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Synthesis, Molecular Structure, and Vibrational Spectra of Tetrakis(2-hydroxyethylammonium) Chloride and Its Triethanolamine Precursor and Metabolite

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Abstract—A unique one-stage synthesis of tetrakis(2-hydroxyethylammonium) salts, precursors of new hypervalent silicon compounds, has been developed. The vibration spectra of tetrakis(2-hydroxyethylammonium) chloride and its triethanolamine precursor and metabolite have been studied by IR spectroscopy and quantum chemistry. Analysis of alterations in the modes with increasing number of $HOCH_2CH_2$ groups has been performed.

Keywords: triethanolamine, tetrakis(2-hydroxyethylammonium) chloride, molecular structure, vibration spectra

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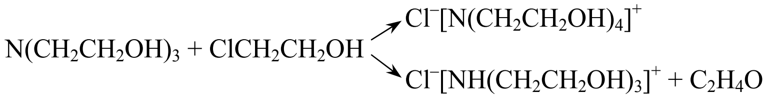
Organic derivatives of triethanolamine are of particular interest among atranes. Triethanolammonium salts of protic acids $[HN(CH_2CH_2OH)_3]^+X^-$ (protatranes [1]) have an *endo* atrane structure and are much more bioactive [2, 3] than their precursor and metabolite triethanolamine, as well as acids HX, which are widely used in medicine and agriculture. Further research on compounds of this class resulted in the development of new medicines [4]. Later Walker and Bruce suggested compounds with flexible hydroxyalkyl groups in the cation to be applied as ionic liquids capable to dissolve, stabilize, and activate enzymes [5, 6]. Tris(hydroxymethyl)aminomethane (Tris) added in even small amounts to various ionic liquids much enhanced the activity of horseradish peroxidase [7]. An even stronger effect can be obtained if to increase the number and flexibility of hydroxyalkyl substituents in the ammonium cation. The activity of enzymes in a tetrakis(2-hydroxyethylammonium) chloride $[N(CH_2CH_2OH)_4]^+Cl^-$ ionic liquid was 30–240 times higher than in other ionic liquids [8]. On the whole, the reactivity, molecular and stereoelectronic structure, as well as bioactivity of this class of compounds have never been studied. Moreover, tetrakis(2-hydroxyethylammonium) salts can be considered as precursors of previously unknown hypermetallatranes, in particular, hypersilatranes.

Aimed at preparing tetrakis(2-hydroxyethylammonium) chloride, we have studied the reaction of 2-chloroethanol with triethanolamine. The reaction was performed under reflux for 24 h in the absence of a solvent, as well as in different solvents (butanol, dioxane, acetonitrile) and at different reagent ratios. However, we failed to obtain tetrakis(2-hydroxyethylammonium) chloride by this procedure. The reaction yielded no other products but chloroprotatrane $[NH(CH_2CH_2OH)_3]^+Cl^-$. A similar reaction of triethanolamine with iodoethanol in an open reaction system resulted too in an exclusive formation of iodoprotatrane [9]. Tetrakis(2-hydroxyethylammonium) chloride could only be prepared by the procedure described in [10]. However, also herethe major reaction product was chloroprotatrane (as a powder insoluble in methanol). The formation of chloroprotatrane is due to a high proton affinity of the triethanolamine nitrogen; as a consequence, the latter abstracts proton from the 2-chloroethanol hydroxyl (Scheme 1).

Possibly, tetrakis(2-hydroxyethylammonium) chloride obtained by the latter procedure is a secondary

Scheme 1.



$$\mathrm{N(CH_2CH_2OH)_3 + ClCH_2CH_2OH}\begin{array}{l}\nearrow \mathrm{Cl^-[N(CH_2CH_2OH)_4]^+} \\ \searrow \mathrm{Cl^-[NH(CH_2CH_2OH)_3]^+ + C_2H_4O}\end{array}$$

reaction product of chloroprotatrane with ethylene oxide in a closed system under increased pressure. Such chemical reaction has been described in a number of patents [11].

