



HAL
open science

Crystal structure of cyclohexylammonium hydrogen maleate salt hemi-hydrated

Boucar Diouf, Bougar Sarr, Waly Diallo, Mouhamadou Sembéne Boye, Cheikh Abdoul Khadir Diop, Stanislav Pechev, François Michaud

► **To cite this version:**

Boucar Diouf, Bougar Sarr, Waly Diallo, Mouhamadou Sembéne Boye, Cheikh Abdoul Khadir Diop, et al.. Crystal structure of cyclohexylammonium hydrogen maleate salt hemi-hydrated. *Mediterranean Journal of Chemistry*, 2023, 13 (1), pp.1-7. 10.13171/mjc02301041662diallo . hal-03946684

HAL Id: hal-03946684

<https://hal.science/hal-03946684v1>

Submitted on 19 Jan 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Crystal structure of cyclohexylammonium hydrogen maleate salt hemi-hydrated

Boucar Diouf¹, Bougar Sarr¹, Waly Diallo^{1,*}, Mouhamadou Sembéne Boye², Cheikh Abdoul Khadir Diop¹, Pechev Stanislav Pavlo³, and François Michaud⁴

¹ Laboratoire de Chimie Minérale et Analytique – Département de Chimie – Faculté des Sciences et Techniques – Université Cheikh Anta Diop de Dakar

² Département de Physique-Chimie - Faculté des Sciences et Technologie de l'Éducation et la Formation - Université Cheikh Anta Diop Dakar

³ ICMCB, CNRS, Université de Bordeaux- 87 avenue Dr A. Schweitzer, 33608 Pessac – France

⁴ Service Commun d'Analyse par Diffraction des Rayons X, Université de Bretagne Occidentale, 6, avenue Victor Le Gorgeu, CS 93837, F-29238 Brest cedex 3, France

Abstract: The compound $\text{C}_6\text{H}_{11}\text{NH}_3[\text{HOOC}(\text{CH}_2)_2\text{COO}]\cdot\text{H}_2\text{O}$ has been obtained using one pot-synthesis process by mixing, in methanol, $\text{HOOC}(\text{CH}_2)_2\text{COOH}$, $\text{C}_6\text{H}_{11}\text{NH}_2$ and SnPh_3Cl in a 1:1:1 molar ratio. X-ray diffraction analysis of the compound reveals that in the crystal structure, hydrogen maleate $[\text{HOOC}(\text{CH}_2)_2\text{COO}]^-$ in cis configuration interacts with $[\text{C}_6\text{H}_{11}\text{NH}_3]^+$ cations and water molecules to generate an $R_6^6(22)$ ring. The interconnections of the rings via simple ($\text{N}-\text{H}\cdots\text{O}$ and $\text{O}-\text{H}\cdots\text{O}$) and bifurcated ($\text{N}-\text{H}\cdots(\text{O}, \text{O})$) hydrogen bonds give rise to a 2D supramolecular structure.

Keywords: Crystal structure; maleate anion; $\text{N}-\text{H}\cdots\text{O}$ hydrogen bond; an infinite 2D network graph set notation.

1. Introduction

Maleic acid is a key molecule in crystal engineering due to its structural aspect in deprotonation and inter and intramolecular hydrogen bonding functionality. It is recognized as an effective ingredient in pharmaceutical formulations and has been placed on a list of pharmaceutically acceptable acids^{1,2}. Maleate anions are frequently used to prepare complexes, organic compounds, and especially pharmaceutical products³⁻⁷. As a dicarboxylic acid, it forms two salts with active pharmaceutical ingredients: maleates and hydrogen-maleates (HMAL). In pharmacokinetics, for example, some maleate salts are used as the free basis or enalapril maleate to study the influence of some active agents in healthy patients^{8,9}. In genetic medicine, maleate salts are used as amlodipine salts in genetic disease treatment¹⁰. In fundamental chemistry, Madsen et al. reported the methylammonium hydrogen maleate and studied the very short intermolecular hydrogen bonds¹¹.

