

MERCAPTOETHYLAMINETRIACETIC ACID*

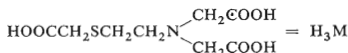
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Mercaptoethylaminetriacetic acid (H_3M), a complexing agent containing three kinds of donor atoms, has been studied and its acid-base dissociation constants and the dissociation mechanism have been determined. The compounds H_3M , $H_3M.H_2O$, $H_3M.HCl$, $H_3M.HCl.H_2O$ and Na_3M were prepared and were characterized by the powder X-ray method and by their infrared spectra.

In the course of a systematic study of the structural analogues of EDTA containing heteroatoms other than nitrogen, such as sulphur¹ and phosphorus², we have found that the complexing properties of these substances can be considerably affected by introducing a sulphidic sulphur into their aliphatic chain. We considered mercaptoethylaminetriacetic acid as a potentially interesting ligand of this kind; it contains simultaneously nitrogen, sulphur and oxygen as donor atoms:



This substance was studied by Dyatlova and coworkers³⁻⁶ and by Jing-Chi Chu⁷, but their results are limited to qualitative measurements in solutions. More detailed data on the ligand synthesis are also missing.

Thus the topic of the present paper is the synthesis of mercaptoethylaminetriacetic acid and of its salts and the determination of qualitative data on the properties of these substances, which could serve as a basis for a study of their complexing abilities.

EXPERIMENTAL

Reagents and Apparatus

β -aminoethanol, technical grade, from Lachema, was fractionated *in vacuo* before use. A 10M-DCI solution in D_2O was obtained by saturation of deuterium oxide (isotopic purity, 99.7%, from the Institute for Research, Preparation and Utilization of Radioisotopes, Prague) with gaseous DCI,

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obtained from sodium chloride and 96% D_2SO_4 (Soyuzkhimexport, isotopic purity, 97%). Other chemicals were of p.a. purity from Lachema and Merck.

The apparatus have been described in a previous communication².

Analytical Methods

The ligand content was determined by potentiometric titration with nascent bromine ($KBrO_3 + KBr$ solution) in 2M-HCl, during which the sulphidic sulphur is oxidized to sulphoxide. Chloride was determined gravimetrically as $AgCl$, sodium as Na_2SO_4 , after digestion of Na_3M with sulphuric acid and water by drying to a constant weight and from GTA curves.

RESULTS AND DISCUSSION

Preparation of the Compounds

H_3M : β -mercaptoethylamine hydrochloride, obtained from β -aminoethanol by condensation with carbon disulphide followed by hydrolysis of the thiazolidine-2-thione formed⁸, was alkylated by a slight excess of sodium chloroacetate in a weakly alkaline aqueous solution: 116 g $HSCH_2 \cdot CH_2NH_2 \cdot HCl$ (0.98 mol) were dissolved in 800 ml of 4M sodium chloroacetate, with cooling with water, stirring and passage of nitrogen through the mixture. After heating to 80°C, 30% NaOH was added at a rate such that the solution refluxed gently and its alkalinity corresponded to the phenolphthalein colour change. After completion of the reaction (overall consumption of NaOH being 3.95 mol), the solution was boiled under reflux for one hour, cooled, neutralized to pH 6 with concentrated hydrochloric acid, purified with active charcoal, filtered and acidified with concentrated hydrochloric acid to pH 1.5. After two week's standing at 5°C, the crystals which separated were filtered off, washed with ice water and recrystallized from hot water. The substance was dried first at 40°C and then at 150°C. The yield was 103 g (42%) of a white crystalline substance with m.p. 207–208°C (decomp.). Analysis: $C_8H_{13}NO_6S$ (m.w. 251.3) calculated: 38.24% C, 5.21% H, 5.58% N, 12.76% S; found: 38.96% C, 5.69% H, 5.53% N, 12.78% S. The alkalimetric equivalent: calculated 83.8; found 83.9.

