Supplementary Information

Strength from weakness: Opportunistic CH…O interactions dictate the conformational fate

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Table of contents

Supplementary Information

General Methods

Chromatograms were visualized under UV light and by dipping plates into either phosphomolybdic acid in MeOH or anisaldehyde in ethanol, followed by heating. Proton ^{1}H NMR, COSY, NOESY and HMQC spectra were recorded either on a Bruker (500 MHz) or Mercury Plus (Varian 400 MHz) NMR spectrometer. Proton chemical shifts are reported in ppm (δ) relative to the internal tetramethylsilane (TMS, δ 0.0 ppm) or with the solvent reference relative to TMS employed as the internal standard ($CDCl_3$, δ 7.26 ppm; D_2O, δ 4.79 ppm). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m)], integration, coupling constants [Hz] and peak identification). All NMR signals were assigned on the basis of ^{1}H NMR, ^{13}C NMR, COSY and HMQC experiments. ^{13}C spectra were recorded with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard. All NMR data were collected at 25 °C. The concentrations of the NMR samples were 5 mg per 0.5 mL and 20 mg per 0.5 mL for ^{1}H NMR and ^{13}C NMR respectively. Melting points were determined using Stuart SMP30 melting point apparatus and are uncorrected. Flash column chromatography was performed using Silica Gel 200-400 mesh. All reactions were carried out under argon or nitrogen atmosphere employing oven dried glassware.

General procedure for preparation of 3,4-di-*O*-acyl-1,2:5,6-di-*O*-isopropylidene-*myo*-inositol

Supplementary Information

To a solution of 1,2:5,6-di-*O*-isopropylidene-*myo*-inositol (**1**)[1] (1 mmol) and DMAP (10 mg) in dry pyridine (5 mL), acyl chloride/anhydride (3 mmol) was added drop wise at 0 °C and the reaction was stirred overnight gradually allowing the mixture to warm to rt. When TLC showed complete disappearance of starting material, reaction was quenched by adding a few drops of water and the mixture was concentrated under reduced pressure. The resulting residue was dissolved in ethyl acetate (60 mL) and was washed successively with 10% ascorbic acid solution, saturated sodium bicarbonate solution, water and finally with brine. The organic layer was dried over anhyd. $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography to get the corresponding 3,4-di-*O*-acyl,1,2:5,6-di-*O*-isopropylidene-*myo*-inositol.

Determination of the structure in solution

Haasnoot-Altona equation[2] (eqn 1) is the most reliable form of Karplus equation which not only relates the vicinal $^3J_{HH}$ coupling constant with the dihedral angle between the coupling partners but also takes into consideration the effect of electronegativity and the orientation of the substituents in HC-CH fragment on the $^3J_{HH}$ value.

$$^3J_{HH} = 13.86 \cos^2\phi - 0.81 \cos\phi + \Sigma \Delta\chi_i \{0.56 - 2.32 \cos^2(\xi_i.\phi + 17.9° \mid \Delta\chi_i \mid)\} \quad \ldots\ldots(1)$$

$\Delta\chi_i$ is the electronegativity difference between the substituent attached to the HC-CH fragment and hydrogen; ξ_i is either +1 or -1 depending on the orientation of the substituent.

Supplementary Information

We[3-8] and others[9-11] have used this equation very reliably and frequently for the determination of the solution conformation of various cyclitol derivatives. Thus we have used this equation for the determination of the conformation of the esters **2-10** in different solvents. Vicinal $^3J_{HH}$ values for the different set of vicinal protons on the inositol ring in different solvents were measured from ^{1}H NMR spectra in the corresponding solution. From each $^3J_{HH}$ value, the dihedral angle (ϕ) between the two hydrogens was calculated using the above equation. It is interesting to note that ϕ values for any particular set of vicinal protons in all the seven solvents tested were more or less same. In order to determine the conformation of **2-10** in these solutions, these compounds were energy minimized by MM2 method after fixing the dihedral angles between the vicinal protons as those obtained from the NMR method.

Conformation of diacetate 3 in solution

Table ESI 1. Experimental $^3J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the diacetate **3** in solvents of different polarity

H-C-C-H	$CDCl_3$	DMSO-d6	Acetone-d6	CD_2Cl_2	CD_3OD	C_6D_6	CD_3CN
H1-C1-C2-H2	6.7 (-5)	6.4 (-13)	6.5 (-10)	6.7 (-5)	6.4 (-13)	6.5 (-10)	6.4 (-13)
H2-C2-C3-H3	4.2 (40)	4.5 (37)	4.1 (41)	4.1 (41)	3.7 (44)	4.4 (38)	3.6 (45)
H3-C3-C4-H4	3.8 (60)	5.0 (50)	4.3 (56)	3.9 (59)	--	4.4 (55)	--
H4-C4-C5-H5	8.8 (-157)	9.1 (-165)	8.7 (-156)	8.7 (-156)	9.3 (-165)	9.2 (-165)	9.3 (-165)
H5-C5-C6-H6	10.5 (-166)	10.4 (-167)	10.5 (-166)	10.5 (-166)	10.5 (-166)	10.4 (-167)	10.5 (-166)
H6-C6-C1-H1	7.9 (-172)	7.9 (-172)	7.9 (-172)	7.9 (-172)	8.0 (-173)	7.9 (-172)	8.1 (-173)

Supplementary Information

It is clear from **Table ESI 1** that, in all the solvents acetate **3** adopts a boat conformation. As a representative example, the conformation of **3** in $CDCl_3$ is shown in **Figure ESI 1**. It is noteworthy that in this conformation, H6…O3 distance is 2.23 Å, much smaller than the van der Waal distance of 2.72 Å.

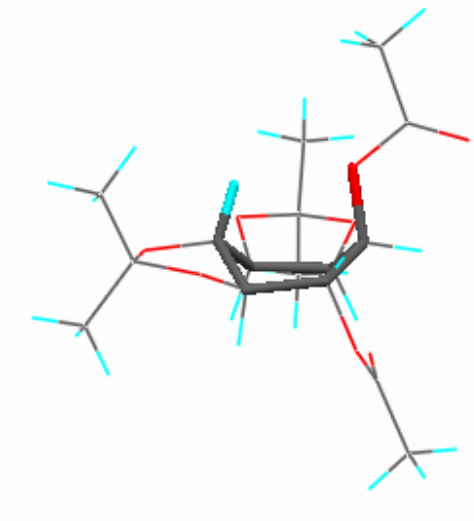


Figure ESI 1. Conformation of diacetate **3** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Conformation of dipivaloate 4 in solution

Table ESI 2: Experimental $^3J_{HH}$ values (in Hz) and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of dipivaloate **4** in solvents of different polarity

H-C-C-H	$CDCl_3$	DMSO-d6	Acetone-d6	CD_2Cl_2	CD_3OD	C_6D_6	CD_3CN
H1-C1-C2-H2	6.3 (-15)	5.7 (-24)	5.9 (-21)	6.1 (-18)	5.6 (-25)	5.5 (-26)	5.9 (-21)
H2-C2-C3-H3	4.7 (35)	4.7 (35)	4.7 (35)	4.7 (35)	4.9 (33)	4.9 (33)	4.7 (35)
H3-C3-C4-H4	5.2 (48)	6.5 (34)	6.2 (38)	5.4 (46)	6.7 (31)	6. 9 (28)	6.0 (40)

Supplementary Information

H4-C4-C5-H5	9.0 (-152)	9.2 (-154)	9.4 (-155)	9.1 (-153)	9.7 (-158)	9.8 (-159)	9.4 (-155)
H5-C5-C6-H6	10.3 (-165)	10.1 (-162)	10.1 (-162)	10.2 (-163)	10.1 (-162)	10.0 (-160)	10.2 (-163)
H6-C6-C1-H1	8.3 (-177)	8.3 (-177)	8.4 (-178)	8.4 (-178)	8.5 (-179)	8.6 (-179)	8.4 (-178)

As in the case of benzoate **2** and acetate **3**, it is very clear from the **Table S2** that pivaloate **4** also adopts boat conformation in all these solvents. The conformation of **4** in $CDCl_3$ solution is shown in **Figure ESI 2** as a representative example. In this case, the H6…O3 distance is 2.19 Å.

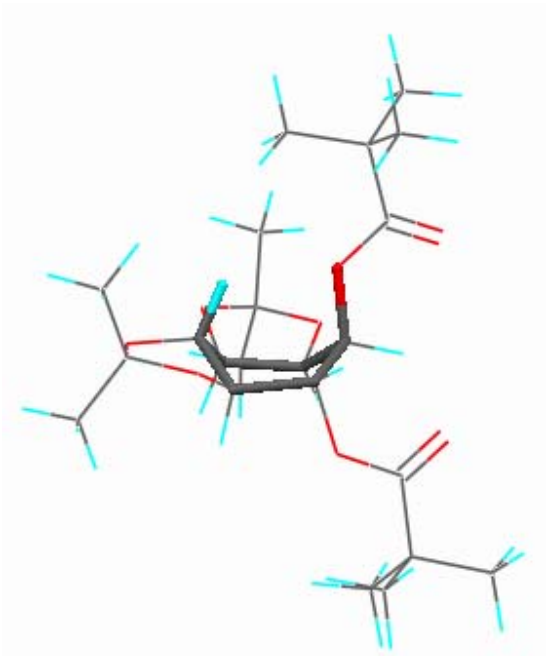


Figure ESI 2. Conformation of dipivaloate **4** in $CDCl_3$ solution. The interacting partners (H6 and O3) and the resultant boat form of the cyclitol ring is highlighted as capped stick model for clarity.

