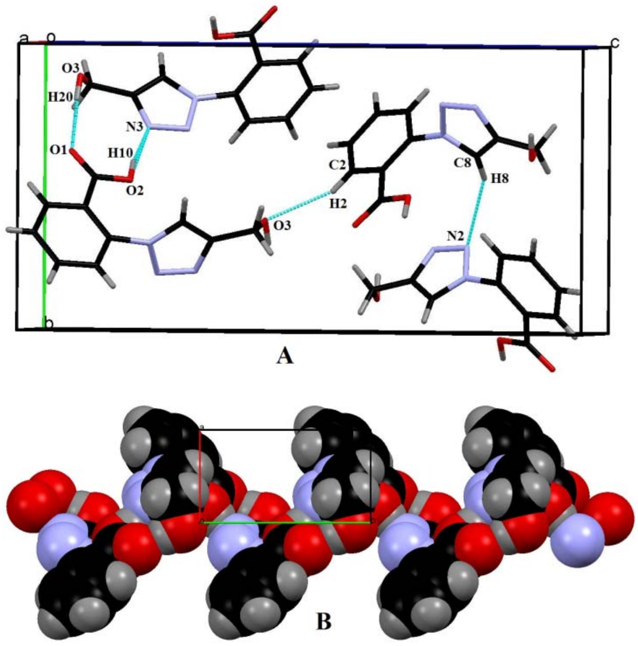


1 Y = 2-COOH, X = CH_2OH, 68%, method A
2 Y = 2-COOH, X = Ph, 80%, method B
3 Y = 2-COOH, X = COOH, 71%, method C
4 Y = 2-OH, X = COOH, 75%, method B
5 Y = 2-OH, X = CH_2OH, 65%, method D
6 Y = 4-COOH, X = CH_2OH, 85%, method B

Scheme 1 Synthesis of phenyltriazole derivatives **1-6**. Reaction conditions (A) toluene, 90 °C, 12 h; (B) $CuSO_4.5H_2O$, sodium ascorbate, *t*-BuOH/H_2O (1:1, v/v), rt, 48 h; (C) CuI, DMSO/H_2O (9:1, v/v), rt, 24 h; (D) $CuSO_4.5H_2O$, sodium ascorbate, PEG-600, rt, 48 h.

Structure of 1

Hydroxy acid **1** crystallized in the orthorhombic system with $P2_12_12_1$ space group, the most common space group observed in the chiral crystals of organic molecules.[27] The dihedral angle between the *N*-aryl plane and the triazole plane is 72.75°. The carboxyl acid group of one molecule is doubly hydrogen bonded (O1 and O2 and H10,) to the triazole nitrogen and hydroxyl group (N3, O3 and H20) of another molecule that is related through 2_1 screw translation parallel to the b-axis (Fig. 1A). Such extensive intermolecular hydrogen bonding among molecules that are related through 2_1 screw translation parallel to the b-axis forms a helical hydrogen bond synthon with the pitch of the helix as the b-axis (9.6714 Å) itself (Fig. 2B and 2C). The bond lengths and angles are O1-O3 = 2.830 Å, O1-H20 1.958 Å, O1-H20-O3 = 176.60° O2-N3 = 2.659 Å, N3-H10 = 1.791 Å, , O2-H10-N3 = 169.50°. In addition there are C-H…O (H2 and O3, O3-C2 = 3.387 Å, O3-H2 = 2.511 Å, C2-H2-O3 = 157.14°) hydrogen bonding between molecules that are related through 2_1 screw axis parallel to the b-axis and C-H…N (H8 and N2, N2-C8 = 3.432 Å, N2-H8 = 2.603 Å, C8-H8-N2 = 148.76°) hydrogen bonding between molecules that are related through 2_1 screw axis parallel to the c-axis. These intermolecular hydrogen bonding interactions are shown in Fig. 2A. Although absolute configuration of the HTA molecule in the crystal is not determined, all the four molecules in the unit cell have the same absolute configuration. Hence the crystal is chiral.



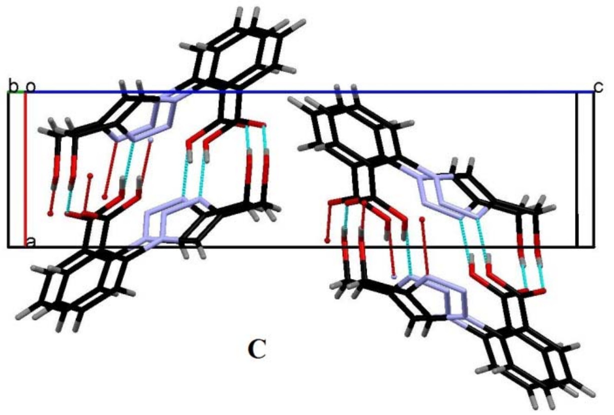
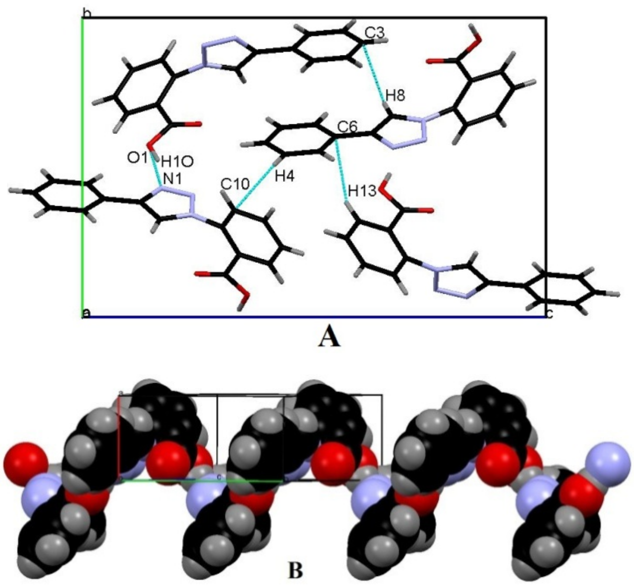


