One hydrogen bond doesn't make a separation or does it? Resolution of amines by diacetoneketogulonic acid

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1. Experimental section

Materials. All compounds were purchased from Aldrich and of ACS (≥99%) quality.

Preparation of diastereomeric salts. 100 mg of (−)-2,3:4,6-Di-O-isopropylidene-2-keto-L-gulonic acid, (diacetoneketogulonic acid, DAG) was dissolved in excess amount of the related amines and the crystals were harvested immediately after appearance. Many attempts were made to crystallize DAG with S-MeBUAM (rate of evaporation was varied, as well as the crystallisation temperature) but all experiments yielded gels.

Single Crystal X-Ray Diffraction. Diffraction data for all compounds were collected on a Bruker DUO APEX II diffractometer[1] with graphite monochromated Mo Kα1 radiation (λ = 0.71073 Å) at 173 K using an Oxford Cryostream 700. Data reduction and cell refinement were performed using SAINT-Plus[2] and the space groups were determined from systematic absences by XPREP[3] and further justified by the refinement results. In all cases, the structures were solved in the aid of X-Seed[4] by direct methods using SHELXS-97[5] and refined using full-matrix least-squares/difference Fourier techniques using SHELXL-97.[5] The hydrogen atoms bound to carbon atoms were placed at idealized positions and refined as riding atoms with U_{iso} (H) = 1.2 U_{eq} (Ar-H, CH_2) or 1.5 U_{eq} (CH_3). Diagrams and publication material were generated using PLATON[6] and X-Seed. Experimental details of the X-ray analyses are provided in Table S1. CIFs for each structure have been deposited with the Cambridge Structural Database (CCDC 950602-950607).

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[1] Bruker **2005**. *APEX*2. Version 1.0-27. Bruker AXS Inc., Madison,Wisconsin, USA.
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[3] Bruker **2003**, *XPREP2*. Version 6.14. Bruker AXS Inc., Madison, Wisconsin, USA.
[4] L. J. Barbour, *J. Supramol. Chem.*, **2001**, *1,* 189-191**.**
[5] G. M. Sheldrick, SHELXS-97 and SHELXL-97 *Programs for crystal structure determination and refinement.* University of Göttingen, 1997.
[6] A. L. Spek, *J. Appl. Crystallogr*. **2003**, *36*, 7-13.