Conformation of dinaphthoate 5 in solution

Supplementary Information

Table ESI 3. Experimental $^{3}J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the dinaphthoate **5** in solvents of different polarity

H-C-C-H	**$CDCl_3$**	**DMSO-d6**	**Acetone-d6**	**CD_2Cl_2**	**C_6D_6**	**CD_3CN**
H1-C1-C2-H2	6.6 (-9)	6.0 (-20)	6.2 (-16)	6.5 (-10)	6.3 (-15)	6.0 (-20)
H2-C2-C3-H3	4.3 (39)	4.7 (35)	3.8 (44)	4.5 (37)	4.7 (35)	4.0 (42)
H3-C3-C4-H4	4.3 (56)	5.7 (43)	--	4.7 (52)	5.0 (50)	--
H4-C4-C5-H5	9.4 (-166)	8.6 (-154)	9.5 (-166)	9.1 (-164)	9.4 (-166)	9.6 (-167)
H5-C5-C6-H6	10.2 (-167)	--	10.3 (-167)	10.4 (-167)	10.2 (-167)	10.2 (-167)
H6-C6-C1-H1	8.0 (-173)	7.4 (-167)	8.1 (-174)	8.0 (-173)	8.0 (-173)	8.3 (-177)

Supplementary Information

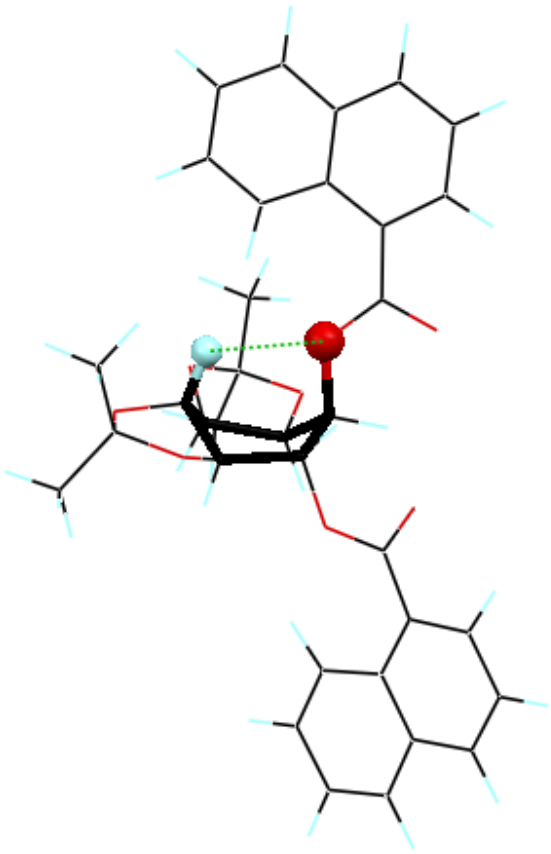


Figure ESI 3. Conformation of dinaphthoate **5** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Conformation of dipyrenoate 6 in solution

Table ESI 4. Experimental $^3J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the dipyrenoate **6** in solvents of different polarity

H-C-C-H	$CDCl_3$	DMSO-d6	Acetone-d6	CD_2Cl_2	C_6D_6	CD_3CN

Supplementary Information

H1-C1-C2-H2	6.6 (-9)	6.1 (-18)	6.2 (-16)	6.3 (-15)	6.3 (-15)	5.8 (-22)
H2-C2-C3-H3	4.2 (40)	4.7 (35)	3.6 (46)	4.3 (39)	--	4.0 (42)
H3-C3-C4-H4	4.2 (57)	5.4 (46)	--	4.6 (54)	5.0 (50)	--
H4-C4-C5-H5	8.7 (-155)	8.6 (-154)	9.6 (-166)	9.0 (-164)	9.5 (-166)	9.7 (-167)
H5-C5-C6-H6	10.4 (-167)	--	10.1 (-167)	10.3 (-167)	9.9 (-167)	10.1 (-167)
H6-C6-C1-H1	8.0 (-173)	7.0 (-164)	8.1 (-174)	7.9 (-172)	7.9 (-172)	8.4 (-178)

Supplementary Information

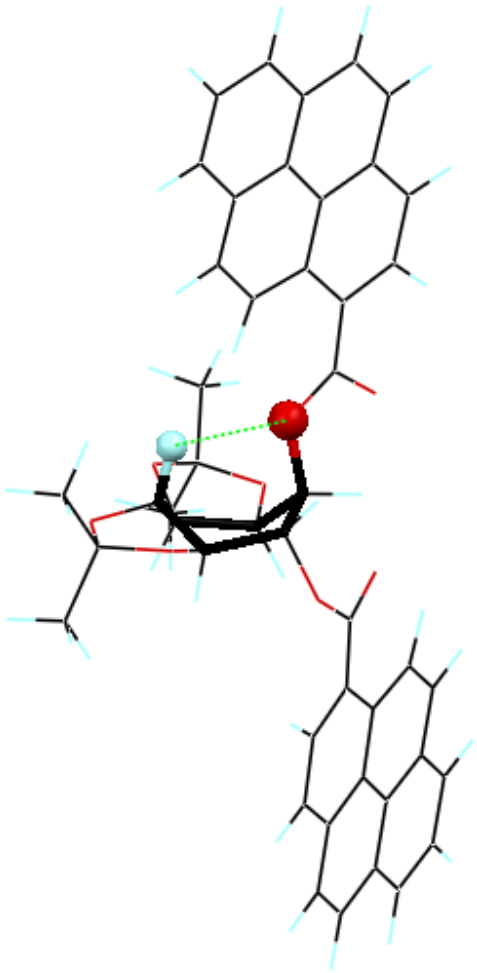


Figure ESI 4. Conformation of dipyrenoate **6** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Conformation of monopivaloate 7 in solution

Table ESI 5. Experimental $^3J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the monopivaloate **7** in solvents of different polarity

H-C-C-H	$CDCl_3$	DMSO-d6	Acetone-d6	CD_2Cl_2	CD_3OD	C_6D_6	CD_3CN

Supplementary Information

H1-C1-C2-H2	6.3 (-15)	6.7 (-5)	6.6 (-9)	6.2 (-16)	6.2 (-16)	5.8 (-22)	6.2 (-16)
H2-C2-C3-H3	4.5 (37)	4.2 (40)	4.3 (39)	4.5 (37)	4.5 (37)	4.6 (36)	4.5 (37)
H3-C3-C4-H4	5.0 (50)	4.2 (57)	4.4 (55)	5.3 (47)	5.3(47)	4.8 (51)	5.1 (49)
H4-C4-C5-H5	8.8 (-158)	8.4 (-151)	8.4 (-151)	8.8 (-158)	8.8 (-158)	8.8 (-158)	8.8 (-158)
H5-C5-C6-H6	10.4 (-167)	10.5 (-167)	10.5 (-167)	10.4 (-167)	10.4 (-167)	9.8 (-167)	10.4 (-167)
H6-C6-C1-H1	8.2 (-176)	8.0 (-174)	8.1 (-174)	8.3 (-177)	8.3 (-177)	--	8.3 (-177)

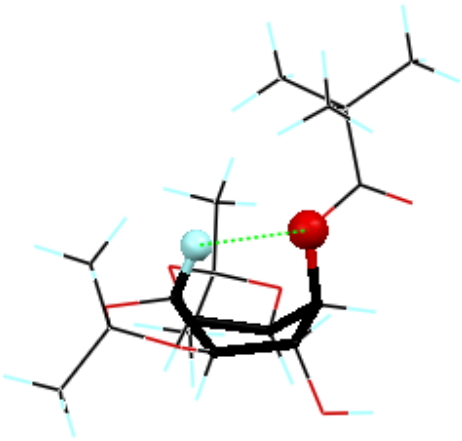


Figure ESI 5. Conformation of monopivaloate **7** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Conformation of monobenzoate 8 in solution

Table ESI 6. Experimental $^3J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the monobenzoate **8** in solvents of different polarity

H-C-C-H	**$CDCl_3$**	**DMSO-d6**	**Acetone-d6**	**CD_2Cl_2**	**CD_3OD**	**C_6D_6**	**CD_3CN**
H1-C1-C2-H2	6.6 (-9)	6.7 (-5)	6.7 (-5)	6.5 (-10)	6.6 (-9)	6.6 (-9)	6.5 (-10)

Supplementary Information

H2-C2-C3-H3	4.2 (40)	4.0 (42)	4.0 (42)	4.3 (39)	4.1 (41)	4.1 (41)	4.3 (39)
H3-C3-C4-H4	4.1 (58)	3.9 (59)	3.8 (60)	4.2 (57)	4.2 (57)	3.9 (59)	4.4 (55)
H4-C4-C5-H5	8.6 (-154)	8.5 (-152)	8.3 (-150)	8.6 (-154)	8.6 (-154)	8.3 (-150)	8.7 (-156)
H5-C5-C6-H6	10.6 (-167)	10.6 (-167)	10.6 (-167)	10.6 (-167)	10.6 (-167)	10.6 (-167)	10.6 (-167)
H6-C6-C1-H1	7.8 (-171)	7.8 (-171)	7.0 (-164)	7.8 (-171)	7.7 (-170)	7.8 (-171)	8.0 (-173)