Fig.2 (A) Hydrogen bonding among the molecules in the unit cell, (B) helical hydrogen bond synthon (view along c axis), (C) helical hydrogen bond synthon (view along b axis).

Structure of 2

Carboxylic acid **2** also crystallized in the orthorhombic system with $P2_12_12_1$ space group forming chiral crystals. The dihedral angle between the *N*-aryl plane and the triazole plane is 78.14°. The *C*-phenyl and the triazole rings are nearly coplanar with a dihedral angle of only 7.8°. The carboxylic acid and the triazole nitrogen are hydrogen bonded (O1, H10 and N1, O1-N1 = 2.732 Å, H10-N1 = 1.725 Å and O1-H10N1 = 165.36°) resulting in helical hydrogen bond network propagating along the b axis with the pitch of the helix as the b axis (11.9294 Å) itself (Fig, 3A and 3B). In addition adjacent helices are connected through C-H…π interactions (C3-H8 = 2.815 Å, C6-H13 = 2.86 Å, C10-H4 = 2.862 Å) (Fig. 3A and 3C). All the four molecules in the unit cell have the same absolute configuration. Hence the crystal is chiral.



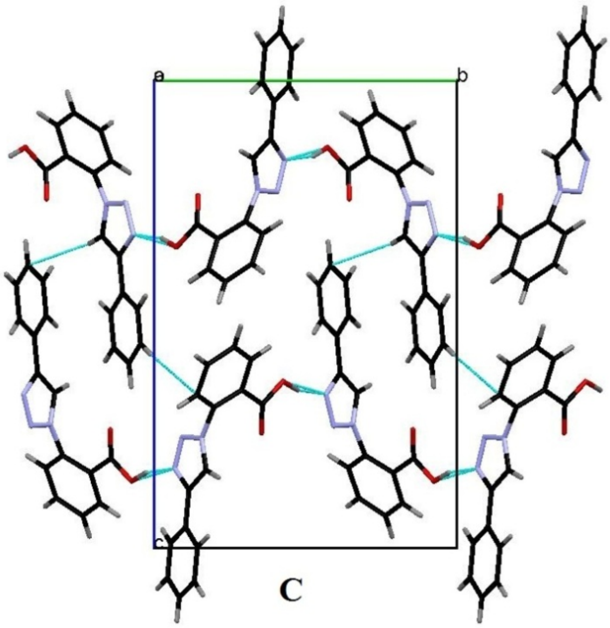


Fig.3 (A) Hydrogen bonding among the molecules in the unit cell, (B) helical hydrogen bond network, (C) inter helical C-H…π network (view along a axis).

Structure of 3

Diacid derivative **3** crystallized in the monoclinic system with $P2_1/n$ space group. The dihedral angle between the aryl plane and the triazole plane is 85.75°, the highest among these derivatives **1-6**. The unit cell contained four molecules, two pairs of enantiomers with respect to the inversion center. Both the carboxylic acid groups in the molecule have *syn* orientation and the dihedral angle between the planes containing the carboxylic acid groups is 81.36°. The molecules related through 2_1 screw translation parallel to b-axis form a hydrogen bonded helix (say left-handed helix) with pitch of the helix as b-axis (9.3768 Å) itself (Fig. 4A). The O-H…N (N3, H10, O1) hydrogen bond is between the carboxylic acid of the phenyl group (O1, H10) and the nitrogen (N3) of the triazole ring (N3-O1 = 2.781 Å, N3-H10 = 1.803 Å, O1-H10-N3 = 177.12°) (Fig. 4A). Molecules that are inversion equivalents also form O-H…N hydrogen bonded helix of opposite handedness (say right handed helix). These two *untwined* helices of opposite chirality are connected to each other at every turn (pitch of the helix) by centrosymmetric dimeric O-H…O (O4, H20, O3) hydrogen bonds between the carboxylic acid groups of the triazole rings (O3-O4 = 2.684 Å, O3-H20 = 1.671 Å, O4-H20-O3 = 173.48°) forming a very interesting supramolecular 3D hydrogen bond network (Fig.4B and 4C).