Table S1 Crystal data for amine salts of DAG

Compound	**(DAG$^-$)(BUAM$^+$)**	**(DAG$^-$)(*R*-MeBUAM$^+$)**	**(DAG$^-$)(*R*-PEA$^+$)**	**(DAG$^-$)(*S*-PEA$^+$)**	**(DAG$^-$)(*S*-NEA$^+$)**	**(DAG$^-$)(*R*-NEA$^+$)**
CCDC no.	950602	950603	950605	950607	950606	950604
Chemical formula	$(C_{12}H_{17}O_7^-)(C_4H_{12}N^+)$	$(C_{12}H_{17}O_7^-)(C_5H_{14}N^+)$	$(C_{12}H_{17}O_7^-)(C_8H_{12}N^+)$	$(C_{12}H_{17}O_7^-)(C_8H_{12}N^+)$	$(C_{12}H_{17}O_7^-)(C_{12}H_{14}N^+)$	$(C_{12}H_{17}O_7^-)(C_{12}H_{14}N^+)$
M_r	347.40	361.43	395.44	395.44	445.50	445.50
Cell setting, space group	Orthorhombic, $P2_12_12_1$	Orthorhombic, $P2_12_12_1$	Monoclinic, $P2_1$	Monoclinic, $P2_1$	Monoclinic, $P2_1$	Orthorhombic, $P2_12_12_1$
Temperature (K)	173(2)	173(2)	173(2)	173(2)	173(2)	173(2)
a, b, c (Å)	6.1806(13), 14.641(3), 20.360(4)	6.3376(5), 15.4586(12), 20.0153(17)	14.4045(11), 6.2322(5), 23.4872(18)	14.634(3), 6.2305(12), 11.855(2)	13.740(5), 6.188(3), 15.056(6)	7.6206(4), 11.4755(9), 26.5274(16)
α, β, γ (°)	90.00, 90.00, 90.00	90.00, 90.00, 90.00	90.00, 103.762(2), 90.00	90.00, 102.86(3), 90.00	90.00, 113.998(8), 90.00	90.00, 90.00, 90.00
V (Å^3)	1842.3(7)	1960.9(3)	2048.0(3)	1053.8(4)	1169.4(8)	2319.8(3)
Z	4	4	4	2	2	4
D_x (Mg m^{-3})	1.252	1.224	1.283	1.246	1.265	1.276
Radiation type	MoKα (λ= 0.71073)	MoKα (λ= 0.71073)	MoKα (λ= 0.71073)	MoKα (λ= 0.71073)	MoKα (λ= 0.71073)	MoKα (λ= 0.71073)
μ (mm^{-1})	0.098	0.094	0.097	0.094	0.093	0.094
Crystal form, colour	rod, colourless	rod, colourless	rod, colourless	rod, colourless	rod, colourless	rod, colourless
Crystal size (mm)	0.41 x 0.35 x 0.35	0.35 x 0.19 x 0.18	0.2 x 0.2 x 0.2	0.20 x 0.18 x 0.15	0.18 x 0.16 x 0.16	0.42 x 0.33 x 0.24
No. of measured, independent and observed reflections	9142, 4552, 3677	11503, 4035, 3545	10530, 7077, 5714	8188, 4682, 4129	6011, 4368, 3950	8259, 4679, 4396
h, k, l (min, max)	-8, 8; -10, 19; -27, 27	-7, 7; -17, 19; -25, 25	-17, 17; -5, 7; -28, 28	-19, 15, -8, 8, -15, 15	-16, 17; -7, 7; -17, 18	-9, 5; -4, -14; -33, 33
Θ (min, max.)	1.71, 28.40	1.66, 26.49	1.46, 25.84	2.01, 28.37	2.60, 26.51	2.35, 26.31
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.0374, 0.0953, 0.982	0.0323, 0.0812, 0.921	0.0382, 0.0872, 1.007	0.0351, 0.0888, 1.016	0.0429, 0.1191, 1.052	0.0365, 0.0968, 1.023
No. of parameters/ restrains	274/6	236/3	516/7	262/4	298/4	298/3
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.231, -0.168	0.192, -0.146	0.160, -0.151	0.239, -0.158	0.250, -0.214	0.285, -0.320

Table S2 Hydrogen bond metrics for the amine salts of DAG

D-H...A	*D-H (Å)*	*H...A (Å)*	*D...A (Å)*	*D-H...A (°)*	*Symmetry descriptor*
(DAG$^-$)(BUAM$^+$)*					
N24−H24A…O15*	0.91	1.85	2.7520(6)	171	x-1/2,1/2-y,-z
N24−H24B...O14*	0.91	1.92	2.8115(6)	167	x-1,y,z
N24−H24C...O15	0.91	1.93	2.8009(6)	160	
(DAG$^-$)(*R*-MeBUAM$^+$)					
N25−H25A...O15	0.91	1.93	2.8360(2)	169	
N25−H25B...O14*	0.91	1.94	2.8087(2)	159	x-1,y,z
N25−H25C...O15*	0.91	1.86	2.7735(2)	175	x-1/2,1/2-y,-z
(DAG$^-$)(*R*-PEA$^+$)					
N28−H28A...O14*	0.94	1.89	2.8210(2)	174	x,y-1,z
N28−H28B...O15	0.93	1.95	2.8500(2)	161	
N28−H28B...O1	0.93	2.52	3.0806(2)	119	
N28−H28C...O43*	0.88	2.03	2.8907(2)	166	x,y-1,z
N56−H56A...O15	0.94	1.93	2.8640(2)	172	
N56−H56B...O42*	0.92	1.83	2.7468(2)	177	x,y-1,z
N56−H56C...O43	0.85	2.04	2.8471(2)	158	
N56−H56C...O31	0.85	2.60	3.079(2)	116	
N56−H56C...O29	0.85	2.717	3.311(2)	128	
(DAG$^-$)(*S*-PEA$^+$)					
N28−H28A...O15	0.91	1.90	2.7688(6)	161	
N28−H28A...O3	0.91	2.56	3.1319(6)	121	
N28−H28B...O15*	0.91	1.96	2.8464(6)	165	1-x,y-1/2,-z
N28−H28C...O14*	0.91	1.88	2.7898(6)	174	x,y-1,z
C23−H23...O6*	0.95	2.55	3.5011(7)	177	x,y,z-1
C27−H27B…O3*	0.98	2.44	3.3967(7)	165	1-x,y-1/2,-z
(DAG$^-$)(*S*-NEA$^+$)					
N32−H32A…O15	0.91	1.82	2.7334(11)	175	
N32−H32B…O15*	0.91	2.00	2.8899(12)	165	1-x,1/2+y,-z
N32−H32C…O14*	0.91	1.92	2.8352(11)	177	x,1+y,z
C30−H30...O6	1.00	2.68	3.671(1)	169	
(DAG$^-$)(*R*-NEA$^+$)					
N32−H32A…O15	0.92	1.81	2.7203(2)	168	
N32−H32B…O14*	0.92	1.80	2.7237(2)	175	1-x,-1/2+y,1/2-z
N32−H32C…O6	0.92	1.98	2.8753(2)	162	
C5−H5A…O15*	0.99	2.40	3.3777(3)	170	1-x,-1/2+y,1/2-z