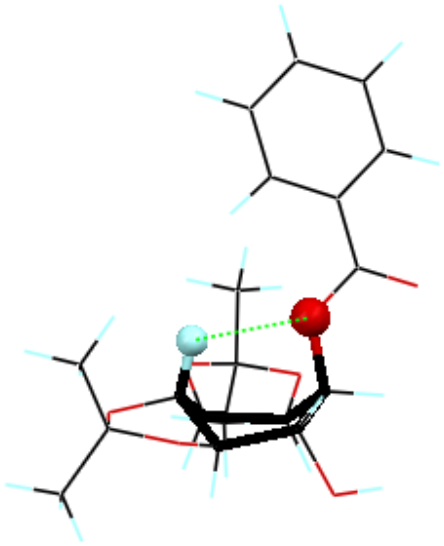


Figure ESI 6. Conformation of monobenzoate **8** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Conformation of mononaphthoate 9 in solution

Table ESI 7. Experimental $^3J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the mononaphthoate **9** in solvents of different polarity

H-C-C-H	**$CDCl_3$**	**DMSO-d6**	**Acetone-d6**	**CD_2Cl_2**	**CD_3OD**	**C_6D_6**	**CD_3CN**
H1-C1-C2-H2	6.1 (-18)	6.3 (-15)	6.4 (-13)	6.1 (-18)	6.2 (-16)	6.3 (-15)	6.1 (-18)

Supplementary Information

H2-C2-C3-H3	4.7 (35)	4.5 (37)	4.4 (38)	4.6 (36)	4.5 (37)	4.4 (38)	4.5 (37)
H3-C3-C4-H4	4.7 (52)	4.5 (54)	4.4 (55)	5.2 (48)	5.1(44)	4.7 (52)	5.3 (47)
H4-C4-C5-H5	9.0 (-164)	9.2 (-164)	8.6 (-154)	9.0 (-164)	8.9 (-161)	8.7 (-155)	9.1 (-164)
H5-C5-C6-H6	10.4 (-167)	10.4 (-167)	10.5 (-167)	10.4 (-167)	10.4 (-167)	10.5 (-167)	10.3 (-167)
H6-C6-C1-H1	8.1(-174)	8.1(-174)	8.0 (-173)	8.2 (-176)	8.2 (-176)	8.0 (-173)	8.3 (-177)

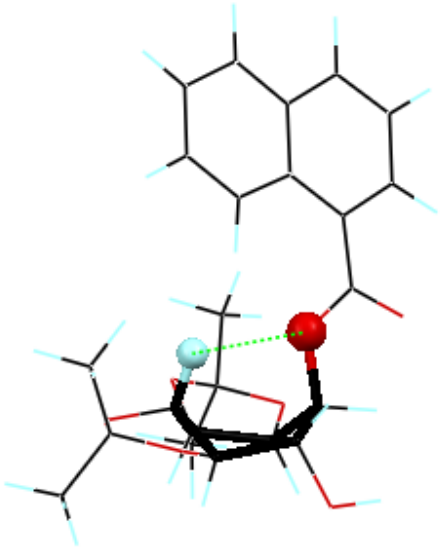


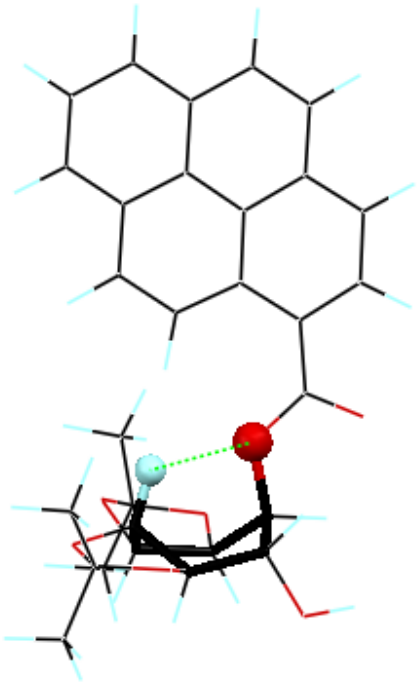
Figure ESI 7. Conformation of mononaphthoate **9** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Conformation of monopyrenoate 10 in solution

Table ESI 8. Experimental $^3J_{HH}$ values in Hz and corresponding calculated dihedral angle ϕ (in parenthesis in degrees) of various vicinal protons of the monopyrenoate **10** in solvents of different polarity.

Supplementary Information

H-C-C-H	$CDCl_3$	DMSO-d6	Acetone-d6	CD_2Cl_2	CD_3OD	C_6D_6	CD_3CN
H1-C1-C2-H2	6.2 (-16)	6.3 (-15)	6.4 (-13)	6.1 (-18)	6.3 (-15)	6.4 (-13)	6.0 (-20)
H2-C2-C3-H3	4.6 (36)	4.4 (38)	4.3 (39)	4.7 (35)	4.7 (35)	4.3 (39)	4.6 (36)
H3-C3-C4-H4	4.6 (54)	4.5 (54)	4.5 (54)	5.0 (50)	5.0 (50)	4.4 (55)	5.2 (48)
H4-C4-C5-H5	8.9 (-161)	8.9 (-161)	8.6 (-154)	8.9 (-161)	9.0 (-164)	8.6 (-154)	8.9 (-161)
H5-C5-C6-H6	10.4 (-167)	10.3 (-167)	10.5 (-167)	10.3 (-167)	10.3 (-167)	10.5 (-167)	10.3 (-167)
H6-C6-C1-H1	8.0 (-173)	8.0 (-173)	8.0 (-173)	8.1 (-174)	8.1 (-174)	7.9 (-172)	8.3 (-177)



Supplementary Information

Figure ESI 8. Conformation of monopyrenoate **10** in $CDCl_3$ solution. The interacting donor (C6-H6) and the acceptor (O3) and the resultant boat form of the cyclitol ring are shown as capped stick model for clarity.

Thus in compounds **2-10**, the inositol ring adopts a boat conformation due to intramolecular CH…O interaction between H6 and O3. In general, more acidic C-H forms stronger bond.[12] Like in sugars, the cyclitol hydrogens are significantly acidic to form relatively strong H-bond. Steric strain around C6 may also be contributing to the increased CH acidity and hence the donor strength.[13,14]

Determination of the conformation in solid states

The solid state structures of these compounds were determined by solving their single crystal X-ray structures.

Crystal structure of dibenzoate 2

Refined formula: $C_{26}H_{28}O_8$, Formula weight: 468.48, space group: P-1, Unit cell dimensions and volume: a = 11.5979(10); b = 12.7445(11); c = 18.9854(16); V = 2521.3(4), No of formula units in the unit cell *Z*:4, Calculated density $\rho_{calcd:}$ 1.234, Linear absorption coefficient μ: 0.091, Radiation and wavelength: 0.71073 Temperature: 297K, $2\theta_{max}$; 25.0, No of measured and independent reflections: R: 0.0500 (7236), $_{w}$R 0.1222 (8860).

The dibenzoate **2** crystallized in P -1 space group with two molecules having slightly different conformations in the asymmetric unit (**Figure ESI 9**). Both the conformers (conformer A and conformer B) have distorted chair conformations for their

cyclitol ring (**Figures ESI 10 & ESI 11**). Several intermolecular interactions (**Table ESI 9**) stabilize the chair conformation of both the conformers and the overall crystal packing.

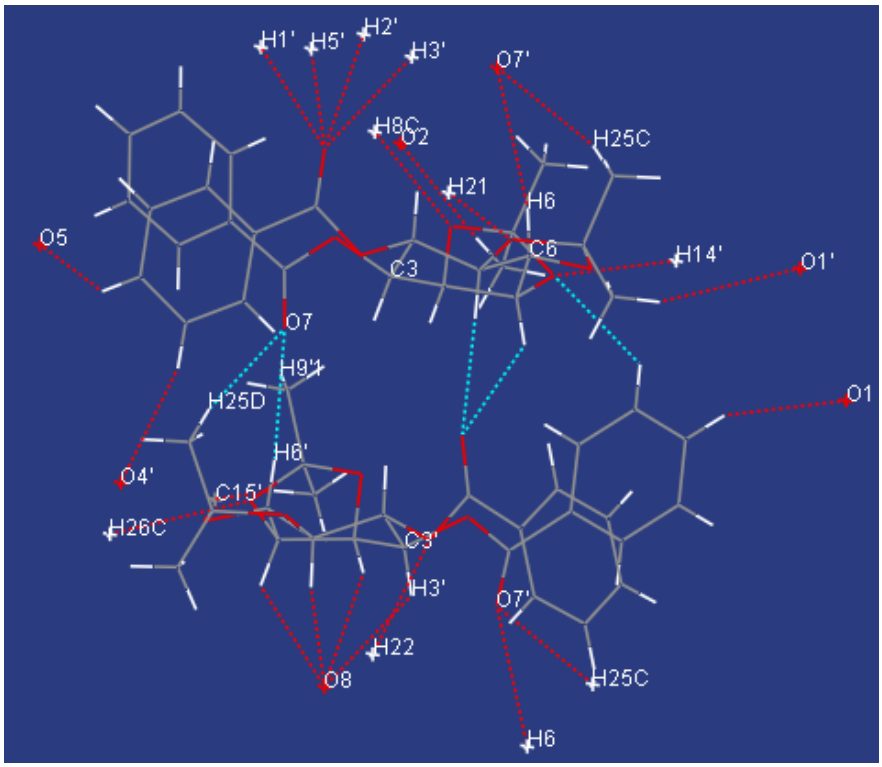


Figure ESI 9. Crystal structure of the dibenzoate **2** showing two conformers in the asymmetric unit. Also various intermolecular CH…O interactions are shown.

