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**N-METHYLACETAMIDE:
PURIFICATION AND TESTS
FOR PURITY**

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PURIFICATION OF N-METHYLACETAMIDE
AND TESTS FOR PURITY

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N-methylacetamide (abbreviated NMA in this report) is one of a small group of non-aqueous solvents which have dielectric constants greater than that of water [The dielectric constant of NMA is 165.5 at 40° (ref. 1)]. Solubilities of inorganic salts in NMA consequently are quite high compared with those in other, low dielectric constant organic solvents. For example, the alkali halides studied conductometrically by Dawson and his co-workers¹ exhibit solubilities greater than 0.1 M. Likewise it is possible to prepare a 0.1 M solution of tetraethylammonium perchlorate or sodium perchlorate in NMA².

PHYSICAL PROPERTIES OF NMA

The physical properties of NMA are summarized in the following table.

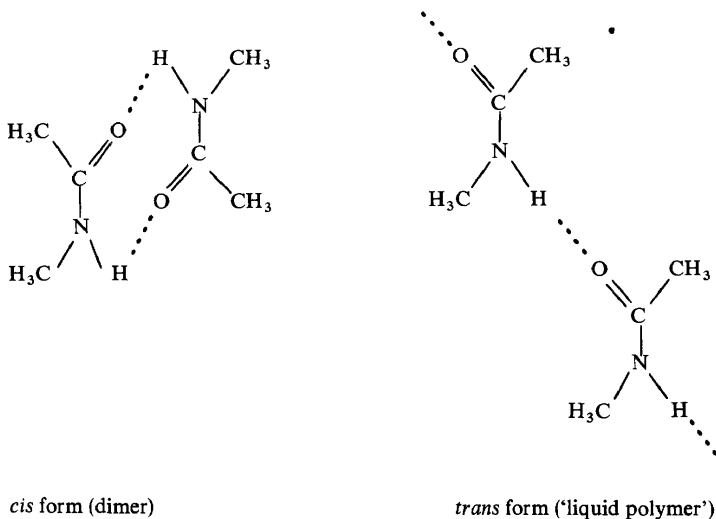
Melting point	29.5° (ref. 1)
	30.6° (ref. 3)
	30.35–30.55° (ref. 4)
Boiling point	206° (ref. 1)
Specific conductance (ohm ⁻¹ cm ⁻¹)	1–3 × 10 ⁻⁷ at 40° (ref. 1, 2)
	2.5 × 10 ⁻⁸ at 40° (ref. 5)

Temperature (°C)	Density (g/ml)	Viscosity (cP)	Dielectric constant
30.0	0.9503 (ref. 1)	3.885 (ref. 1)	178.9 (ref. 1); 179.0 (ref. 8)
30.5			175.7 (ref. 6)
32.5			172.9 (ref. 6)
35.0	0.9460 (ref. 7)	3.23 (ref. 7)	169.7 (ref. 6)
37.5			166.1 (ref. 6)
40.0	0.9421 (ref. 1)	3.019 (ref. 1)	162.7 (ref. 6); 165.5 (ref. 1)
			165.0 (ref. 8); 184.3† (ref. 4)
45.0	0.9376 (ref. 7)	2.54 (ref. 7)	156.0 (ref. 7)
50.0	0.9336 (ref. 1)	2.411 (ref. 1)	151.8 (ref. 1)
60.0	0.9254 (ref. 1)	1.958 (ref. 1)	138.6 (ref. 1); 139.5 (ref. 8)
80.0			118.5 (ref. 8)
100			101.0 (ref. 8)
120			87.2 (ref. 8)
140			75.5 (ref. 8)
160			65.0 (ref. 8)
180			56.0 (ref. 8)
200			48.0 (ref. 8)

†Decreased rapidly with time.

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Mizushima *et al.*⁹ have determined the structure of NMA by studying its Raman, infra-red and ultra-violet spectra and by making dipole moment measurements on dilute solutions of NMA in carbon tetrachloride and in dioxane. All experimental evidence and theoretical calculations lead to the conclusion that the molecules of NMA in the liquid state exist in the *trans* rather than the *cis* configuration and that there is extensive intermolecular hydrogen bonding through which 'polymers' of chain structure are formed. These structures are shown in the following figure.



