[CONTRIBUTION FROM JET-PROPULSION LABORATORY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Synthesis of Nitric Esters by the Addition of Nitric Acid to the Ethylene Oxide Ring[1]

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A study of factors influencing the yield of products resulting from the addition of nitric acid to ethylene oxide (oxirane) compounds has been made. For reactions in aqueous solutions, it was demonstrated that the ratio of nitrated products to side products was directly proportional to the ratio of nitrate ion (in moles per liter) to water (in moles per liter) at a given temperature. An increase in temperature increased the yield of nitrated product. Several new nitrato alcohols have been prepared in good yield by two nitration procedures. In addition, information relating to positional isomerism, heats of reaction, and major side reactions is included.

Nitric esters have been synthesized primarily by the reaction of alcohols with a mixture of concentrated nitric and sulfuric acids.[2] In addition to the potential hazard of this method, a difficulty arises when partial nitration of a polyhydric alcohol is desired. In particular, if an investigator is interested in obtaining 2-nitratoethanol[3] by the nitration of ethylene glycol, the product must be separated from 1,2-dinitratoethane. A more specific method for producing nitric esters, but on a laboratory scale only, is that of treating alkyl halides with silver nitrate. Owing to numerous possible side reactions[5] this method usually gives low yields, besides requiring an expensive reagent.

It has been demonstrated on several occasions that the nitrate ion adds to the oxirane ring to produce nitric esters[6–8] Nevertheless, little has been done in the way of developing synthetic methods for nitric esters based on this reaction. For example, in recent work[4] the reaction of ethylene chlorohydrin or bromohydrin with silver nitrate was used for the preparation of 2-nitratoethanol. Therefore it was decided that a careful study of the reaction of oxirane compounds with nitric acid would be desirable. The reaction has been studied in both aqueous and non-aqueous solutions. The methods which have been developed are not only convenient laboratory methods of synthesis but might well serve as bases for the large-scale synthesis of nitrato alcohols. Nitric acid was added to the following compounds: ethylene oxide, propylene oxide, 2,3-epoxybutane, epichlorohydrin, allyl glycidyl ether, glycidol, methyl glycidyl ether, 2-methoxyethyl glycidyl ether and styrene oxide. New compounds were prepared with the exception of the products from ethylene oxide, glycidol, and epichlorohydrin. Nitrated products could be isolated in pure condition except from the reaction mixture of styrene oxide. The exceptional reactivity of the nitric ester group with the phenyl group presumably caused thermal decomposition at elevated temperatures and thereby prevented distillation of the crude product even under reduced pressure.

Investigation of the two major side reactions, glycol formation and polymerization, was made, together with the determination of the effect of temperature on yields of final products. Also, heats of reaction have been measured under several different experimental conditions. An attempt was made to decide upon the position of entry of the nitrate ion by the familiar benzoylation-rate method[9–11] The nitrato alcohols are benzoylated at somewhat slower rates than are the corresponding aliphatic alcohols. However, the results indicate that a secondary alcohol was obtained from all unsymmetrical oxides except propylene oxide which gave a mixture of the two isomers.

The thermal sensitivity of these compounds has been studied briefly to increase safety in handling, as described in the experimental section of the paper.

Experimental

Aqueous Solution Procedure.—The general procedure was as follows: A solution of 464 g. (5.8 moles) of ammonium nitrate and 132 g. of concentrated nitric acid (1.5 moles nitric acid) in 332 g. of water was prepared in a 2-liter, three-necked flask equipped with mechanical stirrer, thermometer and dropping funnel. One mole of oxirane compound was added at a moderate rate from the dropping funnel to the stirred solution. A cold-water-bath was applied to keep the temperature from rising above about 35° during the course of the reaction, which is highly exothermic. When addition was complete, the cooling bath was removed and the mixture stirred for 1 to 2 hours. The solution was then neutralized by the addition of solid sodium bicarbonate. The neutral solution was extracted with six 150-ml. portions of ether or by using a continuous extractor. After the extract was dried over anhydrous sodium sulfate, the ether was removed and the residue distilled at reduced pressure through an 18-inch Vigreux column. Of the nitric ester obtained in solution as determined by separate titration, 60 to 90% was easily isolated. In the case of ethylene oxide, its volatility required the use of a slightly modified method of addition to the reaction mixture. Ethylene oxide was either bubbled into the nitrating solution through a fritted glass disk or was dissolved in an equal volume of ice-water and added from a cold dropping funnel. By either method, some loss of ethylene oxide by evaporation was encountered.