We suggested that the yield of tetrakis(2-hydroxyethylammonium) chloride could be increased by introducing ethylene oxide to the closed reaction system. Therefore, before reaction varied quantities of ethylene oxide were dissolved in a cold 2-chloroethanol or its mixture with methanol. The triethanolamine–2-chlototoethanol–ethlene oxide molar ratio was 1.01 : 1 : (0.15–0.50). The weight fraction of methanol in the reaction mixture was 30%. In view of the fact that tetrakis(2-hydroxyethylammonium) chloride is highly sensitive to moisture, after the reaction performed with no solvent the required quantity of methanol was added to the reactor to dissolve the reaction product. When ethylene oxide was added (even in a very small quantity), no precipitation of methanol-insoluble chloroprotatrane was observed. Tetrakis(2-hydroxyethylammonium) chloride was recrystallized from ethanol taken in a quantity double the weight of the methanol solution. The recrystallized product was dissolved in methanol, and its concentration in the solution was determined by chloride gravimetry. The yield of tetrakis(2-hydroxyethylammonium) chloride after recrystallization, calculated per 2-chloroethanol in the initial methanol solution, was 73%. According to X-ray diffraction data, tetrakis (2-hydroxyethylammonium) chloride has several polymorphic modifications which are likely to have quite different melting points. The salt starts to melt at 80°C but does not liquefy completely until it starts to decompose. Derivatographic analysis (heating rate 2.5 deg/min) showed that tetrakis(2-hydroxyethylammonium) chloride is a fairly thermally stable compound. It starts to decompose at about 200°C. Decomposition sharply accelerates with temperature. When thermal treatment of tetrakis(2-hydroxyethylammonium) chloride is performed using an oil bath, at the beginning of the decomposition the salt irreversibly transforms into a liquid more viscous than triethanolamine.

As the molecular structure of tetrakis(2-hydroxyethylammonium) chloride has never been studied, we have studied its structure and vibration spectra and compared them with those of triethylamine. The equilibrium structures of triethanolamine and tetrakis-(2-hydroxyethyl)ammonium $[\mathrm{N(CH_2CH_2OH)_4}]^+$, optimized at the B3LYP level with the aug-cc-pVTZ basis set (including diffuse functions), are shown in Figs. 1 and 2. The structure of monomeric triethanolamine (Fig. 1a) belongs to the C_3 point group. The feature of this structure is that the hydroxy groups of each of the $\mathrm{HOCH_2CH_2N}$ "blades" form hydrogen bonds with each other with the O···H distance of 2.023 A.

Monomeric triethanolamine is likely to exist in the gas phase (no experimental data are available), but in the crystal phase it exists exclusively as dimers, where monomer molecules are held together by six strong hydrogen bonds [12]. As follows from X-ray diffraction data and the first quantum-chemical calculation [13], the molecule of triethanolamine has an *endo* conformation, where the nitrogen lone electron pair is directed inside the "dome." The equilibrium structure of the dimer is shown in Fig. 1b. The structure belongs to the S_6 point group. The arrangement of hydrogen bonds in the dimer differs from that in the monomer: The hydroxy groups of one of the monomers are hydrogen-bonded to the hydroxy groups of the other, and each hydroxy group acts both as a donor and as an acceptor. Therefore, the monomers are held together by six hydrogen bonds; the length of these bonds is 1.711 A, which is appreciably shorter compared to the hydrogen bonds in the monomer. The other bonds lengths in the dimer are close to the bonds in the monomer: C–N bonds are slightly longer and C–C bonds are slightly shorter. In the whole, the equilibrium bond lengths in the dimer are closer to the experimental values.

We obtained an IR spectrum of triethanolamine and tetrakis(2-hydroxyethylammonium) chloride films in the range 4000–800 cm^{-1}. The table lists the vibration frequencies of these two compounds. To assign the frequencies, we calculated harmonic vibration frequencies for the triethanolamine monomer and dimer and the $[\mathrm{N(CH_2CH_2OH)_4}]^+$ cation by the B3LYP/aug-cc-pVDZ method. As we showed previously [14, 15], the

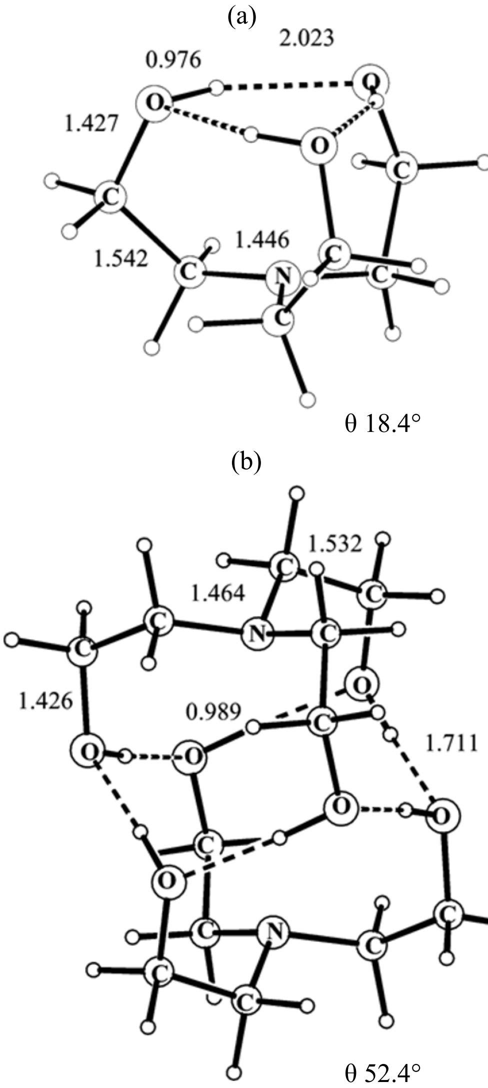


Fig. 1. Equilibrium structure of triethanolamine: (a) monomer and (b) dimer.

