Desiccant efficiency in solvent drying. 3. Dipolar aprotic solvents

David R. Burfield, and Roger H. Smithers

J. Org. Chem., 1978, 43 (20), 3966-3968 • DOI: 10.1021/jo00414a038 • Publication Date (Web): 01 May 2002

Downloaded from http://pubs.acs.org on May 1, 2009

More About This Article

The permalink http://dx.doi.org/10.1021/jo00414a038 provides access to:

- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article
Other acetics which are commonly used as protecting groups for alcohols are the tetrahydropyranyl ether (ref 4, p 104), ethoxycarbonyl ether (S. Chiduk and J. Stone, J. Chem. Soc. (London), 1719 (1969)), 2-methoxyisopropyl ether (ref 4, p 107), and 4-methoxymethyl ether (ref 4, p 108). Removal of all of these groups can be accomplished with dilute aqueous acid. They are prepared from the corresponding vinyl ether with acid catalysis. The methoxymethyl ether, as well as our tert-butoxymethyl ether, is prepared from the chloro ether with base catalysis.


Methods for the free-radical halogenation of organic compounds have been reviewed: E. S. Huyser, Synthesia, 7 (1970).

Sulfuryl chloride has been used to chlorinate tetrahydrofuran (THF); C. G. J. F. Norris and G. W. Rigby, J. F. Norris and G. W. Rigby, J. Chem. Soc., 54, 2088 (1932).

There is no reaction at 0 °C after 4 h but a satisfactory reaction rate is obtained at room temperature. The water bath is used for cooling purposes only.

The 1H NMR spectra of the tert-butoxymethyl ethers show singlets at δ 4.1–4.7 (2 H) and 1.2–1.25 (9 H). The corresponding 13C NMR spectra are also consistent with the proposed structures. For example, the acetal and quaternary carbons are found at δ 85.248 and 74.251, respectively, for the benzyl alcohol acetal and δ 90.038 and 94.066, respectively, for the 1-tetrahydropyranyl ether.

It is generally acknowledged that dipolar aprotic solvents are the media of choice in some reactions and are unique in facilitating others. The special solvent effects of molecules such as DMF and Me$_2$SO are attributable to their large dielectric constants coupled with the absence of solvation by hydrogen bonding and typically manifest themselves in properties such as poor anion solvation, voracious cation solvation, and a marked hydropolarity. For the chemist, this latter feature is unfortunate since small amounts of water in these systems can diminish their nucleophilicity and may even be hazardous to some operations. The drying of these solvents is thus of paramount importance, but in these cases, all attempts to isolate the chloro ether by concentration have led to decomposition.

Caution!

No. 1260

Drying of Hexamethylphosphoric Triamide (HMPT).

Caution! HMPT is a suspected carcinogen. Although in recent years the favored desiccant for HMPT appeared to be calcium hydride, drying has also been previously accomplished with alkali metals, alkali metal earth oxides, and 4A and 13X molecular sieves. The results with the siccatives summarized in Table I are largely self-evident, but the following points are worth noting.

The extreme resistance to desiccation is demonstrated by the impossibility of obtaining super-dry HMPT under any of the conditions used here. Even sequential drying, which was previously found to be effective with acetonitrile, falls short in this case. The use of sodium–potassium alloy as a drying agent seems questionable in view of the thermal instability of solutions of alkali metals in solvents of this type.

Since phosphorus pentoxide causes loss of material through side reactions, the best procedure for drying HMPT appears to be distillation from calcium hydride followed by storage over molecular sieves.

Drying of Dimethylformamide

One source observes that it is doubtful whether distillation alone can remove water from this solvent and recommends a chemical method for the elimination of protonic impurities. 4A molecular sieves, alumina, potassium hydroxide, and calcium hydride have all been endorsed as siccatives for DMF.

The results in Table II indicate the powerful hydrophilicity of this solvent, although sequential drying with 5A sieves almost achieves super-dryness. Interestingly, and contrary to an earlier suggestion, while some of the basic desiccants investigated are totally inept, e.g., alumina and potassium carbonate, others such as calcium hydride and potassium hydroxide achieve quite reasonable drying levels. Also, although seldom advocated for use in this circumstance, phosphorus pentoxide is a commendable desiccant. For DMF, however, barring impurities other than water, by far the

### Desiccant Efficiency in Solvent Drying. 3.

**Dipolar Aprotic Solvents**

David R. Burfield* and Roger H. Smithers

Department of Chemistry, University of Malaya, Kuala Lumpur 22-11, Malaysia

Received May 2, 1978

It is generally acknowledged that dipolar aprotic solvents are the media of choice in some reactions and are unique in facilitating others. The special solvent effects of molecules such as DMF and Me$_2$SO are attributable to their large dielectric constants coupled with the absence of solvation by hydrogen bonding and typically manifest themselves in properties such as poor anion solvation, voracious cation solvation, and a marked hydropolarity. For the chemist, this latter feature is unfortunate since small amounts of water in these systems can diminish their nucleophilicity and may even be hazardous to some operations. The drying of these solvents is thus of paramount importance, but in these cases, all attempts to isolate the chloro ether by concentration have led to decomposition.

