cis- and trans-Δ⁵,¹⁷-Pregnadiene-3β,20-diol Diacetates (VII, VIII).—A solution of 4.4 g. of Δ⁵-pregnene-3β-ol-20-one and 2.45 g. of p-toluenesulfonic acid in 500 cc. of acetic anhydride was boiled gently and the solvent allowed to distil. After about seven hours the residual dark solution (100–150 cc.) was poured into ice-water, and after a short interval the product was extracted with ether and the solution was washed with water, sodium carbonate solution, and again with water, dried and evaporated. The residue (5.06 g.) was dissolved in a small amount of benzene and the solution diluted with 150 cc. of petroleum ether (30–60°), chromatographed on alumina, and eluted with petroleum ether, benzene–petroleum ether (1:2 and 1:1) and with benzene. The initial crystalline fractions melting over the range 120–133° were combined and on repeated crystallization from methanol gave enol acetate-A as long prisms, m. p. 144–146° (1.84 g., 33%). A sample recrystallized again for analysis melted at 147°, [α]²⁵D −50.0° (C = 2% in chloroform).

Anal. Calcd. for $C_{25}H_{36}O_4$: C, 74.95; H, 9.06. Found: C, 74.82; H, 9.01.

Processing of later chromatographic fractions and of mother liquor material by further chromatography and recrystallization from methanol eventually afforded 0.22 g. of pure enol acetate-B, as plates, m. p. 171–172°, [α]²⁵D −52° (C = 2% in chloroform).

Anal. Calcd. for $C_{25}H_{36}O_4$: C, 74.95; H, 9.06. Found: C, 74.58; H, 8.94.

The methanol mother liquors afforded 1.2 g. of a mixture of A and B, m. p. 115–117°, that showed no depression when mixed with either isomer.

Bromination of Enol Acetate-A (m. p. 147°).—A solution of 0.08 g. of bromine in chloroform was added dropwise at room temperature to a solution of 0.1 g. of A in 5 cc. of chloroform. Removal of the solvent in vacuum and crystallization from acetone–ligroin (70–90°) gave 90 mg. (60%) of bromo product melting at 162°, dec. Recrystallization from the same solvent gave pure material in the form of plates, m. p. 166–168°, dec. Plattner and co-workers[7] have reported the preparation of 3β-acetoxy-20-keto-5,6,17-tribromopregnane (IX) by bromination of pregnenolone acetate, but they report merely the melting point 149–151° and give no analysis. We prepared the tribromo compound according to their procedure and on repeated recrystallization from acetone–ligroin formed plates, m. p. 167–168°, dec., that gave no depression when mixed with the substance from enol acetate-A.

Anal. Calcd. for $C_{23}H_{33}O_3Br_3$: C, 46.25; H, 5.56. Found: C, 46.26; H, 5.56.

The bromination of isomer-A was conducted more conveniently in acetic acid; dilution with water precipitated the product and one crystallization from acetone–ligroin gave plates, m. p. 161–162° in 71% yield. The fully purified sample melted at 166–167° dec., and gave no depression with either of the above samples.

Bromination of Enol Acetate-B (M. p. 171°).—Bromination in acetic acid as above gave plates, m. p., and mixed m. p. with the product from A, 167–168°, dec.

Anal. Calcd. for $C_{23}H_{33}O_3Br_3$: C, 46.26; H, 5.56. Found: C, 46.19; H, 5.31.

Saponification of the Enol Acetates.—A solution of 0.1 g. of isomer A or B in 10 cc. of methanol was treated with a solution of 0.1 g. of potassium carbonate in 1 cc. each of water and methanol and let stand at room temperature for five hours. The product, precipitated by water, on crystallization from dilute alcohol gave plates identified by crystal form, m. p. and mixed m. p. (189–190°) as Δ⁵-pregnene-3β-ol-20-one; yield, 60 mg. (76%) from A, 58 mg. (73%) from B.