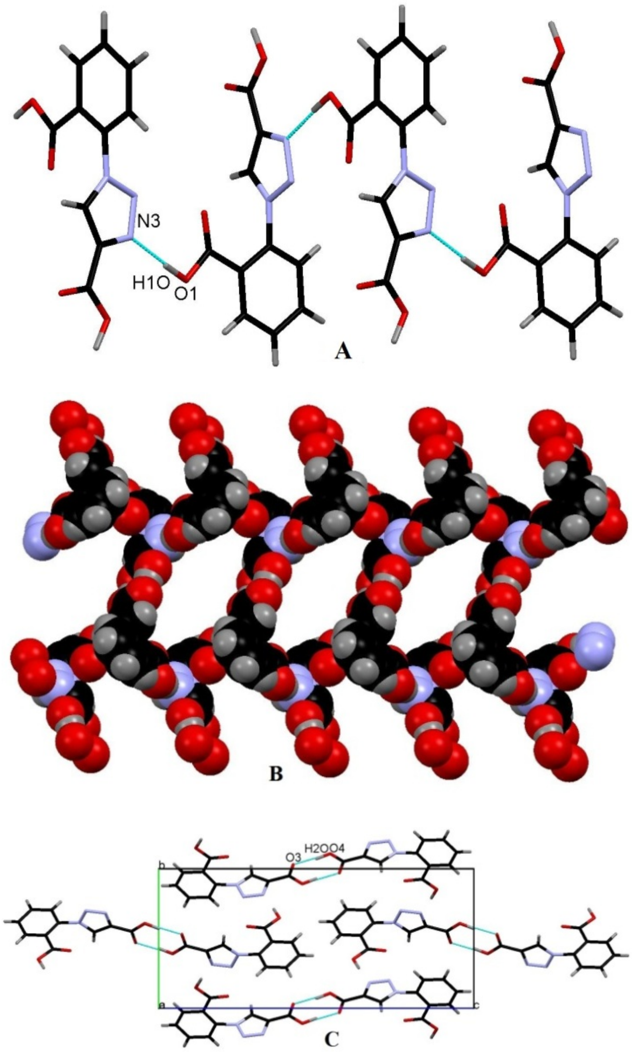


Fig.4 (A) Helical hydrogen bonded network in **3**, (B) centrosymmetric bridging of two helices of opposite chirality through hydrogen bonding between COOH groups of the triazole ring (view along a axis), (C) centrosymmetric hydrogen bonding (bridging units of the helices) of molecules in the asymmetric unit (view along a axis).

Structure of 4

Phenolic acid **4** crystallized in the monoclinic system with $P2_1/c$ space group. The phenyl and triazole rings are twisted with an angle of 70.4^o and the carboxylic acid group and the triazole ring are nearly coplanar. The unit cell contained four molecules, two pairs of enantiomers with respect to the inversion center as in the case of **3**. The carboxylic acid group in the molecule has *syn* orientation. In this case, molecules that are related through glide plane form hydrogen bonded helix along the c-axis (glide component 0, 0, ½) with pitch of the helix as c-axis itself (Fig. 5A). The hydrogen bond is between the phenolic OH and the triazole nitrogen (O1, H10 and N3, O1-N3 = 2.804 Å, H10-N3 = 1.912 Å, O1-H10-N3 = 176.3^o). The carboxylic acid group connects molecules related through the inversion center to the adjacent helices of opposite chirality through a centrosymmetric hydrogen bonded dimer (Fig. 5B) as in the case of **3**.

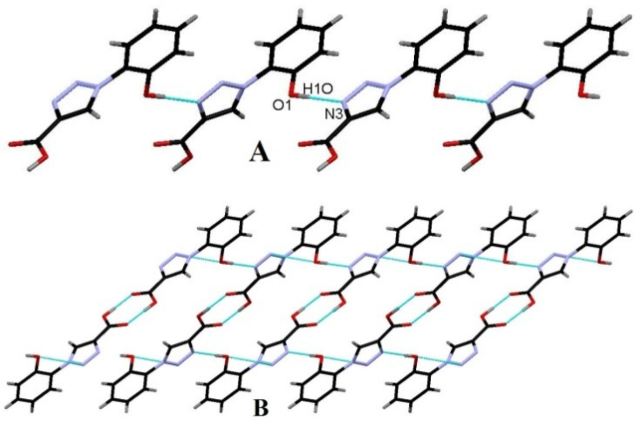


Fig.5 (A) Helical hydrogen bond network in **4**, (B) bridging through centrosymmetric hydrogen bonded dimer of adjacent helices (both views along b-axis).