General Method for Obtaining Yield Data in Aqueous Solution Method.—Preliminary to establishing optimum conditions for the aqueous solution method, exploratory information on yield was obtained. A sample of oxide was added to a given reaction mixture which contained a known acid concentration. After allowing the solution to stand until reaction was practically complete (usually 30 minutes

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[1] This paper presents the results of one phase of research carried out at the Jet Propulsion Laboratory, California Institute of Technology, under Contract No. DA-04-495-ord 18, sponsored by the Department of the Army, Ordnance Corps.

[2] T. L. Davis, "Chemistry of Powders and Explosives," John Wiley and Sons, Inc., New York, N. Y., 1943.

[3] The nomenclature used throughout this paper is that of Marans and Zelinski.[4] Although not widely used as yet, it provides a simple classification of compounds reported herein.

[4] N. S. Marans and R. P. Zelinski, THIS JOURNAL, **72**, 5330 (1950).

[5] W. A. Cowdrey, *et al., J. Chem. Soc.*, 1252 (1937).

[6] M. Hanriot, *Ann. chim. phys.*, [5] **17**, 118 (1879).

[7] C. Blétry, French Patent 846,575 (1939).

[8] L. Smith, G. Wode and T. Widhe, *Z. physik. Chem.*, **130**, 154 (1927).

[9] R. G. Kadesch, THIS JOURNAL, **68**, 41 (1946).

[10] J. F. Norris and E. C. Haines, *ibid.*, **57**, 1425 (1935).

[11] D. Swern, G. Billen and H. B. Knight, *ibid.*, **71**, 1152 (1949).

or less), the amount of acid remaining in solution was ascertained by titration.

Non-aqueous Solution Procedure.—The general procedure was as follows: One mole of the oxide dissolved in 200 ml. of chloroform was placed in a 500-ml. 3-necked flask equipped with a 250-ml. graduated dropping funnel, a 50-ml. graduated dropping funnel, stirrer, cold-water condenser and thermometer. The top of the funnel containing the oxide solution was connected with the reaction flask by means of an open tube. To the small funnel was added 50 ml. (approximately 1 mole) of white fuming nitric acid. Approximately 3 to 5 ml. of the nitrating solution was added to the flask, and the stirrer was turned on. The flask was surrounded by an ice-bath, and the nitric acid and ethylene oxide solutions were then added simultaneously at such a rate that there was always a slight excess of acid present in the reaction mixture. After the addition of both reactants was complete, which required about 2.5 hours, the contents of the flask were heated and the temperature maintained at 40° for 60 minutes. The unreacted acid was then neutralized with about 30 g. of sodium bicarbonate. Any solids present were removed by filtration. The chloroform was removed under reduced pressure. The crude product was then distilled under vacuum to give a 60 to 70% yield of a product of practically pure nitrato alcohol containing no glycol.

A product containing some glycol contamination was prepared in about the same yields if white fuming nitric acid was replaced by 60% aqueous nitric acid saturated with ammonium nitrate.

An example of a procedure for removing glycol is given in the following purification of nitratopropanol. As an alternate procedure, a highly efficient distilling column could be used in the purification of some nitrato alcohols. Sixty grams (0.496 mole) of nitratopropanol of approximately 90% purity was shaken with 12.8 g. (0.06 mole) of sodium periodate dissolved in 150 ml. of water. The mixture was allowed to stand at room temperature for 30 minutes and was then stored in the 0° refrigerator overnight. Some crystals, presumably sodium iodate, had separated. The mixture, which smelled strongly of lower aldehydes, was placed in the continuous extractor and extracted with ether until no further decrease in volume was noted. On removal of the ether by evaporation and distillation of the residual product, 48 g. (or 80%) of pure nitratopropanol was recovered; b.p. 37–40° (0.5 mm.); nitrogen analysis, 11.50% (11.57%, calcd.).