Table ESI 9: Intermolecular CH…O interactions in dibenzoate **2**

No	D-H…A	d (Å)	d-vdW	Angle	Symmetry operation
1	C1-H1…O8′	2.53	-0.19	135	x, y, z conformer B
2	C5-H5…O8′	2.53	-0.19	149	x, y, z conformer B
3	C21-H21…O5	2.67	-0.05	132	1-x,2-y,1-z
4	C22-H22…O4′	2.73	0.01	158	-x,2-y,1-z
5	C25-H25c…O7′	2.76	0.04	160	1+x,y,z
6	C26-H26c…O1′	2.87	0.15	159	1+x, -1+y, z

Supplementary Information

7	C8-H8c…O2	2.88	0.16	176	1-x, 2-y, -z
8	C6-H6…O7′	2.90	0.18	154	1+x,y,z
9	C1′-H1′…O8	2.44	-0.28	125	-1+x, y, z
10	C3′-H3′…O8	2.54	-0.18	125	-1+x, y, z
11	C5′-H5′…O8	2.68	-0.04	139	-1+x, y, z
12	C14′-H14′…O1	2.52	-0.20	143	1-x,1-y, -z
13	C6-H6′…O7	2.62	-0.10	170	x, y, z conformer A
14	C9′-H9′1…O7	2.56	-0.16	170	x, y, z conformer A
15	C25′-H25D…O7	2.75	0.03	170	x, y, z conformer A
16	C15′-H15′…O1	2.80	0.08	133	x, y, z conformer A

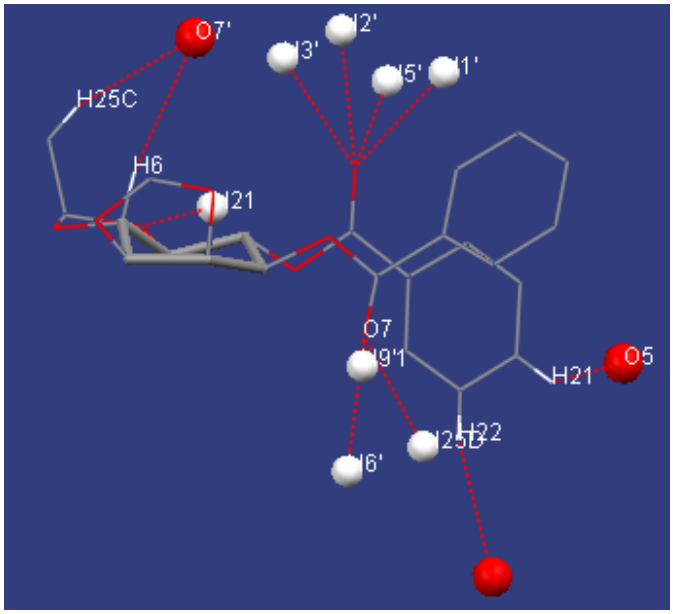


Figure ESI 10. Conformer A in the crystal structure of **2**. The chair form is highlighted at the capped stick model and the important CH…O interactions responsible for pulling the C3 end opposite to the conformationally stiff C6 end so as to form the chair conformation are highlighted.

Supplementary Information

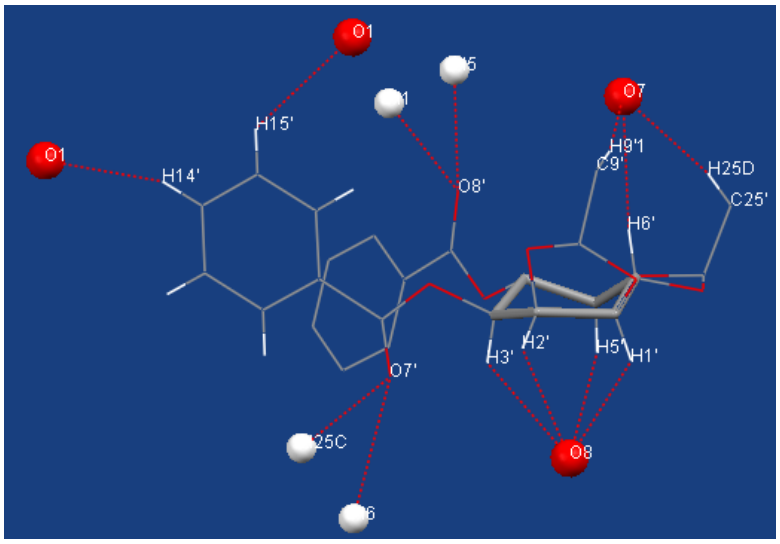


Figure ESI 11. Conformer B in the crystal structure of **2**. The chair form is highlighted as the capped stick model and the important CH…O interactions responsible for forcing C3' end to orient in a direction opposite to C6' end in order to form the chair conformation are highlighted.

Crystal structure of acetate 3

Refined formula: $C_{16}H_{24}O_8$, Formula weight: 344.35, space group: P21/c, Unit cell dimensions and volume: a = 19.6432(17); b = 10.0493(8); c = 9.1485(8); V = 1784.2(3), No of formula units in the unit cell Z:4, Calculated density $\rho_{calcd:}$ 1.282, Linear absorption coefficient μ: 0.103, Radiation and wavelength: 0.71073 Temperature: 293K, $2\theta_{max}$; 26.36, No of measured and independent reflections: R: 0.0516 (1369), $_{w}$R 0.1198 (3637).

Acetate **3** crystallizes in $P2_1/c$ space group with a single molecule in the asymmetric unit. The cyclitol ring adopts a chair conformation in consistence with the solid state conformation of **2**. As in the case of benzoate **2**, the crystal structure of acetate **3** is also dictated by intermolecular CH…O interactions alone. Each molecule is involved in twenty CH…O interactions (**Table ESI 10**) with six of its neighboring molecules.

Supplementary Information

(**Figure ESI 12**). The C3 carbon is pulled to a direction opposite to C6 mainly by four CH…O interactions (**Figure ESI 12**) stabilizing the chair conformation.

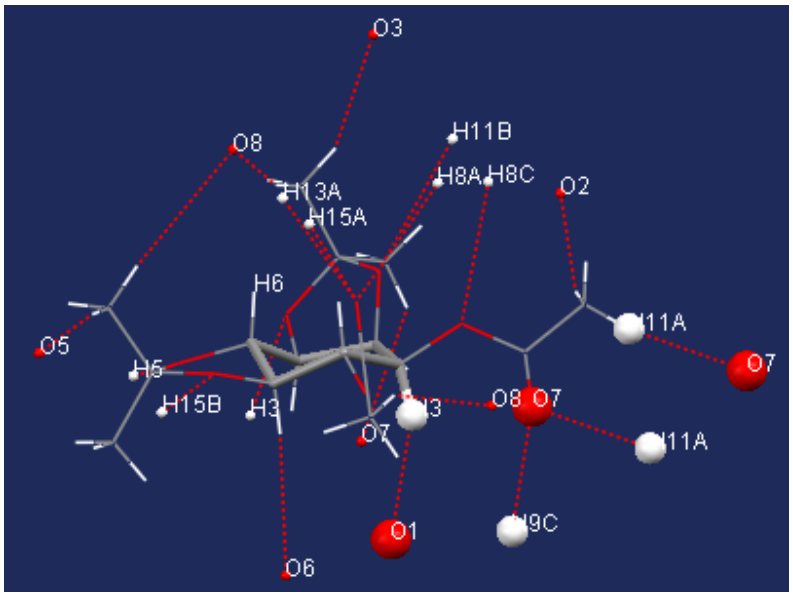


Figure ESI 12. Intermolecular CH…O interactions in the crystal structure of acetate **3**. The chair form of cyclitol ring is highlighted in capped stick model and the main CH…O interactions responsible for pulling the C3 lobe opposite to C6 is shown as ball model.

Table ESI 10. Intermolecular CH…O interactions in acetate **3**

No	D-H…A	d (Å)	d-vdW	angle	Symmetry operation
1	C11-H11a…O7	2.54	-0.18	159	-x, 1-y, -z
2	C15-H15B…O5	2.71	-0.01	171	1-x, 1-y, 1-z
3	C3-H3…O1	2.52	-0.20	148	x,1/2-y,-1/2+z
4	C13-H13A…O8	2.44	-0.28	146	x,1.5-y,-1/2+z
5	C5-H5…O6	2.83	0.11	146	x,1/2-y, -1/2+z
6	C9-H9C…O7	2.88	0.16	132	x, ½-y, ½+z
7	C11-H11B…O2	2.82	0.10	154	x, 1.5-y, -1/2+z

Supplementary Information

8	C8-H8A…O8	2.86	0.14	1623	x,1.5-y,1/2+z
9	C8-H8C…O3	2.87	0.15	134	x, 1.5-y, ½+z
10	C15-H15A…O8	2.82	0.10	175	x, 1.5-y, ½+z

Crystal structure of pivaloate 4

Refined formula: $C_{22}H_{36}O_8$, Formula weight: 428.51, space group: P-1, Unit cell dimensions and volume: a = 6.2347(3); b = 9.7994(5); c = 21.2685(12); V = 1281.64(12), No of formula units in the unit cell Z:2, Calculated density $\rho_{calcd:}$ 1.110, Linear absorption coefficient μ: 0.692, Radiation and wavelength: 1.54184 Temperature: 293K, $2\theta_{max}$; 61.74, No of measured and independent reflections: R: 0.0706 (2473), $_{w}$R 0.2389 (3898).

