Electronic Supplementary Information (ESI)

Cetirizine derived supramolecular topical gel in action: rational design, characterization and *in vivo* self-delivery application in treating skin allergy in mice

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E-mail addresses: ocpd@iacs.res.in, bcssj@iacs.res.in

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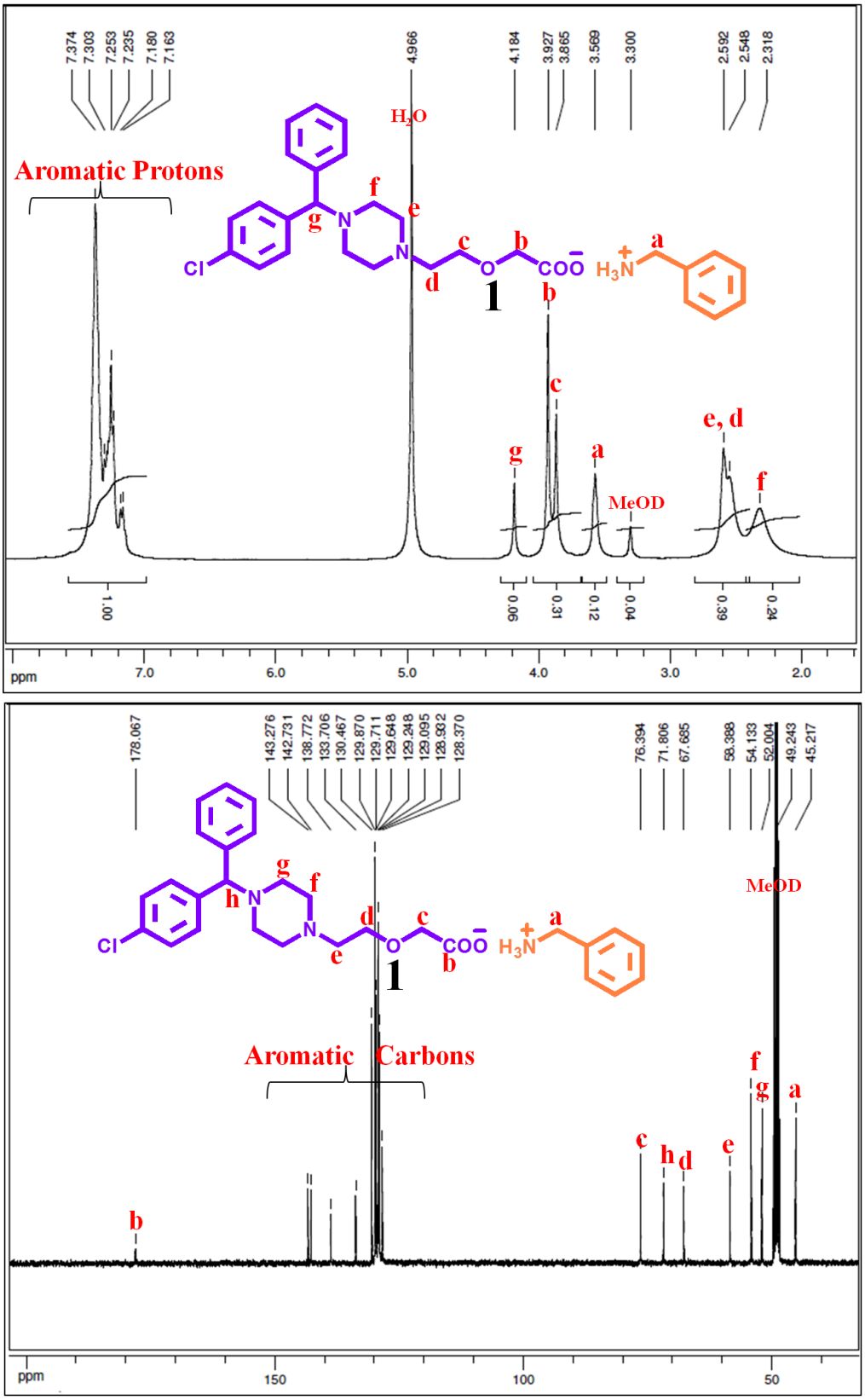

Figure S1: ^{1}H-NMR and ^{13}C-NMR spectra of **1** in MeOD.

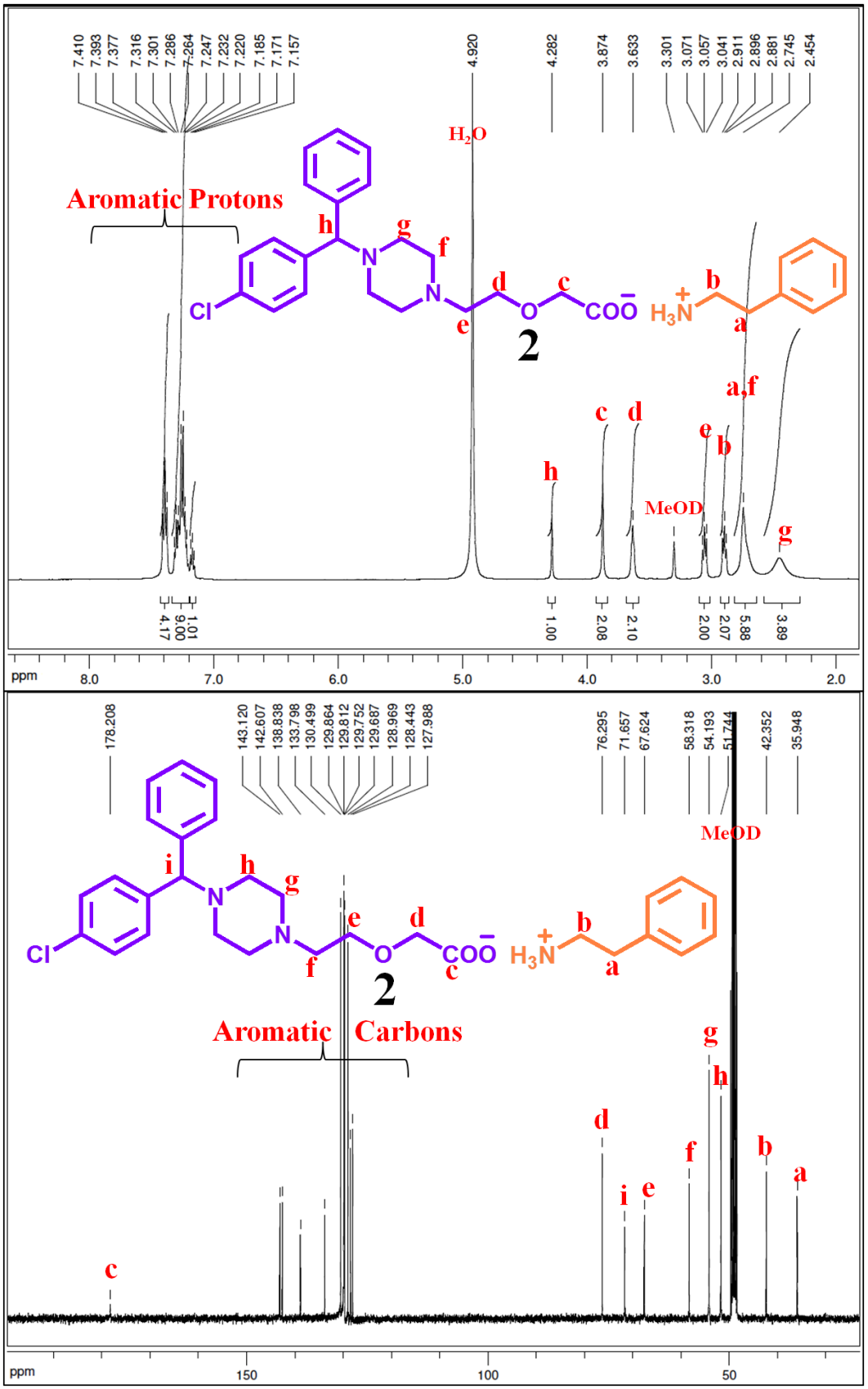

Figure S2: ^{1}H-NMR and ^{13}C-NMR spectra of **2** in MeOD.