When the nitrato alcohol to be prepared is a high explosive, it may be desirable to employ a distillation technique based on the principle of leaving a low-oxygen-balance material in the still pot, as suggested by Gold.[12] Adaptation to the preparation of nitrato alcohols is illustrated in the following purification of 2-nitratoethanol: Fifteen milliliters of 2-nitratoethanol of approximately 93% purity and 5 ml. of dibutyl phthalate were mixed together, and the resulting solution was fractionated. A heated column, 1 cm. i.d. and 30 cm. in length, packed with Podbielniak random packing was used at approximately 0.5 mm. pressure. About 12.7 g. (85%) of the product was recovered, boiling over the range 37.5–42.0° (0.5 mm.). Approximately the last third boiled at 40.0–41.0° (0.5 mm.); nitrogen content, 12.88% (13.08%, calcd.); saponification equivalent, 111.0 (107.0, calcd.).

Benzoylation Rate Method.—The method used was only a slight modification of that previously described.[9–11]

Thermal Sensitivity Tests.—Gradual heating of 50- to 100-mg. samples of 2-nitratoethanol in a sealed, heavy-walled capillary tube placed in a copper block resulted in violent explosion (possibly detonation) at 187°. Under the same conditions nitratopropanol decomposed but did not explode. Tests of this kind are complicated by dependence of the results on sample size and rate of heating.

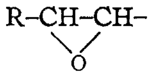
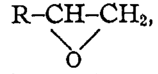
Determination of Heat of Reaction.—The apparatus used for obtaining heat of reaction data consisted of a dewar flask equipped with a nichrome heating coil and a thermometer reading to hundredths of a degree. A magnetic stirrer was used throughout each run. A device for introducing the sample of oxirane compound into the nitrating solution without undue loss owing to evaporation consisted of a gelatin capsule fitting snugly over the end of a glass tube. A close-fitting glass plunger inserted into the glass tube through a sleeve of rubber tubing was used to push the capsule off the end of the glass tube. After the sample was placed in the capsule, the capsule was slipped a short way onto the end of the glass tube, and the whole assembly was weighed on an analytical balance.

One hundred grams of solution was weighed into the dewar flask and stirred. After the initial temperature was recorded, the sample of oxirane compound was introduced under the surface of the solution by means of the plunger just described. The peak temperature, which was reached in a few minutes, was recorded. Temperature rise obtained was between 1.5 and 2.5°.

The heat capacity of the solution was then obtained by measuring the amount of power required to raise the temperature of the solution through the same temperature interval, using the heating coil. The value used was an average of two or three determinations. The temperature rise resulting from solution of the gelatin capsule was determined and found to be small (on the order of 0.02°).

Analytical Procedures.—Information regarding purity of the nitrato alcohols was obtained in three ways. Nitrogen content was determined[13] by the micro-Dumas procedure of Shelberg.[14] Vicinal hydroxyls were determined by the improved periodate method of Dal Nogare and Oemler.[15] The saponification equivalents were determined by the usual method[16] or by a slightly modified procedure which is particularly adapted to small samples as follows: A 100- to 200-mg. sample of ester was weighed into a 3-inch Pyrex test-tube. An accurately measured excess of alcoholic potassium hydroxide solution (approximately 1 *N* in 95% ethanol) was added. The test-tube was closed with a rubber stopper wired in place, and the sample and a similarly treated blank were heated in a boiling water-bath for 30 minutes. The contents of the tubes were then rinsed into separate erlenmeyer flasks and titrated with 0.1 *N* hydrochloric acid.