In the crystal of pivaloate **4,** each molecule is involved in twenty CH…O interactions (**Table ESI 11**) with seven of its neighboring molecules (**Figure ESI 13**). In consistence with benzoate **2** and acetate **3**, C3 carbon is pulled to a direction opposite to C6 mainly by intermolecular CH…O interactions (**Figure ESI 13**) stabilizing the chair conformation.

Table ESI 11. Prominent intermolecular CH…O interactions in pivaloate **4**

No	D-H…A	d (Å)	d-vdW	angle	Symmetry operation
1	C1-H1…O8	2.69	-0.03	125	1+x, y, z
2	C3-H3…O8	2.58	-0.14	130	1+x, y, z
3	C5-H5…O8	2.48	-0.24	149	1+x, y, z
4	C14-H14A…O7	2.55	-0.17	149	-1+x,y,z
5	C17-H17B…O6	2.72	0.00	165	-1+x,-1+y,z

Supplementary Information

6	C21-H21B…O5	2.65	-0.07	175	-x,1-y,-z

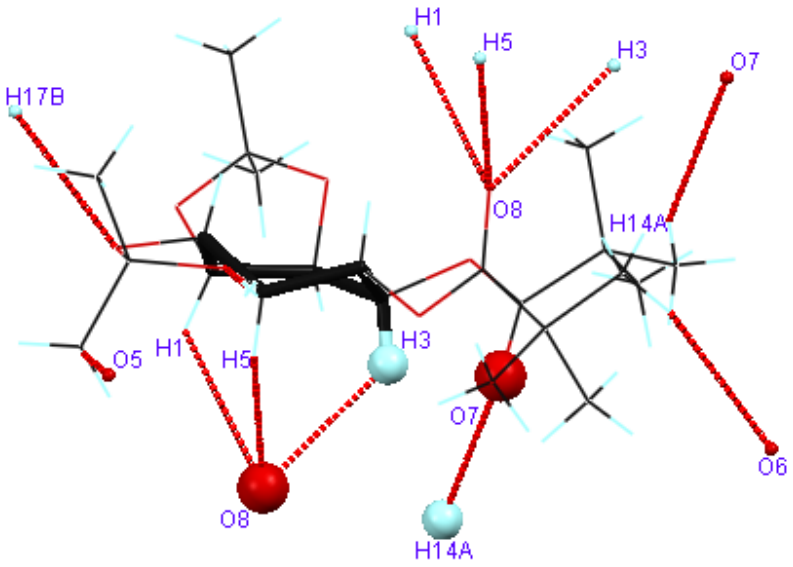


Figure ESI 13. Intermolecular CH…O interactions in crystals of pivaloate **4**. The chair form of cyclitol ring is highlighted in capped stick model and the main CH…O interactions responsible for pulling the C3 lobe opposite to C6 is shown as ball model.

Conformation of dipyrenoate 6 from Fluorescence studies

Supplementary Information

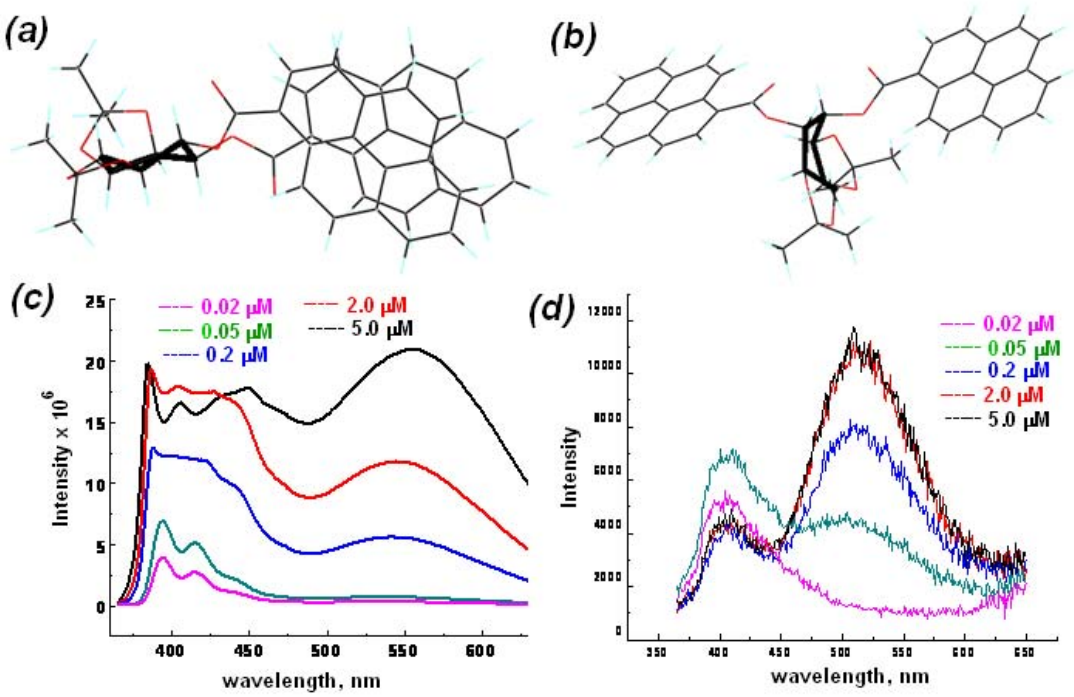


Figure ESI 14. (a) Chair conformation of **6** showing the pyrene-pyrene stacking. (b) Boat conformation of **6**. (c) Fluorescence changes in emission spectra of the dipyrenoate **6** (λ_{exn} 350 nm) with different concentration of **6** in chloroform. (d) Fluorescence changes in emission spectra of the dipyrenoate **6** in solid state (λ_{exn} 350 nm). The spectra were recorded by drop-casting a thin layer of **6** on a glass plate from its chloroform solutions of different concentrations.

Supplementary Information

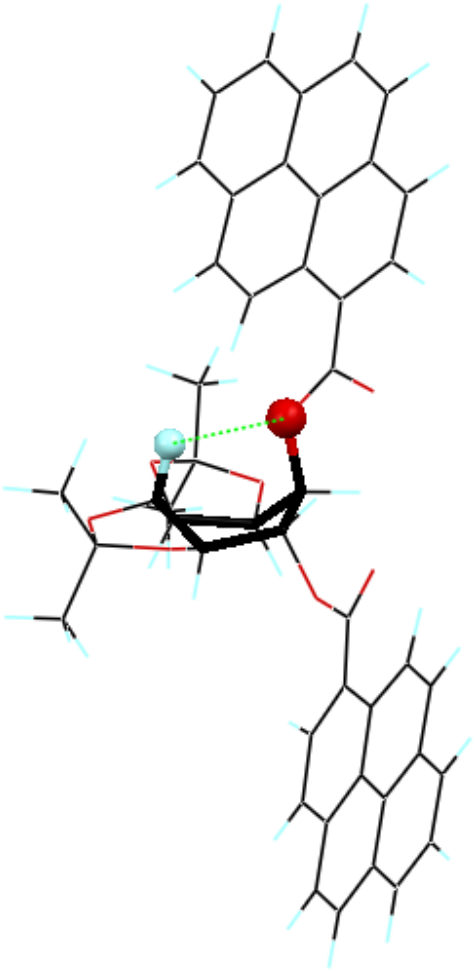


Figure ESI 15. Conformation of dipyrenoate **6** in solid. The conformation of the cyclitol ring is highlighted as capped stick model and the CH…O hydrogen bonds responsible for the particular conformation are highlighted as ball model for clarity.