Structure of 5

Dihydroxy derivative (**5**) crystallized in the triclinic system with P-1 space group. The dihedral angle between the aryl plane and the triazole plane is only 20.79^o, the smallest among the *ortho* substituted derivatives **1-5**. Considering that the phenolic hydroxyl group in **5** is smaller in size compared to a carboxylic acid group in **1**,**2** and **3**, a smaller dihedral angle might be justified for this derivative. However, in **4** which also contains an *ortho* hydroxy group, the dihedral angle is 70.4^o. This large difference in the dihedral angles between **4** and **5** might be due to the differences in the hydrogen bond mode. Formation of the centrosymmetric hydrogen bond between the two hydroxyl groups in **5** might be responsible for the relatively planar structure in **5** compared to the twisted structure in **4**. The molecule and its inversion equivalent are doubly hydrogen bonded through O-H…O (O2 and H1, O1-O2 = 2.687 Å, O2-H1 = 1.869 Å, O1-H1-O2 = 175.45^o) bonds forming a centrosymmetric dimeric structure (Fig. 6A). The bc diagonal translation equivalents of the pair in the dimer are further doubly bonded through O-H…N (N3 and H2A, N3-O2 = 2.836 Å, N3-H2A = 2.206 Å, N3-H2A-O2 = 168.97^o) bonds resulting in an one dimensional ribbon (Fig. 6C). The ribbons are further linked through weak C-H…N (N2 and H5, N5-H5 = 2.705 Å) interactions leading to a 3D hydrogen bond network (Fig. 6B). The ribbons are also further networked by C-H…π (C4 and H8, C4-H8 = 2.871 Å) interactions through the triazole ring hydrogen and π–π (C1 and C3) interactions through the phenyl rings (Fig. 6A and 6D). The π–π interactions are through slipped π stacking of the phenyl rings and the vertical inter-planar distance is 3.358 Å.

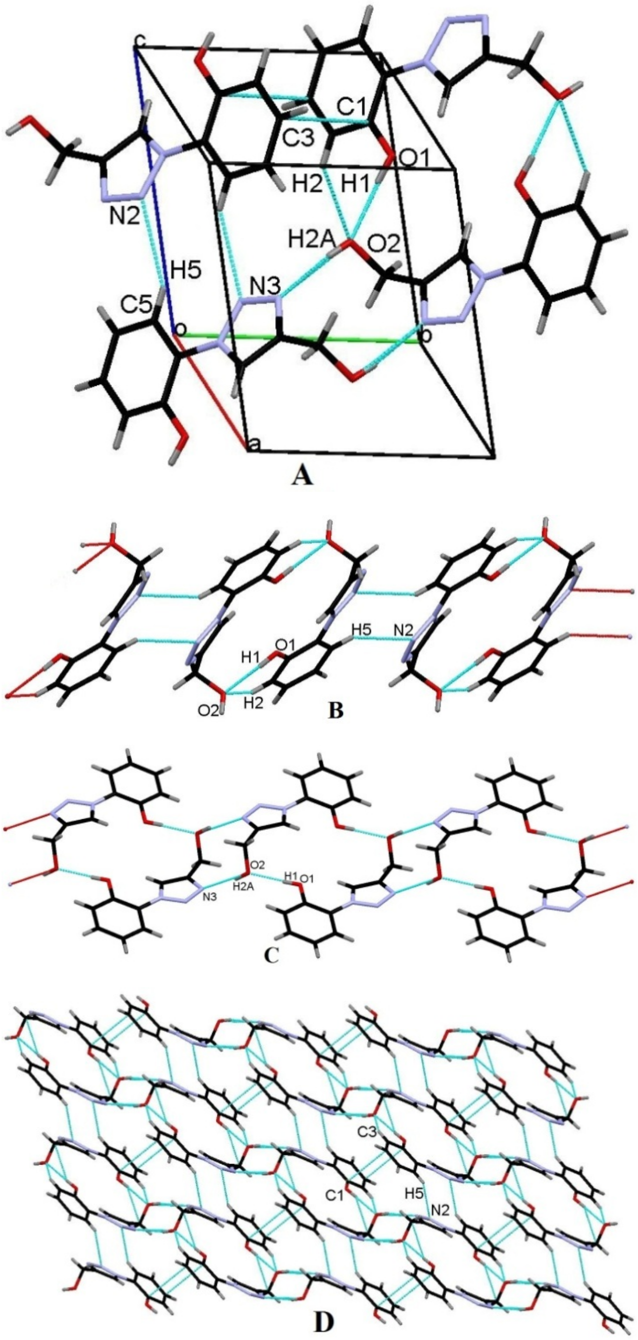


Fig.6 (A) Various non-covalent intermolecular interactions in **5** in the crystal forming a hydrogen bond network, (B) formation of 1D ribbon like structure through O-H…O and C-H…N hydrogen bonds synthon, (C) formation of 1D ribbon like structure through O-H…O and O-H…N hydrogen bonds synthon, (D) inter linking of the ribbons through π–π and C-H…N interactions to a 3D hydrogen bonded network.