The unusually high dielectric constant of NMA is explained on the basis of this 'liquid polymer' structure. Studies of various types by other workers^{6, 10-12} substantiate this conclusion regarding the structure of NMA in the liquid state.

The crystal structure and polymorphism of solid NMA has been studied by Katz¹³.

NMA is completely miscible with water; however, the value of water-NMA mixtures as solvent media is doubtful owing to the hydrolysis of the amide, particularly in the presence of bases and, to a lesser extent, acids.

Pure NMA is not hygroscopic; however, it does take up moisture slowly if exposed to a humid atmosphere. Since NMA is a nearly neutral solvent, it does not absorb carbon dioxide from the air rapidly; however, the solubility of carbon dioxide in this solvent has not been determined. Oxygen is appreciably soluble in NMA and can be detected polarographically. It is easily removed, as presumably carbon dioxide is also, by purging the solvent with nitrogen. NMA apparently is stable in the presence of air for periods exceeding a month (however, see ref. 4), but for long-term storage it is probably best to keep pure anhydrous NMA under an atmosphere of dry nitrogen and in the solid state, i.e. at room temperature or below.

NMA is not known to have any toxic properties. When pure it is colourless and virtually odourless. Because of these innocuous properties, and except for

its melting point being inconveniently just above room temperature and its viscosity somewhat high, it is a convenient and pleasant solvent to work with.

The autoprotolysis constant of NMA has not been determined; however, some data are available which give good indications as to the basic strength of this solvent. Unfortunately the same is not true regarding its acidic strength as explained below. Polarographic, conductometric and glass electrode pH titration results of Knecht^{2,14} show that perchloric and hydrochloric acids are completely dissociated in NMA, that the second proton of sulphuric acid is less dissociated in NMA than in water (two breaks appear in the pH titration curve), and that acetic and salicylic acids are both weaker acids in NMA than they are in water. Conductance measurements of Knecht¹⁴ yield a value $K_a = 1.4 \times 10^{-4}$ (in water $K_a = 1.06 \times 10^{-3}$) for salicylic acid in NMA. Conductance measurements of Dawson¹⁵ yield a value $K_a = 7.3 \times 10^{-8}$ (in water $K_a = 1.75 \times 10^{-5}$) for acetic acid in NMA. These data indicate that NMA is a weaker base than water. The available data relating to acidic strength of NMA are inconclusive, largely because strong bases cause decomposition of the solvent. Conductance measurements on weaker bases are inaccurate due to the relatively large contribution to the overall conductance by the solvent itself.

TESTS FOR PURITY

The major impurities commonly found in NMA are acetic acid, methylamine, a third impurity of unknown composition which is formed when NMA is heated strongly (e.g. during distillation at atmospheric pressure), and of course water. The following tests can be employed to detect these common impurities, the same tests undoubtedly serving as well to reveal the presence of other impurities. These tests are:

- (1) Water content by Karl Fischer titration.
- (2) Polarographic range.

When tetraethylammonium perchlorate is used as the supporting electrolyte, a deaerated solution prepared from pure NMA has a polarographic range extending from +0.35 to -2.75 V (versus aqueous saturated calomel electrode) over which the residual current at the dropping mercury electrode does not exceed 0.4 microamp. Acetic acid impurity will show up as a cathodic discharge (or wave if only small amounts are present) in the region -1.7 to -1.9 V (versus aq. SCE). Methylamine impurity will result in an anodic discharge (or wave) at potentials less positive than +0.35 V. The impurity of unknown composition mentioned above gives rise to a cathodic discharge beginning at about -2.2 V. Water as an impurity is undetected polarographically.

- (3) Specific conductance.

It is relatively easy to prepare NMA that has a specific conductance of 1 to 5×10^{-7} ohm⁻¹ cm⁻¹. The lowest value reported is 2.5×10^{-8} ohm⁻¹ cm⁻¹ (ref. 5).