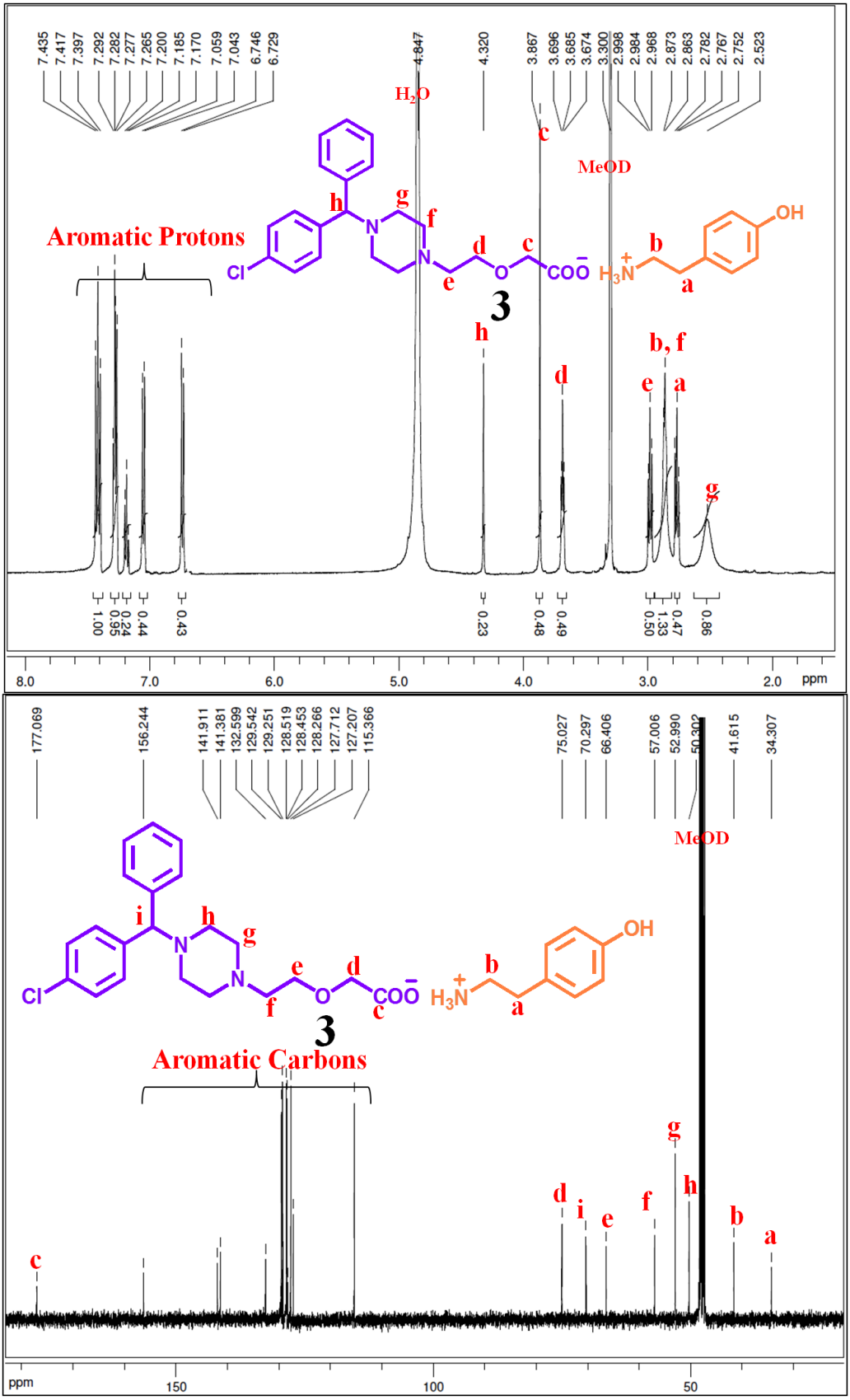

Figure S3: ^{1}H-NMR and ^{13}C-NMR spectra of **3** in MeOD.

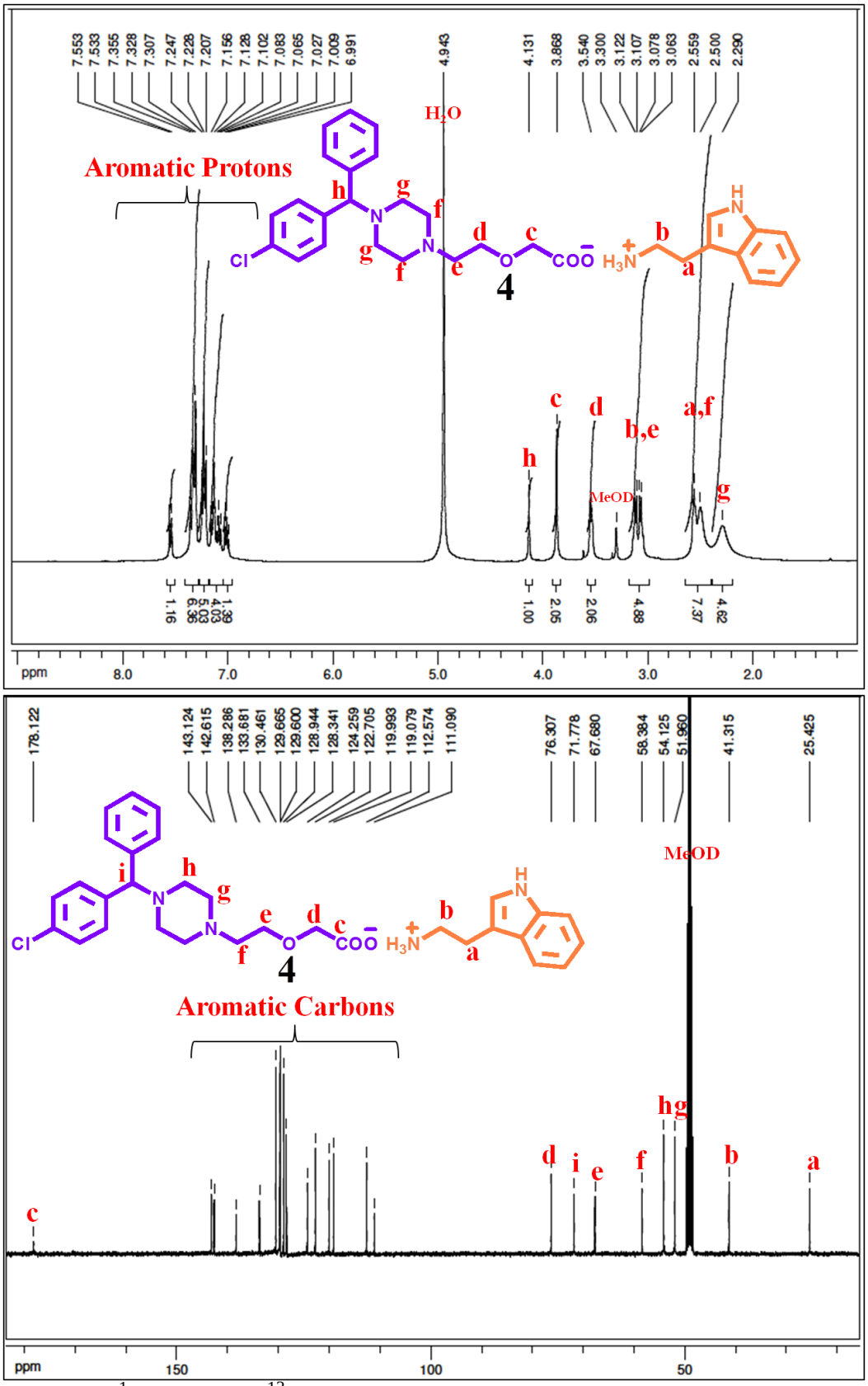

Figure S4: ^{1}H-NMR and ^{13}C-NMR spectra of **4** in MeOD.