Poreba and al.¹² have reported structures of alkali hydrogen maleates. Thus, to better understand the mode of formation of maleates and hydrogen maleates, this new salt $\text{C}_6\text{H}_{11}\text{NH}_3[\text{HOOC}(\text{CH}_2)_2\text{COO}]\cdot\text{H}_2\text{O}$ (**1**) was isolated as a

suitable crystal by reacting the maleic acid, the cyclohexylammonium and SnPh_3Cl in one “pot” process.

2. Experimental

Compound **1** was obtained by mixing methanol solutions of maleic acid (0.300g, 2.584 mmol), cyclohexylamine (0.256g, 2.584 mmol), and SnPh_3Cl (0.994g, 2.584 mmol) in 1:1:1 ratio. A white precipitate is obtained after two hours of steering up.

This precipitate is filtered, and the obtained filtrate is made to slow solvent evaporation at room temperature. After one week of slow solvent evaporation, colorless suitable single crystals are obtained corresponding to **1**. The white precipitate is made for elemental analysis and corresponds to $(\text{C}_6\text{H}_{11}\text{NH}_3)\text{HOOC}(\text{CH}_2)_2\text{COO}\cdot\text{SnPh}_3\text{Cl}$.

Elemental analyses were performed at the “Plateforme d'Analyse Chimique et de Synthèse Moléculaire de l'Université de Bourgogne (PACSMUB)” on a Fisons EA 1108 CHNS-O apparatus. The elemental analysis has been made, and the data are in good agreement: Calculated: C: 53.56%, H: 8.09%, N: 6.25%; found: C: 53.58%, H: 8.17%, N: 6.12%.

*Corresponding author: Waly Diallo

Email address: waly.diallo@ucad.edu.sn

DOI: <http://dx.doi.org/10.13171/mjc02301041662diallo>

Received November 21, 2022

Accepted December 12, 2022

Published January 4, 2023

A crystal of **1** was selected and mounted on a mylar loop with oil. Crystallographic data collection was recorded with a Bruker Kappa Apex II diffractometer. The crystal ($0.25 \times 0.06 \times 0.05 \text{ mm}^3$) was kept at $T = 296\text{K}$ during data collection. Data collection: *CrysAlis PRO*¹³; cell refinement: *CrysAlis PRO*¹³; data reduction: *CrysAlis PRO*¹³; program(s) used to solve structure: *SIR92*¹⁴; program(s) used to refine structure: *SHELXL97*¹⁵; molecular graphics: *ORTEP-3 for Windows*¹⁶ (Farrugia, 2012) and *Mercury*¹⁷; software used to prepare material for publication: *WinGX*¹⁶ (Farrugia, 2012) and *PLATON*¹⁸. Absorption correction: Multi-scan SADABS2014/5 (Bruker, 2014) was used for absorption correction. $wR2(\text{int})$ was 0.0735 before and 0.0385 after correction. The Ratio of minimum to maximum transmission is 0.8059. The $\lambda/2$ correction factor is 0.00150.

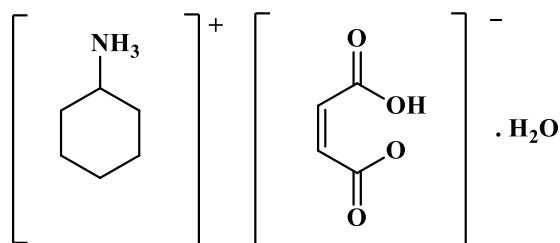
Crystallographic data for the structural analysis has been deposited with the Cambridge Crystallographic Data Centre, CCDC, number 2080826. This information may be copied free of charge. The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or <http://www.ccdc.cam.ac.uk>).