Results and Discussion

When an oxirane compound of the symmetrical type  $\underset{\diagdown O \diagup}{R{-}CH{-}CH{-}R}$ is treated with nitric acid, only one nitrato alcohol is produced, *viz.*, $RCHOHCHONO_2R$. Unsymmetrical oxides,  $\underset{\diagdown O \diagup}{R{-}CH{-}CH_2}$, allow the possibility of two isomeric products, $R{-}CHOHCH_2ONO_2$ and $R{-}CHONO_2CH_2OH$. Information in the literature suggests[17,18] that acid-catalyzed reactions sometimes lead to the production of appreciable amounts of each isomer, whereas in base-catalyzed reactions the secondary alcohol is produced mostly. When allylic structures are involved, acid-catalyzed reactions can give predominantly the primary alcohol.[9] Since the object of the present paper was primarily the development of methods for producing addition products in the best possible yields, only a preliminary evaluation of the positional-isomerism aspect was attempted. The benzoylation rate method used by previous investigators[9–11] gave results shown in Table I. Although the results are not conclusive, they indicate that a mixture of isomers results when nitric acid adds to propylene oxide, but there was a predominance of secondary alcohol from the other oxides studied.

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[12] M. H. Gold, private communication.

[13] Stephen Vango of this Laboratory performed all micro-Dumas nitrogen analyses reported.

[14] E. F. Shelberg, *Anal. Chem.*, **23**, 1492 (1951).

[15] S. Dal Nogare and A. N. Oemler, *ibid.*, **24**, 902 (1952).

[16] A. I. Vogel, "A Text-Book of Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1948.

[17] H. C. Chitwood and B. T. Freure, THIS JOURNAL, **68**, 680 (1946).

[18] *Cf.* discussion by S. Winstein and R. B. Henderson in R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 27–42.

TABLE I

BENZOYLATION RATE STUDIES

Alcohol	Reacn. with benzoyl chloride in 90 min., %	Predominant structural formula[a]
2-Nitratoethanol	67	$CH_2OHCH_2ONO_2$
Nitratopropanol	35	
Nitratobutanol	12	$CH_3CHOHCH_2ONO_2CH_3$
Nitratochloropropanol	21	$ClCH_2CHOHCH_2ONO_2$
Nitratohydroxypropanol	51	$HOCH_2CHOHCH_2ONO_2$
Nitratoallyloxypropanol	16	$CH_2{=}CHCH_2OCH_2CHOHCH_2ONO_2$
Ethanol	82	CH_3CH_2OH
Isopropanol	27	$CH_3CHOHCH_3$
Nitratomethoxyethoxypropanol	14	$CH_3OCH_2CH_2OCH_2CHOHCH_2ONO_2$
Nitratomethoxypropanol	15	$CH_3OCH_2CHOHCH_2ONO_2$

[a] In cases where uncertainty prevails, the predominant isomer on the basis of the benzoylation rate is given.

The physical properties of various nitrato alcohols synthesized by the addition of nitric acid to oxirane compounds are shown in Table II. The yields reported in this table represent the best obtained with the given compound during the course of this investigation but not the maximum yield obtainable since results of the more systematic study of yield were not available at the time of their preparation. Using oxygen balance as an index,[19] it is also apparent from Table II that most of the alcohols synthesized are fairly high explosives and that due precaution should be exerted in handling them.

TABLE II

PHYSICAL PROPERTIES OF NITRATO ALCOHOLS PRODUCED BY ADDITION OF HNO_3 TO OXIRANE COMPOUNDS

Compound	Yield, %	B.p. °C.	B.p. Mm.	$n^{20}D$	d^{20}_4	Nitrogen, % Calcd.	Nitrogen, % Found	Sapn. equiv. Calcd.	Sapn. equiv. Found	Mol. refraction Calcd.	Mol. refraction Found	Oxygen balance[a]
2-Nitratoethanol	58	44–46	1	1.4373	1.3483	13.08	13.13	107.1	106.3	21.09	20.83	−37.4
Nitratopropanol[b]	65	50–52	1	1.4357	1.2233	11.57	11.81	121.1	121.7	25.71	25.49	−72.7
Nitratobutanol	41	44–45	1	1.4382	1.1811	10.37	10.50	135.1	134.2	30.33	30.02	−53.2
Chloronitratopropanol	60	75	7	1.4751	1.4411	9.00	8.51	77.8	77.9	30.57	30.38	−51.4
Methoxynitratopropanol	50	93–94	3	1.4400	1.2605	9.26	9.31	151.1	151.5	31.97	31.82	−79.5
Methoxyethoxy nitratopropanol	43	118	1	1.4495	1.2225	7.18	7.04	195.2	198.3	42.85	42.82	−102.6
Allyloxy nitratopropanol	43	80	1	1.4586	1.1960	7.91	7.33	177.1	184.0	40.75	40.88	−113
Nitratohydroxypropanol	61	100–102	1	1.4698	1.4164	10.22	10.19	137.1	136.1	27.23	26.98	−52.6

