120. *On the Structure of Knudsen's Base and of Related Compounds. Part I.*

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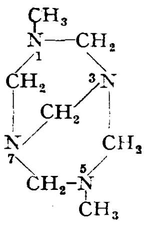
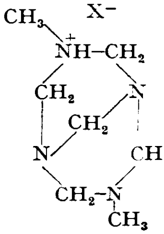
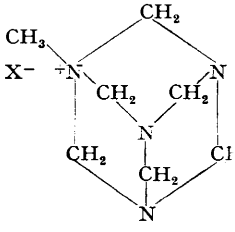
The corresponding salts of Knudsen's base, and those of the base obtained by treating hexamine dinitrate with hot solvents, are identical with one another and with the corresponding salts of the 1-methylhexamine ammonium cation.

Knudsen (*Ber.*, 1914, **47**, 2694) described the preparation of a base, since called "Knudsen's base," in the form of its sulphate, by the action of aqueous formaldehyde on ammonium sulphate. On the basis of carbon, hydrogen, and nitrogen analyses of the salts, Knudsen assigned to the base the structure (I), 1 : 5-dimethylpentamethylenetetramine. The salts were regarded as hydrosalts of type (II).


(I.)


(II.)


(III.)

We had found that, when hexamine dinitrate is treated with hot water, methyl alcohol, ethyl alcohol, *iso*propyl alcohol, or *tert.*-butyl alcohol, the main product isolated, the nitrate, m. p. 195°,* of an organic base (*A*), is independent of the solvent. This compound was identified by carbon, hydrogen, nitrogen, " CH_2 as CH_2O," and nitrate ion analyses, and by mixed m. p., as the hexamine methonitrate (1-methylhexamine 1-nitrate) (III; $X = NO_3$) prepared by Hahn and Walter (*Ber.*, 1921, **54**, 1531) by addition of methyl nitrate to hexamine. This compound was also prepared *via* hexamine methiodide and most carefully investigated in the University of Pennsylvania where it was independently shown that, when hexamine dinitrate is extracted with hot chloroform, hexamine methonitrate is produced (private communication from Professor Marvin Carmack).

We then noticed that corresponding salts of base *A* and of Knudsen's base had many identical chemical and physical properties, indicating that the two bases probably have identical structures. If this is so, then, either the identification of the salts of base *A* as (III), or Knudsen's formulation of the salts of his base as (II), must be in error, and in this connection we note the observation of Hahn and Walter (*loc. cit.*) who had prepared a compound by a reaction similar to Knudsen's reaction (using aqueous formaldehyde, ammonia, and ammonium sulphate) and designated it as (III; $X = NH_4SO_4^-$) on the basis of analyses for carbon, hydrogen, nitrogen, and sulphur only. They did not consider the alternative structure and do not refer to Knudsen's work.

It was therefore decided to re-examine the points named in the headings below.

Evidence for the Identification of the Salts of Base A *as having Structure* (III).—This problem is treated in two parts, showing (*a*) that the main product *A* is the same for a range of solvents, and (*b*) that the product *A* is a nitrate having structure (III; $X = NO_3$).

(*a*) The analytical data and the m. p. and mixed m. p. data for the products *A* isolated by treatment of hexamine dinitrate with several hot solvents are given in Table I and leave little doubt that the various products are identical.

(*b*) The identification of the product *A* as (III; $X = NO_3$) was carried out on the specimen obtained by hot water. The analytical results for the nitrate, picrate, and chloride are given in Table III. For all three, the theoretical figures for carbon, hydrogen, nitrogen, and anion are so similar for the alternative structures (II) and (III) that no differentiation on this basis can be made. The theoretical figures for *N*-methyl and methylene, however, are markedly different, and the experimental data favour the formulation (III) (methylhexamine salts).

TABLE I.