* *For (DAG$^-$)(BUAM$^+$) only one of the disorder is included. The hydrogen bonding of the other disorder is virtually the same.*

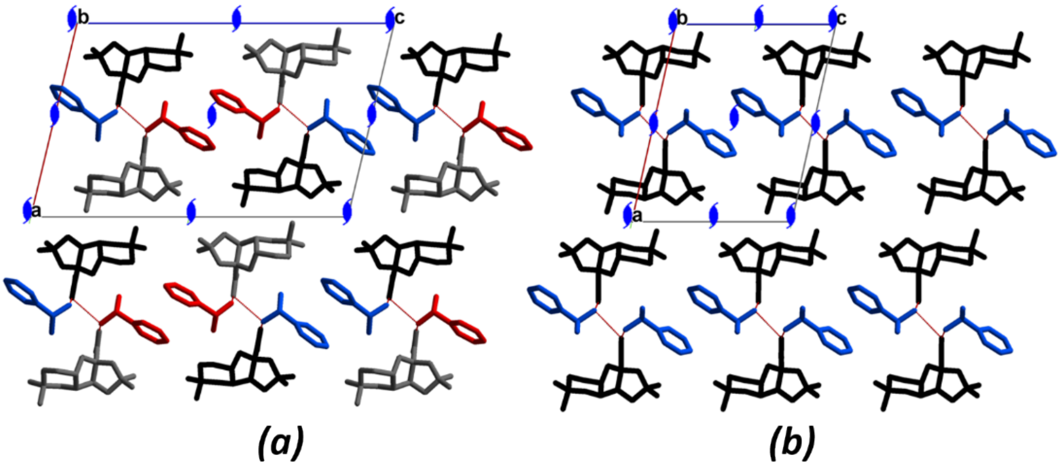


Figure S1 Packing diagrams of (DAG$^-$)(*R*-PEA$^+$) (DAG$^-$)(*S*-PEA$^+$), *a* and *b* respectively. The symmetry equivalent molecules are coloured accordingly and the unit cells are presented with the positions of the 2 fold screw axes.

Table S3 Torsion angles of the –*COO*$^-$ moiety of DAG in the different structures

	C10-C2-C13-O14 (°)
(DAG$^-$)(BUAM$^+$)	0.1
(DAG$^-$)(*R*-MeBUAM$^+$)	-5.9
(DAG$^-$)(*R*-PEA$^+$) mol A	-0.5
mol B	-2.7*
(DAG$^-$)(*S*-PEA$^+$)	-12.1
(DAG$^-$)(*S*-NEA$^+$)	-10.8
(DAG$^-$)(*R*-NEA$^+$)	-50.6

