Episodic knowledge on first and foremost crystalline structural report of ethylenediamineteraacetic acid (EDTA) itself

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ABSTRACT

An investigation into the precise crystalline structural report of ethylenediaminetetraacetic acid (EDTA), a representative chelator learned in the education of analytical chemistry, was initiated as there appeared to be apparent ambiguity regarding the accurate notation of EDTA as a neutral molecule or a zwitterion. Consequently, the first and foremost article reporting EDTA as 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 are also summarized herein. This episodic knowledge will be fundamental for not only chemical education but also related fundamental and applied sciences.

Keywords: chemical analysis, history, polyaminocarboxylic acid, salt.

Introduction

Ethylenediaminetetraacetic acid (2,2',2",2"'-(ethane-1,2-diyldinitrilo)tetraacetic acid; EDTA) 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

describes 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 were 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 (Fig. 1).[11,12]

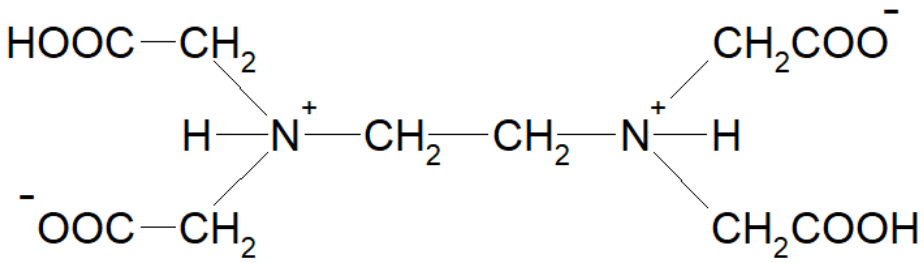

Fig. 1 Zwitterionic notation reported by crystal structure of EDTA.[11,12]

Materials and methods

Information as to crystal compounds at Cambridge Crystallographic Data Centre (CCDC) have been searched through the Internet with no fee (https://www.ccdc.cam.ac.uk/structures/).

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] have been reported. However, they have been neglected by almost all researchers reporting 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 Cambridge Crystallographic Data Centre (CCDC) exhibiting a search result, it is shown that the data by Lu & Shao (1962) was deposited in 1971 as "L.Y.Tsein, S.M.Chen, Scientia Sinica, 1962, 9, 496". I tried to obtain a report through the Internet, but the article was not available online. Thus, I ordered a copy of the article via the University Library. Eventually, I found that as the original article by Lu & Shao (1962) 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 '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, in addition to unavailability through the Internet, 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. Here should be also emphasized that none of them never mentioned the actual first and foremost report by Lu & Shao (1961), even though posterior Chinse researchers who rediscovered and deposited the crystal structural data of EDTA itself on the CCDC.[15]

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,[16] 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[17] through this investigational process after reporting an addendum.[18] Accordingly, a total of 33 entries related to EDTA themselves and non-chelating salts thereof are shown in Table 1. Here, $(EDTA+2H)^{2+}$ denotes ethylenediammoniotetra-acetic acid $(HOOCCH_2)_2NH^+CH_2CH_2NH^+(CH_2COOH)_2$; $(EDTA+H)^+$ denotes ethylenediammonioacetato-tri-acetic acid $(HOOCCH_2)_2NH^+CH_2CH_2NH^+(CH_2COO^-)CH_2COOH$; EDTA denotes ethylenediammoniodiacetato-di-acetic acid $HOOCCH_2(^-OOCCH_2)NH^+CH_2CH_2NH^+(CH_2COO^-)CH_2COOH$; and $(EDTA–2H)^{2-}$ denotes ethylenediammoniotetra-acetate $(^-OOCCH_2)_2NH^+CH_2CH_2NH^+(CH_2COO^-)_2$, respectively. 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 sciences afterwards.

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Table 1. Non-chelating zwitterionic EDTA molecules and their salts with reported crystal structural data deposited on the CCDC (types of EDTA, entry numbers, chemical formulae, CCDC numbers) sorted by the CCDC Nos.

Type	Entry No.	Chemical formula	CCDC No.
$(EDTA+2H)^{2+}$	1	$EDTA\cdot 2HCl\cdot 3H_2O$	657759
	2	$EDTA\cdot 2HCl\cdot 3H_2O$	1163542
	3	$EDTA\cdot H_2SO_4\cdot H_2O$	1300053
$(EDTA+H)^{+}$	4	$EDTA\cdot HBr\cdot H_2O$	1283049
EDTA	5	$EDTA\cdot 0.39H_2O$	1101398
	6	EDTA	1148825
	7	EDTA	1148826
	8	EDTA	1148827
	9	EDTA	1148828
	10	$EDTA\cdot(H_3O)Na_2[Ni(EDTA–2H)]PW_{12}O_{40}\cdot 5H_2O$	1433251
$(EDTA–2H)^{2–}$	11	$[Mn(H_2O)_6](EDTA–2H)$	285809
	12	$N_2H_5(EDTA–2H)$	656243
	13	$(N_2H_5)_2(EDTA–2H)$	656246
	14	$Sr_2(EDTA–2H)Cl_2\cdot 5H_2O$	686018
	15	$Sr_2(EDTA–2H)(HCO_3)_2\cdot 4H_2O$	686020
	16	$\{HC_3N_3(NH_2)_3\}_2(EDTA–2H)\cdot 2H_2O$	741062
	17	$K_2(EDTA–2H)\cdot 2H_2O$	838146
	18	$Na_2(EDTA–2H)\cdot 2H_2O$	1020814
	19	$(NH_4)(N_2H_5)(EDTA–2H)\cdot NH_3\cdot 2H_2O$	1033967
	20	$[Mg(H_2O)_6](EDTA–2H)$	1103464
	21	$Rb_2(EDTA–2H)\cdot 2H_2O$	1147983
	22	$K_2(EDTA–2H)\cdot 2H_2O$	1148821
	23	$Ca(EDTA–2H)\cdot 2H_2O$	1166578
	24	$Na_2(EDTA–2H)\cdot 2H_2O$	1171161
	25	$Na_2(EDTA–2H)[Te(OH)_6]\cdot 2H_2O$	1309261
	26	$K_2(EDTA–2H)\cdot 2H_2O$	1968403
	27	$Ag_2(EDTA–2H)$	2006750
	28	$Na_2(EDTA–2H)\cdot 2H_2O$	2051489
	29	$Ba(EDTA–2H)\cdot 4H_2O$	2054973
	30	$Sr_2(EDTA–2H)_2\cdot 6H_2O$	2054974
	31	$(HOCH_2CH_2NH_3)_2(EDTA–2H)$	2144221
	32	$\{(HOCH_2)_3CNH_3\}_2(EDTA–2H)\cdot 3H_2O$	2172960
	33	$[Mg(H_2O)_6](EDTA–2H)$	2241171

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93 **Conclusions**

94 The first and foremost crystalline structural reports exhibiting an exact zwitterionic EDTA itself has
95 provided valuable insights into its history in chemistry. However, the bibliographic data of this
96 monumental article reported by Lu & Shao in 1961 was misinterpreted when registered in the
97 CCDC, and subsequent studies also erroneously cited. This episodic knowledge would be of
98 significance for not only chemical education but also scientific research in the near future.

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Conflict of interests

The Author declares no conflict of interests.