Caution!

No. 1260

Drying of Hexamethylphosphoric Triamide (HMPT).

Caution! HMPT is a suspected carcinogen. Although in recent years the favored desiccant for HMPT appeared to be calcium hydride, drying has also been previously accomplished with alkali metals, alkali metal earth oxides, and 4A and 13X molecular sieves. The results with the siccatives summarized in Table I are largely self-evident, but the following points are worth noting.

The extreme resistance to desiccation is demonstrated by the impossibility of obtaining super-dry HMPT under any of the conditions used here. Even sequential drying, which was previously found to be effective with acetonitrile, falls short in this case. The use of sodium–potassium alloy as a drying agent seems questionable in view of the thermal instability of solutions of alkali metals in solvents of this type.

Since phosphorus pentoxide causes loss of material through side reactions, the best procedure for drying HMPT appears to be distillation from calcium hydride followed by storage over molecular sieves.

Drying of Dimethylformamide

One source observes that it is doubtful whether distillation alone can remove water from this solvent and recommends a chemical method for the elimination of protonic impurities. 4A molecular sieves, alumina, potassium hydroxide, and calcium hydride have all been endorsed as siccatives for DMF.

The results in Table II indicate the powerful hydrophilicity of this solvent, although sequential drying with 5A sieves almost achieves super-dryness. Interestingly, and contrary to an earlier suggestion, while some of the basic desiccants investigated are totally inept, e.g., alumina and potassium carbonate, others such as calcium hydride and potassium hydroxide achieve quite reasonable drying levels. Also, although seldom advocated for use in this circumstance, phosphorus pentoxide is a commendable desiccant. For DMF, however, barring impurities other than water, by far the
A1203
B203
4A molecular sieves
P2O5
CaH2
KOH (powdered)
CaO
K2CO3
B2O3
Al2O3
CaSO4
K2CO3

with a large variety of other siccatives.8 Calcium sulfate, alkali earth metal oxides, alkali metal hydroxides, alumina, and, surprisingly perhaps, fractional distillation alone15 have all been utilized.

Perhaps the most unexpected result (Table III) is that fractional distillation, discarding the first 20% of the distillate, affords desiccation of similar magnitude to that obtained with molecular sieves! This result is most surprising in view of the high dielectric constant and hygroscopicity of Me2SO.

The interpretation of other results for Me2SO is not so straightforward. For many of the basic desiccants, e.g., calcium hydride and calcium and barium oxides, initial dehydration is followed by an increase in apparent water content, and this indicates a base-catalyzed exchange between the acidic protons of Me2SO and labeled water. This suggestion is supported by a desiccation experiment with powdered potassium hydroxide which gave very little apparent drying. In this case, standing for 2 or 3 h over the desiccant produced yellow solutions, most likely indicating the presence of the dimethyl ion, which would of course lead to labeled solvent through exchange processes.

Although the results with the basic desiccants are therefore not very conclusive, a necessary corollary in the case of calcium hydride is, however, that drying is relatively slow, and perhaps not very efficient. A similar result for this desiccant was noted earlier with acetoneitrile.1

In summary, although phosphorus pentoxide gave the best drying, it also induced significant decomposition, and the method of choice for Me2SO would appear to be initial fractional distillation followed by sequential drying with molecular sieves.

Drying of Acetone. Acetone has been dried with a wide spectrum of desiccants.8 Thus, alumina, calcium chloride, phosphorus pentoxide, and 4A molecular sieves,16 as well as calcium and (anhydrous) cupric sulfate, have all been used.

Since acetone has the lowest dielectric constant of the solvents investigated here, it might be predicted that its drying should be relatively easy. In fact, in many respects the drying of acetone proved to be the most difficult case. As with Me2SO, the root of the difficulty is the acidic protons, which in this case compounds the drying problem not only by inflating apparent water content by exchange process but also by providing a pathway to self-condensation through enol intermediates. This facet of acetone chemistry makes the choice of a successful desiccant a delicate process. As Table IV shows, mild siccatives such as calcium sulfate are inept; more potent desiccants such as molecular sieves exhibit a short initial drying action but thereafter actually cause disastrous increases in water content by displacement of the condensation equilibrium. This interpretation was confirmed for molecular sieves and other basic desiccants such as barium oxide by gas chromatographic analysis which demonstrated the presence of mesityl oxide in the dried solvent (see Table IV).