* *C38-C30-C41-O42*

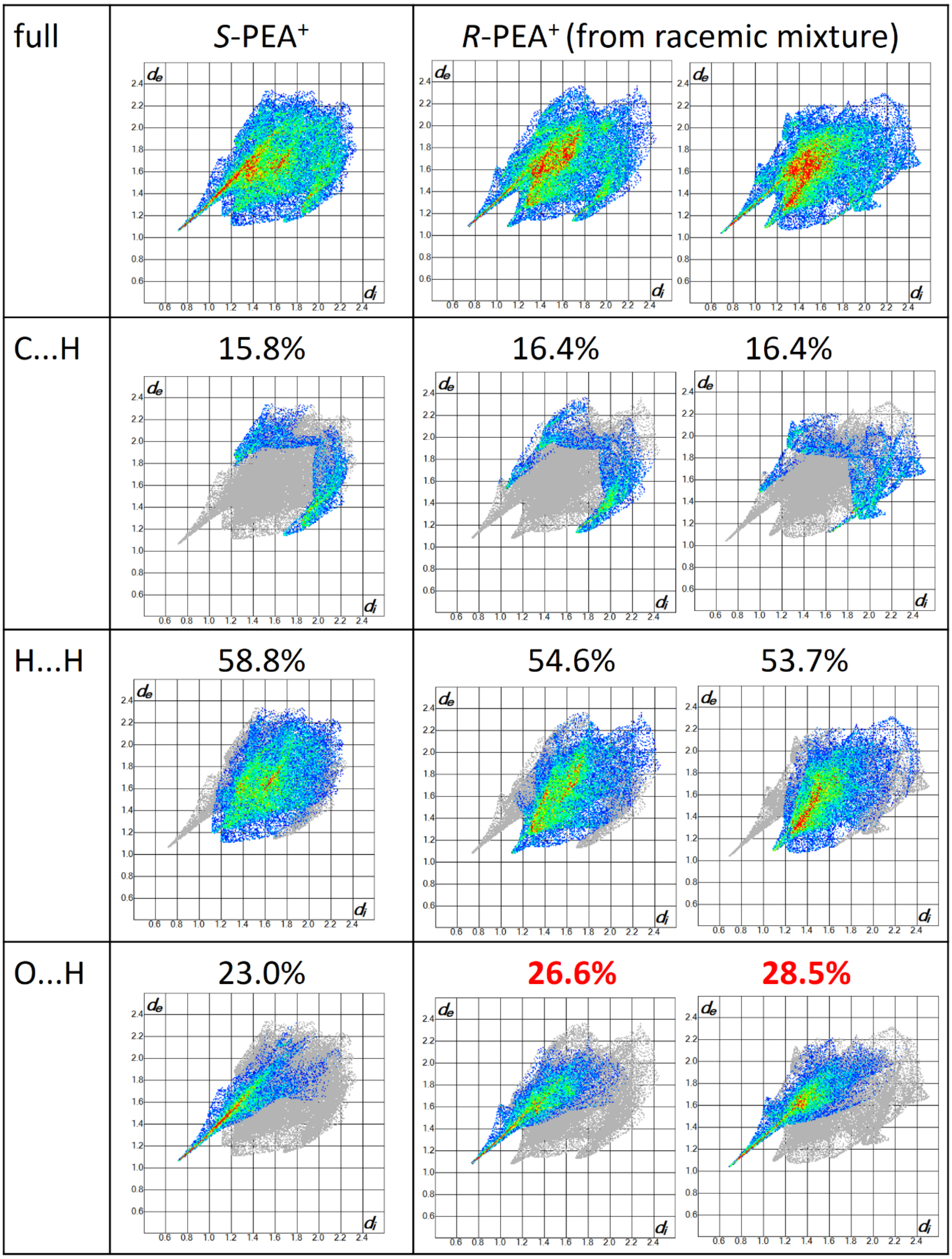


Figure S2 Fingerprint plots for the guest components *S*-PEA$^+$ and *R*-PEA$^+$ (full and highlighted sections of the relevant interactions, such as C…H, H…H and O…H) in structures (DAG$^-$)(*S*-PEA$^+$) and (DAG$^-$)(*R*-PEA$^+$), respectively. Note the higher amount of O…H contacts of the *R*-PEA$^+$ cation (red) in the crystal obtained from the racemic mixture of the amine.