Saponification of 30 mg. of A or B in 4 cc. of methanol was also conducted by adding a solution of 30 mg. of potassium bicarbonate in a few drops of water and 2 cc. of methanol. After forty-eight hours at room temperature, processing as above gave crude pregnenolone, m. p. 184–188°: 19.5 mg. (82%) from A, and 19.0 mg. (80%) from B. The recrystallized samples had the m. p. and mixed m. p. 189–190°.

## Summary

A statement in the literature indicating that the Serini reaction in one instance proceeds without inversion at $C_{17}$ has been shown to be in error.

A pair of cis–trans- Δ¹⁷-enol-20-acetates prepared from pregnenolone both yield pregnenolone and not 17-isopregnenolone on saponification. Such substances therefore cannot be intermediates in the Serini reaction, and this probably proceeds through the oxide.

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CAMBRIDGE 38, MASS.          RECEIVED JANUARY 20, 1949

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# A New Method of Preparing the High Explosive RDX[1]

By W. E. BACHMANN AND JOHN C. SHEEHAN[2]

Cyclotrimethylenetrinitramine (also called cyclonite and more recently RDX)[3] was first prepared in 1899 from nitric acid and the dinitrate of hexamethylenetetramine by Henning,[4] who gave few details and offered no structure for the prod-

uct. Herz[5] proposed the correct structure for the compound and recognized its explosive properties, and Hale[6] reported improved directions for its preparation. In 1940 we learned that Ross and Schiessler[7] had obtained RDX from formaldehyde, ammonium nitrate and acetic anhydride in the absence of nitric acid, but no details of their experiments were available to us.

In the conventional process for making RDX, hexamethylenetetramine is treated with 98–100% nitric acid. The reaction has been formulated by Hale[6] as shown in Equation 1.

(1) This investigation was carried out in 1941 under a contract recommended by the NDRC between the OSRD and the Regents of the University of Michigan.

(2) Present address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts.

(3) According to various reports RDX played a critical role in World War II as one of the most powerful high explosives. For an excellent popular discussion of the development and large scale production of RDX and its importance to the war effort see James Phinney Baxter 3rd, "Scientists Against Time," Little, Brown and Company, Boston, 1946, pp. 256–259.

(4) Henning, German Patent 104,280 (1899).

(5) Herz, Swiss Patent 88,759 (1920); Chem. Zentr., 92, IV, 926 (1921).

(6) Hale, THIS JOURNAL, 47, 2754 (1925).

(7) Ross and Schiessler, McGill University, unpublished results.
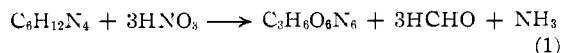
$$C_6H_{12}N_4 + 3HNO_3 \longrightarrow C_3H_6O_6N_6 + 3HCHO + NH_3$$

$$(1)$$

This method possesses two serious disadvantages: a large excess of nitric acid must be employed for the best results, and one-half of the equivalent of formaldehyde is not utilized but is lost usually through oxidation by the nitric acid in the "fume-off," which is carried out after dilution with water. As a result, considerable equipment is required to reconvert the oxides of nitrogen to nitric acid and to concentrate the dilute acid. The maximum amount of RDX possible is one mole per mole of hexamethylenetetramine, and appreciably less than this is obtained even under optimum conditions.

Although Equation 1 seemed to be an overly simplified representation of the reaction, it occurred to us to try to utilize the by-products to obtain a second mole of RDX. Thus, if two moles of ammonium nitrate and six moles of acetic anhydride were present during the reaction of hexamethylenetetramine with nitric acid, then *two* moles of RDX might be obtainable from one mole of hexamethylenetetramine according to Equation 2.[8]