$H_3M \cdot H_2O$: 3 g H_3M were dissolved in 200 ml of hot water and the solution was allowed to crystallize at laboratory temperature. The white needles were filtered off under vacuum, washed with ethanol and ether and dried at room temperature. The yield was 2.4 g (72%). The substance loses water at 110°C and melts at 208°C (decomp.) Analysis: $C_8H_{15}NO_7S$ (m.w. 279.3) calculated: 88.88% M^{3-} , 6.45% H_2O ; found: 88.43% M^{3-} , 7.22% H_2O .

$H_3M \cdot HCl \cdot H_2O$: 10 g H_3M were dissolved in 20 ml of hot 6M-HCl; the solution was saturated with hydrogen chloride at -10°C, and allowed to crystallize at -5°C. The crystals were filtered off, washed with ethanol previously saturated with hydrogen chloride and with ether, and were dried at room temperature. The yield was 5.3 g (43%) of white crystals. The substance is decomposed to $H_3M \cdot H_2O$ by water; it melts at 114°C and decomposes at 140–145°C with liberation of HCl. Analysis: $C_8H_{16}ClNO_7S$ (m.w. 305.7) calculated: 81.20% M^{3-} , 5.89% H_2O , 11.59% Cl; found: 80.81% M^{3-} , 5.32% H_2O , 11.68% Cl.

$H_3M \cdot HCl$ was obtained by dehydration of this substance at 80°C over phosphorus pentoxide. White crystals with similar properties as those of the hydrate decompose at about 140°C. Analysis: $C_8H_{14}ClNO_6S$ (m.w. 287.7) calculated: 86.12% M^{3-} , 12.32% Cl; found: 86.27% M^{3-} , 12.09% Cl.

Deuterated substances were prepared by triple recrystallization from D_2O and from 10M-DCI in D_2O , respectively.

Na_3M was obtained by neutralization of H_3M with sodium hydroxide to pH 11 and by evaporation of the solution near to dryness. The white crystalline powder was filtered off, washed with ethanol and ether, and dried at laboratory temperature. The yield was 75%. The substance is readily soluble in water. It decomposes at 340°C without melting. Analysis: $\text{C}_8\text{H}_{10}\text{NNa}_3\text{O}_6\text{S}$ (m.w. 317.2) calculated: 78.26% M^{3-} , 21.74% Na; found: 78.07% M^{3-} , 21.25% Na.

Attempts to prepare hydrogen sodium salts were unsuccessful. Na_2HM forms only an oily material and NaH_2M disproportionates to H_3M and Na_2HM .

Properties in Solution

The dissociation constants were determined by titration of $4 \cdot 10^{-3}\text{M}$ H_3M with a 0.1M hydroxide solution at 25°C and $I = 0.1$. Both sodium hydroxide in a NaClO_4 medium and tetraethylammonium hydroxide in a NEt_4Cl medium were used. The titration curves were identical within experimental error, thus indicating that no complex of sodium ions with the ligand is formed. The dissociation constants, given in Table I, were calculated from the titration curves using the SCOGS program⁹. The distribution of individual acid-base forms of the ligand is shown in Fig. 1. The formation of $\text{H}_3\text{M} \cdot \text{HCl}$ was verified by study of the H_3M solubility in HCl solutions of various concentrations (Fig. 2). $\text{H}_3\text{M} \cdot \text{HCl} \cdot \text{H}_2\text{O}$ is formed as a solid phase at HCl concentrations of 3M and higher.

The dissociation mechanism was elucidated by measurement of infrared and ultraviolet spectra in solutions of various acidities. The infrared spectra of 0.3M solutions of Na_3M in D_2O , whose pD (i.e. "pH" + 0.41, see¹⁰) was adjusted by a DCl solution in D_2O , were measured in the region, $1500-1800\text{ cm}^{-1}$. Calcium fluoride cells with a sample thickness of 0.04 mm were used. The positions and relative intensities of three kinds of $\nu_a(\text{COO})$ maxima in this region are given in Table II; their assignment is in agreement with the literature¹¹. It is evident from the table that the third dissociation constant corresponds to the dissociation of the weakly acidic betain hydrogen.

