[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Determination of Isomer Distribution in the Nitration of *p*-Nitrotoluene by Isotope Dilution Analysis[1]

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The proportion of 2,4- and 3,4-dinitrotoluene formed by nitration of *p*-nitrotoluene with mixed acids has been determined using isotope dilution analysis. The amount of 3,4-dinitrotoluene formed is no more than 0.2% of the total amount of dinitrotoluene.

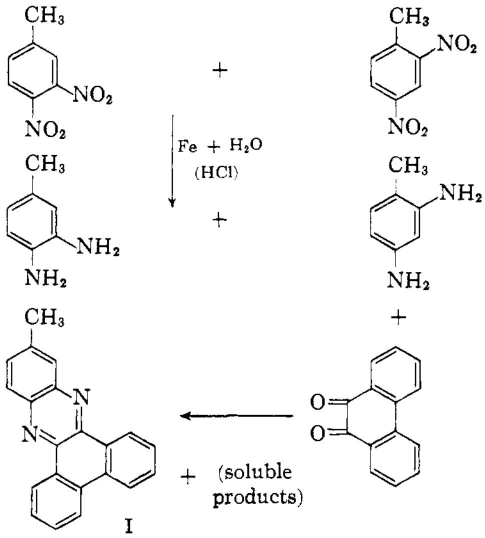
All of the five isomers of 2,4,6-trinitrotoluene which may contaminate the symmetrical isomer desired as a military explosive may possibly arise from the continued nitration of *m*-nitrotoluene. The amount of *m*-nitrotoluene produced in the first stage of nitration of toluene is known to be small; we have recently reported results from isotope dilution analysis which confirm this fact.[2] Three of the unsymmetrical trinitrotoluenes may possibly arise from the continued nitration of *p*-nitrotoluene. A number of workers have stated that nitration of *p*-nitrotoluene gives only 2,4-dinitrotoluene,[3] but, to our knowledge, no careful attempt has ever been made to determine if a small amount of 3,4-dinitrotoluene may also be formed. Such an attempt was the subject of this research.

Isotope dilution analysis was chosen as a technique suitable for this study and one particularly capable of giving an accurate figure for the upper limit of the proportion of an isomer produced in minor amount. The procedure planned involved nitrating radioactive *p*-nitrotoluene, "diluting" the dinitrotoluene produced with non-radioactive 3,4-dinitrotoluene, separating the 3,4- and 2,4-dinitrotoluene and determining the radioactivity of the recovered 3,4-dinitrotoluene.

Two methods which were applied with limited success to the separation of the isomeric dinitrotoluenes will be mentioned briefly. The first was a systematic study of fractional crystallization from various solvents. The solubilities of the two isomers are very similar in ethanol, methanol, ethyl acetate, Skellysolve B and Skellysolve C, both at 0° and at higher temperatures. However, the 3,4-isomer is slightly more soluble in the alcohols and the 2,4-isomer slightly more soluble in the hydrocarbon solvents.[4] It was found that a fractional recrystallization scheme based on these differences would effect separation of the isomers, but it was abandoned as being too laborious and because melting points are unsatisfactory criteria of the purity of the dinitrotoluenes.

The second method involved reduction of the dinitrotoluenes to diaminotoluenes.[5] Advantage was then taken of the *ortho* relationship of the two amino groups in 3,4-diaminotoluene for reaction with formic acid to produce 5-methylbenzimidazole,[6] while 2,4-diaminotoluene was converted to 2,4-diformylaminotoluene. However, the crystallization and purification of 5-methylbenzimidazole presented more difficulty than was expected. The formation of benzimidazoles from higher homologs of formic acid did not produce the necessary improvement in crystallization properties.

A scheme related to the above was found to be much more successful and was adopted as a satisfactory method of separating the isomers. This involved reduction of the dinitrotoluenes to diaminotoluenes as before, followed by treatment with *o*-phenanthrenequinone in alcoholic acetic acid solution. 3,4-Diaminotoluene condensed with the quinone to form insoluble 7-methyl-1,2; 3,4-dibenzophenazine[7,8] (I) while 2,4-diaminotoluene gave no products which interfered with the precipitation of the phenazine. The phenazine served as the form in which the "diluted" 3,4-dinitrotoluene was radioassayed.