In summary, while both cupric sulfate and 3A molecular sieves are clearly at least useful preliminary desiccants, the agent par excellence for acetone is powdered boric anhydride. Using stirring and sequential drying conditions, this siccative gave a solvent containing only 18 ppm of water and caused detectable condensation. In fact, the true water content likely to be lower as even with the premise that drying occurs considerably faster than other processes, some labeling via enol surely occurs on preparation of the standard wet solution.

In view of the remarkable efficiency of this desiccant: acetone and acetoneitrile,1 it is puzzling that boric anhydride is not particularly outstanding for other members of this series (Tables I–III). This finding emphasizes once more the danger in assuming the existence of any kind of absolute scale in the efficiency of desiccants for solvent drying.

Table II. Efficiency of Desiccants in the Dryinga of DMFb

<table>
<thead>
<tr>
<th>desiccant</th>
<th>residual solvent water content, ppm</th>
<th>other conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 h</td>
<td>24 h</td>
</tr>
<tr>
<td>3A molecular sieves</td>
<td>500</td>
<td>187</td>
</tr>
<tr>
<td>P2O5</td>
<td>879</td>
<td>105</td>
</tr>
<tr>
<td>CaH2</td>
<td>641</td>
<td>227</td>
</tr>
<tr>
<td>4A molecular sieves</td>
<td>454</td>
<td>134</td>
</tr>
<tr>
<td>KOH (powdered)</td>
<td>1360</td>
<td>1110</td>
</tr>
<tr>
<td>B2O3</td>
<td>2060</td>
<td>1520</td>
</tr>
<tr>
<td>CaO</td>
<td>2090</td>
<td>2030</td>
</tr>
<tr>
<td>Al2O3</td>
<td>1970</td>
<td>1920</td>
</tr>
<tr>
<td>CaSO4</td>
<td>2310</td>
<td>2030</td>
</tr>
<tr>
<td>K2CO3</td>
<td>2500</td>
<td></td>
</tr>
</tbody>
</table>

Table III. Efficiency of Desiccants in the Dryinga of Me2SOb

<table>
<thead>
<tr>
<th>desiccant</th>
<th>residual solvent water content, ppm</th>
<th>other conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 h</td>
<td>24 h</td>
</tr>
<tr>
<td>4A molecular sieves</td>
<td>978</td>
<td>471</td>
</tr>
<tr>
<td>3A molecular sieves</td>
<td>1050</td>
<td>448</td>
</tr>
<tr>
<td>none</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2O5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2O3</td>
<td>1560</td>
<td>1820</td>
</tr>
<tr>
<td>CaH2</td>
<td>1450</td>
<td>1330</td>
</tr>
<tr>
<td>BaO</td>
<td>2080</td>
<td>1740</td>
</tr>
<tr>
<td>Al2O3</td>
<td>1840</td>
<td>1900</td>
</tr>
<tr>
<td>K2CO3</td>
<td>2280</td>
<td>2200</td>
</tr>
<tr>
<td>KOH (powdered)</td>
<td>2130</td>
<td></td>
</tr>
<tr>
<td>CaSO4</td>
<td>2140</td>
<td></td>
</tr>
</tbody>
</table>

a Static drying modes unless otherwise specified. b Desiccant loading 5% w/v; initial water content 2560 ppm (0.256% w/w). c Sequentially dried sample, 72 h. d Fractionally distilled sample. e Distilled sample. f Contaminated by decomposition products. g Stirring for 24 h followed by distillation. h Yellow colored solutions.
Table IV. Efficiency of Desiccants in the Drying of Acetone

<table>
<thead>
<tr>
<th>desiccant</th>
<th>residual solvent water content, ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>B$_2$O$_3$</td>
<td>0.18$^a$, 0.47$^e$</td>
</tr>
<tr>
<td>3A molecular sieves</td>
<td>115, 152, 322$^a$, 322$^b$</td>
</tr>
<tr>
<td>CuSO$_4$ (anhydrous)</td>
<td>1920, 972, 579, 1700$^h$</td>
</tr>
<tr>
<td>Cs$_2$SO$_4$</td>
<td>1590, 1600</td>
</tr>
<tr>
<td>BaO</td>
<td>1910, 1870$^i$</td>
</tr>
<tr>
<td>P$_2$O$_5$</td>
<td>1970$^f$</td>
</tr>
<tr>
<td>K$_2$CO$_3$</td>
<td>2057, 2250</td>
</tr>
</tbody>
</table>

$^a$ Static drying modes unless specified otherwise.
$^b$ Desiccant loading 5% w/v; initial water content 2710 ppm (0.271% w/w), unless specified otherwise.
$^c$ Initial water content 2880 ppm (0.289% w/w).
$^d$ Stirred, distilled, and sequentially dried, 24 h.
$^e$ Stirred for 24 h and distilled.
$^f$ Dried for 24 h and then distilled.
$^g$ Contamination (2%) by mesityl oxide.
$^h$ Fractionated sample.
$^i$ Contamination (12%) by mesityl oxide.