3. Structure description

The asymmetric unit of compound **1** consists of one hydrogen maleate anion, one cyclohexylammonium cation, and an {OH} entity from the lattice water

molecule (Figure 1). The interconnection of two hydrogen maleate anions, two water molecules, and two cyclohexylammonium cations through simple ($\text{N1} \cdots \text{H1A} \cdots \text{O5} = 2.952(3) \text{ \AA}$, $\text{O5} \cdots \text{H5} \cdots \text{O4} = 2.926(3) \text{ \AA}$) and bifurcated ($\text{N1} \cdots \text{H1B} \cdots (\text{O1}, \text{O2}) = (3.204(3), 3.054(2)) \text{ \AA}$) hydrogen bonds leads to the dimer $\{\text{CyNH}_3[\text{HOOC}(\text{CH})_2\text{COO}] \cdot \text{H}_2\text{O}\}_2$. Compared to $\text{NH} \cdots \text{O}$ and $\text{OH} \cdots \text{O}$ reported by Zeller and al. in the X-ray structure of maleate salts bedaquiline¹⁹, the lengths of intramolecular hydrogen bonds are similar. This dimer (motif) symbolized by a ring containing a total of twenty-two atoms, including six donors and six acceptors, is designated by this graphic notation $\text{R}_6^6(22)$ ²⁰ where R alludes to "ring" (Figure 2).

At this ring, each hydrogen maleate interacts with a cyclohexylammonium cation and a water molecule. As in some previous works²¹, within the maleate anion, the intramolecular hydrogen bond ($\text{O3} \cdots \text{H3} \cdots \text{O2} = 2.428(3) \text{ \AA}$) assisted by resonance locks the hydrogen maleate ion in a rigid and planar cis conformation. On the other hand, due to the double character of the water molecule (hydrogen bond donor and acceptor characters) and the three protons of the $-\text{NH}_3$ group of cyclohexylammonium, other similar rings $\{\text{CyNH}_3(\text{HOOC}(\text{CH})_2\text{COO})\text{H}_2\text{O}\}_2$ take shape and propagate. In Figure 3, along the b-axis is a structure comprising three rings interconnected by hydrogen bonds. The supramolecular structure of the compound is an infinite 2D network that can be described as a superposition along the b-axis of similar rings Figure 4.



Chemical Scheme

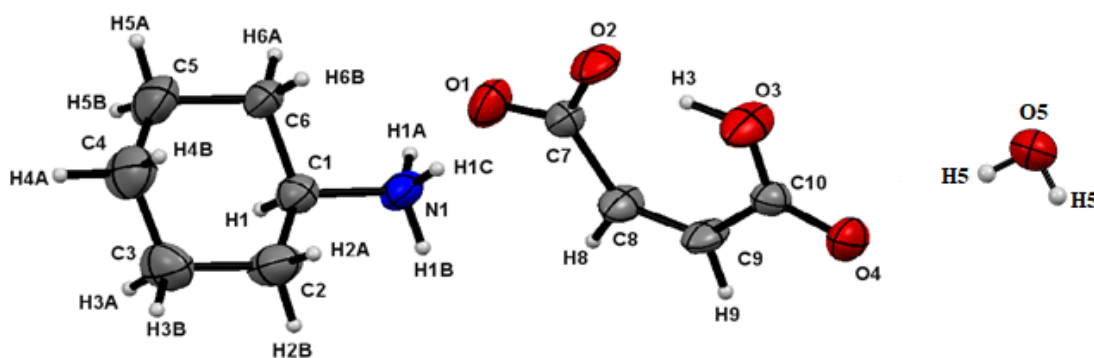


Figure 1. Asymmetric unit of $\text{CyNH}_3[\text{HOOC}(\text{CH})_2\text{COO}] \cdot \text{H}_2\text{O}$ [Symmetry operation (i): $-x+1, -y+1, -z+1$; (ii) $-x+1, -y, -z+1$; (iii) $x, -y, z-1/2$; (iv) $x, y-1, z$].

We have represented the two hydrogen atoms of the water molecule, but for reasons of symmetry, one of

the hydrogen atoms belongs to the represented unit and the other to the neighboring unit.