$$4HNO_3 + 2NH_4NO_3 + 6 (CH_3CO)_2O \longrightarrow$$

$$2 \qquad + 12CH_3COOH \quad (2)$$

RDX
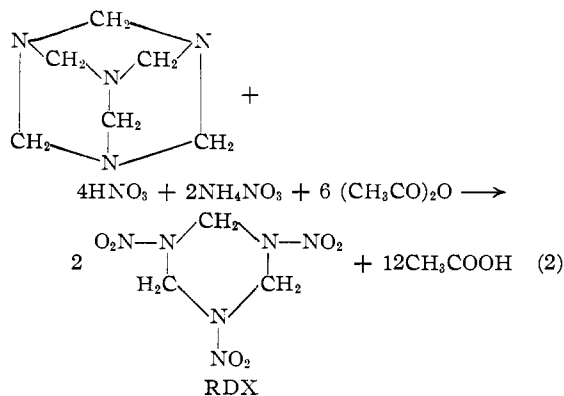
Exploratory experiments led to spectacular "fume-offs," to viscous honey-like products after drowning, and sometimes to RDX of varying degrees of purity. After considerable experimentation, procedures were worked out whereby RDX could be prepared by the new reaction under carefully controlled conditions in 70% yields calculated on the basis of two moles of RDX per mole of hexamethylenetetramine. In other words, approximately twice as much RDX can be obtained by this method as was possible by direct nitrolysis of hexamethylenetetramine with nitric acid alone. It is evident that two of the six amino nitrogen atoms in the two molecules of RDX are contributed by the ammonium nitrate.

The reaction leading to the formation of RDX was carried out at about 75°. The reagents were employed in nearly the amounts required by the

equation with the exception of the nitric acid which was used in slight excess. Since the reaction was carried out in an anhydrous medium (presence of acetic anhydride), 98–100% nitric acid was employed. By using the dinitrate salt of hexamethylenetetramine, which can be prepared in excellent yield from hexamethylenetetramine and 70% nitric acid, less 98% acid is required in the nitrolysis reaction. The ammonium nitrate was used in finely divided form or most advantageously in solution in the nitric acid. The acetic anhydride may be used alone or mixed with the nitric acid. Obviously many variations in the procedure are possible.

In the presence of acetic anhydride and ammonium nitrate it is important to keep the ratio of nitric acid to hexamethylenetetramine practically constant throughout the reaction. It follows that the hexamethylenetetramine should not be added gradually to a flask containing all of the nitric acid and the other reagents; nor should the nitric acid be added gradually to the hexamethylenetetramine and other reagents. Because of the exothermic nature of the reaction, it is not possible to mix at one time more than relatively small amounts of the reagents. Accordingly, the best procedure is to add the hexamethylenetetramine and the nitric acid simultaneously and equivalently in portions to the reaction flask; the ammonium nitrate and acetic anhydride may be introduced portionwise with these reagents or may be placed in the flask before the reaction is started. During the portionwise addition of a mixture of 98% nitric acid and acetic anhydride and a mixture of hexamethylenetetramine dinitrate and ammonium nitrate simultaneously and equivalently to a flask at such a rate that the temperature was kept at 75°, colorless crystals of RDX precipitated from the reaction mixture in practically pure form in 60% yield.

The product obtained in 68–70% yield by filtration of the anhydrous reaction mixture or in 81–87% yield by drowning the mixture contained another compound besides RDX; its presence was indicated by the lowered melting point of the product even after purification. The compound was isolated in the form of colorless crystals which melted higher than RDX.[9] This new nitrolysis product was found to be less soluble than RDX and more stable to the action of hot aqueous nitric acid.

The reaction took an entirely different course when the reagents in the same proportions were mixed in the cold and the temperature was raised slowly to 75°. Under these conditions a new compound (termed BSX) was produced, which was found to be unstable to warm 70% nitric acid and to aqueous ammonia. Evidently acetylation by the acetic anhydride as well as nitration occurred

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(8) Superficially, the reaction appears to be a combination of the nitration reaction and the procedure of Ross and Schiessler. However, the new reaction would be run under conditions alien to both of the other reactions.

(9) This compound was designated HMX (HM for high-melting) by Dr. G. F. Wright, University of Toronto, who isolated it independently and practically simultaneously. The structure proposed by one of us (W. E. B.) will be discussed in a subsequent paper.

in the reaction since a different compound was produced when propionic anhydride was substituted for the acetic anhydride.[10]

In addition to serving as an efficient method for preparing RDX, the new reaction led directly or indirectly to the preparation of numerous new nitramines (as exemplified by HMX and BSX) and to the unfolding of much new chemistry of hexamethylenetetramine. These results will be reported in communications from this laboratory and others in this country and in Canada.