Crystal structure of monobenzoate 8

Table ESI 12. Prominent intermolecular interactions in monobenzoate **8**

No	D-H…A	d (Å)	d-vdW	angle	Symmetry operation
1	C19-H19c…O4	2.486	-0.234	152	x, 1+y, z
2	C19-H19a…O1	2.825	0.105	132	x, 1.5-y, ½+z
3	C19-H19b…O5	3.011	0.291	117	x, 1+y, z

4	C16-H16c…O6	2.563	-0.157	146	-x, 1-y, -z
5	C1-H1…O5	2.594	-0.126	161	x, ½-y, -½+z
6	C2-H2…O4	2.987	0.267	126	x, ½-y, -½+z
7	C3-H3…O4	2.996	0.276	129	x, ½-y, -½+z
8	C11-H11…O2	2.837	0.117	135	1-x, -½+y, ½-z
9	C11-H11…O4	2.874	0.154	116	1-x, ½+y, ½-z
10	O4-H4…O7	2.012	-0.708	166	x, ½-y, ½+z

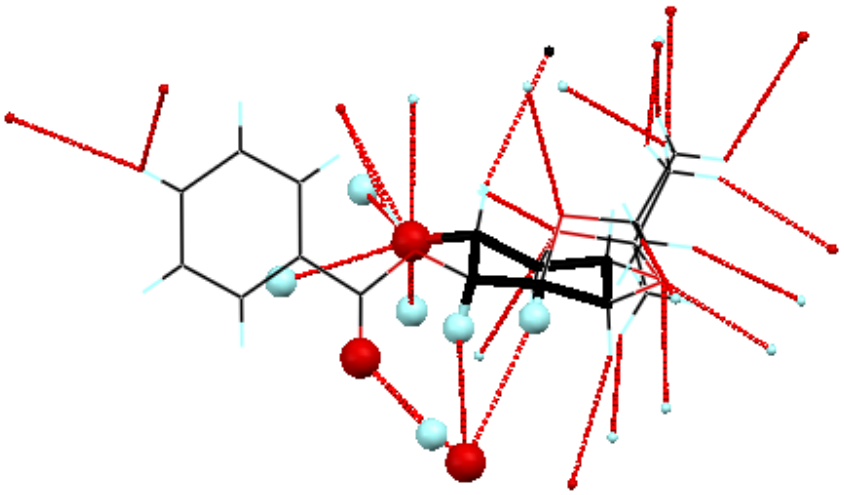


Figure ESI 16. Intermolecular interactions in crystals of monobenzoate **8**. The chair form of cyclitol ring is highlighted in capped stick model and the main interactions responsible for pulling the C3 lobe opposite to C6 is shown as ball model.

Crystal structure of mononaphthoate 9

Table ESI 13. Prominent intermolecular interactions in mononaphthoate **9**

No	D-H…A	d (Å)	d-vdW	Angle	Symmetry operation
1	C3-H3…O7	2.60	-0.12	140	1.5-x, ½+y, z

2	C2-H2…C20	2.89	-0.01	140	1-x, ½+y, ½-z
3	C2-H2…C19	2.87	-0.03	156	1-x, ½+y, ½-z
4	C1-H1…O3	2.40	-0.32	154	1.5-x, -½+y, z
5	O6-H6A…O4	1.94	-0.78	174	1.5-x, -½+y, z
6	C5-H5…O3	2.60	-0.12	151	1.5-x, -½+y, z
7	C5-H5…O4	2.69	-0.03	113	1.5-x, -½+y, z
8	C16-H16…O2	2.61	-0.11	128	½-x, -½+y, z
9	C17-H17…O1	2.67	-0.05	143	½-x, -½+y, z
10	C19-H19…O7	2.62	-0.10	146	1-x, -½+y, ½-z

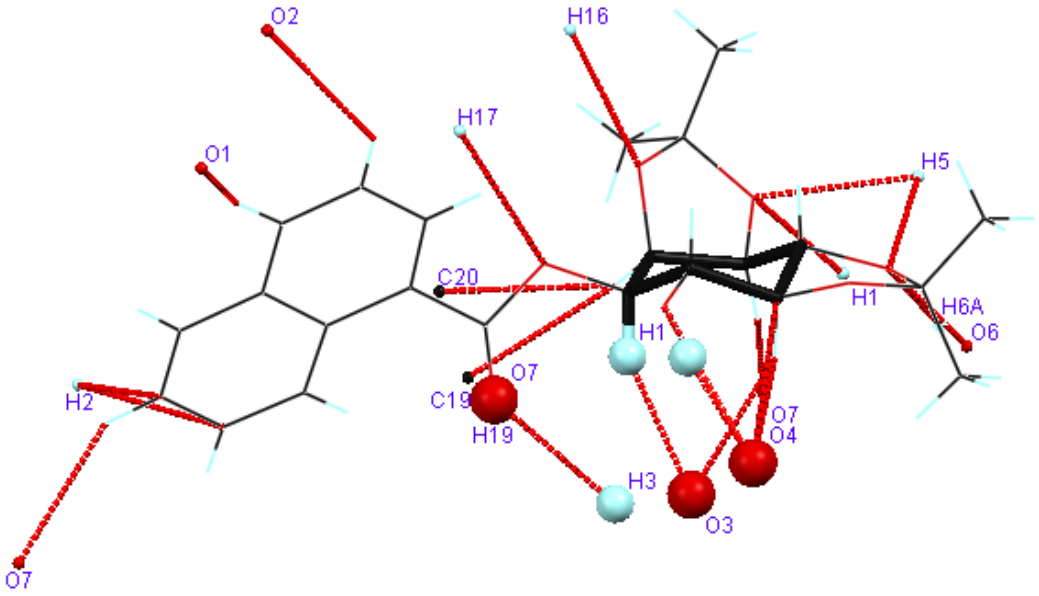


Figure ESI 17. Intermolecular interactions in crystals of mononaphthoate **9**. The chair form of cyclitol ring is highlighted in capped stick model and the main interactions responsible for pulling the C3 lobe opposite to C6 is shown as ball model.

Crystal structure of monopyrenoate 10

Supplementary Information

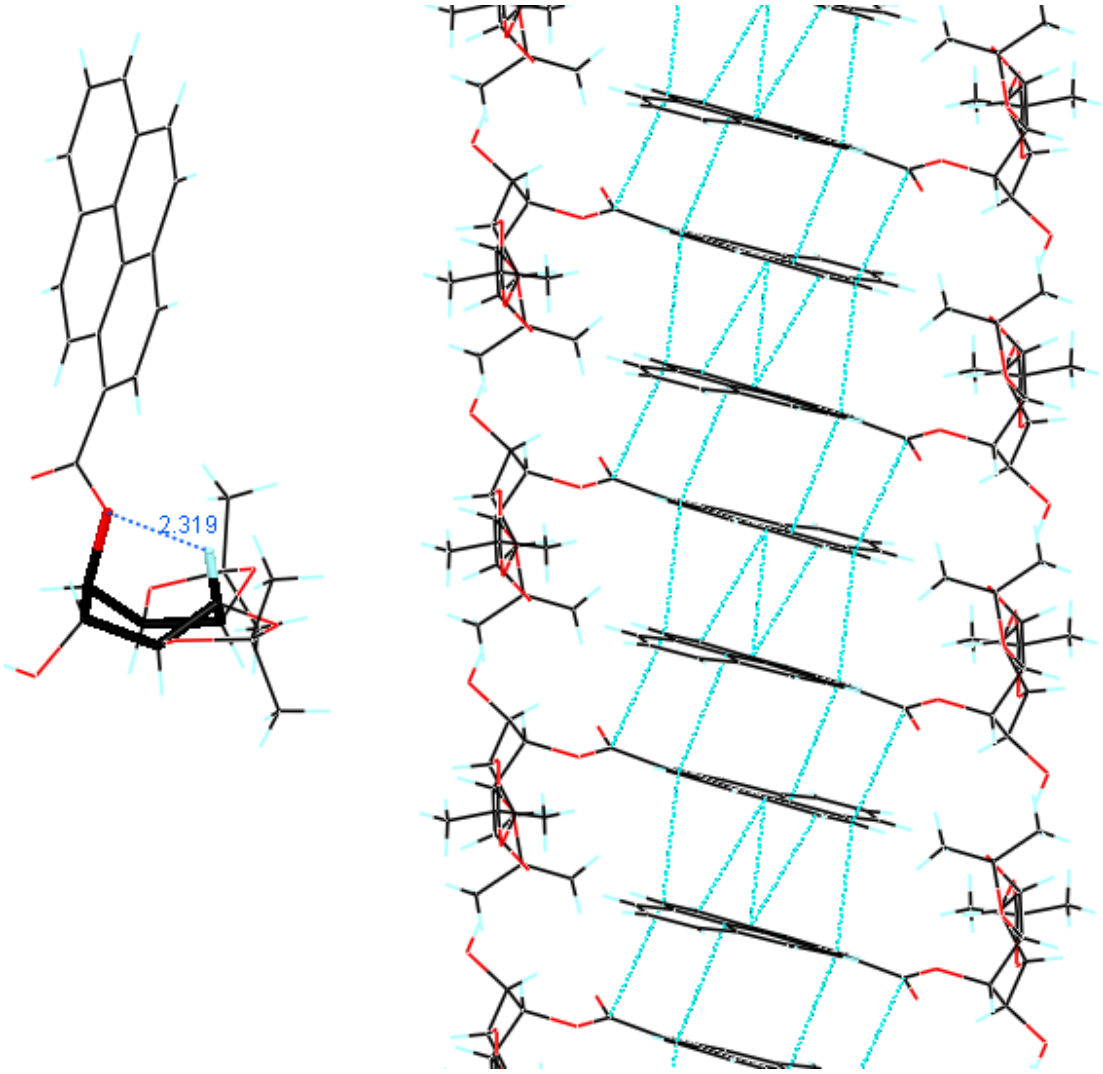


Figure ESI 18. (a) Boat conformation of monopyrenoate **10** in its crystals. Intramolecular CH…O hydrogen bond (C6-H6…O3) is shown as blue dotted line. The distance is 2.319 Å and the angle is 112.6°. (b) Crystal packing in **10**. Intermolecular π-π stacking (Stacking distance of 3.3 Å) between pyrene units to a ladder type arrangement is shown.