The conditions of Kobe, Skinner and Prindle[9] were used for the nitration of *p*-nitrotoluene, with slight modifications. In runs 1 and 2 the theo-

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[1] Supported by U. S. Army Ordnance Research under Contract No. DAI-23-072-501-ORD-(P)-6. Taken from the M. A. thesis of H. P. Browder, Jr., The University of Texas, 1956.

[2] R. M. Roberts, P. Heiberger, J. D. Watkins, H. P. Browder, Jr., and K. A. Kobe, THIS JOURNAL, **80**, 4285 (1958).

[3] (a) W. H. Gibson, R. Duckham and R. Fairbairn, *J. Chem. Soc.*, **121**, 270 (1922); (b) P. de Beule, "La Fabrication du Trinitrotoluene en Deux Phases," Brussels, Belgium, 1949, p. 99; (c) T. L. Davis, "The Chemistry of Powder and Explosives," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 142.

[4] This is in line with the expected greater dipole moment of 3,4-dinitrotoluene.

[5] S. A. Mahood and P. V. L. Schaffner, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 160.

[6] E. Bamberger and B. Berle, *Ann.*, **273**, 321 (1893).

[7] O. Hinsberg, *ibid.*, **237**, 341 (1887).

[8] A. G. Williams, THIS JOURNAL, **43**, 1913 (1921).

[9] K. A. Kobe, C. G. Skinner and H. B. Prindle, *Ind. Eng. Chem.* **47**, 785 (1955).

retical amount of nitric acid plus a 10% excess was used. These two nitrations were carried out under identical conditions; the temperature of the reaction mixture was kept between 65 and 75°. The crude dinitrotoluene was recrystallized once before it was "diluted" with non-radioactive 3,4-dinitrotoluene. In this crystallization, no attempt was made to separate dinitrotoluene isomers from one another, since this would defeat the purpose of the isotope dilution analysis. Mixed solvents were used, and a large amount of the poor solvent was added finally to ensure complete recovery of the dinitrotoluenes from the mother liquor.

The calculation of the proportion of 3,4-dinitrotoluene present in the dinitrotoluene product was made in the usual way for an inverse isotope dilution analysis.[2] The value calculated in run 1 from the first sample of phenazine radioassayed was 0.08%; after a further recrystallization of the phenazine a second radioassay indicated 0.04%. The value calculated in run 2 from the first sample of phenazine radioassayed was 0.12%; recrystallization of the phenazine and re-assay gave 0.04%, as in run 1. It would have been desirable to recrystallize and re-assay until a constant value was reached, but the small amount of phenazine available prevented this. Thus, it was impossible to conclude from these results whether nitration of *p*-nitrotoluene actually produced 0.04% of 3,4-dinitrotoluene along with 99.96% of 2,4-dinitrotoluene, or whether the small amount of radioactivity in the phenazine represented a trace of contamination.

Run 3 was made under slightly different conditions. A lower concentration of sulfuric acid was used and an amount of nitric acid 14.8% less than the theoretical amount, based on the *p*-nitrotoluene. These changes were made to reduce the possibility of formation of trinitrotoluenes from the dinitrotoluenes, which presumably might be nitrated at different rates with the result that the proportion of dinitrotoluenes remaining after complete reaction might not be the same as that originally produced. Under these conditions, an appreciable amount of *p*-nitrotoluene remained unchanged at the end of the reaction, and it was necessary to remove it from the dinitrotoluene by steam distillation. A larger amount of phenazine available for radioassay in this run allowed recrystallization to almost constant radioactivity. The final assay corresponded to 0.2% of 3,4-dinitrotoluene formed in this nitration, which was higher than the value found in runs 1 and 2. It is possible that this figure does not represent a significantly larger proportion of this isomer formed in this run than in the first two, because the presence of unchanged *p*-nitrotoluene in this reaction mixture represents an additional source of higher activity contamination not present in runs 1 and 2. Another possibility is that there was some loss of the minor isomer in the recrystallizations of the crude products in runs 1 and 2, in spite of the precautions taken, while there was none in the steam distillation used in run 3.[10]

In either event, it is obvious that the nitration of *p*-nitrotoluene under the usual conditions does not produce a significant amount of 3,4-dinitrotoluene, the upper limit being about 0.2%.