Structure of 6

Hydroxyacid **6** crystallized in the triclinic system with P-1 space group. In **6** the carboxylic acid group is present in the *para* position of the phenyl ring. As a result the phenyl ring, triazole ring and the carboxylic acid groups are nearly coplanar. The twist between the phenyl ring and the triazole ring is only 6.27°, the lowest among derivatives **1-6**. The unit cell contained two molecules that are related through an inversion center. In this structure one molecule is centrosymmetrically doubly hydrogen bonded with each of its neighbours (Fig. 7A) forming an interesting hydrogen bonded supramolecular stepped-layered network. A molecule (x, y, z) is centrosymmetrically hydrogen bonded through O-H…O bonds to its neighbor (-x, 1-y, 1-z), through O-H…N bonds to another neighbor (-x, 2-y, -z) and through C-H…O bonds to yet another neighbor (1-x, 1-y, -z) (Fig. 7A). The hydrogen bond distances and angles are O1-H2 = 1.808 Å, O1-O2 = 2.62 Å, N3-H10 = 1.778 Å, O3-H8 = 2.261 Å and O1-H2-O2 = 170.55°, respectively, well within the range. The inter layer distance is 3.357 Å, well within the π stacking distance (Fig. 7B).

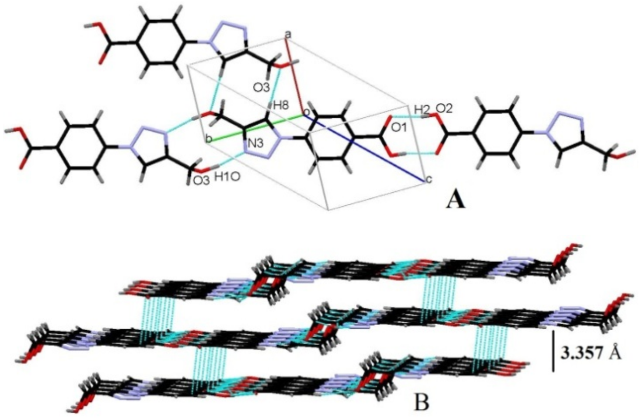


Fig.7 (A) Centrosymmetric hydrogen bond network in **6**, (B) hydrogen bond mediated layered structure of **6** in the crystal.

Correlation of crystal structures to conformation of 1-6 in the solid state

The crystallographic data for compounds **1-6** are presented in Table 1. From the analysis of the crystal structures of **1-6** the following inferences can be clearly made. In all the cases the triazole hydrogen acted as a hydrogen bond donor and the triazole nitrogen acted as a hydrogen bond acceptor for the formation of hydrogen bonds. The dihedral (twist) angle between the *N*-phenyl and the triazole rings is crucial for the formation of helical hydrogen bonded structures. Compounds **1-4** with twist angles in the range of 70 to 85° formed helical hydrogen bonded solid state supramolecular structures due to the relative orientation of the hydrogen bond donor group (COOH or phenolic OH) and hydrogen bond acceptor (triazole nitrogen). In case of derivatives **5** and **6** the twist angles were only 20.79° and 6.27°, respectively, not sufficient for the formation of helical hydrogen bond network. They are sufficiently planar to form only layered structures and hence they both formed only hydrogen bonded layered structures in the crystal. In both cases the layers were within π stacking distance (3.35 Å). In derivative **6** the bulky COOH group is deliberately placed in the *para* position to test the hypothesis that the phenyltriazoles must have a twisted conformation to exhibit helical hydrogen bonded structures. Comparison of structures of **1** and **6** (*ortho vs para*) clearly reveals that indeed it is the COOH group placed in the *ortho* position of the phenyl ring on **1** that results in twisted conformation. The twisted conformation in turn results in the chirality of **1** in the solid state. Indeed it is the twisted conformation of the otherwise achiral compounds **1-4** that make them chiral in the solid state. Another interesting

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Table 1 Crystallographic data, data collection and refinement for **1-6**

Parameter	**1**	**2**	**3**	**4**	**5**	**6**
Formula	$C_{10}H_9N_3O_3$	$C_{15}H_{11}N_3O_2$	$C_{10}H_7N_3O_4$	$C_9H_7N_3O_3$	$C_9H_9N_3O_2$	$C_{10}H_9N_3O_3$
Formula weight	219.20	265.27	233.19	205.18	191.19	219.20
Radiation	Mo K_α	Mo K_α	Mo K_α	Mo K_α	Mo K_α	Mo K_α
Wavelength	0.71073 Å	0.71073 Å	0.71073 Å	0.71073 Å	0.71073 Å	0.71073 Å
Crystal system	orthorhombic	orthorhombic	monoclinic	monoclinic	triclinic	triclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_1/n$	$P2_1/c$	P-1	P-1
a/Å	5.2611 (2)	5.7364 (2)	5.0172 (11)	14.5117 (7)	6.9540 (3)	5.5178 (8)
b/ Å	9.6714 (4)	11.9294 (5)	9.3768 (19)	5.1416 (2)	7.6099 (3)	6.7350 (10)
c/ Å	19.3615 (8)	18.4660 (9)	21.357 (4)	12.3092 (6)	8.6454 (3)	13.337 (2)
α/°	90	90	90	90	106.098 (2)	87.308 (6)
β/ °	90	90	96.602 (10)	107.607 (2)	101.881 (2)	82.823 (6)
γ/ °	90	90	90	90	93.586 (2)	74.791 (6)
V/ Å^3	985.16 (7)	1263.66 (9)	998.1 (4)	875.41 (7)	426.66 (3)	
T/K	298 (2)	298 (2)	298 (2)	298 (2)	298 (2)	298 (2)
Z	4	4	4	4	2	2
Reflections/ unique	3807/1871	5076/2639	6029/1729	5304/1521	5888/2247	4813/1568
R_{int}	0.0146	0.0240	0.0382	0.0170	0.0184	0.0359
μ/mm^{-1}	0.112	0.096	0.124	0.121	0.109	0.117
F(000)	456	552	480	424	200	228
θ range	2.10-28.40	2.03-27.28	1.92-25.00	2.95-25.00	2.52-33.88	3.08-25.00
Goodness of fit on F^2	1.067	1.043	1.074	0.907	1.603	1.178
R_1 and wR_2 [I > 2σ(I)]	0.0295 0.0745	0.0476 0.0852	0.0546 0.1173	0.0323 0.1036	0.0401 0.1273	0.0591 0.1584
R_1 and wR_2 (all data)	0.0316 0.0767	0.0765 0.0973	0.0316 0.0767	0.0395 0.1186	0.0316 0.0767	0.0839 0.1933

