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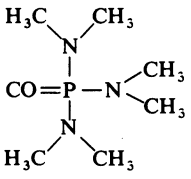
Hexamethylphosphoramide [tris(dimethylamino)phosphine oxide, hexamethylphosphoric triamide, hexametapol, often abbreviated HMPA or HMPT] (see formula I below) is a colourless, mobile, aprotic solvent having a somewhat unpleasant odour. It is liquid over a wide range of temperatures and has a relatively high dielectric constant. Since it is one of the most strongly basic of the aprotic solvents now used for electrochemical studies, its behaviour is very important.

PHYSICAL AND CHEMICAL PROPERTIES OF HMPA

Some physical properties of HMPA are summarized in *Table 1*. The HMPA molecule has a pyramidal structure. Its P—O bond is polar with



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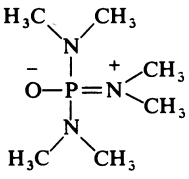

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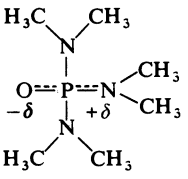

IIb

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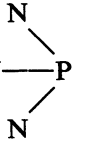
Table 1. Physical properties of HMPA

Freezing point	7.20°C[1]
Boiling point, 760 mmHg	235°C[1]
15 mmHg	115°C[1]
1 mmHg	68–70°C[1]
Refractive index, n_D (20°C)	1.4584[2]
n_D (25°C)	1.4564[2]
Density, 25°C	1.020 g/cm^3 [2,3,4]
Viscosity, 25°C	3.25 cP[3,4], 3.23 cP[5]
Dielectric constant, 20°C	30.5[2]
25°C	29.6[2,3], 30.0[4]
Dipole moment μ, 25°C	
Liquid HMPA	5.38D[2], 4.31D[6]
HMPA in benzene	5.54D[2]
Electrolytic conductivity	0.5–2 × 10^{-8} ohm^{-1} cm^{-1} [3]
	2–4 × 10^{-8} ohm^{-1} cm^{-1} [7]

* For further details of refractive index, density, dielectric constant, and dipole moment of HMPA, see ref. 2.

approximately 50 per cent ionic character and can be described as IIa or IIb[1]. The symmetrical distribution of the positive charge over the



grouping and the high electron density on the oxygen give rise to a large dipole moment and unusually high basicity[1]. The strong basic character of HMPA, as compared with other solvents, is shown in *Table 2* by a chemical shift for the proton of chloroform[1] and by the donor number proposed by Gutmann[8].

HMPA is very hygroscopic and gradually takes up moisture if exposed to a humid atmosphere. It is easily mixed with water in any proportions.

HMPA is miscible in all proportions with a majority of the common solvents. It readily dissolves many organic compounds, some inorganic salts, polymers, and gases such as acetylene[10]. HMPA has a strong solvation power for the cations, and many metal complexes with it have been isolated.

Table 2. Dielectric constants, donor numbers and chemical shifts of some solvents for electrochemical use

Solvent	Dielectric constant[2,9]	Donor number[8]	Chemical shift[1]*
HMPA	29.6	38.8	2.03
Pyridine	12.3	33.1	
DMSO	46.7	29.8	1.34
DMF	36.7	26.6	1.30
Water	78.5	18.0	
Acetone	20.7	17.0	0.94
Propylene carbonate	64.4	15.1	
Acetonitrile	37.5 (20°C)	14.1	

* Chemical shift $\Delta\delta_\infty(CHCl_3) = \delta_\infty - \delta$, where δ_∞ and δ respectively are the chemical shifts at infinite dilution of a solution of chloroform in the solvent in question and in cyclohexane.

Most of the ionic compounds dissolved in it are fairly extensively dissociated[3, 11] because of its relatively high dielectric constant.

In HMPA, free from dissolved oxygen and moisture, alkali and alkaline earth metals dissolve to produce deep blue solutions of solvated electrons[12], which are relatively stable even at ambient temperatures. Organic radical anions are also stable in HMPA[13].

