PROCEEDINGS OF THE YEREVAN STATE UNIVERSITY

Chemistry and Biology 2024, **58**(3), p. 192–196

Chemistry

EPISODIC KNOWLEDGE ON FIRST AND FOREMOST CRYSTALLINE STRUCTURAL REPORT OF ETHYLENEDIAMINETETRAACETIC ACID

D. NOGUCHI *

Graduate School of Integrated Science and Technology, Nagasaki University, Japan

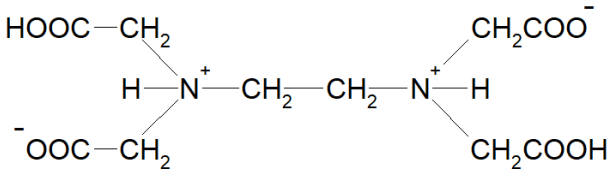
An investigation into the precise ethylenediaminetetraacetic acid (EDTA) crystalline structural report was initiated, as there appeared to be some ambiguity regarding the accurate notation of EDTA as a neutral molecule or a zwitterion. As a result, the first and foremost article reporting EDTA in zwitterionic form was determined after a difficult confirmation. Additionally, crystallographic data of the zwitterionic EDTA itself and non-chelated salts thereof registered on the CCDC were also mentioned herein. This episodic knowledge will be fundamental for not only chemical education but also related science and technology in the future.

https://doi.org/10.46991/PYSUB.2024.58.3.192

***Keywords*:** analytical chemistry, chelator, polyaminocarboxylic acid.

Introduction. Ethylenediaminetetraacetate (EDTA; 2,2',2",2"'-(ethane-1,2--diyldinitrilo)tetraacetate) is a commonly learned chelator in analytical chemistry owing to its ability to form stable metal complexes with four carboxylate groups (R-COO^-) and two tertiary amino groups (R-NR'R") thereof. However, the accurate notation of EDTA itself appears somewhat ambiguous. This would be because there was a controversy about the chemical structure of EDTA itself around the middle of the 20th century [1, 2]. The one group interpreted EDTA as a neutral molecule [3–5], whereas the other group interpreted it as a zwitterion; i.e. $HOOCCH_2(^-OOCCH_2)NH^+CH_2CH_2NH^+(CH_2COO^-)CH_2COOH$ [6–8]. Even afterwards, there are still some textbooks of analytical chemistry that describe it as not a zwitterion, but a neutral molecule [9]. Precise understanding and revealing the historical origin of the chemical structure of EDTA itself should be significant not only for chemical educators, but also for scientific researchers. Therefore, I have investigated and analyzed the reported crystal structures of both zwitterionic EDTA themselves and its non-chelating salts; 27 entries have been demonstrated recently [10]. But at that time, the first and foremost article reporting the crystal structure of EDTA had not yet been determined. Eventually, according to a difficult task to confirm, it was found that the first and foremost crystal structure of EDTA was reported with zwitterionic fashion by Lu & Shao in 1961 and 1962 [11, 12] (see Scheme).

* E-mail: a.chemist.noguchi.d@gmail.com



Scheme of the structural formula of a zwitterionic EDTA molecule in its crystalline state.

Materials and Methods. Information as to crystal compounds at Cambridge Crystallographic Data Centre (CCDC) have been searched through the Internet.

Results and Discussion. Hereafter, the complicated episode found by my investigation is demonstrated in detail. The above-mentioned monumental articles (Lu & Shao 1961; 1962) reporting EDTA crystal structures written in Chinese with an abstract in English [11] and in Russian [12] were published. However, they have been neglected by almost all researchers who reported the crystal structures of EDTA themselves and their salts of non-chelation after that [10]. Why is this such a regrettable situation? From the web-site of the CCDC exhibiting a search result, it is shown that the data by [12] was deposited in 1971 as "L.Y. Tsein, S.M. Chen, Scientia Sinica, 1962, 9, 496". I attempted to obtain the report through the Internet in 2023, but the article was not available online at that time (from 2024 onwards, it is currently available online). Thus, I ordered a copy of the article via the University Library. Eventually, I found that as the original article [12] was written in Russian, the bibliography must be translated into English. Unfortunately, the bibliographic notation is incorrect. In Chinese culture, surnames (family names) are traditionally written before the "first" (given) names. Usually, when translating Chinese names into English, the surname is often swapped with the given name. However, in the present case, swapping was not done; "Tsein" and "Chen" are indeed parts of their given names. These parts of their given names seemed to be treated as surnames during the translation. Second, although the volume number in the bibliography is noted as "9", it is also incorrect. In the original article, the volume number is demonstrated as the Roman numeral "XI"; XI means 11, not 9 (=IX)! Thirdly, the page number is incorrect. In the original paper, the page numbers began from 469, not 496! Triple mistakes are making it be very difficult to identify.