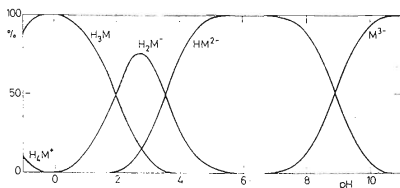


FIG. 1

Distribution Curves of the H_3M Acid-Base Forms

TABLE I

Dissociation Constants of H_3M at $25^\circ C$ and $I = 0.1$ ($NaClO_4$)
Residual⁹ 0.07 ml.

Constant	$-\log K_1^H$	3σ
K_1^H	1.97	0.12
K_2^H	3.53	0.10
K_3^H	8.82	0.07

TABLE II

Infrared Spectra of H_3M in D_2O at Various pD

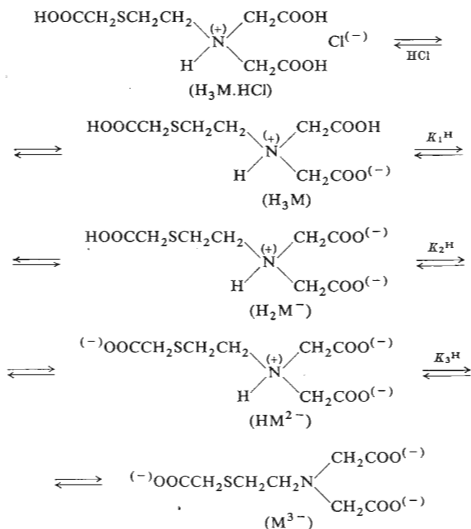
pD	$-\text{COO}^-$	$ \begin{array}{c} \text{CH}_2\text{COO}^- \\ \diagup \\ \text{H}-\text{N}^+ \\ \diagdown \\ \text{CH}_2\text{COOH} \end{array} $ cm^{-1} (relative intensity)	$-\text{COOH}$
10M-DCI	—	—	1 740 (17.0)
1.70	—	1 623 (4.4)	1 695 (10.7)
3.64	1 579 (1.7)	1 623 (11.7)	1 691 (2.7)
5.11	1 576 (8.1)	1 622 (12.7)	—
9.58	1 578 (12.8)	1 616 (7.2)	—
12.88	1 578 (21.2)	—	—

TABLE III

Percent Concentration of $-\text{SCH}_2\text{COOH}$ Groups in Dependence on pH

pH	% $-\text{SCH}_2\text{COOH}$		
	from the UV spectrum	calculated from K_1^H and K_2^H assuming that the dissociation of SCH_2COOH corresponds to constant	
		K_1^H	K_2^H
2.81	89	13	84
3.23	70	5	65
3.59	42	2	43
3.96	26	1	23
4.55	12	0	9

The dissociation order of the two strongly acidic hydrogens was clarified using measurement of ultraviolet spectra in the charge transfer band region between 200 and 300 nm. From reference measurements with model substances it was found that the $-\text{SCH}_2\text{COOH}$ group exhibits a maximum at 235–240 nm, while the $-\text{N}(\text{CH}_2\text{COOH})_2$ group absorbs substantially less in this region (Fig. 3). Band separation using Gaussian analysis gave a maximum position of 236 nm for the $-\text{SCH}_2\text{COOH}$ in H_3M (ϵ_{M} 190). The changes in the spectrum in the region, 200–300 nm, in dependence on pH then unambiguously show that the second H_3M dissociation constant corresponds to the $-\text{SCH}_2\text{COOH}$ group (Table III). The acidobasic equilibria can therefore be described by the following scheme:



Properties of the Crystalline Substances

The substances were characterized by their X-ray powder patterns and infrared spectra. As follows from Table IV, no substances are isostructural. Their infrared spectra are quite complex. Important band groups and their assignment are summarized in Table V, from which some conclusions can be drawn concerning the structure

of the solid substances, especially in comparison with the spectra of their aqueous solutions.