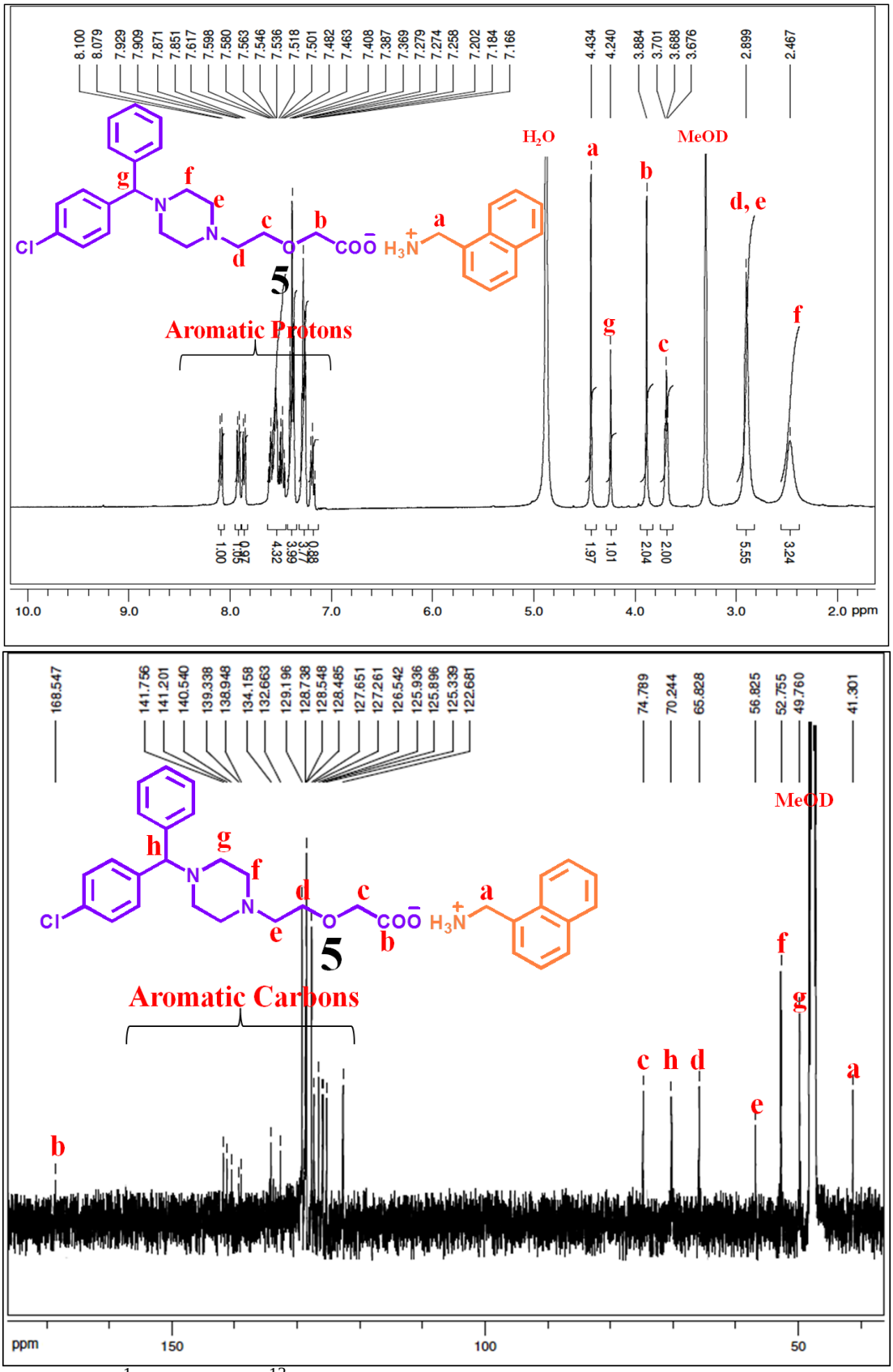

Figure S5: ^{1}H-NMR and ^{13}C-NMR spectra of **5** in MeOD.

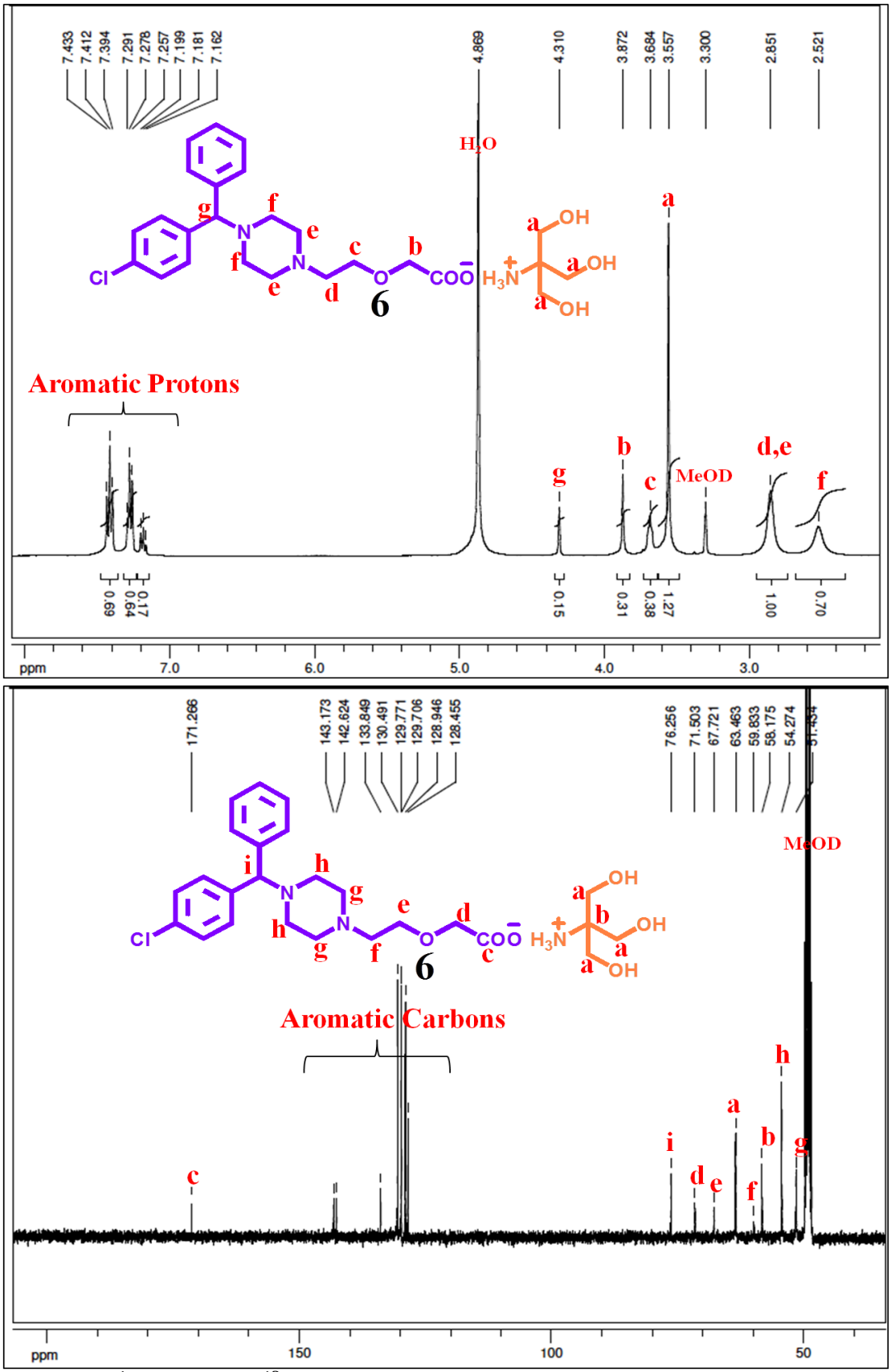

Figure S6: ^{1}H-NMR and ^{13}C-NMR spectra of **6** in MeOD.