- (4) Melting point.

The melting point of the solvent may be taken as an indication of purity; however, this test is less sensitive than those described above. The highest melting point reportedly achieved is 30.6° (ref. 3).

(5) Colour and odour.

Pure NMA is both colourless and odourless (or nearly odourless). Each of the common impurities (acetic acid, methylamine and the impurity of unknown composition) imparts a distinctive odour to the solvent, even when present in relatively small amounts.

PREPARATION OF NMA

NMA is available commercially (e.g. in the USA from Eastman Kodak); however, the commercial product not only is expensive but also invariably contains sufficiently large amounts of impurities (principally acetic acid) to make it unsuitable for any careful studies without purification. Since NMA is easily prepared from inexpensive starting materials, the recommended procedure is to prepare and purify the solvent as described below.

Several methods have been used by various workers^{16, 17} to prepare NMA, but none is as simple, inexpensive and satisfactory as the direct reaction between glacial acetic acid and monomethylamine. The methylamine may be in gaseous form, in which case it is simply bubbled through hot glacial acetic acid, or in a concentrated aqueous solution. The resulting partially aqueous solution of methylammonium acetate is heated to approximately 130° to crack out and distill off water, leaving behind a crude product consisting of NMA contaminated with relatively large amounts of acetic acid, methylamine and water.

PURIFICATION OF NMA

Methods for the purification of NMA are of two general types: (1) fractional freezing, including zone melting, and (2) chemical treatment followed by distillation at reduced pressure. Both methods require more than a single cycle. That is, in the first method several (at least five) fractional freezing cycles must be employed, while in the second method several vacuum distillations, separated by different chemical treatment steps, are required. Both methods, properly handled, yield products whose purities are indistinguishable by the tests described above. [Exceptions are the solvent for which a lower specific conductance was obtained by carrying it through several additional (i.e. more than five) fractional freezing cycles, and the solvent obtained by zone melting.] However, the fractional freezing and zone melting procedures are strongly recommended for the following reasons: (1) they can readily be adapted to the purification of large volumes of solvent, (2) the equipment, at least in the case of simple fractional freezing, is minimal, easily obtained and uncomplicated, (3) they require a minimum of operator attention, (4) the process is simple and therefore not susceptible to the experimental chemical difficulties encountered in the treatment-distillation procedure, and (5) the number of cycles can be extended conveniently to obtain solvent of very low specific conductance.

Fractional freezing and zone refining procedures (recommended)

Dawson and his co-workers have carried out numerous studies^{1, 5, 11, 15, 18-27} using NMA as a solvent and have developed and refined the fractional

freezing technique for purifying the solvent. Their refined procedure is outlined below.

The crude solvent, from which water and much excess acetic acid have been distilled, is fractionally distilled at atmospheric pressure. Five litres of the product of this distillation (fraction collected at 204° to 206°C ?) are introduced into a six-litre Pyrex separatory funnel equipped with an inner glass finger tube which is concentric with the axis of the funnel. During the freezing process, an internal heater assembly is placed inside this finger. The heater assembly described by Dawson consists of 2.44 m of No. 24 Nichrome wire (resistance 1.66 ohm/ft) wrapped as 75 turns around 50 cm of 6 mm tubing and encased in a glass tube. Crystallization is allowed to proceed at room temperature while 3 to 7 V is applied to the heater by means of a variable transformer, the voltage necessary depending upon the temperature of the room and the purity of the NMA. After a period of from five to nine days the remaining liquid is drawn off by suction. The solid is re-melted and the freezing repeated. Throughout the fractional freezing cycles the NMA is kept under an atmosphere of purified nitrogen.

In earlier papers^{1, 11} Dawson and co-workers reported specific conductances of the solvent from 2×10^{-6} to $1-3 \times 10^{-7}$ ohm⁻¹ cm⁻¹ at 40°. However, by extending the number of fractional freezing cycles and using the refined apparatus and procedure described above they were able to obtain solvent having a specific conductance less than 5×10^{-8} ohm⁻¹ cm⁻¹, the lowest value reported being 2.5×10^{-8} ohm⁻¹ cm⁻¹.