The typical splitting of the carboxyl antisymmetric stretch with H_3M and $\text{H}_3\text{M} \cdot \text{H}_2\text{O}$ and the presence of N—H vibration bands (shifting on deuteration) indicate that these substances also have zwitterion structure with protonated nitrogens in the crystalline state. Both undissociated carboxylic groups are simultaneously bound by relatively strong intermolecular hydrogen bonding, as indicated by the low value of the $\nu(\text{OH})$ wavenumber, about 2710 cm^{-1} , shifting on deuteration to about 2090 cm^{-1} . The $\nu(\text{H}_2\text{O})$ and $\nu(\text{D}_2\text{O})$ values, on the other hand, characterize the water molecule as hydrate water, not forming more significant hydrogen bonds.

The hydrochlorides, $\text{H}_3\text{M} \cdot \text{HCl} \cdot \text{H}_2\text{O}$ and $\text{H}_3\text{M} \cdot \text{HCl}$ have all their carboxyl groups protonated and their spectra are consistent with the structure of a quaternary ammonium salt. They contain only a single $\nu_a(\text{COOH})$ maximum and an intense $\nu(\text{NH})$ or $\nu(\text{ND})$ band. The region of the $\nu(\text{OH})$ vibration substantially differs from H_3M . The hydrochloride spectra exhibit independent bands of free hydroxyl groups at 3570 cm^{-1} , shifting to 2650 cm^{-1} on deuteration. This indicates that the hydrochlorides do not form intermolecular hydrogen bonds, which is in agreement with the assumed ionic structure. The character of the water molecule in $\text{H}_3\text{M} \cdot \text{HCl} \cdot \text{H}_2\text{O}$

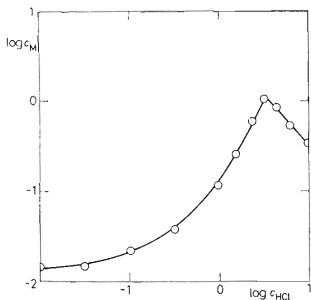


FIG. 2

The H_3M Solubility in Hydrochloric Acid

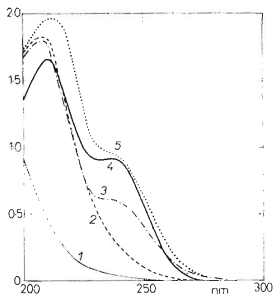


FIG. 3

The Ultraviolet Absorption Spectra of H_3M and of Related Compounds

1 cm cells; curve: 1 $5 \cdot 10^{-3}\text{ M-CH}_3 \cdot \text{N}(\text{CH}_2\text{COOH})_2$; 2 $5 \cdot 10^{-3}\text{ M-H}_4\text{EDTA}$; 3 $2 \cdot 10^{-3}\text{ M-CH}_3\text{SCH}_2\text{COOH}$; 4 $2 \cdot 10^{-3}\text{ M-HOOCCH}_2\text{SCH}_2\text{CH}_2\text{SCH}_2\text{COOH}$; 5 $5 \cdot 10^{-3}\text{ M-H}_3\text{M}$.

TABLE IV
X-Ray Powder Patterns of the Prepared Compounds
CuK α ; goniometric registration with a recorder.