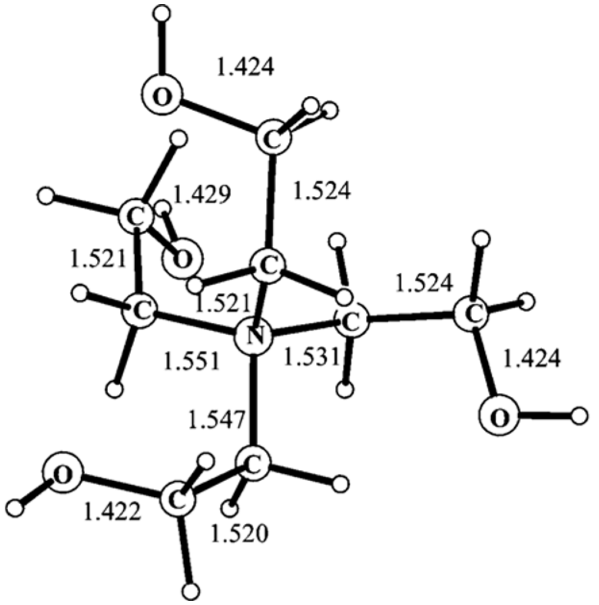


Fig. 2. Equilibrium structure of the tetrakis(2-hydroxyethylammonium) cation.

vibration frequencies of atranes calculated by this method well fit the experimental values, except for the C–H and, especially, O–H stretching vibration frequencies. The reason for the latter finding is that these frequencies are highly anharmonic, whereas the calculation gives harmonic frequencies.

Nevertheless, the OH stretching vibration frequencies in the triethanolamine dimer are close to experimental. This fact may suggest that the strength of the hydrogen bond in the dimer is overestimated. The calculated ν(OH) in the $[N(CH_2CH_2OH)_4]^+$ cation are markedly higher, because our model does not include cation−anion hydrogen bonds. Taking into account that the ν(OH) frequencies in the cation are much higher than the respective vibration frequencies in the triethanolamine dimer, we are safe to state that these bonds are fairly strong.

The calculated COH bending vibration frequencies are higher than 1500 cm^{-1}. In view of the overestimation of the strength of hydrogen bonds in the dimer we can conclude that the experimental frequencies are lower. However, they are likely to be obscured by strong and broad band centered at 1456 cm^{-1}. The δ(CH_2) frequencies, too, fall into this region.

The δ(COH) frequencies in tetrakis(2-hydroxyethylammonium) chloride can be assigned to the band at 1446 cm^{-1}, which is absent from the spectrum of triethanolamine. Even though certain δ(CH_2) and δ(COH) frequencies overlap each other, they are fairly characteristic. The same relates to the wagging and torsional vibrations of the CH_2 groups. However, at frequencies lower than 1200 cm^{-1}, contributions of different vibrations are mixed, which allows nothing more than arbitrary assignments. Vibrations mostly contributed by C–N (correspond to the IR band at 1153 cm^{-1}), C–O (1073 cm^{-1}), and C–C (908 and 883 cm^{-1}) stretching can only be recognized.

The introduction of one more ethanol moiety in going from triethanolamine to tetrakis(2-hydroxyethylammonium) chloride results in that the C–N bond in the latter molecule much elongates and the C–C and C–O bonds respectively shorten and elongate, though

Experimental IR spectra (ν, cm^{-1}) and B3LYP/aug-cc-pVDZ vibration spectra (km/mol) of triethanolamine and tetrakis(2-hydroxyethylammonium) chloride