More recently Bonner and co-workers⁴ described the application of the zone melting technique to the purification of commercial NMA using apparatus specially constructed to be suited for substances melting near room temperature. Their apparatus consisted of Vycor tubes having a radius of 0.7 cm and a length of 78 cm, and ten such tubes containing more than one litre of material could be purified at one time. In order to maintain a small molten zone (usually about 1 cm) they placed cooling coils (cold water circulated) immediately above the heating wires. The zone was heated with a single loop of Nichrome wire, heated electrically, so as to just melt the sample in the tube. They employed a minimum of six complete melting cycles. Taking great care to avoid atmospheric contamination, they obtained a product having a melting point 30.35° to 30.55° and a dielectric constant 184.3 at 40°. This remarkably high dielectric constant decreased with time however, and this behaviour, coupled with results of precise calorimetric measurements and melting point curves, are interpreted as an indication of some decomposition of the material, even in the solid state. They concluded that appreciable changes occur in the hydrogen bonding of the solvent when small quantities of impurities are present. The degree of purity achieved by these authors most probably is higher than any previously reported (direct comparisons cannot be made since they did not employ any of the tests for purity described above); however, the unavoidable (inherent) instability of the initial product renders this degree of purity an unattainable goal for most practical purposes. Nevertheless, zone melting, being a further refinement of the fractional freezing technique, should probably be given precedence over the simple fractional freezing technique outlined above. Assuming the availability of suitable equipment, the zone refining method can be made less

time consuming and less demanding of operator attention. The purified material can be handled with greater ease and less danger of contamination.

Other purification procedures

Fractional distillation alone at atmospheric pressure does not yield pure NMA, the product being contaminated with acetic acid, methylamine and an impurity of unknown composition which produces a cathodic polarographic discharge at about -2.2 V (versus aq. SCE). Despite the large difference in boiling point between NMA on the one hand and acetic acid and methylamine on the other, these two impurities persist even in the fraction distilling at 202° to 204° . The impurity of unknown composition forms whenever NMA is heated to its normal boiling point.

Knecht and Kolthoff² developed two different purification procedures involving chemical treatment steps between successive vacuum distillations. The chemical treatment steps, designed to remove the impurities mentioned above, include extraction of aqueous NMA with petroleum ether, treatment with sulphuric acid, treatment with potassium carbonate, and treatment with calcium oxide. Although both purification procedures yield pure NMA, neither procedure is recommended because both are more difficult, troublesome and time-consuming than the fractional freezing or zone melting procedures. The description of these two procedures nevertheless provides insight into the chemical properties and stability of NMA (see ref. 2).

Attempts to remove water from NMA (even otherwise pure NMA) by treatment with phosphorus pentoxide followed by vacuum distillation yielded an impure product, the impurity giving rise to a cathodic polarographic discharge or wave beginning at -2.2 to -2.4 V. Nevertheless, Reynolds and Weiss²⁸ used solvent prepared in this way for studies requiring extremely anhydrous conditions; the added impurity presumably did not interfere with their spectral measurements. French and Glover⁷ also purified NMA in this way for their conductance studies. Their procedure was to shake the solvent (presumably a commercial product) with phosphorus pentoxide, filter it through glass wool and vacuum distill it. This was repeated three times followed by two more vacuum distillations without previous treatment with phosphorus pentoxide. Their final product had a specific conductance of 4.2 to 6.0×10^{-7} ohm⁻¹ cm⁻¹ at 35° and remained constant with time. Apparently they did not test polarographically for impurities, and it is probable that the impurity mentioned above was present in their solvent.

Distillation of NMA at atmospheric pressure in the presence of calcium oxide results in rapid decomposition of the solvent with the liberation of large amounts of ammonia or methylamine.

No ion exchange or chromatographic methods have been employed for the purification of NMA; however, to purify relatively large amounts of a viscous solvent like NMA by these techniques, even if successful, probably would prove to be more difficult and time-consuming than the procedures mentioned above.

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