Experimental[11]

Materials.—*p*-Nitrotoluene-1-C^{14} was prepared by nitration of toluene-1-C^{14} (Tracerlab, Inc.) at 30° with mixed acids.[2] It was separated from the *o* and *m* isomers by distilling these through the Podbielniak still described before[2] and recrystallizing the residual *p* isomer to constant m.p. (52.0–53.0°) from aqueous ethanol. Ordinary *p*-nitrotoluene used for dilution and trial "dead" runs was Eastman Kodak Co., white lable, as was the 2,4-dinitrotoluene, 4-methyl-2-nitroaniline and *o*-phenanthrenequinone. Sulfuric and nitric acids were reagent grade, standardized by titration.

3,4-Dinitrotoluene was prepared from 4-methyl-2-nitroaniline by oxidation with Caro acid, followed by nitric acid oxidation of the intermediate 3-nitro-4-nitrosotoluene.[12]

Apparatus.—The nitration vessel was a 25-ml. three-necked, pearshaped flask equipped with a thermometer, stirrer and semi-micro buret for addition of the mixed acids. The stirrer was a T-shaped centrifugal type and was turned by a 1700 r.p.m. motor. The reaction mixture was immersed in a 4-l. water-bath, heated electrically.

Radioassays were made by wet-combustion of organic compounds to carbon dioxide which was collected in an ionization chamber and counted on a vibrating reed electrometer.[2]

Nitration of *p*-Nitrotoluene. Run 1.[13]—In the nitration flask was placed 2.38 g. of *p*-nitrotoluene-1-C^{14} (5.50 μc./mmole) and 2.15 g. of 90.0% sulfuric acid. The flask was then placed in the water-bath at 65° and the contents were allowed to come to bath temperature. In a separate flask were mixed 2.04 g. of 96.4% sulfuric acid, 1.31 g. of 91.8% nitric acid and 0.04 g. of water.[9] (The amount of nitric acid used was the theoretical amount, plus 10%). The mixed acids were warmed to bath temperature and then added dropwise to the stirred *p*-nitrotoluene–sulfuric acid mixture through the semi-micro buret during 5.3 minutes, while the temperature of the reaction mixture rose to about 75°. The reaction mixture was stirred an additional 15 minutes. It was then poured into 50 ml. of chipped ice and water. The precipitated crude dinitrotoluene was collected on a filter and dried (3.01 g.). After one recrystallization from ethanol-Skellysolve B it weighed 2.74 g. (87%) and melted at 71.4–72.2° (pure 2,4-dinitrotoluene melts at 71.8–72.2°). This product (2.728 g.) was mixed with 1.821 g. of 3,4-dinitrotoluene, along with 7.5 ml. of 50% ethanol and 9.1 g. of powdered iron. This mixture was heated and stirred under reflux on a steam-cone while a mixture of 0.9 ml. of concd. hydrochloric acid and 2.5 ml. of 50% ethanol was added dropwise during 8 minutes.[5] After an additional 2 hr. of heating and stirring, the acid was neutralized with 15% alcoholic potassium hydroxide solution. The reaction mixture was filtered and the solid material was washed with two 5-ml. portions of 95% ethanol. The filtrate was cooled in an ice-bath and 2.56 g. of concd. sulfuric acid was added dropwise. The hydrogen sulfate salt of the diamines precipitated and was collected on a filter, washed with two 3-ml. portions of 95% ethanol and dried in a vacuum oven at 95° (30 mm.) for 9 hr. The dry salt weighed 4.69 g. (85%). The free diamines were obtained by dissolving the salt in 20 ml. of water and neutralizing with concd. sodium hydroxide solution; an oil separated which then solidified and was collected on a filter and dried in a desiccator over calcium chloride in a nitrogen atmosphere. The crude diamines (2.76 g.) were dissolved in 100 ml. of 95% ethanol and warmed to 55°. This solution was then added to a solution of 6.68 g. of *o*-phenanthrenequinone in 325 ml. of glacial acetic