Subsequently, Cotrait in 1972 reported another data of the crystal structure of EDTA with R index written in French [13]. Cotrait (1972) cited the above-mentioned article as "Tsin L.Y. & Chen S.M. (1962). Acta Sci. Sin. p. 469". The journal name thereof is misleading; "Acta Sci. Sin." is inaccurate, because "Acta" was unnecessary, and another confusing journal of "Acta Chim. Sin." also exists. Moreover, the volume number was not included. Later, the further crystal structure of EDTA itself was also reported by Ladd & Povey (1973) [14], citing the aforementioned paper as "Lu Y. & Shao M. (1962) Sci. Sin. II, 469". As you know by now, they mistaken the volume number "XI" for II!!! These incomplete citations are seemed like another reason for losing the worth of the first-reported invaluable knowledge. When Shkol'nikova & Porai-Koshits (1990) [15] reviewed the structures of uncharged, anionic, and cationic aminoalkylcarboxylic complexones including EDTA, the studies by Lu & Shao (1960, 1961) [11, 12] were not referenced, despite the fact that they were "Russian" scholars. Here should be also emphasized that none

of them ever mentioned the actual first and foremost report by Lu & Shao (1961) [11], even though posterior "Chinese" researchers, who rediscovered and deposited the crystal structural data of EDTA itself on the CCDC [16].

Further information shall be introduced. I also found additional entries of the non-chelation salts of EDTA such as $[Mg(H_2O)_6](EDTA–2H)$ by Tinnemans in 2023 [17], and two entries of $(HOCH_2CH_2NH_3)_2(EDTA–2H)$ and $\{(HOCH_2)_3CNH_3\}_2(EDTA–2H)\cdot 3H_2O$ by Semenov et al. in 2023 [18] through this investigational process. Moreover, I found a crystal structure reporting Ag(EDTA–3H) [19]. Accordingly, a total of 34 entries related to EDTA themselves and non-chelating salts thereof were ensured after my previous work [20]. These existing data of the crystalline structures of zwitterionic EDTA itself and its non-chelational salts are expected to be valuable for both chemical education and materials science and engineering afterwards.

Conclusion. The first and foremost crystalline structural reports exhibiting an exact zwitterionic EDTA itself have provided valuable insights into its history in chemistry. However, the bibliographic data of this monumental article reported by Lu & Shao written in Russian was misinterpreted when registered in the CCDC, and subsequent studies also erroneously cited. This episodic knowledge would be of significance for not only science education, but also advanced research in the near future.

This work is an updated version of my preprint in EdArXiv. The language of the draft was edited using Paperpal, recruited by the NU's Academic Support Office.

The author thanks the partial funding received from the Research Grant of NU WISE Programme for Global Health (2024).