## Experimental[11]

**Hexamethylenetetramine Dinitrate.**—The method of preparation of this salt was essentially that described by Hale.[6] To a solution of 40 g. of hexamethylenetetramine in 70 ml. of water cooled in an ice-salt-bath was added dropwise with stirring 43.5 ml. of 70% nitric acid; the temperature was not allowed to go above 15°. After the mixture had been chilled for fifteen minutes at 5°, the dinitrate was collected by filtration or by centrifuging. After being dried below 30° (low humidity necessary if air dried), the salt weighed 69.8 g. (92%). The filtrate, if kept below 15° at all times, can be used repeatedly. From 120 g. of hexamethylenetetramine 217 g. (95%) of the salt was obtained.

**Preparation of RDX.**—A 2-liter, four-necked, round-bottomed flask was equipped with an efficient mechanical stirrer, a thermometer, a 175-ml. buret which was marked off into 75 7-ml. graduations, and a powder funnel. The flask was set into a small-volume water-bath which fitted the flask fairly snugly and thus contained little water in order that the temperature could be changed quickly by the addition of cold water or steam through inlet tubes. An intimate mixture of 192 g. of hexamethylenetetramine dinitrate and 114 g. of finely divided ammonium nitrate (dried at 80°) was weighed into 75 portions of 4.0-4.1 g. each (placed in test-tubes for convenience and protection). A mixture of acetic anhydride-nitric acid was prepared by the dropwise addition with cooling (5-15°) and stirring of 78 ml. of 98% nitric acid to 480 ml. of acetic anhydride. This solution should be used as soon as it is prepared.

A 20-25 ml. portion of the acetic anhydride-nitric acid solution and about 1 g. of the solid mixture (which inhibits reaction between the anhydride and nitric acid as the temperature is raised and prevents a possible dangerous fume-off) was stirred in the flask and the temperature of the bath was raised quickly to about 80° by introducing steam into the water-bath. As soon as the internal temperature reached 70-75°, the solid and the liquid mixtures were added gradually at such a rate that a 4-g. portion of the mixture of solids was added for every 7 ml. of liquid. Throughout the exothermic reaction the inside temperature was maintained at 73-78°. At the start it was necessary to proceed cautiously, but as the volume of the reaction mixture increased the temperature was easily kept within the desired limits when the additions were made as rapidly

as a portion every half minute. After all of the reagents had been added, the mixture was stirred for fifteen minutes at 75°.

Nearly from the start of the reaction the RDX precipitated from the reaction mixture in practically pure form as dense crystals. When the stirring was stopped, the RDX crystals settled like sand to the bottom of the flask, leaving the supernatant liquid practically clear.

The mixture was filtered while hot (60°), washed with acetic acid and then with warm water, and dried; yield, 195-202.5 g. (61-63%); m. p. 203-204° with previous softening at 198°.[12] When 5 g. of the product was stirred with 25 ml. of 55% nitric acid at 70° for one-half hour, cooled and filtered, a 96% recovery of RDX with a m.p. of 205-206° was obtained.

When the reaction mixture was cooled in the course of one-half hour to 25° with stirring before being filtered, 225-235 g. (70-73.5%) of product was obtained; m.p. 199-202° with previous softening at 191°. Treatment with 55% nitric acid as above for one-half hour gave a product with 95% recovery melting at 203-204° with previous softening at 193°; this represents a 67.5-70% yield.

When the reaction mixture was drowned by addition in one portion of 640 ml. of warm (50°) water with stirring, there was obtained 261 g. (81.5%) of colorless solid with m. p. 180-185°. It was purified by heating 120 g. of the material and a solution of 12 g. of sodium acetate and 5 ml. of concentrated aqueous ammonia in 600 ml. of water on a steam-bath for sixteen hours under a reflux condenser. During the first few hours 5.5 ml. of concentrated aqueous ammonia was added as needed to keep the pH at 6-8; frequent tests were made during the first hour; weight of product, 106 g.; m.p. 198-202°. A 7-g. sample of this product was warmed with 35 ml. of 70% nitric acid for fifteen minutes on a steam-bath with occasional swirling and then brought into solution over a micro burner. The beautiful colorless crystals of RDX obtained by adding an equal volume of water and allowing the mixture to cool weighed 6.47 g.; m. p. 203-204° with softening at 200°.