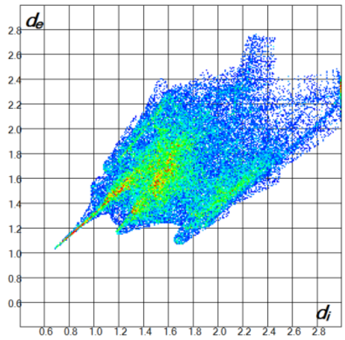
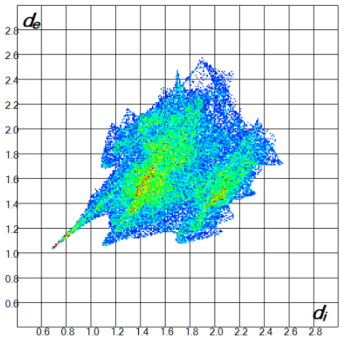
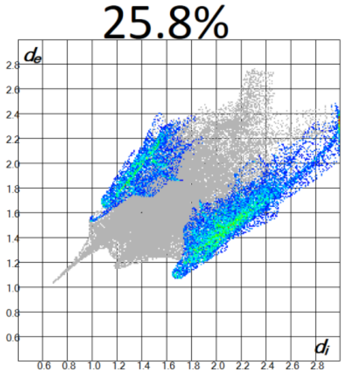
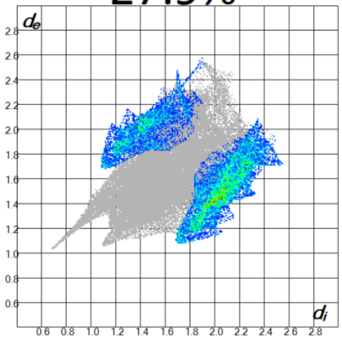
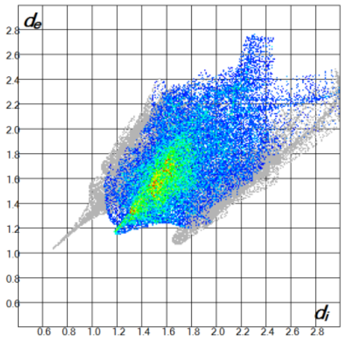
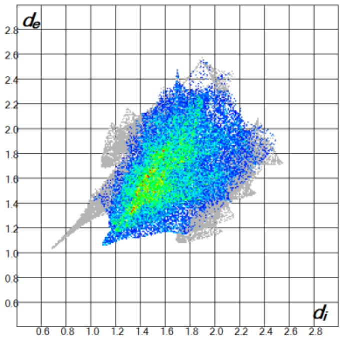
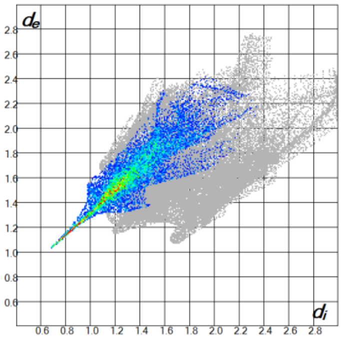
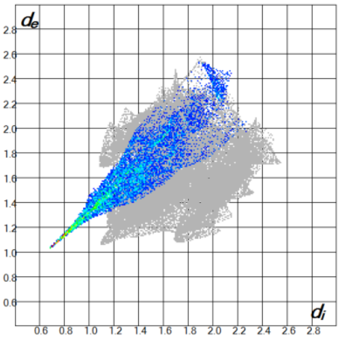
full	*S*-NEA⁺ (from racemic mixture)	*R*-NEA⁺
		
C…H	25.8% 	27.9% 
H…H	53.3% 	58.3% 
O…H	20.8% 	13.8% 

Figure S3 Fingerprint plots for the guest components *S*-NEA$^+$ and *R*-NEA$^+$ (full and highlighted sections of the relevant interactions, such as C…H, H…H and O…H) in structures (DAG$^-$)(*S*-NEA$^+$) and (DAG$^-$)(*R*-NEA$^+$), respectively. Note the higher amount of O…H contacts of the *S*-NEA$^+$ cation (red) in the crystal obtained from the racemic mixture of the amine.

Lattice-energy calculations

The crystal structures were energy-minimised in full (including the unit-cell parameters) with the experimental space-group symmetry imposed. The energy-minimisations were carried out in *GRACE*[1], which in turn calls *VASP*[234] for single-point pure density functional theory calculations. The Perdew-Burke-Ernzerhof (PBE) exchange-correlation functional[5] was employed. *GRACE* adds a dispersion correction[6] and an efficient energy-minimisation algorithm that takes full advantage of chemical information in the form of delocalized internal coordinates and approximate first and second derivatives. The energies are the total lattice enthalpies at T = 0 K and P = 0 GPa. This is the same method and these are the same energies that were used so successfully in the 2007 crystal structure prediction Blind Test[7]. The method was further validated on 225 molecular single crystal structures[8]. The calculation of lattice energies combining ionic interactions, hydrogen bonds, π···π interactions and Van der Waals interactions was validated by means of a successful crystal structure prediction on pyridinium chloride[9]. In addition to the lattice energies, the calculations also provide idealised positions for the hydrogen atoms.