[a] The oxygen balance defined by the quantity (−1600/mol. wt.) [2C + (H/2) − O] has been used by Lothrop and Handrick[19] to measure the explosive performance of numerous materials. On this scale a value of zero as represented by 1,2-dinitratoethane (glycol dinitrate) gives maximum performance, whereas materials such as trinitrotoluene and mononitratoethane have the values −78.9 and −61.5, respectively. [b] In most cases the relative position of the incoming nitrato group has not been established with certainty; therefore only general names are used.

The two procedures which were investigated for synthesis of the nitrato alcohols differed in that the reaction was conducted in an aqueous medium in one case and a non-aqueous medium in the other. Side reactions differed somewhat in the two procedures, and each had certain advantages. The aqueous solution procedure yielded products relatively free from materials other than glycols and proved to be well adapted to the general study of factors influencing yield. Also, the aqueous reaction could be made to take place very rapidly. Certain features of the non-aqueous solution procedure appear desirable when considering its adaptation to large-scale synthesis; *viz.*, the amount of oxirane compound in relation to nitration mixture can be made smaller by virtue of using more concentrated nitric acid, an extraction step is eliminated and excess of reactants is considerably smaller. If white fuming nitric acid is used a glycol-free product is obtained.

The essential agreement in heat of reaction with propylene oxide for the two procedures is shown in Table III. Variation in heat of reaction with composition of the nitrating mixture for the aqueous procedure is also illustrated. Owing to the fact that perchlorate ion has little tendency to add to the oxide ring, the predominant reaction is hydration when 5% perchloric acid is used; accordingly the heat of hydration of propylene oxide was found to be 22.9 ± 0.6 kcal./mole. It can roughly be inferred from the data in Table III that the heat of nitration is approximately 4 or 5 kcal./mole less than the heat of hydration.

In establishing optimum conditions, propylene oxide was treated with varying amounts of nitric acid (0.5–15%) and ammonium nitrate (0–50%).

TABLE III

HEATS OF REACTION OF PROPYLENE OXIDE WITH NITRIC ACID

Composition of solution	Heat of reaction, cal./mole
10% HNO_3; 50% NH_4NO_3	−18,900 ± 23
10% HNO_3; 25% NH_4NO_3	−18,500 ± 244
2% HNO_3	−22,300 ± 17
5% $HClO_4$	−22,900 ± 638
HNO_3 (95%) in $CHCl_3$[a]	−24,900 ± 330

[a] Conducted under actual preparative conditions.

It had been established that the nature of the salt had no effect on the amount of nitration produced as long as the ratio of the moles of nitrate ion to moles of water in the nitrating mixture was kept constant. Three solutions 1.59 *N* in nitric acid and 0.312 *N* in either ammonium nitrate, calcium nitrate or sodium nitrate gave 47.1, 46.3 and 47.8% nitration, respectively, in 30 minutes. Also it was found that in solutions containing 10% nitric acid and higher, the reaction was essentially complete in 5 to 10 minutes independent of the oxide used. Of importance in the use of this type of data was the fact that varying the ratio of the moles of acid to moles of oxirane compound had little influence on total amount of nitration in the range of values 2 to 9. Another significant ob-

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(19) W. C. Lothrop and G. P. Handrick, *Chem. Revs.*, **44**, 419 (1949).