Substance *A* prepared by	C, %.	H, %.	N, %.	CH_2, %.	NO_3^-, %.*	M. p.	Mixed m. p.
H_2O	38·8	6·9	32·2	38·4	28·2	192°	190°
MeOH	38·5	7·0	33·0	38·2	28·0	190	191
EtOH	38·9	6·8	32·4	38·6	28·3	191	190
Pr^iOH	38·8	6·9	32·5	38·0	28·2	192	190
Bu^nOH	38·7	6·9	31·9	38·1	28·3	192	
$CHCl_3$ *	39·0	7·0	32·6	—	27·4	193	

The analytical data reported in this paper were obtained as follows: The C, H, N, and *N*-CH_3 (Herzig–Meyer) determinations were by Drs. Weiler and Strauss (Oxford); CH_2 was determined gravimetrically as CH_2O by dinitrophenylhydrazine, following Brady (*J.*, 1931, 757); NO_3^- and picrate$^-$ were determined by nitron, following Cope and Barab (*J. Amer. Chem. Soc.*, 1917, **39**, 509); Cl^- was determined as AgCl.

* Data obtained in the University of Pennsylvania (private communication from Professor Marvin Carmack).

TABLE II.

	M. p. of salt.		
Base.	Nitrate.	Picrate.	Chloride.
(*a*) Authentic methylhexamine	190°	210°	—
(*b*) Base *A* (hot H_2O)	192	212	202°
(*c*) Knudsen's base	190	209 *	202
Mixed *a*–*b*	190	212	—
Mixed *b*–*c*	190	209 *	202

* Data obtained by A. T. T. and T. U. at Explosives Research and Development Establishment (E.R.D.E.). The m. p. of this picrate is discussed below.

As was expected, *N*-methyl determinations were not very satisfactory. The Herzig–Meyer micro-procedure might well lead to anomalous results with compounds capable of yielding

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* The melting of this substance, and of all other new substances discussed in this work, is accompanied by decomposition.

relatively large amounts of formaldehyde, especially with a tetra-alkylammonium cation such as in (III).

TABLE III.

Analysis of salts of base A *and Knudsen's base.*

	C, %.	H, %.	N, %.	*N*-CH$_3$, %.	CH$_2$, %.	Anion, %.	
Found for base *A*	38·8	6·9	32·2	10·0	38·4	28·2	nitrate
Found for Knudsen's base	38·7	7·4	32·2	9·8	38·5	28·3	
Calc. for $C_7H_{15}O_3N_5$ (III; X = NO$_3$) ...	38·7	6·9	32·3	13·4	38·8	28·6	
Calc. for $C_7H_{17}O_3N_5$ (II; X = NO$_3$)	38·4	7·8	32·0	26·5	32·0	28·3	
Found for base *A*	40·6	4·7	25·4	5·0	21·8	59·7	picrate
Found for Knudsen's base	40·6	4·6	25·6	5·2	21·5	59·3	
Calc. for $C_{13}H_{17}O_7N_7$ (III; X = picrate)	40·8	4·4	25·6	7·6	22·0	59·6	
Calc. for $C_{13}H_{19}O_7N_7$ (II; X = picrate)	40·6	5·0	25·5	15·1	18·2	59·3	
Found for base *A*	43·5	8·9	29·8	12·6	43·8	18·7	chloride
Found for Knudsen's base	43·7	9·0	29·5	11·9	44·0	18·7	
Calc. for $C_7H_{15}N_4Cl$ (III; X = Cl)	44·1	7·9	19·4	15·2	44·1	18·6	
Calc. for $C_7H_{17}N_4Cl$ (II; X = Cl)	43·6	8·8	29·1	30·1	36·4	18·4	

Authentic specimens of hexamine methonitrate and methopicrate (III; X = NO$_3$ or picrate) were prepared from hexamine by the successive action of methyl iodide and silver nitrate or picric acid. Mixed m. p.s of each of these substances and of the corresponding salts of base *A* are given in Table II.

The identity of authentic hexamine methonitrate and the nitrate of base *A* obtained by chloroform has been established by Dr. A. T. Blomquist of Cornell University by microscopic examination (private communication from Professor Marvin Carmack).

As a final check, specimens of authentic hexamine methopicrate and the picrate of base *A* (obtained by hot water) were submitted to Professor F. J. Llewellyn (then of Birmingham University) for comparison by the *X*-ray powder method. He reported that the specimens gave identical patterns (Fig. 1).

The identity of the salts of base *A* with the corresponding salts of the methylhexamine cation is thus established.