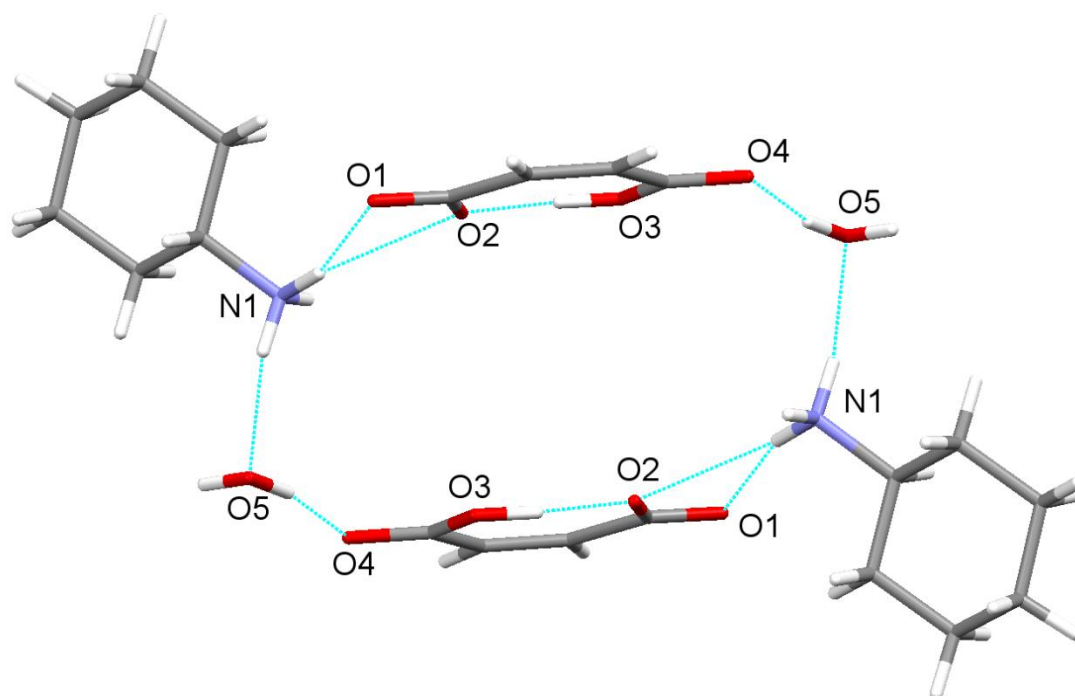


Figure 2. Perspective view of one ring in $\{\text{CyNH}_3 \cdot (\text{HOOC}(\text{CH}_2)_2\text{COO}) \cdot \text{H}_2\text{O}\}_2$