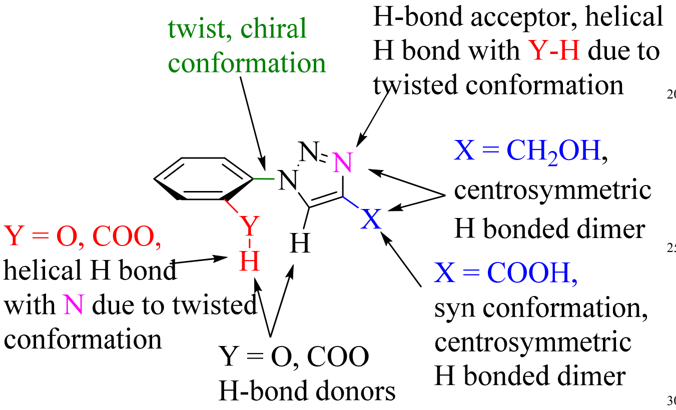

Fig.8 Correlation of structural features of the triazole derivatives to the observed hydrogen bonded supramolecular structures in the crystals.

observation is the role of carboxylic acid group when placed on the triazole ring to form centrosymmetric hydrogen bonded dimer. In all the examples (**1-4** and **6**) the COOH group is in the *syn* conformation. In both **3** and **4** the acid group on the triazole ring is engaged in the formation of centrosymmetric hydrogen bonded dimer through O-H…O homosynthons. As a result of the centrosymmetric hydrogen bonded dimer formation these derivatives crystallized as only racemic compounds in spite of the fact that helical hydrogen bonding motif is present in these structures. In triazoles containing COOH and OH groups both homo and hetero hydrogen bond synthons can be involved in the formation of the solid state supramolecular structures. The interplay of homo and hetero hydrogen bond synthons is clearly evident from the observed solid state supramolecular hydrogen bond networks in **1-6**. The heterosynthon, namely O-H…N is predominant in all the structures and is responsible for the supramolecular helical hydrogen bond network in case of **1-4**. In case of **5** both O-H…O homosynthon involving both the OH groups and the O-H…N heterosynthon involving one of the hydroxyl groups and the triazole nitrogen are involved in the formation of two distinct centrosymmetric supramolecular hydrogen bond networks. In the present investigation all the helical motifs in the supramolecular structures of **1-4** are due to heterosynthon, namely O-H…N hydrogen bond whereas the centrosymmetric motifs are due to both homo- and hetero hydrogen bond synthons. The inferences discussed above are pictorially depicted in Figure 8.

Experimental

2-(4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)benzoic acid (1)

Method A: 2-Azidobenzoic acid (360 mg, 2.20 mmol) and propargyl alcohol (1.23 g, 22.0 mmol) were dissolved in 10 mL of toluene. The reaction mixture was stirred at room temperature for 10 minutes and then heated at 90 °C for 12 h to give a white precipitate. The precipitate was filtered, washed with water and dichloromethane/ hexane mixture (1:1 v/v). The product HTA was obtained as a white powder. Recrystallization from a mixture of acetonitrile and methanol (1:1 v/v) afforded colorless crystals of **1**. Yield: 68%. mp 177 °C, IR (KBr) / cm^{-1} 3420 (broad), 3135, 2958, 1675, 1603, 1470, 1356, 1301, 1018 ; ^{1}H NMR δ_H (400 MHz, DMSO-d$_6$) 8.33 (1H, s), 7.90 (1H, d, *J* = 8 Hz), 7.74 (1H, t, *J* = 8 Hz), 7.65 (1H, t, *J* = 8 Hz), 7.58 (1H, d, *J* = 8 Hz), 5.32 (1H, broad, s), 4.60 (2H, s); ^{13}C NMR δ_C (100 MHz, DMSO-d$_6$) 166.6, 147.9, 135.2, 132.2, 130.2, 129.6, 128.6, 126.2, 123.9, 54.8; HRMS calcd. for $C_{10}H_{10}N_3O_3$ (M+H)$^+$ 220.0722, found 220.0712.