Comparison of the Properties of Corresponding Salts of Base A *and of Knudsen's Base.*—Hot water was used to produce the base *A*. The nitrates, picrates, and chlorides of base *A* and of Knudsen's base were prepared and analysed (see Tables II and III). The oily hydroxides prepared from the two bases had identical refractive indices (1·4475 at 20°).

It was found that aqueous solutions of the nitrate, chloride, dichromate, neutral sulphate, and hydroxide of base *A*, on treatment with aqueous picric acid, all gave the same picrate, m. p. 208—209° (m. p.s determined at E.R.D.E.), seemingly identical with the picrate obtained from Knudsen's base.

The findings presented in this section seem to indicate strongly the probable identity of the two bases.

Evidence for the Formulation of the Salts of Knudsen's Base.—The two lines of work described above indicate that salts of Knudsen's base have structure (III), whereas Knudsen (*loc. cit.*) had advocated structure (II). Its picrate was therefore subjected to tests analogous to those used for the identification of the picrate of base *A*.

The first batches of the picrate of Knudsen's base prepared in Manchester (M. E. F., E. L. H., J. K. N. J., H. D. S.) had the m. p. 210° reported from E.R.D.E. All subsequent preparations gave the m. p. 195° recorded by Knudsen. The two specimens of hexamine methopicrate first prepared gave the expected m. p. 210—212°, but a mixed m. p. between them and Knudsen's picrate, m. p. 195°, gave no depression below 195° and all subsequent preparations of hexamine methopicrate in Manchester have shown m. p. 195—198°. It seems probable that hexamine methopicrate is dimorphic and that, the lower-melting dimorph being now obtained, we shall not be able to make again the other modification.

X-Ray powder photographs of Knudsen's picrate and of authentic hexamine methopicrate, kindly supplied by Professor F. J. Llewellyn, showed complete identity (Fig. 2), thus confirming the analytical data—the CH$_2$ content figure being especially significant—and the rather slight m. p. data.

Further evidence for the methylhexamine cation structure for Knudsen's compounds is furnished by our observation that the direct synthesis of the parent hydroxide of these compounds can be achieved from formaldehyde, methylamine, and ammonia, and that the yield

FIG. 1.

X-Ray powder diagrams for hexamine methopicrate (north and south quadrants) and the picrate of base A *(east and west quadrants).*

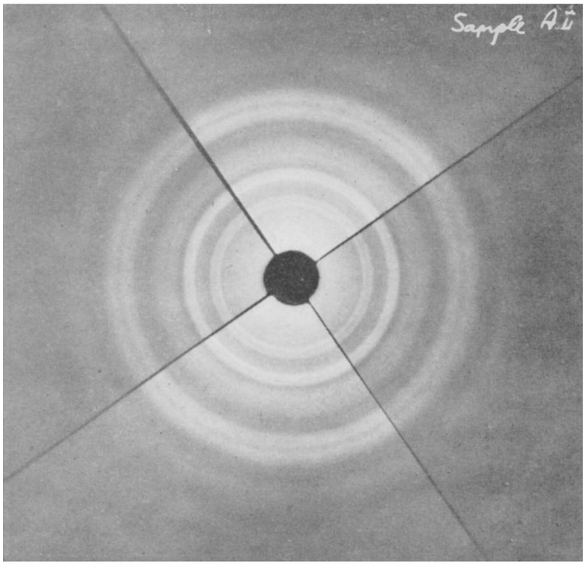
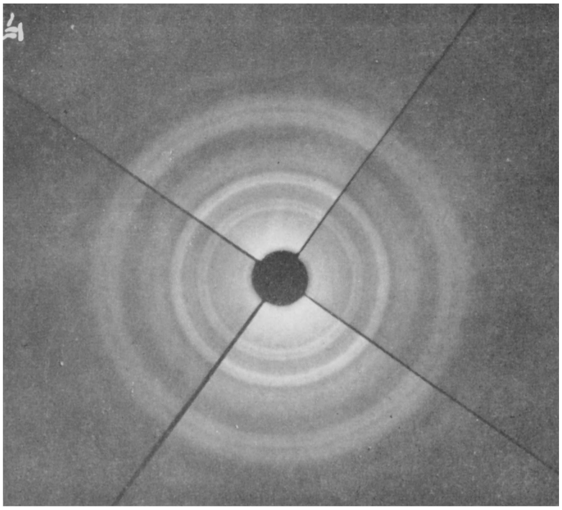


FIG. 2.