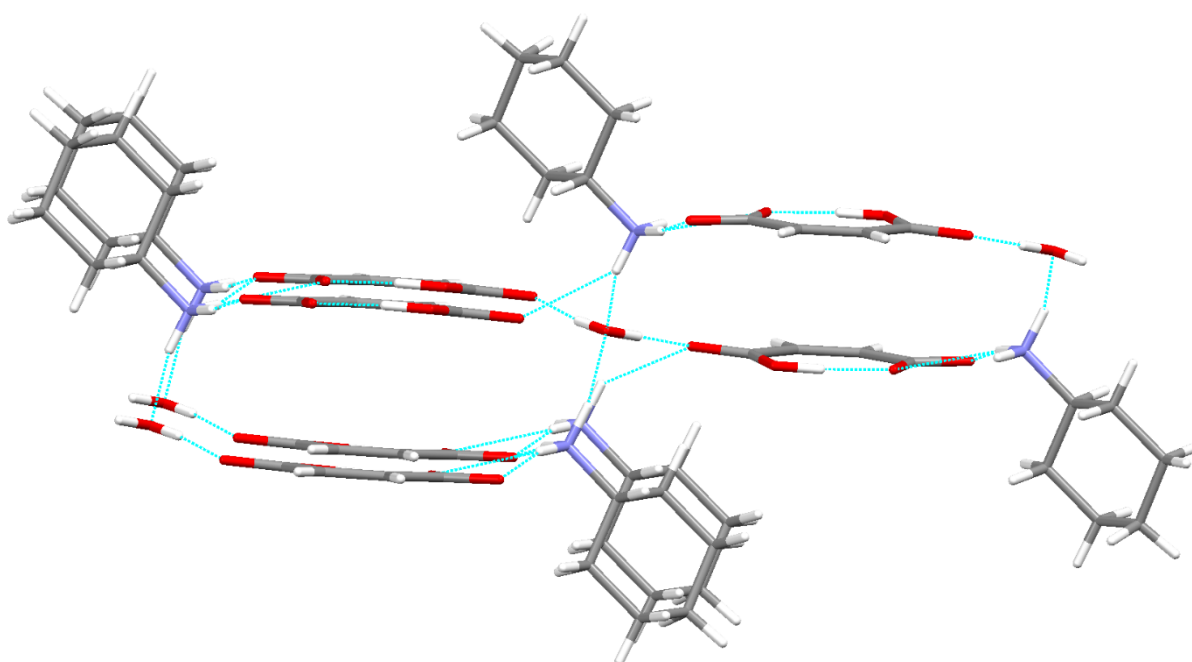


Figure 3. Perspective view of three rings in $\text{CyNH}_3 \cdot (\text{HOOC}(\text{CH}_2)_2\text{COO}) \cdot \text{H}_2\text{O}$ along b axis

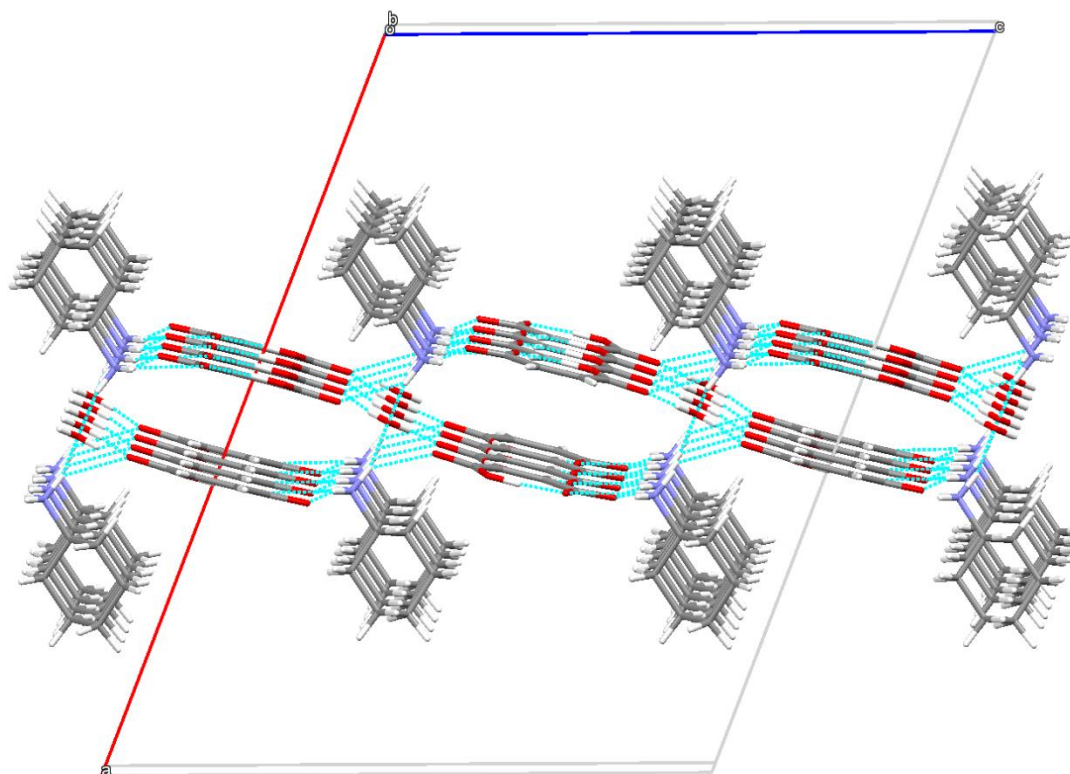


Figure 4. The crystal partial packing for the $\text{CyNH}_3[\text{HOOC}(\text{CH}_2)_2\text{COO}]\cdot\text{H}_2\text{O}$ in 2D viewed down [010]

4. Collection data and refinement details

refinement details are summarized in [Table 1](#).