Table ESI 14. Prominent intermolecular interactions in monopyrenoate **10**

No	D-H…A	d (Å)	d-vdW	angle	Symmetry operation
1	C1-H1…O5	2.736	0.016	144	-x, ½+y, ½-z

Supplementary Information

2	C25-H25c…O4	2.584	-0.136	159	x,1+y, z
3	C28-H28c…O4	2.686	-0.034	124	x, ½-y, -½+z
4	C28- H28c…O1	2.75	0.031	158	x, ½-y, -½+z
5	C13-H13…O2	2.746	0.026	174	1-x, 1-y, 1-z
6	O5-H5…O7	2.092	-0.628	170	x, -1+y, z
7	Cg4…Cg4	3.6932(9)		0	1-x, -y, 1-z
8	Cg4…Cg5	3.4856(9)		1.89(7)	1-x, -y, 1-z
9	Cg4…Cg5	3.7799(9)		1.89(7)	1-x, 1-y, 1-z
10	Cg7…Cg4	3.8207(10)		2.52(7)	1-x, -y, 1-z

Cg = centroid of the phenyl ring; Cg4 = C8-C17, Cg5 = C11-C16, Cg7 = C15-C20

Supplementary Information

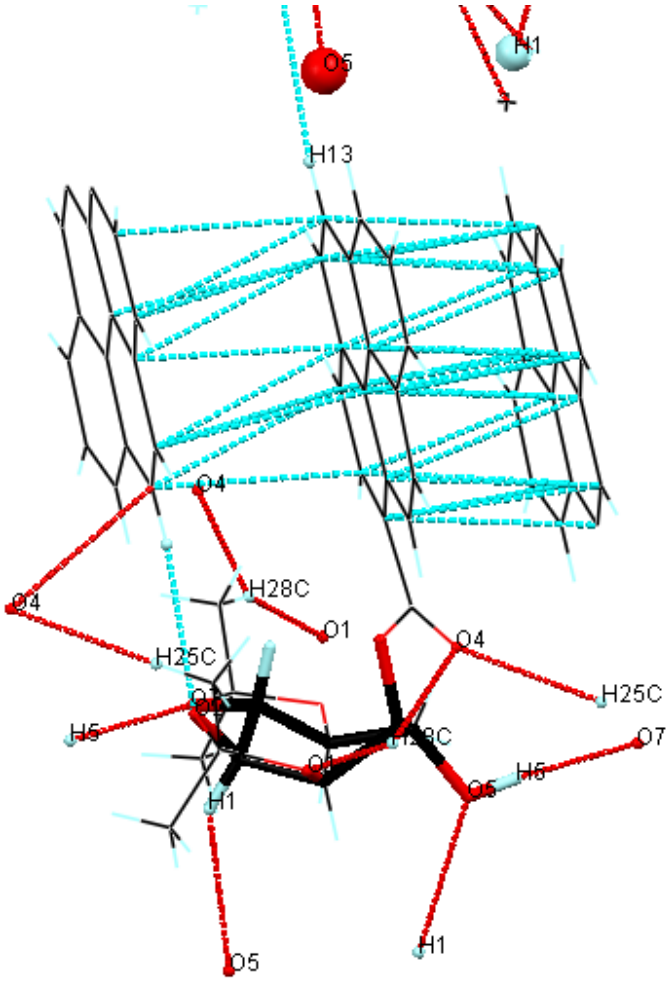


Figure ESI 19. Intermolecular interactions in crystals of monopyrenoate **10**. The boat form of cyclitol ring is highlighted in capped stick model and the main intermolecular interactions in the crystal are shown as red dotted lines.

Supplementary Information

Lattice energy calculations and estimation of interaction energies

The estimation of lattice energies for all the structures were carried out using OPROP module of the OPIX program suite[15] by summation of atom–atom pair potential energies described by the UNI force field.[16] In addition to the lattice energies, OPROP calculates molecule–molecule interaction energies and estimate the energies of the intermolecular interactions and their contribution to the overall lattice stabilization. However, the OPIX program has the limitation of considering only hydroxyl oxygen and the carbonyl oxygen as proton acceptors. The lattice energies of all the structures and the intermolecular interactions energies are given in the table below (**Table ESI 15**).

Table ESI 15. Lattice energies and the intermolecular interactions energies

Dibenzoate **2**				Lattice Energy = -249.3 KJ/mol	
No	D-H…A	H…A	∠D-H…A	Symmetry operation	Energy, kJ/mol
1	C1-H1…O8′	2.53	135	x, y, z conformer B	-19.8
2	C5-H5…O8′	2.53	149	x, y, z conformer B	-19.4
3	C1′-H1′…O8	2.44	125	-1+x, y, z	-20.6
4	C3′-H3′…O8	2.54	125	-1+x, y, z	-19.9
Acetate **3**				Lattice Energy = -176.1 KJ/mol	
1	C11-H11a…O7	2.54	159	-x, 1-y, -z	-21.6
2	C3-H3…O1	2.52	148	x,1/2-y,-1/2+z	-17.1
3	C13-H13A…O8	2.44	146	x,1.5-y,-1/2+z	-23.8
monobenzoate **8**				Lattice Energy = -194.2 KJ/mol	
1	C19-H19c…O4	2.49	152	x, 1+y, z	-21.5
2	O4-H4…O7	2.01	166	x, ½-y, ½+z	-57.7
Mononaphthoate **9**				Lattice Energy = -211.2 KJ/mol	
1	C1-H1…O3	2.40	154	1.5-x, -½+y, z	-17.9
2	O6-H6A…O4	1.94	174	1.5-x, -½+y, z	-51.6
Monopyrenoate **10**				Lattice Energy = -237.2 KJ/mol	
1	O5-H5…O7	2.09	170	x, -1+y, z	-47.0
2	C13…C7 (π…π interaction)	3.28	Dihedral angle 3.93°	1-x, -y, 1-z	-18.5

Supplementary Information

Energies of the strong O-H…O interaction fall within the range of -45 to -60 kJ/mol whereas those of all the C-H…O interactions have interaction energies in the range of -16 to -24 kJ/mol.

Ab initio Calculations

In order to understand the conformational preferences of various cyclitol derivatives better and to support our experimental findings, we have performed *ab initio* calculations on two cyclitol derivatives, **3** and **8**. The derivatives, **3** and **8** were chosen as representative examples from among the series of cyclitol derivatives that we have experimentally studied. We have used the GAUSSIAN-03 program[17] for the *ab initio* calculations. The boat and the chair form conformers of **3** and **8** were optimized at the second order Møller-Plesset perturbation (MP2) level of theory using 6-31G as the basis set. From the predicted energies for these optimized conformers, the relative energies (in kcal/mol) for the boat and the chair form of **3** were found to be 0 and 1.1 respectively, while the relative energies for the boat and the chair form of **8** were found to be 0 and 2.7 respectively. Further, the C6H6…O3 distances in the boat forms of **3** and **8** were found to be 2.367 Å and 2.368 Å respectively, much smaller than the van der Waal distance of 2.720 Å. This is suggestive of a CH…O hydrogen bonding interaction, as has been found from our experiments on a series of cyclitol derivatives. The use of high level *ab initio* calculations like MP2 theory to calculate the conformational energies of organic molecules is already well known and is employed frequently,[18] particularly because experiments to measure such small energy differences between conformers are rather difficult.

Supplementary Information

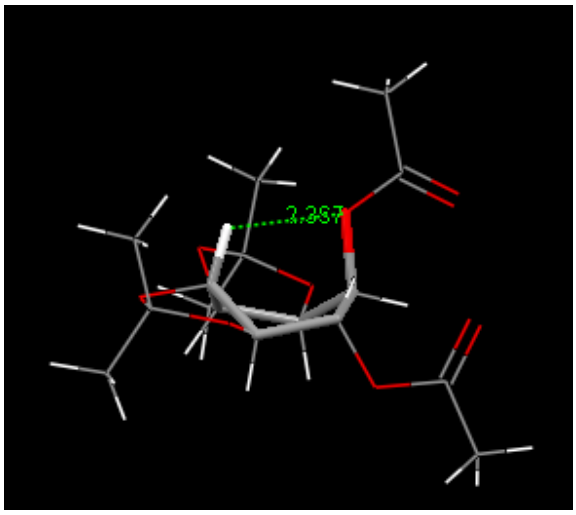


Figure ESI 20. The optimized geometry of the boat form of **3** at the MP2/6-31G level. H6…O3 distance of 2.367 Å and C6H6…O3 angle of 109.2° are in agreement with the solution conformation.

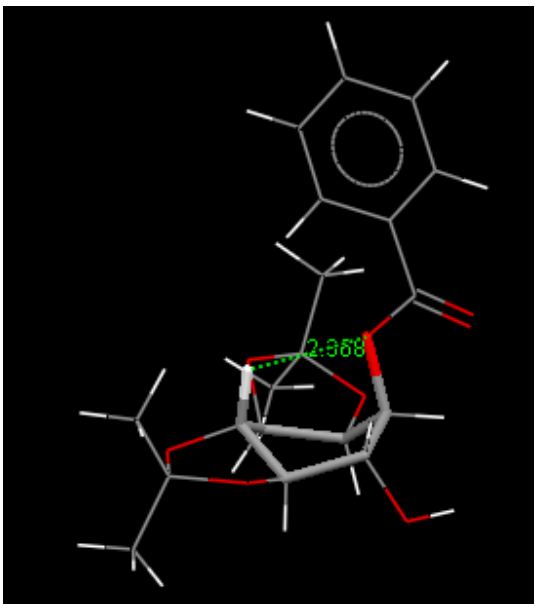


Figure ESI 21. The optimized geometry of the boat form of **8** at the MP2/6-31G level. H6…O3 distance of 2.368 Å and C6H6…O3 angle of 106.1° are in agreement with the solution conformation.