X-Ray powder diagrams for hexamine methopicrate (north and south quadrants) and the picrate of Knudsen's base (east and west quadrants).



is much better (70%) when the reagents are mixed in the correct stoicheiometric proportions for structure (II; X = OH) (yield 50%).

EXPERIMENTAL.

(Analytical data quoted in the tables are not repeated below.)

Hexamine Dinitrate–Solvent Reactions. Base A.—(*a*) *Water.* Hexamine dinitrate (100 g.) and water (500 ml.) were refluxed for 1½ hours. The resulting solution was cooled, neutralised with aqueous sodium carbonate, and evaporated to dryness. The residue was extracted with hot methyl alcohol, and the extract cooled. The white needles deposited were recrystallised from alcohol. The nitrate of base *A* had m. p. 192° (6·5 g.).

The methyl-alcoholic filtrate was evaporated yielding a syrup (52 g.), which was dissolved in cold nitric acid (150 ml. of 70%). Methyl alcohol was added carefully, producing a white crystalline precipitate, which was collected, washed with cold ether, and dried in air. This compound, m. p. 140—145° (11 g.), differs from the above nitrate in being insoluble in hot dioxan, acetone, or acetic acid. It gives a strongly acidic solution in water which with the calculated amount of N/10-sodium hydroxide gives the nitrate, m. p. 192—195°, in good yield. The compound, m. p. 142°, is probably 1-methylhexamine 1 : 5-dinitrate (Found : C, 30·1; H, 5·6; N, 30·5; CH_2, 31·1; NO_3^-, 44·5. Calc. for $C_7H_{16}O_6$: C, 30·0; H, 5·7; N, 30·0; CH_2, 30·0; NO_3^-, 44·3%).

The nitrate of base *A* was prepared in better yield as follows. Hexamine dinitrate (25 g.) in water (50 ml.) was refluxed for 2½ hours, and then cooled and evaporated under reduced pressure. The crystalline residue, recrystallised from alcohol, had m. p. 190° (9 g.).

(*b*) *Methyl alcohol.* Hexamine dinitrate (40 g.) was refluxed in methyl alcohol (200 ml.) for 4 hours, evaporated under reduced pressure to 50 ml., and then kept at 0° overnight. The crystals which separated were recrystallised twice from alcohol, giving a nitrate as white needles, m. p. 190° (3·2 g.).

Similar experiments with the dinitrate (40 g.) and ethyl, *iso*propyl, and *tert.*-butyl alcohol gave the nitrate in yields of 3·5 g. (see Table I).

Salts of Base A (*obtained by hot* H_2O).—*Picrate.* To the nitrate (10 g.) in water (150 ml.), saturated aqueous picric acid was added at 0° until no further precipitation occurred. The orange-red picrate, recrystallised from hot water, had m. p. 208° (12 g.).

Chloride. Prepared as was the corresponding nitrate, starting from hexamine hydrochloride, this was obtained as white needles, m. p. 202° (after softening at 130°, and hardening at 135°) (yield 10—15%). It was also isolated, in good yield, from the filtrate from the precipitation of the nitrate of base *A* by nitron hydrochloride (Found : C, 43·5; H, 8·9; N, 29·8; Cl^-, 18·3. Calc. for $C_7H_{15}N_4Cl$: C, 43·9; H, 7·9; N, 29·4; Cl^-, 18·7%).

Dichromate. Hexamine tetrachromate was prepared by the method of Cambier and Brochet (*Bull. Soc. chim.*, 1895, **13**, 400) by the action of aqueous chromium trioxide on aqueous hexamine. The tetrachromate (42 g.) and water (500 ml.) were heated for 1½ hours on the steam-bath (after the initial dissolution, a dark brown amorphous solid was precipitated). The suspension was cooled and filtered, and the filtrate evaporated to 200 ml. On cooling, orange-yellow crystals separated; when dried, these had m. p. 215° (7 g.) (Found : C, 32·0; H, 6·5; N, 21·1; Cr, 20·0. Calc. for $C_{14}H_{30}O_{14}N_8Cr$: C, 32·0; H, 5·7; N, 21·4; Cr, 20·6%).