Crystal data, data collection, and structure

Table 1. Crystal data and structure refinement of **1**.

Crystal data	
Chemical formula	$(\text{C}_6\text{H}_{14}\text{N}^+)_2\cdot(\text{C}_4\text{H}_3\text{O}_4^-)_2\cdot\text{H}_2\text{O}$
Formula weight ($\text{g}\cdot\text{mol}^{-1}$)	448.51
Crystal system	Monoclinic
Space group	C2/c
a (Å)	24.3982 (9)
b (Å)	5.5452 (2)
c (Å)	18.7405 (6)
β (°)	111.268 (1)
V (Å ³)	2362.78 (14)
Radiation	Mo K α radiation ($\lambda = 0.71073$ Å)
μ (mm^{-1})	0.099
ρ , $\text{g}\cdot\text{cm}^{-3}$	1.263
T, K	296
F(000)	968
θ_{max} , °	27.480
h,k,lmax	31,7,24
Crystal size (mm^3)	$0.25 \times 0.06 \times 0.05$

Z	4
Data collection	
Diffractionmeter	Nonius Kappa APEXII
T min , T max	0.601, 0.746
No. of measured	13892
No. of observed reflections with $[I > 2 \sigma (I)]$	2710
No. of Independent reflections	1740
Rint	0.033
Refinement	
$R[F^2 > 2\sigma(F^2)]$	0.060
$wR(F^2)$	0.184
Goodness-of-fit on F^2	1.03
No. of restraints	1
No. of restraints	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{\max}, \Delta\rho_{\min}$ ($e \text{ \AA}^{-3}$)	0.55, -0.23
CCDC number	2110795

Table 2. Geometric parameters (\AA , $^\circ$) for compound.

Bond lengths (\AA)			
C1—C2	1.472 (4)	C6—H6A	0.97
C1—N1	1.475 (3)	C6—H6B	0.97
C1—C6	1.510 (3)	N1—H1A	0.89
C1—H1	0.98	N1—H1B	0.89
C2—C3	1.516 (4)	N1—H1C	0.89
C2—H2A	0.97	C7—O1	1.232 (3)
C2—H2B	0.97	C7—O2	1.266 (3)
C3—C4	1.508 (4)	C7—C8	1.479 (3)
C3—H3A	0.97	C8—C9	1.329 (3)
C3—H3B	0.97	C8—H8	0.93
C4—C5	1.465 (5)	C9—C10	1.474 (3)
C4—H4A	0.97	C9—H9	0.93
C4—H4B	0.97	C10—O4	1.225 (3)
C5—C6	1.524 (4)	C10—O3	1.279 (3)
C5—H5A	0.97	O3—H3	0.935 (19)
C5—H5B	0.97	O5—H5	0.85 (3)
Bond angles ($^\circ$)			
C2—C1—N1	113.0 (2)	C6—C5—H5B	109
C2—C1—C6	112.3 (2)	H5A—C5—H5B	107.8
N1—C1—C6	109.8 (2)	C1—C6—C5	110.5 (2)
C2—C1—H1	107.1	C1—C6—H6A	109.6