Received 19.07.2024
Reviewed 19.09.2024
Accepted 10.10.2024

REFERENCES

1. Chapman D., Lloyd D.R., Prince R.H. An Infrared and Nuclear Magnetic Resonance Study of the Nature of Ethylenediaminetetra-acetic Acid and Some Related Substances in Solution: Hydrogen Bonding in α-Amino-polycarboxylic Acid Systems. *J. Chem. Soc. (Resumed)* (1963), 3645–3658. https://doi.org/10.1039/JR9630003645
2. Martynenko L.I., Pechurova N.I., et al. Infrared Spectroscopy Investigation of the Structure of Ethylenediaminetetraacetic Acid and Its Salts. *Russ Chem. Bull.* **19** (1970), 1172–1177. https://doi.org/10.1007/BF00852653
3. Busch D.H., Bailar J.C.Jr. The Stereochemistry of Complex Inorganic Compounds. XVII. The Stereochemistry of Hexadentate Ethylenediaminetetraacetic Acid Complexes. *J. Am. Chem. Soc.***75** (1953), 4574–4575. https://doi.org/10.1021/ja01114a054
4. Chapman D. The Infrared Spectra of Ethylenediaminetetra-acetic Acid and Its Di- and Tetra-sodium Salts. *J. Chem. Soc. (Resumed)* (1955), 1766–1769. https://doi.org/10.1039/JR9550001766
5. Langer H.G. Infrared Spectra of Ethylenediaminetetraacetic Acid (EDTA). *Inorg. Chem.* **2** (1963), 1080–1081. https://doi.org/10.1021/ic50009a057

6. Schwarzenbach G., Ackermann H., Komplexone V. Die Äthylendiamin-tetraessigsäure (Complexone V. The Ethylenediamine-tetraacetic Acid). *Helv. Chim. Acta* **30** (1947), 1798–1804 (in German).
https://doi.org/10.1002/hlca.19470300649
7. Nakamoto K., Morimoto, Y., Martell A.E. Infrared Spectra of Aqueous Solutions. III. Ethylenediaminetetraacetic acid, N-hydroxyethylethylenediaminetriacetic Acid and Diethylene-triaminepentaacetic Acid. *J. Am. Chem. Soc.* **85** (1963), 309–313.
https://doi.org/10.1021/ja00886a014
8. Sawyer D.T., Tackett J.E. Properties and Infrared Spectra of Ethylenediaminetetraacetic Acid Complexes. IV. Structure of the Ligand in Solution. *J. Am. Chem. Soc.* **85** (1963), 314–316.
https://doi.org/10.1021/ja00886a015
9. Noguchi D. Confusion in the Notation of the Chemical Structure of EDTA: Molecule or Zwitterion? *J. Technol. Educ.* **28** (2021), 27–36.
https://doi.org/10.13140/RG.2.2.25433.33120
10. Noguchi D. Analysis of Specialties of Crystal Structure for Non-chelate Conformations of Ethylene-diaminetetraacetic Acid and Its Salts with Alkali and Alkaline Earth Metals. *Ukr. Chem. J.* **88** (2022), 55–69 (in Japanese).
https://doi.org/10.33609/2708-129X.88.10.2022.55-69
11. Lu Y., Shao M. The Crystal Structure of Ethylenediaminetetra Acetic Acid. *Acta Phys. Sin.* **17** (1961), 304–309 (in Chinese).
https://doi.org/10.7498/aps.17.304
12. Lu Y., Shao M. Определение кристаллической структуры этилендиамина четырех-уксусной кислоты (Determination of the Crystal Structure of Ethylenediamine Tetra-acetic Acid). *Sci. Sin.* **11** (1962), 469–476 (in Russian).
https://doi.org/10.1360/ya1962-11-4-469
13. Cotrait M. Structure Cristalline d'un Sel Birubidique de l'EDTA (Crystal Structure of an EDTA Dirubidium Salt). *Acta Cryst. B* **26** (1970), 1152–1161 (in French).
https://doi.org/10.1107/S0567740870003758
14. Ladd M.F.C., Povey D.C. Crystallographic and Spectroscopic Studies on Ethylenediamine-tetraacetic Acid (Edta) I. Crystal and Molecular Structure of β-Edta. *J. Cryst. Mol. Struct.* **3** (1973), 15–23.
https://doi.org/10.1007/BF01270899
15. Shkol'nikova L.M., Porai-Koshits M.A. Structure of the Uncharged, Anionic, and Cationic Forms of Aminoalkylcarboxylic and Aminoalkylphosphonic Complexones. *Russ. Chem. Rev.* **59** (1990), 40–43.
https://doi.org/10.1070/RC1990v059n07ABEH003548
16. Wang J., Zhang X., et al. Investigation on the Coordinate Structures of the Rare Earth Metal Complexes with Edta and Cydta Ligands. *Wuhan Univ. J. Nat. Sci.* **8** (2003), 1131–1137.
https://doi.org/10.1007/BF02903686
17. Tinnemans P. CCDC 2241171: Experimental Crystal Structure Determination. *CSD Commun.* (2023).
https://doi.org/10.5517/ccdc.csd.cc2f73vn
18. Semenov V.V., Zolotareva N.V., et al. Complexes of Ethylenediaminetetraacetic Acid with Amines. Molecular Structures of Bis(monoethanolaminium) Ethylenediaminetetraacetate and Bis[tris(hydroxymethyl)methylaminium] Ethylenediaminetetraacetate Trihydrate. *Crystallogr. Rep.* **68** (2023), 247–258.
https://doi.org/10.1134/S1063774523020141
19. Wimmer A., Urstoeger A., et al. Separating Dissolved Silver from Nano-Particulate Silver is the Key: Improved Cloud-point-extraction Hyphenated to Single Particle ICP-MS for Comprehensive Analysis of Silver-Based Nanoparticles in Real Environmental Samples Down to Single-digit nm Particle Sizes. *Anal. Chim. Acta* **1150** (2021), 238198.
https://doi.org/10.1016/j.aca.2021.01.001
20. Noguchi D. Episodic Knowledge on First and Foremost Crystal Structural Report of Ethylenediaminetetraacetic Acid (EDTA) Itself. *EdArXiv* (2024).
https://doi.org/10.35542/osf.io/n9jf4