HMPA is fairly stable to electrochemical reduction, but is not stable against anodic oxidation. In a HMPA–0.1M lithium perchlorate solution, the potential range extends from +0.8 V to −3.6 V versus Ag/0.01 M Ag^+ on a platinum electrode[14, 15] and from +0.1 V to −2.8 V versus Ag/0.01 M Ag^+ on a mercury electrode[7, 15] when measured at current densities of *ca.* 4 mA/cm^2. At the platinum electrode, the cathodic potential limit in this solution is determined by the generation of solvated electrons from the electrode[16]. In HMPA–0.05M Bu_4NClO_4, the cathodic potential limit at a mercury electrode is −3.3 V versus Ag/0.01 M Ag^+ electrode[7, 15]. Metal ions, which are strongly solvated in HMPA, are less easily reduced than in other solvents and their reduction behaviours are significantly influenced by the cation of the supporting electrolyte[7, 17].

In HMPA, perchloric, nitric and *p*-toluenesulfonic acids act as strong acids. The values of pK_a of benzoic acid, acetic acid and phenol have been reported by Madic and Trémillon[18] to be 8.25, 11.9* and 14.15, respectively, which are several units larger than those in aqueous solutions.

Under ordinary conditions of storage, HMPA is very unstable. For the electrochemical use of HMPA, the degradation of the purified solvent by the rapid formation of its peroxide (III) is most troublesome. The formation of the peroxide has been studied in detail by Gal and Yvernault[11, 19, 20]. Oxygen and light are responsible for its formation. When freshly purified HMPA is exposed to the air and the light in a room for a few hours, a reduction wave as shown in *Figure 1* is observed to appear in the polarographic

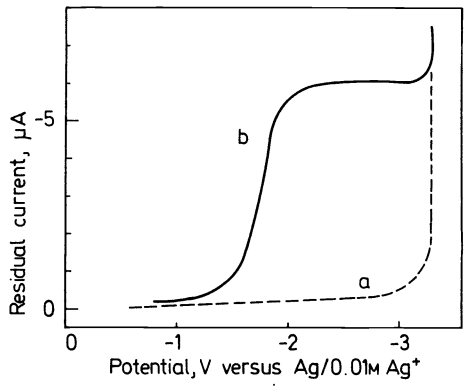
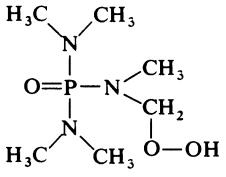


Figure 1. Polarograms of a 0.1M Et_4NClO_4–HMPA solution at the dropping mercury electrode: (a) With freshly distilled HMPA and (b) with the same solvent kept for four days under light. From ref. 11.

* This value was obtained from the halfwave potential of the reduction wave of acetic acid at a platinized platinum electrode. It may be desirable to check it.

residual current/potential curves. The rate of the degradation, however, is quite small when HMPA is kept either free from dissolved oxygen or in the dark.



III

The decomposition of HMPA at higher temperatures is not so extensive, and appreciable decomposition products are not detected by gas chromatographic and infra-red spectrophotometric measurements after being heated for five hours in air at 100°C. If heated at 150°C, however, about one per cent of HMPA is decomposed[21].

HMPA irritates the skin on contact for 24 hours or more, and the skin may become inflamed after prolonged use during more than a month. Kimbrough and Gaines[22] found the amount of HMPA fatal to 50 per cent of test male and female rats to be 2650 and 3360 mg/kg, respectively, by oral administration. By dermal administration the corresponding amount was about 4000 mg/kg for both sexes. Testicular atrophy in male rats was noted at a single dose of 1000 mg/kg. Prolonged dietary intake of 40–80 mg/kg produced partial or complete atrophy.

TESTS OF PURITY

The major impurities commonly found in HMPA as received are water, dimethylamine and its salt with hydrochloric acid, which come from the synthetic processes*. The peroxide of HMPA and other unidentified impurities are also found. The following tests can be employed to detect impurities in HMPA.

(1) Water content by the Karl Fischer method

The classical Karl Fischer titration, which needs a considerable amount of sample HMPA, gives unreliable results for smaller water contents, because HMPA forms a complex with iodine and a sharp end point cannot be obtained in the titration[3]. Gal and Yvernault[15] obtained better results by using the coulometric method (of Bizot[23]), in which only 0.05–0.2 ml of sample HMPA, negligibly small compared with the volume of the titration cell, was necessary.