Powder XRD Experiments

Supplementary Information

(a) Dibenzoate 2: The dibenzoate **2** was crystallized from a mixture of dichloromethane and petroleum ether (1:3, v/v) and a mixture of ethyl acetate and petroleum ether (2:3, v/v) by slow evaporation. The crystals obtained from both these solvent systems (sample 1 and 2) were powdered. The residue obtained after concentration of column fractions was used as the bulk material (sample 3). The spectral data was collected at slow and continuous scan rate using Cu as anode material (Kα1(Å) = 1.54060 and Kα2 (Å) = 1.54443). The data points were collected from angle 10.0114 to 89.9794 (2θ). The experiments were carried out at 25 °C. The spectral data of the crystals obtained from two different solvent systems and the bulk material are exactly matching with each other (Figure ESI 22).

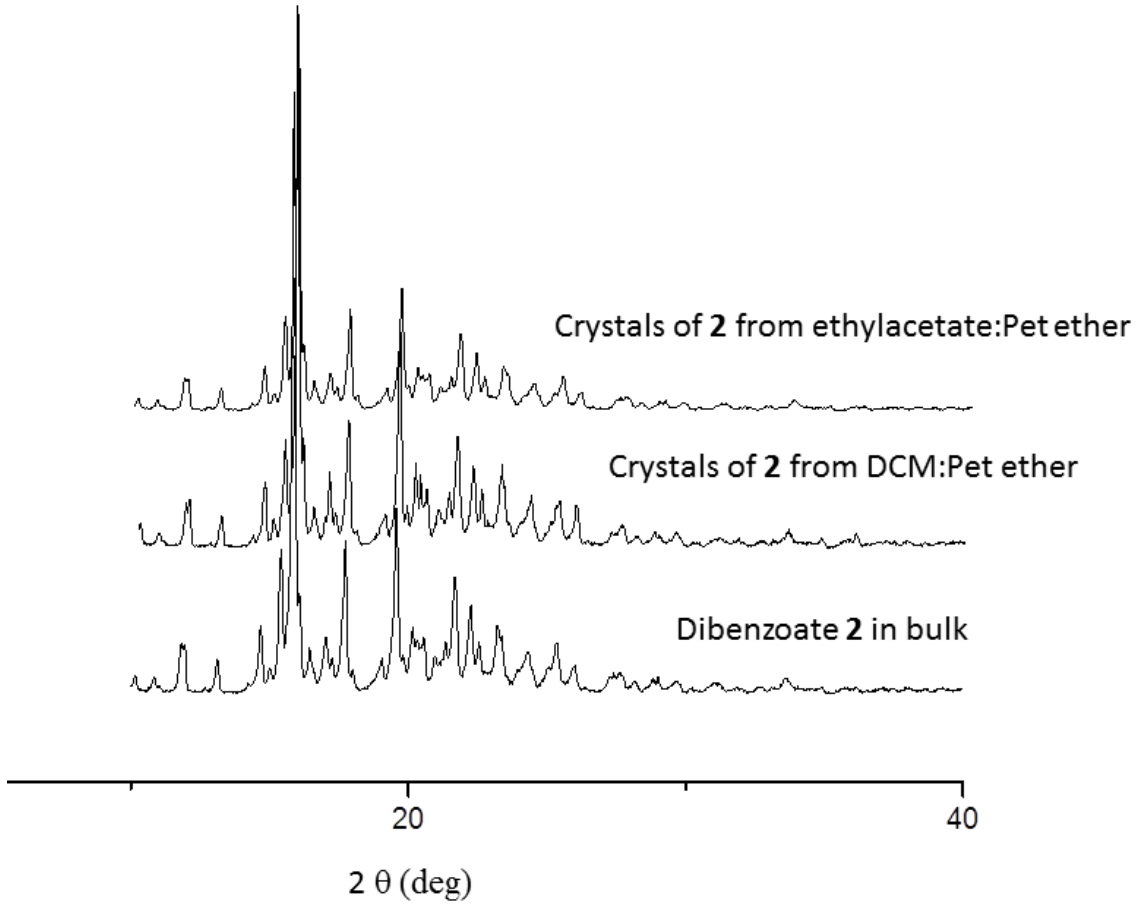


Figure ESI 22. Comparison of PXRD patterns of **2** crystallized from different solvents and the bulk powder.

(b) Diacetate 3: The diacetate **3** was crystallized by slow evaporation from a mixture of chloroform and petroleum ether (2:1, v/v). The crystals obtained were powdered before expt. The residue obtained after concentration of column fractions was used as the bulk material. The spectral data was collected at slow and continuous scan rate using Cu as anode material (Kα1(Å) = 1.54060 and Kα2 (Å) = 1.54443). The data points were collected from angle 10.0114 to 89.9794 (2θ). The experiments were carried out at 25 ^{o}C. The spectral data of the crystalline form and the bulk material are exactly matching with each other (Figure ESI 23).

Supplementary Information

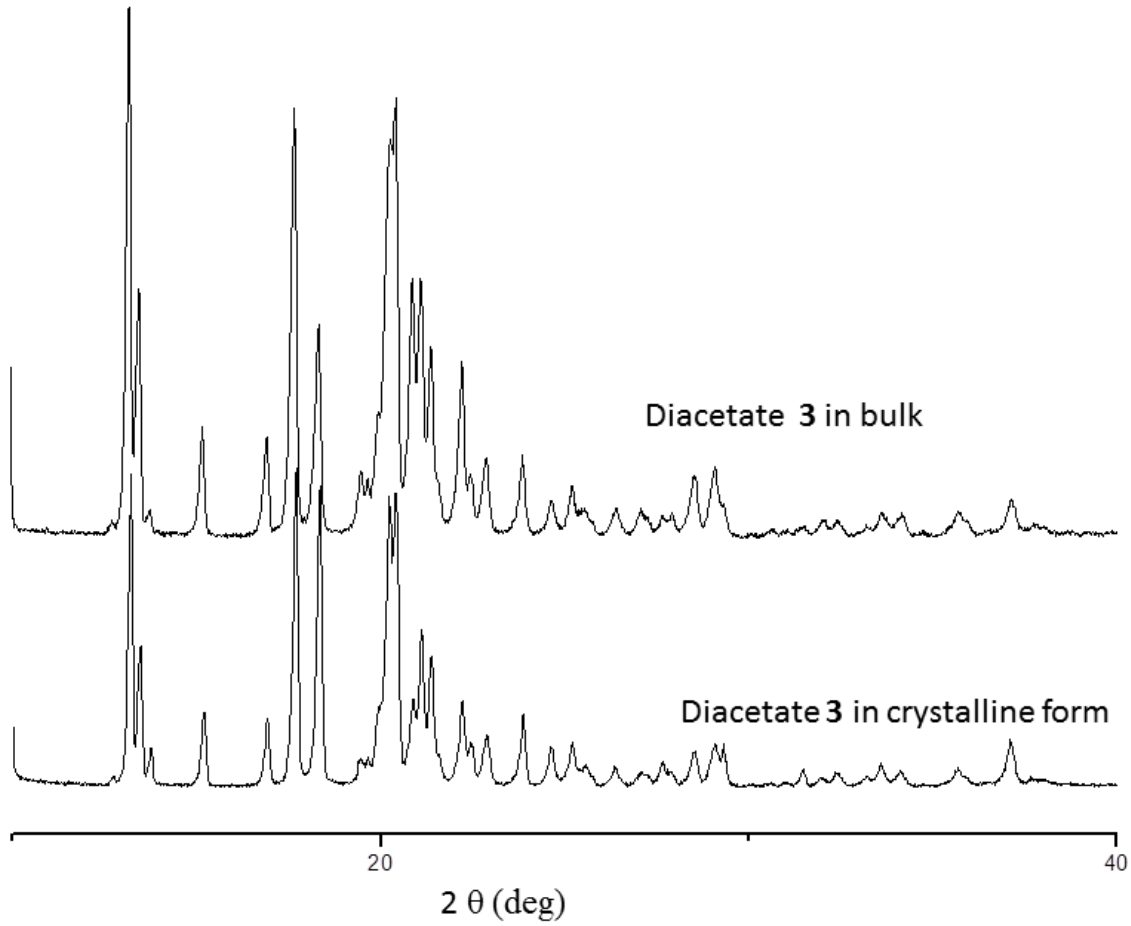


Figure ESI 23. Comparison of PXRD pattern of the crystals of **3** with the bulk powder.

These experiments rule out the possibility of polymeric forms in these compounds under the conditions of our study. Also the simulated PXRD patterns from the crystal structures of these compounds were similar to the experimental PXRD patterns.

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Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G.Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, *Gaussian Inc., Wallingford, CT*, **2003**.

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