Experimental Section

Desiccants. Details of the source, activation, and handling of most of the desiccants have already been described.$^1$ Reagent grade cupric sulfate was activated by heating at 320 °C for 15 h before use. Barium and calcium oxides were of reagent grade, and a fresh batch was used unless specified otherwise.

Sulfates. CuSO$_4$ (anhydrous) was activated by heating at 320 °C for 15 h before use. Barium loading 5% w/v; initial water content 2710 ppm (0.271% w/w), sequentially dried, 24 h.

Sodium acetate was activated by heating at 320 °C for 15 h before use. Barium loading 5% w/v; initial water content 2710 ppm (0.271% w/w), sequentially dried, 24 h.

Potassium carbonate for one day and then over 4A molecular sieves. Gas chromatographic analysis of this material showed it to be free of impurities.

Solutions. DMF, Me$_2$SO, and HMP were commercial synthetic grades of 99% purity (Merck). Acetone was of analytical grade (M&O).

All solvents were rigorously purified by standard methods.$^9$

HMP and Me$_2$SO were treated by standing over barium oxide overnight, followed by filtration, distillation from calcium hydride, and subsequent storage over 20% w/v 4A molecular sieves. Me$_2$SO had bp 74.0–75.0 °C at 12 mmHg, and HMP had bp 89.0–89.5 °C at 3 mmHg.

Commercial DMF was allowed to stand over 4A molecular sieves overnight and was filtered. Distilled from phosphorus pentoxide (bp 55.8–56.0 °C at 20 mmHg), allowed to stand over anhydrous potassium carbonate, and subsequently stored over 4A molecular sieves.

Analytical grade acetone was allowed to stand over anhydrous potassium carbonate for one day and then over 4A molecular sieves overnight. Fractionation gave material, bp 56.2 °C, which was not stored but used immediately. Gas chromatographic analysis of this material showed it to be free of impurities.

Techniques. The procedure used for HMP serves as an example. A stock solution of HMP containing 2620 ppm of labeled water was prepared by the addition of 0.50 g of tritiated water, specific activity 0.5 mCi/mL, to the appropriate mass of purified rigorously dried HMP. Aliquots of the stock solution (15.0 ± 0.1 mL) were syringed directly onto the appropriate desiccant contained in a 25 mL clear-fitting round-bottom flask, which was immediately stopped. Experiments were conducted at ambient temperatures (20–30 °C). Where specified, samples were stirred magnetically. Aliquots (1.00 ± 0.02 mL) were taken at time intervals as specified in Table I and assayed directly by liquid scintillation counting, as previously described.$^1$ Where necessary, viz., in the case of colored solutions or suspected contamination, samples were dissolved by successive dissolution with solvents of increasing polarity. Sequential drying was accomplished by decanting monosiccated solvent onto a fresh charge of 5% w/v desiccant. Sampling was then effected at the time intervals given in the table footnotes.

Registry No.—HMP, 680-31-9; DMF, 68-12-2; Me$_2$SO, 67-68-5; acetone, 67-64-1.

References and Notes

(5) The reaction of sodium hydride with Me$_2$SO has been reported to sometimes give rise to violent explosions; inter alia, see L. Brandsma, "Preparative Acetylenic Chemistry," Elsevier, Amsterdam, 1971, p. 24. However, in our hands, the same reaction has been carried out a number of times using strongly dried solvents with no untoward effects. While the cause of these accidents remains undetermined, it is noteworthy that the equilibrium water content of Me$_2$SO is 10%, and it thus seems not unlikely that the origin of these mishaps may lie in the use of insufficiently dried solvents.
(9) a) F. Tronlin and C. Richardt, Chem., Ber., 110, 2949 (1977); (b) T. J. Wallace and A. Schriesheim, Tetrahedron, 21, 2271 (1965).
(10) Here, as earlier,$^1$ the term super-dry denotes solvents containing less than 1 ppm of water.
(11) See Experimental Section.
(13) See S. S. Plaxx, "Synthetic Reagents", Vol. 1, Ellis Horwood Ltd., Chichester, 1974. This author reports that the use of calcium hydride and other basic desiccants in the drying of DMF could produce significant amounts of dimethylamine. However, the presence of this amine would give rise to inflated apparent water contents, and the values observed here, both for statically dried and distilled samples, suggest that this side reaction is of minor importance for these desiccants.