Դ. ՆՈԳՈՒՉԻ

ԴՐՎԱԾՔԱՅԻՆ ԳԻՏԵԼԻՔ ԷԹԻԼԵՆԴԻԱՄԻՆՏԵՏՐԱՔԱՑԱԽԱԹԹՎԻ ԲՅՈՒՐԵՂԱՅԻՆ ԿԱՌՈՒՑՎԱԾՔԻ ՎԵՐԱԲԵՐՅԱԼ ԱՌԱՋԻՆ ԵՎ ՀԻՄՆԱԿԱՆ ՀԱՂՈՐԴՄԱՆ ՄԱՍԻՆ

Նախաձեռնվել է հետազոտություն էթիլենդիամինտետրաքացախաթթվի (EDTA) բյուրեղային կառուցվածքի ներկայացման վերաբերյալ, քանի որ, ըստ երևույթին, որոշակի երկիմաստություն կար՝ կապված EDTA-ի ճշգրիտ նշման հետ՝ որպես չեզոք մոլեկուլի կամ ցվիտերիոնի: Արդյունքում, դժվար հաստատումից հետո հայտնաբերված է առաջին և հիմնական հոդվածը, որտեղ EDTA-ն ներկայացված է որպես ցվիտերիոնային ձև: Բացի այդ, այստեղ նշված են նաև ցվիտերիոնային EDTA-ի և դրա ոչ քելատային աղերի բյուրեղային կառուցվածքի տվյալները, որոնք գրանցված են CCDC-ում: Այս էպիզոդիկ գիտելիքները ապագայում հիմնարար նշանակություն կունենան ոչ միայն քիմիական կրթության, այլ նաև հարակից գիտության և տեխնոլոգիայի համար:

Д. НОГУЧИ

ЭПИЗОДИЧЕСКИЕ ЗНАНИЯ О ПЕРВОМ И ГЛАВНОМ ОТЧЕТЕ О КРИСТАЛЛИЧЕСКОЙ СТРУКТУРЕ ЭТИЛЕНДИАМИНТЕТРАУКСУСНОЙ КИСЛОТЫ

Было начато исследование отчета о кристаллической структуре этилендиаминтетрауксусной кислоты (ЭДТА), поскольку, по-видимому, существовала некоторая двусмысленность относительно точного обозначения ЭДТА как нейтральной молекулы или цвиттер-иона. В результате после сложного подтверждения приводится первая и главная статья, сообщающая об ЭДТА как о цвиттер-ионной форме. Кроме того, здесь также упоминаются кристаллографические данные самой цвиттер-ионной ЭДТА и ее нехелатированных солей, зарегистрированных в Кембриджском центре кристаллографических данных. Эти эпизодические знания будут иметь основополагающее значение не только для химического образования, но и для смежных наук и технологии в будущем.