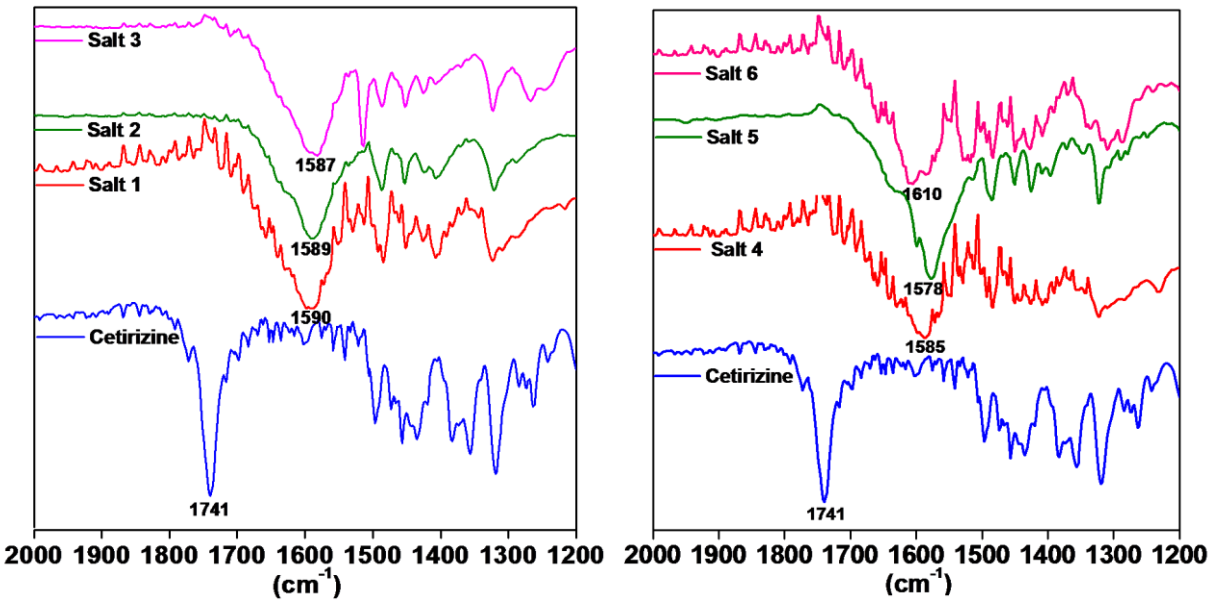

Figure S7: FT-IR spectra of cetirizine and its salts **1-6**.

Table S1: Gelation data of the salts **1-6**[a].

Solvents	**1**	**2**	**3**	**4**	**5**	**6**
Water	CS	CS	S	CS	CS	S
Ethylinglycol	S	S	S	S	S	S
Acetonitrile	S	S	S	S	P	S
Methylsalicylate	S	S	**Gel/2.0**	S	S	S
Cholorobenzene	S	S	**Gel/2.0**	S	S	S
Bromobenzene	S	S	**Gel/4.0**	S	S	S
Toluene	S	S	CS	S	S	S
o-Xylene	S	S	P	S	S	S
Mesitylene	S	S	CS	S	P	S
Nitrobenzene	S	S	**Gel/3.0**	S	S	S
DMF	S	S	S	S	S	S
DMSO	S	S	S	S	S	S
Sunflower Oil	I	I	P	I	I	I
Soyabin Oil	I	I	P	I	I	I

[a]The numerical values indicate the minimum gelator concentration (MGC) in wt % (w/v), CS=Colliodal Solution , S= Soluble , P=PPT and I= Insoluble.

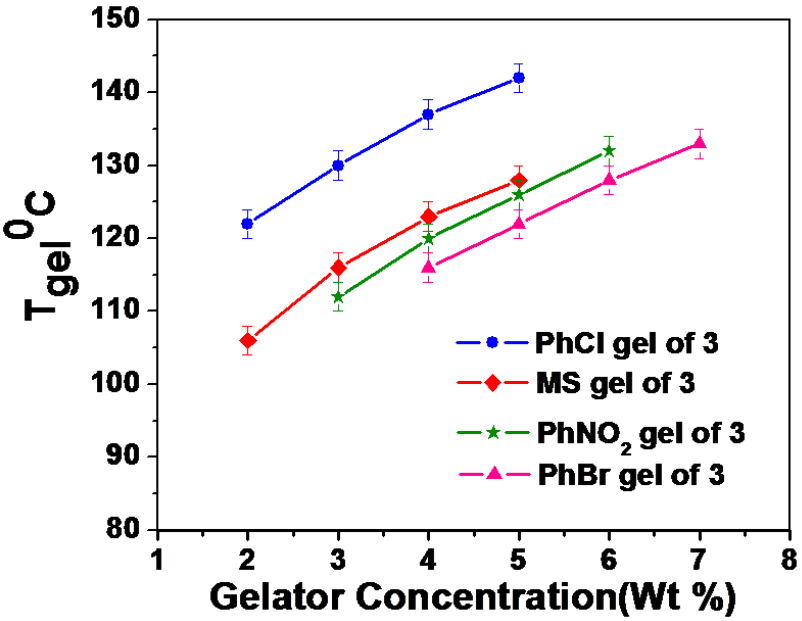

Figure S8: T_{gel} vs gelator concentration plot for the methylsalicylate (MS), chlorobenzene (PhCl), bromobenzene (PhBr) and nitrobenzene ($PhNO_2$) gels of **3**.