Hydroxide. To the chloride (25 g.) in water (150 ml.), moist silver oxide, freshly prepared from silver nitrate (25 g.), was added and the resulting suspension was shaken vigorously for 6 hours at room temperature and then filtered. The filtrate was evaporated under reduced pressure. The oily residue (12 g.), n^{20} 1·4475, of the crude hydroxide was not further purified. The oil is hygroscopic and yields an alkaline solution from which the corresponding picrate can be precipitated in 80% yield.

Salts of Knudsen's Base.—*Nitrate.* This was prepared by a method analogous to that used by Knudsen for the sulphate : a solution of ammonium nitrate (150 g.) in a mixture of aqueous formaldehyde (215 g. of 40%) and water (150 ml.) was heated to 70—80° on a water-bath for 1 hour. The product, isolated as in the case of the nitrate of base *A* and recrystallised from alcohol, had m. p. 190° (12 g.).

Chloride. This was prepared (*a*) by Knudsen's alternative method from pre-formed hexamine, and (*b*) from the nitrate. (*a*) Hexamine (93 g.) was added to a solution of methylamine hydrochloride (90 g.) in hydrochloric acid (229 g.; *d* 1·16) at 20°. The mixture was warmed on a water-bath for ½ hour, and then cooled, neutralised with anhydrous sodium carbonate, and evaporated to dryness. Sodium and ammonium chlorides were removed by extracting the product with hot alcohol (750 ml.). On cooling, the alcoholic extract gave a crop of crystals, mainly methylamine hydrochloride (25 g.) which was collected. Evaporation of the filtrate to 250 ml. gave a mixture (39 g.) of methylamine hydrochloride and Knudsen's chloride. Fractional crystallisation from alcohol gave the chloride, m. p. 202° (8 g.). (*b*) The filtrate from the precipitation of the nitrate from Knudsen's nitrate by nitron hydrochloride was worked up by the usual procedure to give Knudsen's chloride in good yield.

Picrate. This was prepared in 80% yield by addition of picric acid solution to a solution of any of the other salts of Knudsen's base, or the hydroxide.

Hydroxide. This was prepared from the chloride by the method used for base *A*.

Derivatives of 1-*Methylhexamine* (*Hexamine Metho-salts*).—1-*Nitrate.* Hexamine methiodide was prepared by refluxing, for 1 hour, hexamine (35 g.) suspended in methyl alcohol (250 ml.) and methyl iodide (40 g.). The methiodide was treated directly in hot methyl-alcoholic solution with powdered silver nitrate (43 g.). The whole was refluxed for ½ hour, and the resulting suspension was cooled and filtered. The methyl-alcoholic filtrate was worked up as for the nitrate of base *A* prepared by methyl alcohol. The product crystallised in colourless needles, m. p. 190° (40 g.).

1-*Picrate.* This was prepared by adding an equimolecular proportion of picric acid in saturated alcoholic solution at 60° to a solution of authentic hexamine methonitrate in alcohol at 60°. The resulting system was cooled to 0°; the product, hexamine methopicrate, when dried, formed orange-yellow needles, m. p. 210° (85%).

1-*Hydroxide.* This was synthesised from formaldehyde, ammonia, and methylamine as follows. (*a*) Using stoicheiometric proportions of the reagents correct for (III; X = OH). Paraformaldehyde (18 g., 0·6 mol.) was added to a solution of ammonia (17·5 ml., 0·3 mol.; *d* 0·880) and methylamine (9·5 ml., 0·1 mol.; 33%) at room temperature; the paraformaldehyde slowly dissolved, dissolution being accompanied by slight evolution of heat. The solution was kept overnight and then evaporated at 50°/20 mm. The product was extracted with ether, the ethereal solution dried and evaporated, and the product was finally dried *in vacuo* (12 g., 70%). (*b*) Using the stoicheiometric proportions of reagents correct for (II; X = OH), *i.e.*, paraformaldehyde (18 g., 0·6 mol.), ammonia (11 ml., 0·6 mol.; *d* 0·880), and methylamine (19·0 ml., 0·2 mol.; 33%). The yield was 8·5 g. (50%).

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