Results similar to those described were obtained when all of the acetic anhydride was placed in the reaction flask at the start of the reaction. Another variation consisted in dissolving the ammonium nitrate in the 98% nitric acid; some gassing occurs and all of the yellow oxides of nitrogen are driven out. The resulting clear colorless solution does not attack the skin violently as does nitric acid alone. Solid hexamethylenetetramine was used in place of its salt. Although RDX was formed by mixing a solution of hexamethylenetetramine in acetic anhydride with a solution of ammonium nitrate in nitric acid, the yield was not large.

**Isolation of a High-Melting Nitrolysis Product.**—The product obtained in 70-73.5% yield by filtration of the cooled anhydrous reaction mixture was warmed on a steam-bath with 55% nitric acid (5 ml. per gram) for about six hours, and the hot mixture was filtered. The crystals obtained from the chilled filtrate were isolated and warmed with 2-nitropropane (3.5 ml. per gram) in order to dissolve RDX, and the hot solution was decanted from the insoluble crystals of HMX; m. p. 256° or higher, depending on the rate of heating. The compound can be recrystallized from 70% nitric acid without the formation of yellow fumes.

**Preparation of a Nitration and Acetylation Product.**—A mixture of 10.4 g. of hexamethylenetetramine dinitrate and 6.4 g. of ammonium nitrate was added to an ice-cold mixture of 25 ml. of acetic anhydride and 6.84 ml. of 98% nitric acid. The mixture was warmed slowly in the course of one-half hour to 75° with stirring and kept at that temperature for five minutes. Addition of water precipitated 13.8 g. of colorless solid; m. p. 140-145°. By recrystallization from acetone and ethyl acetate the prod-

(10) When the work had progressed to the stage where the new reaction appeared to have possibilities as a practical process for the preparation of RDX on a large scale, other laboratories were asked to coöperate in order to expedite the study of the reaction. The results described in the present paper are substantially those obtained before coöperative contributions were made. Participating continuously or for a short time in the project were groups at the University of Toronto, McGill University, Cornell University, Pennsylvania State College, Harvard University, the University of Pennsylvania, Tennessee Eastman Co., E. I. du Pont de Nemours & Co., Western Cartridge Co., Indiana University, Vanderbilt University, and in Great Britain. The group at the Tennessee Eastman Co. deserves special mention for the masterly way in which it put the reaction into operation as a continuous process. It has been reported (Ref. 3) that RDX was produced by the reaction in Equation 2 at the rate of 360 tons per day.

(11) All melting points are corrected.

(12) A safety shield should be placed between the observer and the melting point apparatus; this precaution is absolutely essential for the higher melting HMX. It is advisable to store the RDX under water, particularly when it is contaminated with the more sensitive forms of HMX.

uct (BSX) was obtained as colorless plates or leaflets; m. p. 154–155°.

*Anal.* Found: C, 26.4; H, 3.7; N, 24.8; molecular weight in acetone (Menzies' method), about 350.

The compound is readily decomposed by hot 70% nitric acid (fume-off) and by hot aqueous ammonia. A different product was obtained when propionic anhydride was substituted for the acetic anhydride.

## Summary

A new synthesis of the high explosive cyclotrimethylenetrinitramine (RDX) is described. From one mole of hexamethylenetetramine it is possible to obtain two moles of RDX by carrying out the nitrolysis at 75° in acetic anhydride in the presence of ammonium nitrate.

Two new nitrolysis products of hexamethylenetetramine were discovered. One (HMX) is formed in the RDX reaction; the other (BSX) is produced when the reagents are mixed cold and the temperature is raised slowly.