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(10) This possibility was suggested by the referee. It is true that a relatively large percentage of the minor isomer might have been lost in the recrystallizations which were applied in runs 1 and 2 to separate the mixed nitrotoluene isomers from starting material and acids. However, it seems unlikely that the total amount of 3,4-dinitrotoluene lost in the recrystallizations could have exceeded 0.2% (the amount found in run 3) since this source of error was not present in run 3, in which the crude product was steam distilled rather than recrystallized.

(11) Melting points were determined on a Koefler micro hot-stage. Boiling points are uncorrected.

(12) H. J. Page and B. R. Heasman, *J. Chem. Soc.*, **123**, 3235 (1923).

(13) Although only the experiments on radioactive materials are described, each step of the procedure was pre-tested thoroughly using ordinary materials.

acid, also warmed to 55°. After several minutes the mixture was cooled in an ice-bath and the crystals of 7-methyl-1,2,3,4-dibenzophenazine were collected on a filter. These were washed with 30 ml. of a 4:1 (v. v.) solution of ethanol-glacial acetic acid and then recrystallized from benzene-acetone solution. After a further treatment with Norite in benzene, 209 mg. of the pure phenazine was obtained,[14] m.p. 220–221° (reported[7] 217°, uncor.).

A 57.2-mg. sample of the phenazine was radioassayed, giving 6.4×10^{-3} μc./mmole (the rate of drift was about nine times that of background). This corresponded to 0.08% of 3,4-dinitrotoluene in the dinitrotoluene. The phenazine was recrystallized from benzene and re-assayed. A 56.7-mg. sample gave 3.5×10^{-3} μc./mmole, corresponding to 0.04% of 3,4-dinitrotoluene.

Run 2.—A 2.00-g. sample of *p*-nitrotoluene-1-C^{14} (5.50 μc./mmole) was nitrated under conditions identical with those of run 1. The crude dinitrotoluene was recrystallized this time from methanol–water, giving 2.541 g. (96%). This product was "diluted" with 1.696 g. of 3,4-dinitrotoluene and reduced as before; the diamine hydrogen sulfates were again obtained in 85% yield. The phenazine was prepared as before and recrystallized from acetone, m.p. 220.5–222.0°.

Radioassay of a 60.0-mg. sample gave 9.6×10^{-3} μc./mmole, corresponding to 0.12% of 3,4-dinitrotoluene. The phenazine was recrystallized from benzene and reassayed. A 60.1-mg. sample gave 3.3×10^{-3} μc./mmole, corresponding to 0.04% of 3,4-dinitrotoluene.

Run 3.—In the nitration flask was placed 2.94 g. of *p*-nitrotoluene-1-C^{14} (5.50 μc./mmole) and 2.81 g. of 85.0% sulfuric acid. The mixed acids added were composed of 2.54 g. of 94.1% sulfuric acid, 1.25 g. of 91.8% nitric acid and 0.18 g. of water. (The amount of nitric acid used was 14.8% less than the theoretical amount.) The reaction temperature and time were the same as in runs 1 and 2. After pouring the reaction mixture into ice and water, the crude dinitrotoluenes were collected on a filter, as before (3.85 g.), but instead of being recrystallized, this time they were steam distilled; 0.381 g. of low-melting *p*-nitrotoluene was recovered from the distillate and 3.028 g. of dinitrotoluene from the residue. This 3.028 g. of material was mixed with 2.010 g. of 3,4-dinitrotoluene, the mixture was reduced as before and the diamines were precipitated as hydrogen sulfate salts (5.31 g., 87%).