N1—C1—H1	107.1	C5—C6—H6A	109.6
C6—C1—H1	107.1	C1—C6—H6B	109.6
C1—C2—C3	111.9 (3)	C5—C6—H6B	109.6
C1—C2—H2A	109.2	H6A—C6—H6B	108.1
C3—C2—H2A	109.2	C1—N1—H1A	109.5
C1—C2—H2B	109.2	C1—N1—H1B	109.5
C3—C2—H2B	109.2	H1A—N1—H1B	109.5
H2A—C2—H2B	107.9	C1—N1—H1C	109.5
C4—C3—C2	111.7 (3)	H1A—N1—H1C	109.5
C4—C3—H3A	109.3	H1B—N1—H1C	109.5
C2—C3—H3A	109.3	O1—C7—O2	122.0 (2)
C4—C3—H3B	109.3	O1—C7—C8	118.3 (2)
C2—C3—H3B	109.3	O2—C7—C8	119.7 (2)
H3A—C3—H3B	107.9	C9—C8—C7	131.1 (2)
C5—C4—C3	112.9 (3)	C9—C8—H8	114.5
C5—C4—H4A	109	C7—C8—H8	114.5
C3—C4—H4A	109	C8—C9—C10	131.1 (2)
C5—C4—H4B	109	C8—C9—H9	114.4
C3—C4—H4B	109	C10—C9—H9	114.4
H4A—C4—H4B	107.8	O4—C10—O3	121.5 (2)
C4—C5—C6	112.9 (3)	O4—C10—C9	119.2 (2)
C4—C5—H5A	109	O3—C10—C9	119.34 (19)
C6—C5—H5A	109	C10—O3—H3	110 (3)
C4—C5—H5B	109		

Table 3. Hydrogen bonds geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O5 ⁱ	0.89	2.34	2.952 (3)	126
N1—H1A···O4 ⁱⁱ	0.89	2.65	3.124 (3)	114
N1—H1A···O4 ⁱⁱⁱ	0.89	2.48	3.148 (3)	132
N1—H1B···O2 ^{iv}	0.89	2.31	3.054 (2)	141
N1—H1B···O1 ^{iv}	0.89	2.35	3.204 (3)	161
N1—H1C···O1	0.89	2.07	2.944 (3)	167
C9—H9···O3 ^{iv}	0.93	2.4	3.213 (3)	146
C8—H8···O2 ^{iv}	0.93	2.48	3.397 (3)	171
O5—H5···O4	0.85 (3)	2.10 (3)	2.926 (3)	164 (3)
O3—H3···O2	0.94 (2)	1.49 (2)	2.428 (3)	176 (4)

5. Conclusion

Reaction between maleic acid and monoalkylamine CyNH₂ in a field containing SnPh₃Cl molecule was studied, leading to the isolation as single-crystals of a monoalkylammonium maleate salt, CyNH₃[HOOC(CH₂)₂COO]·H₂O. The salt crystallizes

in the monoclinic system and C2/c space group. Cations and anions are linked *via* secondary contacts, expanding layer-like arrangements. Currently, the reactivity of the maleate salt towards transition metal complexes or organotin complexes is in progress in our research group, intending to access original self-

assembled constructions involving metal center and maleate oxyanion stabilized by ammonium cations.

Acknowledgments

The authors thank Cheikh Anta Diop University Dakar-Senegal, the ICMCB, CNRS, Université de Bordeaux, and the Service Commun d'analyse par diffraction des rayons X, Université de Bretagne Occidentale, France, for their support in taking the analyses.

Funding information

The work was carried out with no funding.