servation is that the amount of nitric acid or *p*H of the solution did not greatly influence the amount of nitration as long as the ratio of moles of nitrate ion to moles of water was kept constant and the nitric acid content varied from 1 to 15 weight per cent. Accordingly all the data for nitrations in aqueous solutions of ionic strength greater than one were readily correlated by the following equation which relates the amounts of products and reactants in moles per liter

$$\frac{n}{s} = K\frac{(NO_3^-)}{(H_2O)} \qquad (1)$$

where n = nitrated product, s = side product (predominantly glycol), (NO_3^-) = nitrate ion, and (H_2O) = water. A plot of the results with propylene oxide using equation (1) is shown in Fig. 1. A kinetic interpretation of these data, together with a comparative study of the rates of addition of other ions, is being presented separately. Of interest in this connection it was observed that, when nitric acid was added to a variety of oxirane compounds in a solution consisting of 10% nitric acid and 50% ammonium nitrate by weight, the percentage of nitration did not vary greatly. Therefore the plot of Fig. 1 might be expected to hold roughly irrespective of the particular oxide used. The maximum variation for the nitrating solution 10% HNO_3–50% NH_4NO_3 was 73% nitration for ethylene oxide and 66% nitration for glycidol. Apparently the ratio of the rate of nitration to the combined rate of side reactions is relatively unaltered by changes in chemical structure under these conditions. This result is somewhat unexpected in view of the kinetic data by Brönsted, *et al.*,[20] on the addition of halogens to glycidol and epichlorohydrin and is probably a result of the effect of the high salt concentration on the rate of nitration.

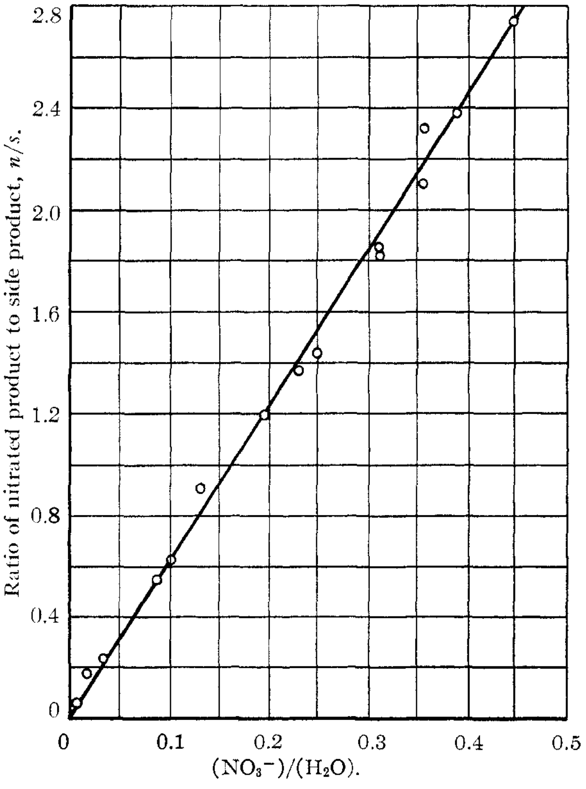

Fig. 1.—Yield data as a function of $(NO_3^-)/(H_2O)$ ratio.

The effect of temperature on the amount of nitration produced is shown in Table IV. At higher temperatures there is a sizable increase in yield which indicates that the activation energy for the nitration reaction is greater than that for hydration.

TABLE IV

VARIATION OF YIELD OF NITRATO ALCOHOL WITH TEMPERATURE BY AQUEOUS SOLUTION PROCEDURE[a]

Temp. of bath, °C.	Nitration, %	Time of reaction
72	55.00	30 min. in bath 30 min. out
52	45.12	30 min. in bath 30 min. out
21	43.44	30 min. in bath 30 min. out
0	41.82	1 hr.
0	41.94	2 hr.
0	41.82	13 min.

[a] The reaction product from the reaction of propylene oxide with nitric acid; moles of oxirane compound/moles of acid = 10; nitrating solution = 10% HNO_3, 25% NH_4NO_3.

The critical nitrato alcohol yield-determining factors were examined for non-aqueous systems and were found to verify qualitatively the conclusions obtained by the aqueous solution procedures. In addition it was observed that unless a slight excess of acid was present in the reaction mixture, appreciable quantities of higher boiling material were obtained. Analyses indicate this material to be dimer of the type $RCH(CH_2ONO_2)OCH_2CHOHR$. Polymerization does not appear to proceed much beyond this stage.

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(20) J. N. Brönsted, M. Kilpatrick and M. Kilpatrick, THIS JOURNAL, **51**, 428 (1929).