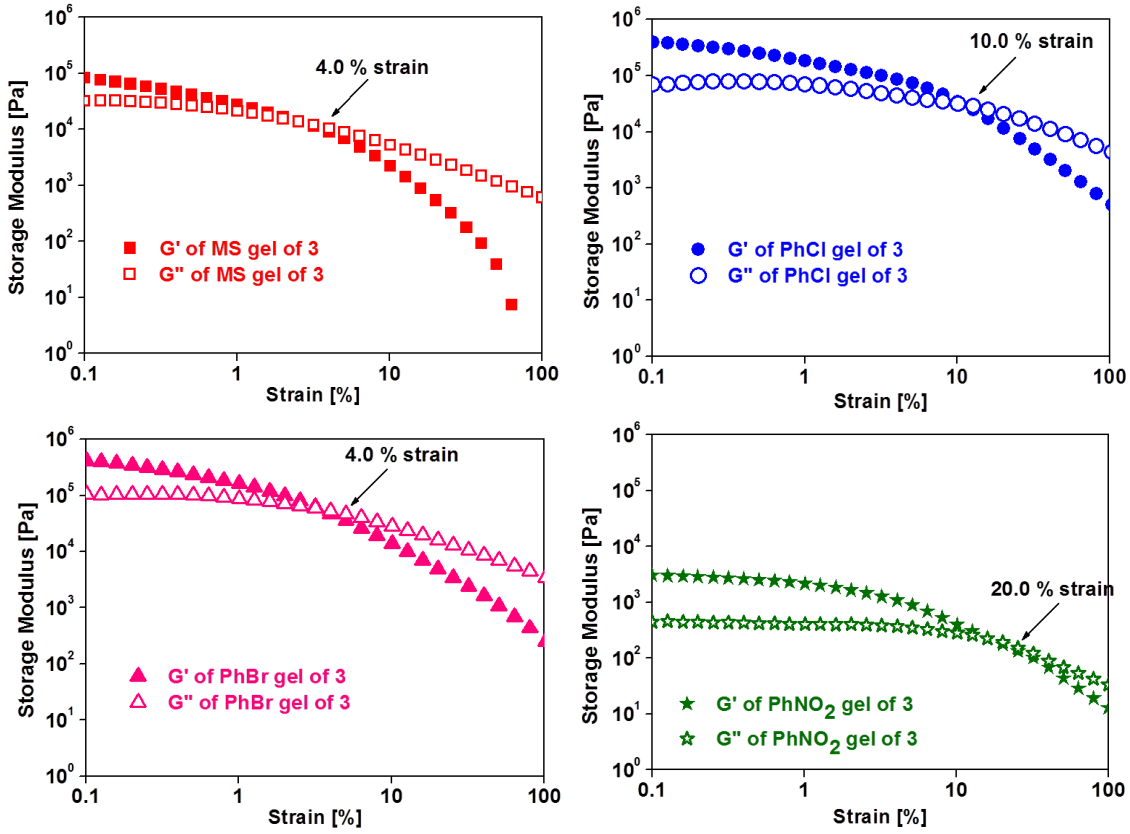

Figure S9: Strain sweep rheological behavior of 4 wt % methylsalicylate (MS), chlorobenzene (PhCl), bromobenzene (PhBr) and nitrobenzene ($PhNO_2$) gels of **3.**

Table S2: Crystallographic parameters for salt **5** and **6**.

Crystal parameters	Salt **5**	Salt **6**
CCDC No.	1053907	1053908
emp. formula	$C_{32}H_{37}N_3O_5Cl$	$C_{50}H_{82}N_6O_{17}Cl_2$
formula weight	579.09	1110.11
temp. (K)	173(2)	100(2)
λ (Å)	0.71073	0.71073
crystal system	monoclinic	triclinic
space group	*I* 2/a	*P* -1
a (Å)	15.4537(14)	10.900(11)
b (Å)	9.1572(8)	11.786(12)
c (Å)	43.467(4)	24.640(3)
α (°)	90	102.078(12)
β (°)	92.602(4)	90.025(13)
λ (°)	90	113.655(12)
V (Å^3)	6144.8(10)	2823(5)
Z	8	2
$\rho_{calc.}$ (gcm^{-3})	1.252	1.306
μ (mm^{-1})	0.168	0.188
F_{000}	2456	1188
crystal size (mm)	0.20x0.15x0.14	0.15x0.10x0.05
θ_{range} (°)	0.93 – 28.39	1.698 – 26.498
miller index ranges	-19≤*h*≤20 -11≤ *k*≤12 -57≤*l*≤56	-13≤*h*≤13 -14≤*k*≤14 -29≤*l*≤30
reflections collected	41706	36556
independent reflections	7443	11364
R_{int}	0.0940	0.1190
completeness to θ_{max} (%)	99.90	98.2
data / restraints /parameters	7443 / 24 / 373	11364 / 1534 / 740
goodness-of-fit on F^2	1.040	0.935
final *R* indices [$I>2\sigma(I)$]	R_1 = 0.0937 wR_2 = 0.02513	R_1 = 0.750 wR_2 = 0.1615
R indices (all data)	R_1 = 0.1662 wR_2 = 0.2803	R_1 = 0.1923 wR_2 = 0.1937
largest diff. peak and hole (e Å^{-3})	0.691 and -0.388	1.379 and -0.474

Table S3: Hydrogen bond parameters for salt **5** [Å and °].

D–H····A	d(H····A)	d(D····A)	<(DHA)	Symmetry transformations
N(1)-H(1A)...N(2)	2.1	2.982(5)	162.1	x,y,z
N(1)-H(1B)...O(1)	1.85	2.745(4)	166.8	x,y,z
N(1)-H(1C)...O(2)	1.96	2.811(4)	156	-x+1/2,y,-z
O(5)-H(5A)...O(2)	1.83	2.696(5)	173.3	-x,-y+1,-z
O(5)-H(5B)...O(6)	1.95	2.789(5)	160.3	x,y,z

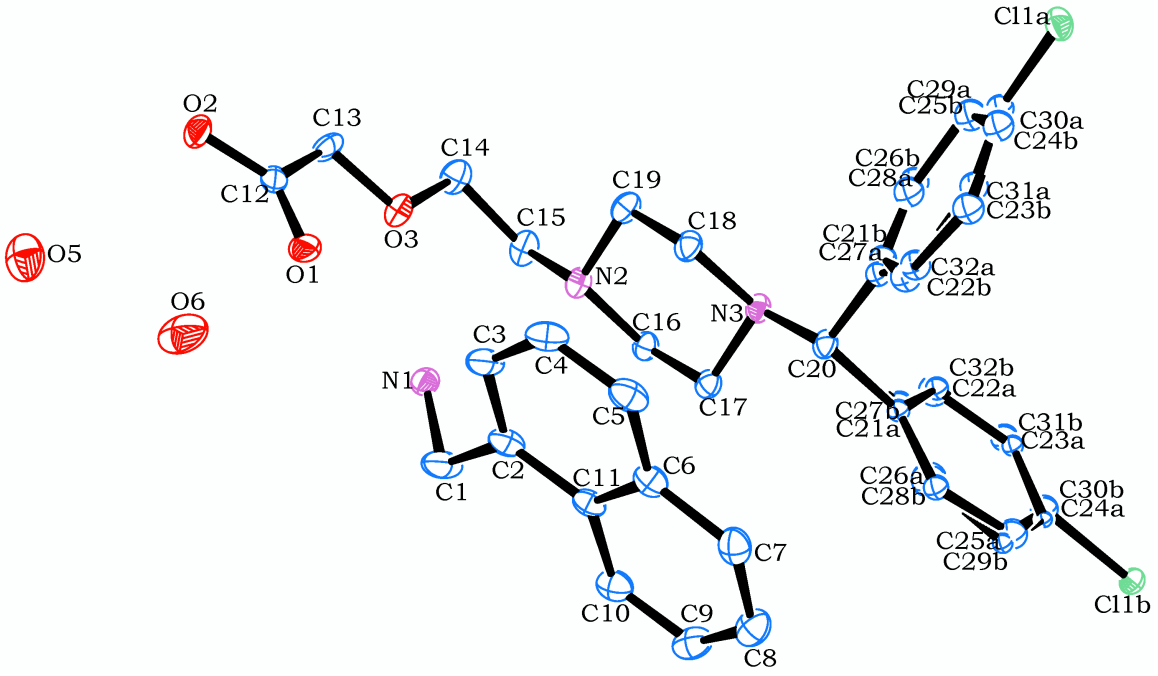

Figure S10: ORTEP representation of crystal structure of salt **5** (Thermal ellipsoids are drawn with 50% probability level).

Table S4: Hydrogen bond parameters for salt **6** [Å and °].

