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HYDROLYSIS AND ANALYTICAL CONTROL OF NITRIC ACID ESTERS ("NITRO-BODIES")

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HYDROLYSIS AND ANALYTICAL CONTROL OF NITRIC ACID ESTERS ("NITRO-BODIES")

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/Following is the translation of an article by E. Schulek, K. Burger and M. Feher in Zeitschrift fur Analytische Chemie, Vol 177, No 2, Berlin, October 1960, pages 81-86./

Nitric acid esters of several polyalcohols and polysaccharides are important products of the explosives industry. Nitric acid esters of certain polyalcohols are also indispensible, often life-saving pharmaceuticals. The quantitative determination of these compounds, the so-called "nitro-bodies," cannot be considered as a satisfactorily solved problem, notwithstanding the many reports of procedures [3] in the literature. According to the reports in literature, many decomposition products are formed from the above-mentioned compounds by an alkaline hydrolysis, as nitrite, nitrate, ammonia, cyanide, formate, acetate, various aldehydes, etc. Several authors have determined that nitrate and nitrite are found in a strictly defined ratio.

In order to elucidate the possibilities of analysis we examined the hydrolysis of several "nitro-bodies," namely that of glycerol trinitrate /nitroglycerin/, pentaerythritol tetranitrate /2,2-bishydroxymethyl-1,3-propanediol tetranitrate/ (Pentrit), nitrocellulose, and nitrostarch. The primary goal of our research was the determination of the formed nitrogen-containing components; the ratio of amounts of these could serve to characterize the individual nitro-bodies. According to the results of our determinations the nitrogen content in the hydrolysates of these compounds was distributed to ammonia, cyanide, nitrite, and nitrate. Suitable procedures therefore were then developed for determination of these four components in mixture [2].

The analyzed materials were hydrolysed according to the following procedure: We dissolved about 0.05 grams of the material, accurately weighed, in 28 milliliters of 96-percent ethanol, and added to the solution two milliliters of 20-percent sodium hydroxide in water. The reaction mixture, containing about 1.5 percent NaOH, was boiled for one hour in a flask [2] with a ground-glass jointed reflux cooler. In order to trap the released ammonia a cotton plug, saturated with hydrochloric acid, was placed between two dry cotton layers in the cup type opening of the reflux cooler. Ammonia formed during the hydrolysis is being released from the strongly alkaline solution and becomes trapped by the

hydrochloric acid containing cotton plug. Upon completion of hydrolysis the flask is removed and the cotton from the upper part of the cooler is washed with about 15 milliliters of water, to which several drops of one normal (1 N) hydrochloric acid has been added. After appropriate adjustment of the pH value, ammonia was distilled from this solution and determined by the customary method [1]. The flask containing the hydrolysate was attached to a ground-glass jointed distillation apparatus and the excess of the solvent was removed by distillation. About three grams of boric acid was added to the liquid residue and the pH of the solution was adjusted to pH 7 to 8 (the pH value can be controlled by an appropriate indicator paper), as necessary for the distillation of cyanide. After the removal of cyanide by distillation the liquid residue was transferred to a 100 milliliter volumetric flask and nitrite and nitrate was determined by using appropriate aliquots from this solution.

With the use of glycerol trinitrate as a model substance we were able to determine that the ratio of the formed hydrolysis products is influenced considerably by the type of solvent, the concentration of alkali, and the presence of several concomitant substances and reducing compounds. For our determinations we used 90-percent ethanol as a solvent, fresh distilled over an alkali, considering that during stratification the acetone would decompose. When the same substance was dissolved in various acetone samples, the measured values gave considerable distribution. When the hydrolysis was performed in the presence of very small amounts of glucose (about 0.1 percent), the ratio of nitrate to nitrite in the hydrolysate showed no change; the same amount of ascorbic acid, however, resulted in about 6-percent rise in the amount of nitrite and thus shifted the ratio of both radicals. We also made similar observations with the hydrolysis of pentaerythritol tetranitrate (Nitropenta) granules which, besides the active ingredient, contained also considerable amounts of reducing carriers (starch, sugar, etc.), that are necessary for the preparation of tablets (see Table 1). In the case of glycerol trinitrate -- the model substance -- hydrolysis of all four nitrogen-containing products were present. With a 10-fold increase of the alkali concentration the amounts of the formed nitrate and nitrite did not show any significant changes; the cyanide, however, disappeared from the hydrolysate and the amount of the released ammonia was doubled.