* HMPA is usually synthesized industrially by the treatment of phosphorus oxide trichloride with an excess of dimethylamine in isopropyl ether. The reaction is

$$POCl_3 + 6HN(CH_3)_2 \rightarrow [(CH_3)_2N]_3PO + 3HCl.HN(CH_3)_2$$

(2) Determination of dimethylamine and chloride ion

The content of dimethylamine and chloride ion can be determined after the addition of water to the sample HMPA. Dimethylamine is determined by acid–base titration with a pH meter. The chloride ion is titrated by conventional argentometry or preferably by coulometry at a silver anode. According to Gal and Yvernault[15], the crude HMPA (product of Prolabo) generally contained at least 1–3 $\times$ 10^{-2}M chloride ion as determined coulometrically after being dissolved in water.

(3) Determination of the peroxide of HMPA by iodometry

Gal and Yvernault[20] proposed an iodometric method in the presence of acetic acid. The mixture consisting of 1 g of potassium iodide, 5 ml of 0.5M acetic acid and 1–2 ml of HMPA is warmed at 40°C for 15 min, and the liberated iodine is then titrated with a solution of 10^{-2}M sodium thiosulfate. It is preferable to add 20 ml of alcohol before titration and to determine the equivalence point by controlled-current potentiometry with two platinum indicator electrodes. Formaldehyde, which is also liberated, does not interfere with this titration.

(4) Polarographic measurements*

The measurement of polarographic residual current/potential curves is very useful as a test for electroactive impurities. The potential range applicable in pure HMPA has been described above (for details, see ref. 15).

Dimethylamine and chloride ion give anodic waves at the dropping mercury electrode (DME). The decomposition product of the solvent, which was identified as the peroxide, can also be detected and determined by the reduction wave at $E_{1/2} = -1.75$ V versus Ag/0.01M Ag^+ at the DME in 0.1M Et_4NClO_4 (*Figure 1*). Gal and Yvernault[20] obtained a linear relation between the limiting current of the wave and the concentration of the peroxide (*ca.* 8 μA for 10^{-2}M). The presence of the peroxide also tends to shift the anodic potential limit in the positive direction, by forming a slightly conductive coverage of mercury oxides on the DME surface. The solvated proton and weakly acidic impurities can also be detected by their reduction waves. At the platinum electrode, the cathodic potential limit in sodium perchlorate–HMPA solutions is very sensitive to traces of water and shifts to less negative values in its presence[14].

(5) Spectrophotometric measurements

Pure HMPA shows little or no absorption in the u.v. region between 260 and 400 nm, but impure HMPA very often absorbs in this region. Therefore, the recording of an u.v. spectrum in this region is a convenient test of the purity of HMPA, though the impurities that give the absorption have not yet been identified.

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* Perchlorates, very often used in polarography in non-aqueous solvents, are explosive at high temperatures, especially when heated in the presence of organic substances. Therefore, in the purification of perchlorates special care must be taken. Tetra-alkylammonium perchlorates should be dried at 50–70 °C under vacuum[26]. Direct flames or infra-red lamps should be avoided. It is advisable to purify only small amounts of the salt in one experiment[28].

(6) Electrolytic conductivity measurements

Purified HMPA has an electrolytic conductivity of less than 4×10^{-8} ohm^{-1} cm^{-1}. Its electrolytic conductivity, however, increases fairly rapidly after distillation as a result of its decomposition (for the effect of the peroxide and dimethylamine on conductivity, see ref. 24). This method is only useful for the detection of ionic impurities.

(7) Gas chromatographic method

A well defined gas chromatographic peak of HMPA itself is obtained by using a column of the stationary phase of Silicone SE-30 at 150°C and a thermal conductivity or a flame ionization detector[11, 25]. The decomposition products in relatively large amounts can be detected on this gas chromatogram, but this method is not useful for the test of trace impurities.

PURIFICATION OF HMPA AND CONSERVATION OF PURIFIED HMPA

Purification of HMPA is usually carried out by chemical pretreatment followed by distillation under reduced pressure or by recrystallization.

For ordinary electrochemical use, the following two procedures seem to be satisfactory and can be recommended.