D–H····A	d(H····A)	d(D····A)	<(DHA)	Symmetry transformations
N(5)-H(5E)...O(5)	1.97	2.776(4)	146.4	-x+2,-y+1,-z
N(5)-H(5C)...O(11)	1.9	2.781(5)	163.4	-x+1,-y,-z
N(5)-H(5D)...O(16)	1.94	2.817(5)	161.7	x,y,z
O(7)-H(7)...O(5)	1.82	2.658(4)	175.2	x-1,y,z
O(8)-H(8)...O(12)	1.91	2.715(4)	161.6	-x,-y,-z
O(9)-H(9)...O(3)	1.88	2.703(4)	165.4	x+1,y,z
N(6)-H(6C)...O(6)	1.96	2.853(5)	167.2	-x+1,-y,-z
O(10)-H(10)...O(14)	1.91	2.741(4)	173.5	x,y,z
O(11)-H(11)...O(3)	1.83	2.672(4)	175.4	x+1,y,z
O(12)-H(12)...O(15)	1.89	2.702(4)	162.8	-x,-y,-z
O(17)-H(17C)...O(7)	1.97	2.784(4)	155.3	x,y,z
O(16)-H(16C)...N(4)	2.01	2.883(5)	179.2	x,y,z
O(16)-H(16D)...O(6)	1.91	2.775(4)	174.5	x,y,z
O(14)-H(14C)...O(2)	1.9	2.766(4)	175.8	x,y,z
O(15)-H(15D)...O(2)	1.88	2.728(4)	163.7	x,y,z
O(15)-H(15C)...O(16)	1.99	2.856(5)	177.2	x-1,y,z

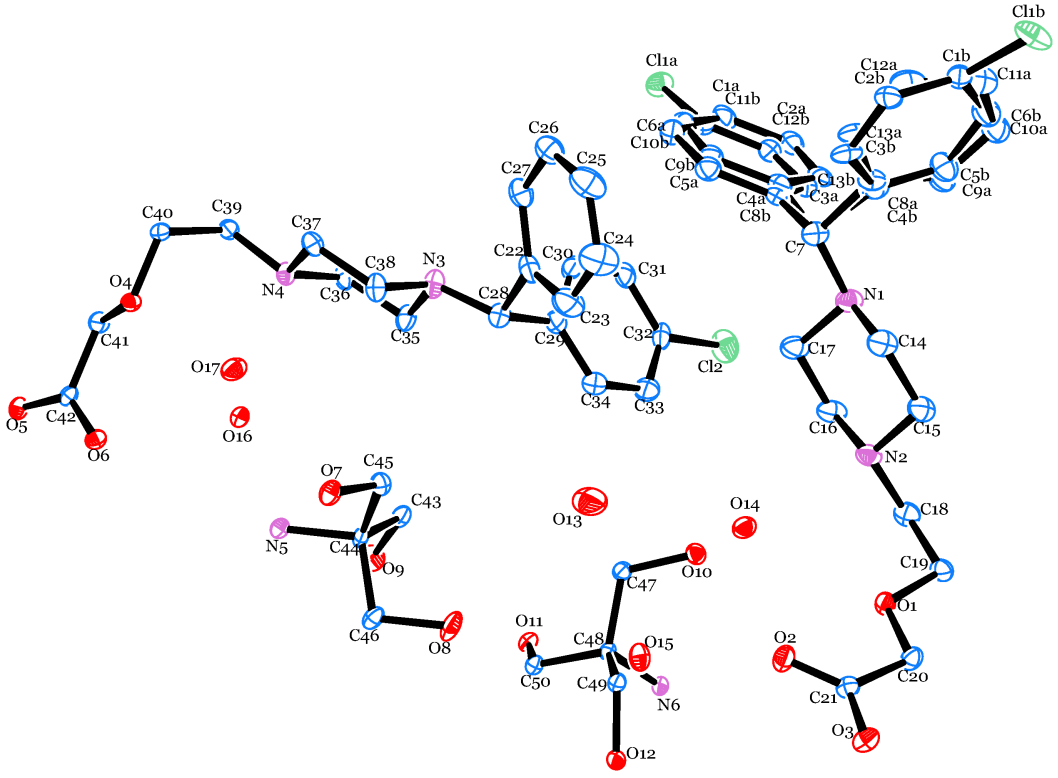

Figure S11: ORTEP representation of crystal structure of salt **6** (Thermal ellipsoids are drawn with 50% probability level).

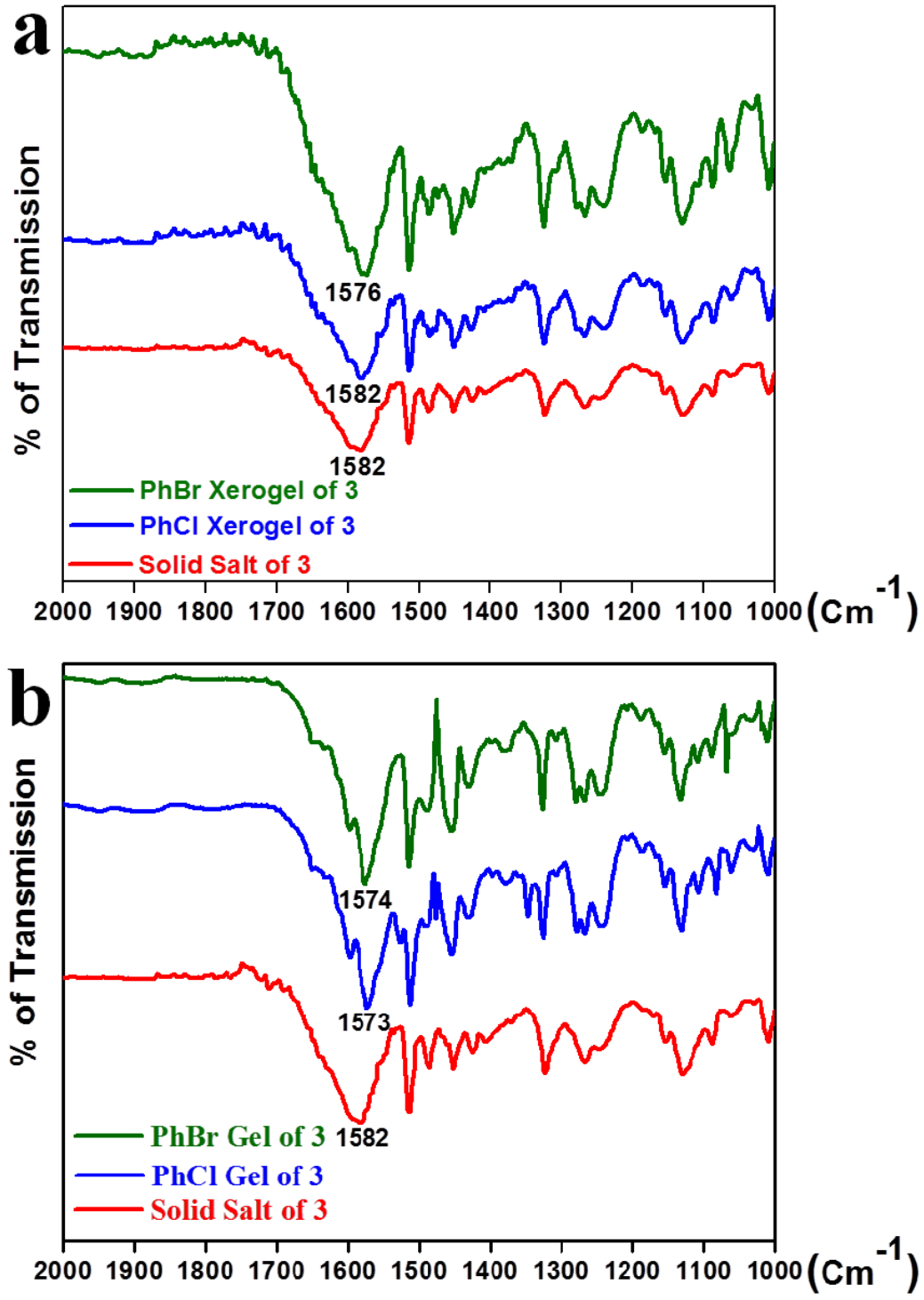

Figure S12: FT-IR spectra of salt **3** in its chlorobenzene (PhCl) and bromobenzene (PhBr) xerogel (a) and gel (b) state.