It follows from the above that in order to obtain reproducable results, the hydrolyses should be performed under completely identical conditions (solvents, alkali concentration, etc.) and with the removal of reducing agents. With changes in conditions there are also changes in concentrations and ratios of the products; however, their sum -- the total nitrogen content -- remains constant within the limits of experimental errors of the analysis of the four components.

During the course of our further experiments we performed the hydrolysis of separate "nitro-bodies" under identical conditions and determined the characteristic ratio of nitrate to nitrite for each of the respective substances (see Table 2). Especially significant this ratio is for pentaerythritol tetranitrate; in its hydrolysate the nitrate part is larger than that of nitrite. It is also significant that during hydrolysis of pentaerythritol tetranitrate there is no formation of cyanide,

as in contrast to other tested nitro-bodies. We assume that the reason for this behavior is that the organic part of the compound -- the pentaerythritol -- acts less reducing than the vicinal polyalcohols of other compounds. Pentaerythritol contains no vicinal hydroxyl groups and thus it can reduce nitrate to nitrite or to nitrogen compounds with a still lower oxidation level only in a limited amount. The correctness of these assumptions are affirmed by the observations that the amount of nitrite increases strongly in the hydrolysate in the presence of organic reducing agents (see Table 1).

Especially significant is the difference between the nitrate-nitrite ratios of nitrocellulose /See note/ and nitrostarch hydrolysates (nitrocellulose 1:1.47; nitrostarch 1:2.15). This difference can be explained on the basis of the different structural and physical properties of both compounds. The nitration of cellulose does not impart any essential changes in the molecular structure and no degradation. The degree of polymerization of cellulose and nitrocellulose is almost the same. Therefore it can be assumed also that the reducing breakdown products are formed in a lesser amount during hydrolysis than it is the case with the less stable compound, the nitrostarch. It is to say that during nitration the compound is partially degraded by the action of the acid, the nitrostarch thus consists of smaller molecules than the original starch and it can be assumed that during hydrolysis further degradation occurs, such degradation being connected with the formation of increasing amounts of reducing agents. (/Note:/ Nitrocellulose was hydrolysed in acetone solution, as it is not soluble in ethanol.)

On the basis of the results of the described tests the formation of nitrogen compounds of lower oxidation level (nitrite, ammonia, cyanide) by the reducing action of the organic molecule released during hydrolysis can be thus partially explained. Cyanide develops as an intermediate during formation of ammonia.

In separate experiments we tested also the rate of hydrolysis of glycerol trinitrate and pentaerythritol tetranitrate which are used as medical remedies. It is known that the action of both compounds is due to their nitrite content which is liberated during degradation in the organism. Glycerol trinitrate (nitroglycerin) is used to induce an immediate, however, soon declining effect, while pentaerythritol tetranitrate (Pentrit) unfolds its effect more slowly, yet has a more lasting action.

We presumed that the difference between the therapeutic effects of both compounds is connected with the rate of their hydrolysis, i.e., with the rate of nitrite formation. As a matter of fact, the results of our determinations show that under identical conditions and the same length of hydrolysis, three times as much nitrite is formed from nitroglycerin as from an equivalent amount of Pentrit. The slower hydrolysis of Pentrit can be well explained with the more difficulty decomposable, more stable structure of the molecule. The pharmacological difference between the effects of both preparations is explained also on the basis of the higher nitrite content in the nitroglycerin hydrolysate (nitrate-nitrite ratio in nitroglycerin hydrolysate is 1:2.13; in Pentrit hydrolysate, 1:0.80).