Triethanolamine			Tetrakis(2-hydroxyethylammonium) chloride		
IR spectrum	monomer[a]	dimer[a,b]	IR spectrum	calculation	assignment
3340 s	3611 (A_u), 3565 (E_u)	3405 (2332), 3303 (2684)	3263 s	3822 (81), 3818 (78), 3817 (84), 3816 (102)	ν(OH)
2950 s	3082 (E_u), 3075 (A_u), 3059 (A_u), 3054 (E_u)	3098 (184), 3092 (1), 3074 (20), 3070 (114)	2972 m	3201 (0), 3188 (4), 3177 (19), 3169 (1), 3129 (4), 3121 (1), 3109 (5), 3106 (7)	$\nu_{as}(CH_2)$
2882 s	3008 (A_u), 3006 (E_u), 2927 (A_u), 2919 (E_u)	3034 (264), 3034 (327), 2898 (545), 2887 (220)	2884 m	3088 (16), 3060 (2), 3055 (29), 3053 (18), 3039 (15), 3023 (33), 3020 (27), 3018 (28)	$\nu_s(CH_2)$
	1467 (A_u), 1431 (E_u)	1562 (234), 1510 (2)	1446 m	1262 (80), 1253 (22), 1247 (17), 1245 (41)	δ(COH)
1456 m	1510 (A_u), 1503 (E_u), 1478 (E_u), 1480 (A_u), 1478 (E_u)	1495 (12), 1487 (30), 1469 (15), 1465 (18)	1467 m	1510 (4), 1506 (1), 1503 (28), 1491 (16), 1488 (1), 1480 (26), 1469 (15), 1457 (2)	$\delta(CH_2)$
1408 m	1410 (E_u), 1394 (A_u)	1413 (8), 1397 (13)	1446 m	1453 (2), 1452 (14), 1446 (5), 1437 (5),	$w(CH_2)$
1360 m	1358 (E_u), 1353 (A_u)	1382 (10), 1389 (84)		1422 (2), 1407 (3), 1400 (0), 1387 (3)	
1338 w	1303 (A_u), 1267 (E_u)	1310 (53), 1299 (30)		1366 (17), 1361 (15)	$tw(CH_2)$
1282 m	1256 (10) (E_u), 1246 (19) (A_u)	1275 (19)	1312 m	1337 (31)	
1250 m		1264 (10)		1328 (2), 1287(4), 1272 (1)	
			1238 m	1240 (28)	
				1234 (12)	
1153 m	1185 (E_u), 1103	1174 (56)		1145 (5), 1140 (2)	ν(CN)
			1110 sh	1126 (34)	
				1117 (44)	
1073 s	1096 (E_u), 1075 (A_u)	1102 (13), 1098 (419)		1112 (7), 1103 (23)	ν(C−O)
			1040 s	1074(29)	
				1068(28)	
	1068 (A_u), 997 (E_u)	1080 (100)	972 m	1030 (50)	$\rho(CH_2)$
1035 s		1060 (70)		1005 (93), 982 (23), 972 (6)	
908 m	904 (E_u), 852 (A_u)	909 (70)	941 s	938 (37)	ν(C−C)
		886 (107)	920 s	926 (32)	
			878 m	898 (16)	
				890 (4)	
883 m	844 (E_u), 734 (E_u)	871 (200)	815 m	835 (3), 818 (9), 786 (6)	$\rho(CH_2)$
		851 (150)		653(1)	

[a] Calculated. [b] Given are only the frequencies of IR-active vibrations of the irreducible representation A_u.

to a lesser degree. This effect reveals itself in the predicted vibration frequencies in the range of C–N stretching vibrations. In going from triethanolamine to tetrakis(2-hydroxyethylammonium) chloride, the highest frequency of these vibrations decreases from 1192 to 1145 cm^{-1} (see the table). The C−C stretching vibration frequencies slightly increase: 938–890 cm^{-1} against 918–892 cm^{-1} in triethanolamine. The CH_2 pendular vibration frequencies decrease. In the whole, the assignment and ranges of vibration frequencies change only slightly, except for COH vibrations, and the $[(HOCH_2CH_2)_4N]^+$ vibrations are fairly well described by the model. The experimental spectra of triethanolamine and tetrakis(2-hydroxyethylammonium) chloride also differ from each other: the $\nu_{as}(CH_2)$, $w(CH_2)$, and ν(C–C) in the latter spectra are higher and the ν(C–N) frequencies are lower. The changes in the OCH_2CH_2N stretching vibration frequencies in going from triethanolamine to tetrakis(2-hydroxyethylammonium) chloride correlate with the changes in the equilibrium (theoretical) lengths of the respective bonds.

EXPERIMENTAL

The IR spectra were measured on a Varian 3100 FT-IR spectrophotometer in KBr. Thermogravimetric and differential thermal analysis were performed on a MOM Paulik–Paulik–Erdey derivatograph in platinum crucibles, heating rate 2.5 deg/min. The equilibrium structures and vibration spectra were calculated by B3LYP with the aug-cc-pVDZ basis set (including diffuse functions).

Tetrakis(2-hydroxyethylammonium) chloride was prepared by the procedure in [10]. The reaction was performed in dry methanol at 115°C in a pressure reactor for 22 h with an excess of triethanolamine. Yield 73%, transparent hygroscopic crystals, mp 80°C (ethanol). Found, %: C 41.52; H 11.11; N 5.97. $C_8H_{20}ClNO_4$. Calculated, %: C 41.82; H 8.79; N 6.10.

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