References

- 1- P. H. Stahl, C. G. Wermuth, *Pharmaceutical Salts: Properties, Selection and Use*, John Wiley & Sons, **2002**.
- 2- D. Seye, A. Toure, M. Lo, C. A. K. Diop, L. Diop, D. Geiger, *Crystal Structure of Diisopropylammonium Hydrogen Maleate*, *Sci. J. Chem.*, **2019**, 7, 110-113.
- 3- C. C. Silva, M. L. Cirqueira, F. T. Martis, *Lamivudine salts with 1, 2-dicarboxylic acids: A new and a rare synthon with double pairing motif fine-tuning their solubility*, *CrystEngComm*, **2013**, 15, 6311–6317.
- 4- L. Orola, I. Sarcevic, A. Kons, A. Actins, M. V. Veidis, *Conformation of the umifenovir cation in the molecular and crystal structures of four carboxylic acid salts*, *J. Mol. Struct.*, **2014**, 1056, 63–69.
- 5- J. M. Chen, Z. Z. Wang, C. B. Wu, S. Li, T. B. Lu, *Crystal engineering approach to improve the solubility of mebendazole*, *Cryst EngComm.*, **2012**, 14, 6221–6229.
- 6- S. Jayanty, T. Akutagawa, T. Nakamura, *Hydrogen-bonded maleate counter anions in tetrathiafulvalene crystals*, *CrystEngComm.*, **2012**, 14, 3875–3881.
- 7- G. T. Gál, N. V. May, P. Bombicz, *Acta Cryst.*, **2016**, E72, 72, 612–615.
- 8- Y-F. Zhang, X-Y. Chen, X-J. Dai, Y-N. Zhang, H-L. Yu, D-F. Zhong, *Influence of omeprazole on pharmacokinetics of domperidone given as free base and maleate salt in healthy Chinese patients*, *Acta Pharmacologica Sinica.*, **2007**, 28, 1243-1246.
- 9- A. E. Till, H. J. Gomez, M. Hichens, A. J. Bolognese, W. R. McNabb, B. A. Brooks, F. Noormohamed, A. F. Lant, *Pharmacokinetics of repeated single oral doses of enalapril maleate (MK-421) in normal volunteers*, *Biopharmaceutics and drugs Disposition*, **1984**, 5, 3, 273-280.
- 10- P. A. Meredith, *Potential concerns about generic substitution: bioequivalence versus therapeutic equivalence of different amlodipine salt forms*, *Current Medical Research and Opinion*, **2009**, 25, 9, 2179-2189.
- 11- D. Madsen, C. Flensburg, S. Larsen, *Properties of the Experimental Crystal Charge Density of Methylammonium Hydrogen Maleate. A Salt with a Very Short Intramolecular O–H–O Hydrogen Bond*, *Phys. Chem. A.*, **1998**, 102, 12, 2177–2188.
- 12- T. Poręba, P. Macchi, N. Casati, *Structural Variety of Alkali Hydrogen Maleates at High Pressure*, *Cryst. Growth Des.*, **2020**, 20, 7, 4375–4386.
- 13- Agilent CrysAlis PRO. Agilent Technologies, Yarnton, England, **2014**.
- 14- A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *SIRPOW. 92—a program for automatic solution of crystal structures by direct methods optimized for powder data*, *J. Appl. Cryst.*, **1992**, 27, 435-436.
- 15- G. M. Sheldrick, *A magic triangle for experimental phasing of macromolecules*, *Acta Cryst.*, **2008**, A64, 112–122.
- 16- C. S. D. Mercury, 2.0: CF Macrae, IJ Bruno, JA Chisholm, PR Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek and PA Wood, *J. Appl. Cryst.*, **2008**, 41, 466–470.
- 17- L. J. Farrugia, *WinGX and ORTEP for Windows: an update*, *J. Appl. Cryst.*, **2012**, 45, 849–854.
- 18- A. L. Spek, *Structure validation in chemical crystallography*, *Acta Cryst.*, **2009**, D65, 148–155.
- 19- M. Zeller, P. Smith, D. K. Purcell, M. Okezue, D. T. Smith, S. R. Byrnh, K. L. Clasee, *Maleate salts of bedaquiline*, *Acta Cryst.*, **2021**, E77, 433–445.
- 20- B. Sarr, A. Mbaye, C. A. K. Diop, F. Melin, P. Hellwig, M. Sidibé, Y. Rousselin, *Crystal structure of bis (diisopropylammonium) molybdate*, *Acta Cryst.*, **2018**, E74, 1682–1685.
- 21- G. Radha, B. V. Pandiyan, P. Deepa, S. Govindarajan, P. Kolandaivel, D. Nataraj, *Synthesis and Experimental Studies on Supramolecular Synthons of Aminoguanidinium Carboxylates: A Case Study of π -Hole Bonded Carbon Bonding via Theoretical Approaches*, *Chemistry Select.*, **2018**, 3, 10032–10048.