A sample of the phenazine was prepared directly from the diamine hydrogen sulfates in this run, dissolving 0.5 g. of the salt in 10 ml. of water and 25 ml. of methanol and adding this solution to a solution of 0.5 g. of *o*-phenanthrenequinone in 25 ml. of acetic acid at 60°. The phenazine was decolorized with charcoal and recrystallized before assay. The radioactivity found corresponded to 0.30% of 3,4-dinitrotoluene. The phenazine was recrystallized and re-assayed twice. The activities found corresponded to 0.25 and 0.20% of 3,4-dinitrotoluene after the second and third recrystallizations.

The remaining diamine salt was converted to free diamine and a sample of the phenazine was prepared as in runs 1 and 2. Radioassay gave an activity corresponding to 0.20% of 3,4-dinitrotoluene. Recrystallization of the phenazine and re-assay gave an activity corresponding to 0.18% of 3,4-dinitrotoluene.

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[14] This was a much smaller yield of the phenazine than was obtained in preliminary experiments with non-radioactive materials. The yields were somewhat higher also in runs 2 and 3 when carried out on a smaller scale and when a smaller proportion of acetic acid was used.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Determination of Isomer Distribution in the Nitration of *o*-Nitrotoluene by Isotope Dilution Analysis. 2,3-Dinitrotoluene[1]

BY ROYSTON M. ROBERTS, JOEL D. WATKINS AND KENNETH A. KOBE

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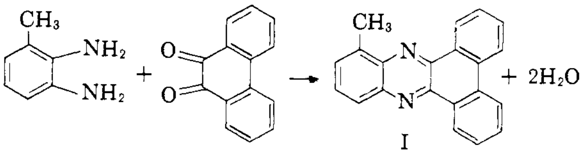
The proportion of 2,3-dinitrotoluene formed by nitration of *o*-nitrotoluene with mixed acids has been determined by isotope dilution analysis. It is less than 0.4% of the total amount of dinitrotoluenes.

Recently we have described studies on isomer distribution among the products of nitration of toluene[2] and *p*-nitrotoluene[3] by mixed acids. The proportions of the minor isomers were determined in each case by isotope dilution analysis. We are now extending this work by a similar study of the nitration of *o*-nitrotoluene.

The nitration of *o*-nitrotoluene has been reported to produce a mixture of 2,4- and 2,6-dinitrotoluene in the proportion of 66.6 and 33.3%, respectively.[4] This analysis was based on comparison of the melting point of a nitration product with melting point-composition curves of known mixtures. There is no record in the literature of the detection or isolation of either of the other two isomeric dinitrotoluenes, 2,3- and 2,5-dinitrotoluene, which may possibly be formed in minor amounts by nitration of *o*-nitrotoluene. The accurate determination of the amount of 2,3-dinitrotoluene produced is the subject of this paper.

The procedure applied to this determination was the inverse isotope dilution technique. This involved nitrating radioactive *o*-nitrotoluene, "diluting" the mixture of dinitrotoluenes produced with non-radioactive 2,3-dinitrotoluene, re-isolating the 2,3-dinitrotoluene in some form from the mixture and determining its radioactivity. The re-isolation of the 2,3-dinitrotoluene was accomplished in a manner analogous to that described for the separation of 2,4- and 3,4-dinitrotoluenes in the preceding paper.[3] This involved reduction of the mixed dinitrotoluenes to mixed toluenediamines and treatment of these in alcoholic acetic acid solution with *o*-phenanthrene-quinone, which condensed with 2,3-diaminotoluene to give insoluble 6-methyl-1,2;-3,4-dibenzophenazine (I). Under the conditions



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of the experiment, the other isomeric diamines do

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[3] R. M. Roberts, H. P. Browder, Jr., and K. A. Kobe, *ibid.*, **80**, 1165 (1958).

[4] W. H. Gibson, R. Duckham and R. Fairbairn, *J. Chem. Soc.*, **121**, 278 (1922).