2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)benzoic acid (2)

Method B: Phenylacetylene (624mg, 6.12 mmol) was added to a stirred mixture of copper sulphate (30 mg, 0.122 mmol), sodium ascorbate (60mg, 0.306mmol) and 2-azidobenzoic acid (500 mg, 3.06 mmol) in *t*-BuOH:H_2O (10 mL : 10 mL).The reaction mixture was stirred at room temperature for 48 h, during which the progress of the reaction was monitored by TLC. The reaction mixture was poured into 50 mL of cold water upon which the product precipitated. The precipitate was washed with water and hexane. Phenyltriazole (**2**) was obtained as a pale yellow powder. Recrystallization from dichloromethane: acetonitrile (1 : 1 v/v) afforded colorless crystals. Yield: 80%. mp 216 °C, IR (KBr) / cm^{-1} 3150, 3090, 1628, 1550, 1408, 1290, 1013 ; ^{1}H NMR δ_H (400 MHz, DMSO-d$_6$) 8.81 (1H, s), 7.92 (3H, m) , 7.62-7.74 (3H, m), 7.43 (2H, t, *J* = 8 Hz), 7.22 (1H, t, *J* = 8 Hz), 4.50 (broad, 1H, OH), ^{13}C NMR δ_C (100 MHz, DMSO-d$_6$) 165.9, 146.4, 135.5, 132.2, 130.6, 130.3, 128.7, 127.8, 126.3, 125.2, 122.6; HRMS calcd. for $C_{15}H_{12}N_3O_2$ (M+H)$^+$ 266.093, found 266.0941.

1-(2-Hydroxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid (4)

Compound **4** was prepared by following method B as described above for **2**. Propiolic acid (338mg, 4.83 mmol) was added to a stirred mixture of copper sulphate (30 mg, 0.120 mmol), sodium ascorbate (79mg, 0.402mmol) and 2-azidophenol (544 mg, 4.029 mmol) in *t*-BuOH:H_2O (10 mL : 10 mL). The reaction mixture was stirred at room temperature for 48 h to give **4** as a brown crystalline powder. Recrystallization from acetone: dichloromethane: methanol (1 : 1 : 1, v/v) afforded pale brown crystals. Yield: 75%. mp 169 °C, IR (KBr) / cm^{-1} 3380 (broad), 3090, 1660, 1450, 1385, 1089; ^{1}H NMR δ_H (400 MHz, DMSO-d$_6$) 10.76 (1H, broad, s), 8.93 (1H,s) , 7.61 (1H, d, *J* = 8 Hz), 7.37 (1H, t, *J* = 8 Hz), 7.12 (1H, d, *J* = 8 Hz), 7.0 (1H, t, *J* = 8 Hz), 3.49 (1H, broad, s, OH); ^{13}C NMR δ_C (100 MHz, DMSO-d$_6$) 161.7, 150.0, 139.5, 130.7, 130.2, 125.4, 124.0, 119.5, 117.0; HRMS calcd. for $C_9H_8N_3O_3$ (M+H)$^+$ 206.0566, found 206.0561.

4-(4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)benzoic acid (6)

Compound **6** was prepared by following method B as described above for **2**. Propargyl alcohol (355mg, 6.13 mmol) was added to a stirred mixture of copper sulphate (15 mg, 0.06 mmol), sodium ascorbate (60mg, 0.306mmol) and 4-azidobenzoic acid (500 mg, 3.06 mmol) in *t*-BuOH:H_2O (10 mL : 10 mL).The reaction mixture was stirred at room temperature for 48 h to give **6** as a pale yellow powder. Recrystallization from dichloromethane: acetonitrile: methanol (1: 1: 1, v/v) afforded colorless crystals. Yield: 85%. mp 252 °C, IR (KBr) / cm^{-1} 3400, 3100, 2890, 2960, 1680, 1506, 1306, 1012 ; ^{1}H NMR δ_H (400 MHz, DMSO-d$_6$) 8.73(1H, s), 8.06 (4H, AB quartet, *J* = 7 Hz), 4.63 (2H, s), 4.50 (broad, 1H, OH); ^{13}C NMR δ_C (100 MHz, DMSO-d$_6$) 165.5, 149.6, 144.0, 139.7, 131.7, 121.2, 119.9, 55.0 ; HRMS calcd. for $C_{10}H_{10}N_3O_3$ (M+H)$^+$ 220.0722, found 220.0716.