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# Chemical Effects of Steric Strains. I. The Effect of Structure upon the Hydrolysis of Tertiary Aliphatic Chlorides[1]

BY HERBERT C. BROWN[2] AND ROSYLN SILBER FLETCHER[2,3]

The introduction of one or two alkyl groups into the ammonia molecule leads to a marked increase in base strength. The introduction of a third alkyl group has the opposite effect. This peculiar weakness of aliphatic tertiary amines has been attributed to a steric effect, termed B-strain. It was suggested that the steric requirements of the three alkyl groups attached to the nitrogen atom are so large as to set up a condition of strain which resists the conversion of the free tertiary amine into the trialkylammonium ion.[4]

If three alkyl groups attached to nitrogen constitute a center of strain, it follows from the similarity in atomic dimensions of nitrogen and carbon that three alkyl groups attached to carbon should also be a center of strain. It is therefore of interest to examine the reactions of highly branched carbon compounds to ascertain whether the steric strain hypothesis has anything to contribute to an understanding of the behavior of these compounds.[5]

It has long been recognized that the chemistry of the branched-chain aliphatic compounds differs significantly from that of the corresponding straight-chain compounds. Several outstanding points of difference may be mentioned.[6]

1. **Tertiary vs. Primary Alcohols.**—The ease with which tertiary alcohols undergo dehydration is in marked contrast to the behavior of primary alcohols.[7] Moreover tertiary alcohols react exceedingly rapidly with the halogen acids at low temperatures; primary alcohols react with difficulty at elevated temperatures.[8]

2. **Tertiary vs. Primary Halides.**—Tertiary halides hydrolyze relatively rapidly in aqueous solvents by a unimolecular mechanism; the rate of hydrolysis is independent of the hydroxide ion concentration. On the other hand, primary halides hydrolyze predominantly by a bimolecular mechanism and the rate of hydrolysis is dependent upon the hydroxide ion concentration.[9]

3. **Rearrangements.**—Highly-branched aliphatic compounds are especially prone toward rearrangements. For example, the replacement of the hydroxyl group in straight-chain primary alcohols proceeds normally, whereas similar reactions involving primary alcohols with a single or double branch in the beta position proceed with rearrangement.[10]

4. **Bond Rupture.**—Reactions involving rupture of the carbon chain usually proceed with

(1) Studies in Stereochemistry. XV.

(2) Present address: Department of Chemistry, Purdue University.

(3) Parke, Davis and Co. Fellow at Wayne University, 1945–1947.

(4) Brown, Bartholomay and Taylor, THIS JOURNAL, **66**, 435 (1944).

(5) Spitzer and Pitzer [*ibid.*, **70**, 1261 (1948)] have attempted a calculation of the steric strain involved in the conversion of the trimethylamine molecule into the trimethylammonium ion. They estimate that the deformation of trimethylamine from a molecule with C–N–C bond angles of 112° to a molecule with tetrahedral angles should require slightly less than 500 calories. They assume that the strain involved in converting the free amine into the trimethylammonium ion should be of the same magnitude and therefore that B-strain cannot be an important factor in the weakness of trimethylamine as a base. No alternative explanation is advanced. Moreover, they state, "B-strain may become important when groups much larger than methyl are attached to the central atom because both the angles of distortion and the angle force constant will increase."

The senior author of the present apper (H. C. B.) believes that the quantity calculated by Spitzer and Pitzer is not identical with the steric strain involved in the conversion of trimethylamine into its ion. However, without more experimental data than are now available, it would be pointless to argue the question. Such data are now being gathered. It is hoped that a full and detailed discussion of the impor

tance of B-strain in trimethylamine and related tertiary amines will be possible in the near future.

In any case, the exact magnitude and importance of B-strain in trimethylamine does not affect the present discussion of the effect of steric strain upon the behavior of highly branched carbon compounds in general and upon the hydrolysis of tertiary aliphatic chlorides in particular.

(6) A preliminary communication outlining the utility of the B-strain hypothesis in correlating the behavior of highly branched carbon compounds was published in *Science*, **103**, 385 (1946).

(7) Hibbert, THIS JOURNAL, **37**, 1748 (1915).

(8) Lucas, *ibid.*, **52**, 802 (1930).

(9) Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941); Bateman, Cooper, Hughes and Ingold, *J. Chem. Soc.*, 925 (1940).

(10) Whitmore and Rothrock, THIS JOURNAL, **54**, 3431 (1932).