Table 1. Analysis of pentaerythritol tetranitrate hydrolysis.

No.	Solvent	Normality of hydroxide	In hydrolysate						Ratio nitrate/nitrite	Notes
			Ammonia-nitrogen %	Cyanide-nitrogen %	Nitrite-nitrogen %		Nitrate-nitrogen %		Total nitrogen %	
					Individual values	Average	Individual values	Average		
1	Ethanol	0.1	0.48	0	7.32 7.38	7.35	9.33 9.41	9.37	17.20	1:0.78	----
2	Ethanol	1.0	0.50	0	7.26 7.34	7.30	8.93 8.88	8.90	16.70	1:0.82	----
3	Ethanol	0.1	0.48	0	10.95 11.25	11.10	5.44 5.60	5.52	17.10	1:2.0	In presence of reducing substance of granules
4	Acetone	0.1	0.27	0	6.11 6.15	6.13	10.56 10.62	10.59	16.99	1:0.58	----

Table 2.

Compound	In hydrolysate						Total nitrogen content of the substance %	Ratio nitrate/ nitrite
	Ammonia-nitrogen %	Cyanide-nitrogen %	Nitrite-nitrogen %		Nitrate-nitrogen %		Total nitrogen %	
			Individual values	Average	Individual values	Average		
Pentaerythritol tetranitrate I	0.48	0	7.32 7.38	7.35	9.33 9.41	9.37	17.20	17.05	1:0.78
Pentaerythritol tetranitrate II	0.67	0	7.09 7.04	7.07	8.67 8.73	8.70	16.44	----	1:0.81
Pentaerythritol tetranitrate III	0.50	0	7.32 7.27	7.30	9.28 9.18	9.23	17.03	17.12	1:0.79
Pentaerythritol tetranitrate IV	0.50	0	7.26 7.34	7.30	8.93 8.88	8.91	16.71	----	1:0.82
Glycerol trinitrate I	0.34	0.21	12.18 12.27	12.23	5.69 5.73	5.71	18.49	18.53	1:2.14
Glycerol trinitrate II	0.32	0.16	11.53 11.59	11.56	5.40 5.45	5.43	17.47	----	1:2.13
"Nitrostarch"	0	0.55	8.56 8.51	8.54	3.85 3.92	3.89	12.98	----	1:2.20
	0	0.48	8.32 8.37	8.35	3.93 4.01	3.97	12.80	----	1:2.10
"Nitrocellulose"**	0.19	0.32	6.90 6.86	6.88	4.71 4.78	4.75	12.14	12.08	1:1.45
	0.25	0.03	7.06 7.12	7.09	4.78 4.82	4.80	12.17	12.08	1:1.48

* Determined as ammonia in hydrolysate after Devarda's reduction.
** Hydrolysed in acetone.

According to the results of these tests the analysis of nitro-bodies can be performed by a quantitative determination of the products which are formed during an alkaline hydrolysis under identical conditions. The products are ammonia, cyanide, nitrate and nitrite. The ratio of hydrolysis products is characteristic for individual compounds.

There are yet many more tests necessary to elucidate the various phases of hydrolysis even semi-quantitatively and the chemical processes taking place during hydrolysis.

Summary

By using previously published methods the authors determined the ammonia, cyanide, nitrite, and nitrate contents in alkaline hydrolysates of several nitric acid esters (glycerol trinitrate, pentaerythritol tetranitrate, "nitrostarch," and "nitrocellulose") prepared under identical conditions, and calculated the alternating ratios of nitrate and nitrite nitrogen in these hydrolysates. The mean values of these ratios were 1:0.83 for pentaerythritol tetranitrate, 1:2.14 for glycerol trinitrate and nitrostarch, and 1:1.46 for nitrocellulose. In contrast to the other tested "nitro-bodies," it was not possible to find cyanide in the hydrolysate of pentaerythritol tetranitrate. The results of analyses are suited for characterization of "nitro-bodies."

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