The –COO torsion angles in S-PEA, R-PEA (Z’=2), S-NEA and R-NEA are 12, 0, 3, 11 and 51°, respectively. The energy difference between the geometries of the DAG molecules in R-NEA and S-NEA is 0.83 kcal/mol in favour of R-NEA as determined from a dispersion-corrected PBE calculation.

2. Vapour sorption experiments

50 g of DAG was dried, sieved (30 μm), spread evenly in a Petri dish (Ø 70 mm) and placed in a vacuum desiccator which contained 100 ml of the racemic amine (PEA or NEA). The system was incubated for 30 mins on 50 °C to obtain an acceptable vapour pressure of the amine (ca. 4 mmHg for PEA and 0.02 mmHg for NEA).

Powder X-ray diffraction experiments were carried out on a Bruker D8 diffractometer using Cu-Kα radiation. The sample was ground to a fine powder and loaded into an aluminium tray. Where available these spectra were compared with those determined from the single crystal structures.

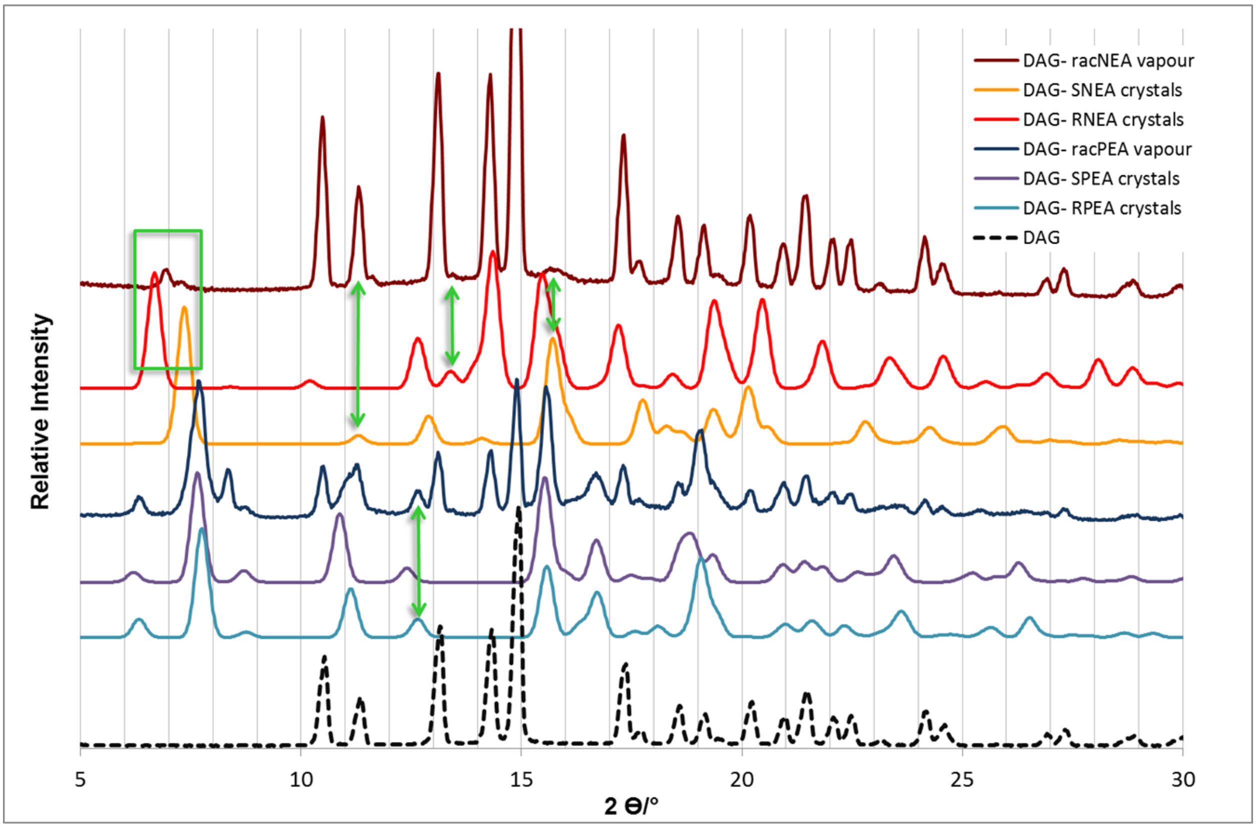


Figure S4 PXRD patterns obtained from DAG exposed to vapor of the different amines are compared to the single crystal structures obtained from crystallization experiments.

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