(1) The purification procedure used by the present authors is as follows. The raw HMPA (product of the Nippon Oil Seal Ind. Co. Ltd, in 1970–74) is refluxed over barium oxide at about 4mmHg in an atmosphere of nitrogen for several hours and then distilled. The middle fraction, about 70 per cent, is collected (b.pt *ca.* 90°C). The distillate is refluxed again over metallic sodium (*ca.* 1 g/kg) under reduced pressure (*ca.* 4 mmHg) and distilled. The distillation is carried out with an adiabatic vacuum fractional distillation column of 1m length and packed with stainless steel Dixon packing. The distillate is kept in a nitrogen atmosphere or under vacuum in the dark at dry-ice temperature. The HMPA thus obtained gives an electrolytic conductivity of $2–4 \times 10^{-8}$ ohm^{-1} cm^{-1} and a water content of approximately 0.01 per cent. This solvent is pure enough for both polarographic and u.v. spectrophotometric experiments.

(2) Gal and Yvernault[11, 15] purified the raw HMPA (product of Prolabo) by two distillations under reduced pressure (< 0.5 mmHg) in an atmosphere of argon, first over sodium (2 g/kg) and then over calcium hydride, using an adiabatic vacuum fractional distillation column of 50 cm length and packed with Multiknit. In order to avoid overheating, the distillation flask was heated in an oil bath. The yield was about 80 per cent of the raw product. The purified solvent was kept under argon in the dark and below 7°C. According to Gal and Yvernault[15], the treatment over sodium reduces the chloride content and that over calcium hydride reduces the dimethylamine. The purified HMPA contained 0.012–0.018 per cent of water, $0.5–4 \times 10^{-3}$M of dimethylamine and below 10^{-5}M of chloride ion; and the conductivity was about 7×10^{-8} $ohm^{-1}cm^{-1}$.

Dubois and others[14] carried out the distillation under reduced pressure (1 mmHg) in the presence of sodium and triphenylmethane and then distilled again under an argon atmosphere. In order to obtain solvent for the volt-

ammetric study of solvated electrons, Kanzaki and Aoyagui[16] refluxed HMPA over calcium hydride for about ten hours in an atmosphere of nitrogen, and then distilled it under vacuum and collected the middle fraction (88°C/4 mmHg). The purified solvent was then introduced into a vacuum line (*ca.* 10^{-5} mmHg). After being degassed very carefully, the solvent was refluxed again over calcium hydride for about one month to remove moisture. Then it was distilled and transferred in a vacuum into ampoules with a break-seal. For electrolytic conductivity measurements, Hanna and others[3] obtained HMPA of conductivity of $0.5–2 \times 10^{-8}$ ohm^{-1} cm^{-1}. Laboratory reagent grade HMPA (product of Pierrefitte Chimie) was distilled at a pressure of 0.8 mmHg through a heated fractionating column packed with small glass rings and the middle fraction of about 80 per cent was collected over calcium hydride. This fraction was then distilled again from calcium hydride, and a similar fraction was collected over barium oxide from which the solvent was distilled before use. All transfers were done under an atmosphere of dry argon.

By a recrystallization procedure, Luehrs and Leddy[17] could reduce the polarographic background current at potentials more negative than −1V. HMPA (Research Organic/Inorganic Chemical Corp.) was purified by fractional distillation under vacuum from calcium hydride at 60°C, and then recrystallized twice in a cold room at 0°C. In order to initiate crystallization, it was necessary to seed the HMPA with a crystal obtained by freezing HMPA with liquid nitrogen. About two thirds of the HMPA was allowed to freeze and the remaining liquid was decanted off. Other purification procedures are summarized in refs. 9 and 27.

To reduce the water content in the purified HMPA, it is effective to pass the solvent through a column of molecular sieves. Gal *et al.*[24] utilized a column of 3A molecular sieves and reduced the water content to about 0.005 per cent. To avoid formation of the peroxide, dry argon was passed over the column for half an hour before passing the solvent and the treatment was carried out in the dark. This treatment also achieved some reduction of the contents of dimethylamine and peroxide. However, extra care is needed when traces of conducting impurities leached out of the molecular sieves interfere with the experimental results.

The rate of decomposition of the purified HMPA may be effectively minimized by storing the HMPA in a cold dark place under an inert atmosphere or under a vacuum. It is, however, advisable to use the purified HMPA as soon as possible (in a day or two) after purification.

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