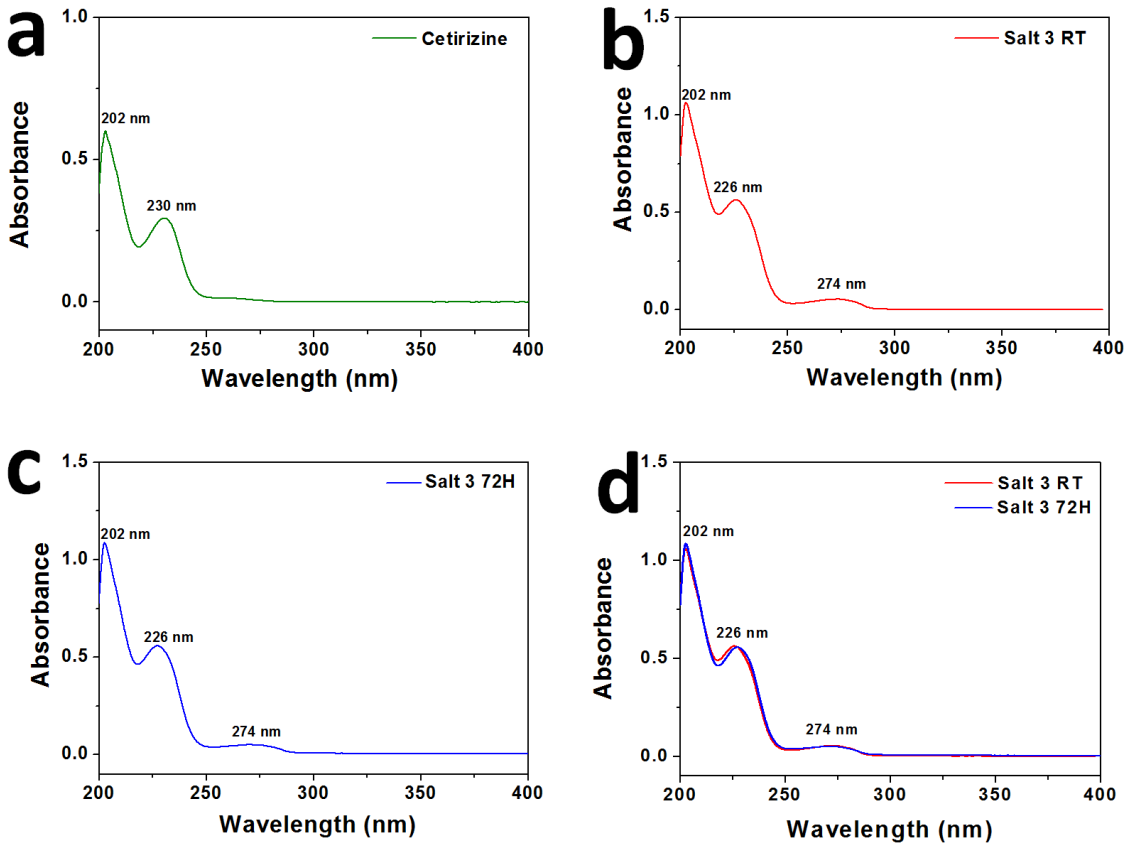

Figure S13: UV-Visible absorbance spectra of cetirizine and its salt **3**; a) UV- Visible spectrum of cetirizine in PBS; b) UV- Visible spectrum of gelator salt **3** in PBS at room temperature (RT)**;** c) UV- Visible spectra of gelator salt **3** after 72 h incubation with PBS and d) UV- Visible spectra of gelator salt **3** at RT and after 72 h incubation with PBS.

Check CIF/ PLATON Report of salt 5

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You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: JM205_0m

Bond precision: C-C = 0.0064 A Wavelength=0.71073

Cell: a=15.4537(14) b=9.1572(8) c=43.467(4)
alpha=90 beta=92.602(4) gamma=90
Temperature: 173 K

	Calculated	Reported
Volume	6144.8(10)	6144.8(10)
Space group	I 2/a	I 2/a
Hall group	-I 2ya	-I 2ya
Moiety formula	C21 H23 Cl N2 O3, C11 H12 N, H2 O, O	C21 H23 Cl N2 O3, C11 H12 N, H2 O, O
Sum formula	C32 H37 Cl N3 O5	C32 H37 Cl N3 O5
Mr	579.10	579.09
Dx,g cm-3	1.252	1.252
Z	8	8
Mu (mm-1)	0.168	0.168
F000	2456.0	2456.0
F000'	2458.23	
h,k,lmax	20,12,58	20,12,57
Nref	7702	7443
Tmin,Tmax	0.970,0.977	0.625,0.746
Tmin'	0.967	

Correction method= # Reported T Limits: Tmin=0.625 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.966 Theta(max)= 28.391

R(reflections)= 0.0937(4167) wR2(reflections)= 0.2803(7443)

S = 1.040 Npar= 373

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level A

PLAT201_ALERT_2_A Isotropic non-H Atoms in Main Residue(s) ..... 12 Report

Author Response: These are disordered C atoms with partial occupancy for which an anisotropic refinement was not permissible. The reflections-to-parameters ratio is also quite low already and should not be impaired by adding further thermal parameters.

Alert level B

PLAT306_ALERT_2_B Isolated Oxygen Atom (H-atoms Missing ?) ..... O6 Check

Author Response: H atoms of water molecule O6 were not located since there was no enough electron density at reasonable distances to be assigned as H atoms.

PLAT430_ALERT_2_B Short Inter D...A Contact O1 .. O6 .. 2.83 Ang.

Author Response: Since H atoms for the water molecules could not be located form the Fourier difference map, it assumes a short contact due to missing H-atoms.

PLAT430_ALERT_2_B Short Inter D...A Contact O6 .. O6 .. 2.77 Ang.

Alert level C

RFACR01_ALERT_3_C The value of the weighted R factor is > 0.25
Weighted R factor given 0.280
PLAT084_ALERT_3_C High wR2 Value (i.e. > 0.25) ..... 0.28 Report
PLAT220_ALERT_2_C Large Non-Solvent C Ueq(max)/Ueq(min) Range 4.8 Ratio
PLAT222_ALERT_3_C Large Non-Solvent H Uiso(max)/Uiso(min) ... 4.4 Ratio
PLAT241_ALERT_2_C High Ueq as Compared to Neighbors for ..... C1 Check
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds ..... 0.0064 Ang.
PLAT410_ALERT_2_C Short Intra H...H Contact H1D .. H10 .. 1.95 Ang.