1-(2-Carboxyphenyl)-1*H*-1,2,3-triazole-4-carboxylic acid (3)

Method C: Propiolic acid (170mg, 2.44 mmol) was added to a stirred mixture of copper iodide (23 mg, 0.122 mmol) and 2-azidobenzoic acid (200 mg, 1.22 mmol) in DMSO:H_2O (4.5 mL : 0.5 mL). The reaction mixture was stirred at room temperature for 24 h, during which the progress of the reaction was monitored by TLC. The reaction mixture was poured into 50 mL of water. It was extracted with ethyl acetate (3 x 50mL), dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure. The crude product was washed with dichloromethane: hexane (1:1) to remove the unreacted starting materials. Compound **3** was obtained as a white powder. Recrystallization from a mixture of benzene : methanol (1:4, v/v) afforded colorless crystals. Yield: 71%. mp 178-180 °C, IR (KBr) / cm^{-1} 3142, 2922, 1725, 1693, 1604, 1555, 1252, 1064; ^{1}H NMR δ_H (400 MHz, DMSO-d$_6$) 9.1 (1H, s), 7.99 (1H, d, *J* = 7.2 Hz), 7.65-7.81 (3H, m); ^{13}C NMR δ_C (100 MHz, , DMSO-d$_6$) 165.9, 161.6, 139.6, 135.0, 132.7, 130.7, 130.6, 130.4, 128.3, 127.1. HRMS calcd. for $C_{10}H_8N_3O_4$ (M+H)$^+$ 234.0515, found: 220.0506.

2-(4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)phenol (5)

Method D: A solution of 2-azidophenol (594 mg, 4.4 mmol) in PEG-600 (10 mL) was degassed with nitrogen. Copper sulphate (11mg, 0.044 mmol) dissolved in 1ml water, sodium ascorbate (87 mg, 0.44 mmol) dissolved in 1 ml water were added to the reaction mixture. Under nitrogen atmosphere propargyl alcohol (492 mg, 8.8 mmol) was added dropwise to the reaction mixture. The reaction mixture was stirred at room temperature for 48 h and then it was poured into 100 mL of water. The aqueous layer was extracted with ethyl acetate (3 x 50mL), dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure. The crude product was washed with ethyl acetate and hexane (1:9, v/v) to remove the unreacted starting materials. Triazloe **5** was obtained as a brown solid. Recrystallization from a mixture of ethyl acetate: methanol (1:1, v/v) afforded pale brown crystals. Yield: 65%. mp 140 °C, IR (KBr) / cm^{-1} 3169 (broad), 3110 (broad), 2950, 1601, 1515, 1474, 1371, 1230, 1008; ^{1}H NMR δ_H (400 MHz, DMSO-d$_6$) 10.24 (1H, broad, s), 8.30 (1H, s) , 7.67 (1H, s), 7.26 (1H, s), 7.11 (1H, s), 6.95 (1H, s), 5.20 (1H, broad s), 4.74 (2H, s); ^{13}C NMR δ_C (100 MHz, DMSO-d$_6$) 148.1, 128.4, 123.6, 123.2, 118.5, 116.2, 54.6. HRMS calcd. for $C_9H_{10}N_3O_2$ (M+H)$^+$ 192.0773, found: 192.0771.

Crystallographic data collection and refinement

All crystals were stable at room temperature and data was carried out at 298 K. The intensity data were collected on a Bruker AXS (Kappa Apex II) diffractometer equipped with graphite monochromated Mo K_α radiation. The data were collected for θ upto 25° for Mo K_α radiation and ω and φ scans were employed for data collection. The frame width for ω was set to 0.5° for data collection. The frames were integrated and data were reduced for Lorentz and polarization correction using SAINT-NT Plus.[28] The multi-scan absorption correction[29] was applied to data. All structures were solved using SIR-92[30] and refined using SHELXL-97.[31] The molecular and packing diagrams were drawn using ORTEP-32[32] and Mercury 2.4.[33] The non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogens could be located in the difference Fourier map. However, hydrogen atoms bonded to carbons were fixed at chemically meaningful positions and were allowed to ride with the parent atom during the refinement. All hydrogen bond donor acceptor distances are well within hydrogen bonding interaction range.

Conclusions

The crystal structures of six structurally related phenyltriazoles endowed with hydrogen bond donor and acceptor groups have been analyzed for the formation of hydrogen bonded supramolecular network in the solid state. The triazole derivatives are achiral in nature. The twisted molecular conformation of derivatives **1-4** makes them chiral in the solid state and the relative orientation of the hydrogen bond donor and acceptor groups enable the formation of helical hydrogen bond network. Whether they would form chiral crystals or not is decided by the presence or absence of carboxylic acid group on the triazole ring. The carboxylic acid group in derivatives **3** and **4** showed preponderance in forming centrosymmetric hydrogen bonded dimers which resulted in the formation of achiral (racemic compound) crystals whereas derivatives **1** and **2** formed chiral (racemic conglomerate) crystals. Derivatives with smaller twist between the phenyl and the triazole ring did not form helical hydrogen bond network, instead they formed layered sheet like structures. The layers are further interconnected through π stacking interactions leading to the formation of a 3D supramolecular network. Derivative **6** with the carboxylic acid group in the *para* position had the lowest dihedral angle (6.27°) and the structure of this derivative in comparison with that of **1** supports our hypothesis that twisted chiral conformation is essential for the formation of helical hydrogen bond network and chiral crystal.

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Notes and references

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