H ₃ M		H ₃ M.H ₂ O		H ₃ M.HCl		H ₃ M.HCl.H ₂ O		Na ₃ M	
<i>d</i> , Å	<i>I</i>	<i>d</i> , Å	<i>I</i>	<i>d</i> , Å	<i>I</i>	<i>d</i> , Å	<i>I</i>	<i>d</i> , Å	<i>I</i>
7.76	1	9.8	3	9.2	2	7.38	4	11.4	10
6.51	4	7.79	1	5.21	6	6.72	1	8.01	3
4.98	4	6.17	1	4.35	10	5.61	1	4.81	5
4.35	7	5.21	3	3.90	2	5.09	2	3.84	2
3.91	8	5.04	3	3.67	3	4.25	5	3.60	2
3.70	6	4.60	1	3.42	7	4.11	3	3.29	3
3.37	10	4.11	3	3.08	5	3.95	6	3.09	2
3.06	1	4.01	3	2.85	4	3.85	5	2.80	8
2.85	2	3.94	3	2.65	4	3.61	5	2.29	2
2.62	3	3.61	2	2.58	3	3.42	10	2.22	1
2.52	1	3.42	10	2.47	1	3.24	2	2.01	2
2.45	2	3.16	2	2.39	4	3.14	4	1.90	2
2.39	1	3.02	6	2.31	2	3.02	1	1.74	1
2.28	1	2.85	1	2.23	1	2.97	3	1.67	2
2.12	1	2.70	2	2.14	1	2.85	5	1.60	1
1.95	2	2.65	1	2.06	2	2.81	1		
1.79	2	2.58	1	2.00	1	2.76	4		
1.76	1	2.44	1	1.91	3	2.72	4		
1.70	2	2.31	1	1.82	3	2.64	3		
1.66	1	2.08	1	1.74	2	2.61	3		
				1.67	1	2.57	3		
				1.62	1	2.47	4		
				1.57	1	2.36	4		
						2.30	3		
						2.20	2		
						2.09	2		
						1.99	1		
						1.80	2		
						1.67	2		

is practically identical with that in H₃M.H₂O. The spectrum of the trisodium salt unambiguously corresponds to the structure of the M³⁻ anion in aqueous solution with dissociated carboxyl groups and with an unprotonated nitrogen atom: it contains a single $\nu_a(\text{COO})$ band at 1595 cm⁻¹ and the $\nu(\text{C—N})$ group region is not split.

TABLE V
Selected Band Groups in the Infrared Spectra

Compound	$\nu(\text{C}-\text{S})$	$\nu(\text{C}-\text{N})$	$\delta(\text{H}_2\text{O})$ (D_2O)	$\nu_a(\text{COO})$	$\nu_a(\text{COOH})$	$\nu(\text{NH})$ (ND)	$\nu(\text{H}_2\text{O})$ (D_2O)	$\nu(\text{OH})$ (OD)
H_3M	686 s	1 059 w 1 085 w		1 671 vs	1 728 vs	3 060 s		2 705 w
D_3M	687 s	1 049 m 1 082 w		1 671 vs	1 728 vs	2 290 m		2 095 w
$\text{H}_3\text{M}.\text{H}_2\text{O}$	660 m	1 062 w 1 080 w	1 641 m	1 680 vs	1 730 sh	3 060 s	3 440 s	2 720 w
$\text{D}_3\text{M}.\text{D}_2\text{O}$	658 m	1 055 w 1 078 w	1 215 w	1 682 vs	1 729 s	2 280 m	2 560 s	2 085 sh
$\text{H}_3\text{M}.\text{HCl}$	677 m	1 048 m 1 083 w			1 730 vs	3 015 s		3 570 s
$\text{D}_3\text{M}.\text{DCl}$	675 m	1 050 m 1 082 w			1 732 vs	2 210 s		2 650 s
$\text{H}_3\text{M}.\text{HCl}.\text{H}_2\text{O}$	675 m	1 060 w 1 085 w	1 640 m		1 730 vs	3 035 s	3 390 vs	3 575 vs
$\text{D}_3\text{M}.\text{DCl}.\text{D}_2\text{O}$	674 m	1 050 m 1 082 m	1 220 m		1 730 vs	2 210 s	2 510 s	2 655 s
Na_2M	683 m	1 035 w		1 595 vs				

CONCLUSIONS

Mercaptoethylaminetriacetic acid is, in its various acid-base forms, a potential mono- to pentadentate ligand, containing three kinds of donor atoms. The dissociation mechanism found is the basis for further study of the complexing ability of the individual acid-base forms, in relation to their structure.

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