Alert level G

PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite 24 Note
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..... 5 Report
PLAT072_ALERT_2_G SHELXL First Parameter in WGHT Unusually Large. 0.13 Report
PLAT083_ALERT_2_G SHELXL Second Parameter in WGHT Unusually Large. 17.20 Why ?
PLAT172_ALERT_4_G The CIF-Embedded .res File Contains DFIX Records 24 Report
PLAT300_ALERT_4_G Atom Site Occupancy of >Cl1B is Constrained at 0.654 Check
PLAT300_ALERT_4_G Atom Site Occupancy of <Cl1A is Constrained at 0.346 Check
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PLAT301_ALERT_3_G Main Residue  Disorder ..... Percentage =        33 Note
PLAT432_ALERT_2_G Short Inter X...Y Contact  Cl1A   ..  C8      ..      3.22 Ang.
PLAT811_ALERT_5_G No ADDSYM Analysis: Too Many Excluded Atoms ....         ! Info
PLAT860_ALERT_3_G Number of Least-Squares Restraints .............        24 Note
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  1 ALERT level A = Most likely a serious problem - resolve or explain
  3 ALERT level B = A potentially serious problem, consider carefully
  7 ALERT level C = Check. Ensure it is not caused by an omission or oversight
 35 ALERT level G = General information/check it is not something unexpected

  0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
 11 ALERT type 2 Indicator that the structure model may be wrong or deficient
  6 ALERT type 3 Indicator that the structure quality may be low
 27 ALERT type 4 Improvement, methodology, query or suggestion
  2 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

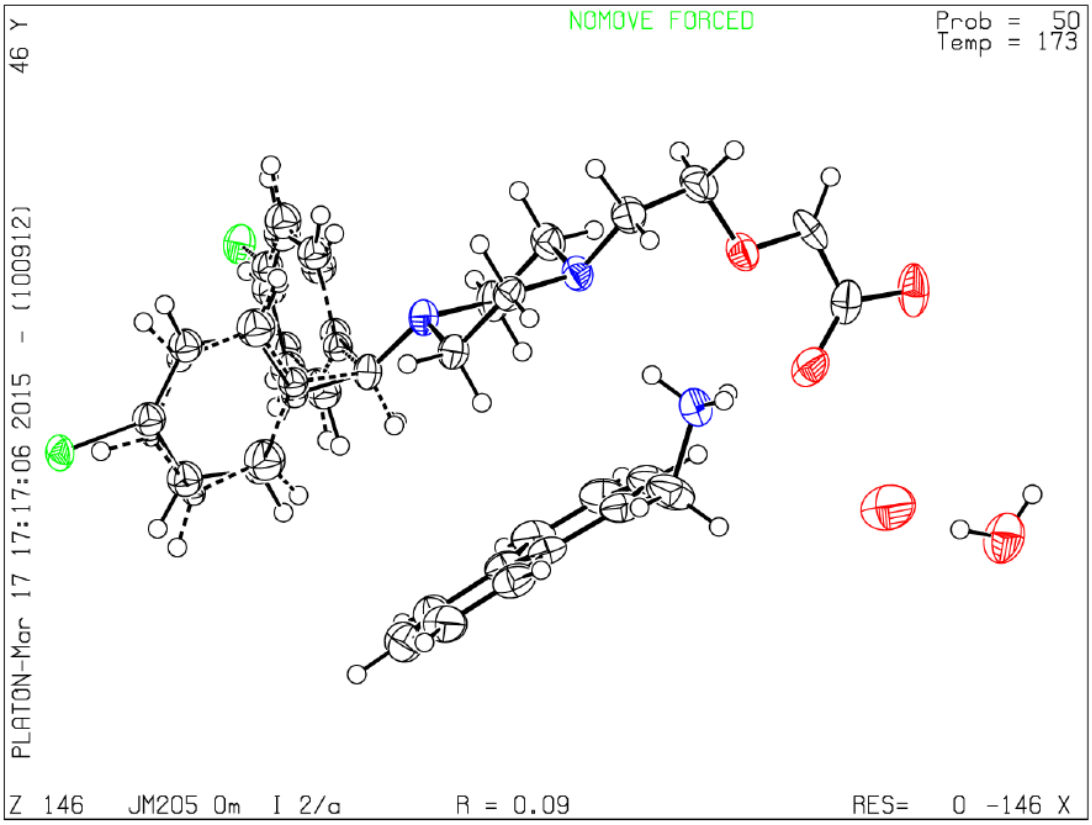
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 29/01/2015; check.def file version of 29/01/2015

Datablock JM205_0m - ellipsoid plot



Check CIF/ PLATON Report of salt 6

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: jm0206ln_0m

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alpha=102.078(12) beta=90.025(13) gamma=113.655(12)
Temperature: 100 K

	Calculated	Reported
Volume	2823(5)	2823(5)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	2(C21 H24 Cl N2 O3), 2(C4 H12 N O3), 5(H2 O)	2(C21 H24 Cl N2 O3), 2(C4 H12 N O3), 5(H2 O)
Sum formula	C50 H82 Cl2 N6 O17	C50 H82 Cl2 N6 O17
Mr	1110.12	1110.11
Dx,g cm-3	1.306	1.306
Z	2	2
Mu (mm-1)	0.188	0.188
F000	1188.0	1188.0
F000'	1189.19	
h,k,lmax	13,14,30	13,14,30
Nref	11709	11364
Tmin,Tmax	0.978,0.991	0.678,0.745
Tmin'	0.972	

Correction method= MULTI-SCAN

Data completeness= 0.971 Theta(max)= 26.498

R(reflections)= 0.0741(5158) wR2(reflections)= 0.1891(11364)

S = 0.924 Npar= 754

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level B

PLAT417_ALERT_2_B Short Inter D-H..H-D H15C .. H16C .. 2.09 Ang.

Author Response: The H atoms bonded to the O atoms of the solvent water atoms were based on the most likely location for these atoms to be involved in O-H...O hydrogen bonding. The idealized positions for the H atoms is reflected in the close intermolecular distances.

Alert level C

DIFMX01_ALERT_2_C The maximum difference density is > 0.1*ZMAX*0.75
_refine_diff_density_max given = 1.358
Test value = 1.275
DIFMX02_ALERT_1_C The maximum difference density is > 0.1*ZMAX*0.75
The relevant atom site should be identified.

PLAT026_ALERT_3_C	Ratio Observed / Unique Reflections too Low	45 %
PLAT029_ALERT_3_C	_diffrn_measured_fraction_theta_full Low	0.970 Note
PLAT094_ALERT_2_C	Ratio of Maximum / Minimum Residual Density	2.88 Report
PLAT097_ALERT_2_C	Large Reported Max. (Positive) Residual Density	1.36 eA-3
PLAT148_ALERT_3_C	su on the a - Axis is (Too) Large	0.011 Ang.
PLAT148_ALERT_3_C	su on the b - Axis is (Too) Large	0.012 Ang.
PLAT148_ALERT_3_C	su on the c - Axis is (Too) Large	0.030 Ang.
PLAT245_ALERT_2_C	U(iso) H13C Smaller than U(eq) O13 by ...	0.019 AngSq
PLAT245_ALERT_2_C	U(iso) H13D Smaller than U(eq) O13 by ...	0.019 AngSq
PLAT340_ALERT_3_C	Low Bond Precision on C-C Bonds	0.0067 Ang.

Alert level G

PLAT002_ALERT_2_G	Number of Distance or Angle Restraints on AtSite	30 Note
PLAT003_ALERT_2_G	Number of Uiso or Uij Restrained non-H Atoms ...	88 Report
PLAT007_ALERT_5_G	Number of Unrefined Donor-H Atoms	19 Report
PLAT171_ALERT_4_G	The CIF-Embedded .res File Contains EADP Records	5 Report
PLAT172_ALERT_4_G	The CIF-Embedded .res File Contains DFIX Records	30 Report
PLAT177_ALERT_4_G	The CIF-Embedded .res File Contains DELU Records	1 Report
PLAT178_ALERT_4_G	The CIF-Embedded .res File Contains SIMU Records	1 Report
PLAT301_ALERT_3_G	Main Residue Disorder ..... Percentage =	24 Note
PLAT793_ALERT_4_G	The Model has Chirality at C7	S Verify
PLAT793_ALERT_4_G	The Model has Chirality at C28	R Verify
PLAT860_ALERT_3_G	Number of Least-Squares Restraints	946 Note

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0 **ALERT level A** = Most likely a serious problem - resolve or explain
1 **ALERT level B** = A potentially serious problem, consider carefully
12 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
11 **ALERT level G** = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
8 ALERT type 2 Indicator that the structure model may be wrong or deficient
8 ALERT type 3 Indicator that the structure quality may be low
6 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 20/08/2014; check.def file version of 18/08/2014

Datablock jm0206ln_0m - ellipsoid plot