The Journal of Organic Chemistry

Desiccant efficiency in solvent and reagent drying. 7. Alcohols

David R. Burfield, and Roger H. Smithers

J. Org. Chem., **1983**, 48 (14), 2420-2422• DOI: 10.1021/jo00162a026 • Publication Date (Web): 01 May 2002

ACS Publications
High quality. High impact.

The Journal of Organic Chemistry is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

2 Hz), 1.18 (d, 3 H, J = 7 Hz); mass spectrum, m/e 110 (M^+).

Acknowledgment. We are grateful to Professor Samuel Danishefsky, Yale University, for encouragement and support through Grant No. AI 16943-03.

Registry No. 1, 85736-25-0; 2, 43124-56-7; 3, 75337-05-2; (+)-pulegone, 89-82-7.

Desiccant Efficiency in Solvent and Reagent Drying. 7. Alcohols[1-6]

David R. Burfield and Roger H. Smithers*

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

Received October 22, 1982

For many of their applications in synthesis, the lower monohydric alcohols are required to be scrupulously dry, and in contrast to alcohols containing six C atoms or more, whose desiccation does not appear difficult,[7] alcohols containing one to four C atoms have long been recognized as posing a formidable drying problem. In the case of ethanol for instance, numerous synthetic procedures contain statements such as "traces of water depress the yield considerably",[8] a practical result of which is that samples dried with CaO, for example (containing up to 5000 ppm of water), are often completely unacceptable.[9] There is also no doubt that for this group, as with other cases,[1-6] the problem of desiccant selection has been compounded by a lack of reliable quantitative data. As an illustration, when discussing the efficiency of magnesium or alkyl phthalate–Na as desiccants, many authorities[7c] continue to quote figures for water contents which were obtained in the original investigations[10] and which must now be viewed with some scepticism. In the light of this, we now report the results of a study of desiccant efficiency for this important group.

General Indications.[7c,11] Both chemical and absorptive-type desiccants have been proposed for drying alcohols, and these include[7c,11a,c] Al, BaO, CaO, Mg, Na, and K_2CO_3, while molecular sieves of Type 3A and 4A have been recommended for further drying.[11b] CaH_2 is also widely quoted,[11d] although some sources[11a] advise caution in its use with the lower alcohols.

While bearing in mind the well-known hygroscopic and hydrophilic properties of these compounds, the experiments reported below were not carried out by using any special techniques to obviate the entry of the atmosphere into drying systems other than those routinely used by the bench chemist.

Methanol. As one authority has observed,[11d] water is the dominant impurity in this solvent, and, unless *extraordinary* care is exercised, this content increases each time MeOH is handled. It is therfore quite remarkable that a survey of the literature on the drying of EtOH and MeOH points up a curious dichotomy: while references to EtOH[8,9] are characterized by numerous strictures as to the importance of achieving perfectly dry solvent, in contrast, MeOH is treated in a rather offhand manner, even though many of its applications parallel those of its higher homologue. "All MeOH used must be anhydrous" is a typical comment,[12] although information on how to realize this is lacking. The cause may lie in the belief that fractionation alone gives a solvent of adequate dryness, although the water content is still an admitted 1000 ppm.[7c,11d] Where drying methods have been indicated, the use of Mg seems most often advised.[11,13]

The results shown in Table I certainly suggest that, on the whole, MeOH is more difficult to dry than its higher homologue. These figures require little comment, but it is worth highlighting the poor performance of 3A molecular sieve powder for MeOH in comparison with other alcohols. This is almost certainly an effect of molecular size and nonselective adsorption on the large surface area which occurs *extremely rapidly* with this desiccant.[14] On account of its small size, MeOH is able to compete with water for entry into the sieve pore. Similar reasons also explain the relative ineffectiveness of the 4A and 5A bead forms of molecular sieve. On the other hand, the 3A *bead* form constitutes a useful desiccant, whose success is presumably due to a much slower rate of absorption which occurs with greater selectivity. It is also worth noting that a combination of methods is often the most effective strategy: a 1-L sample of MeOH distilled from Mg/I_2 onto 10% w/v 3A molecular sieve beads and then allowed to stand 48 h had residual water content of only 12 ppm. Finally, the unimpressive results obtained with BaO and CaO tend to support an earlier assessment of these agents as "tedious and wasteful".[15]

Ethanol. As stated above, references to the use of ethanol as a nucleophile,[16] as a solvent for Bouveault–Blanc

---

[1] Part 1: Burfield, D. R.; Lee, K. H.; Smithers, R. H. *J. Org. Chem.* **1977**, *42*, 3060.

[2] Part 2: Burfield, D. R., Gan, G. H.; Smithers, R. H. *J. Appl. Chem. Biotechnol.* **1978**, *28*, 23.

[3] Part 3: Burfield, D. R.; Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 3966.

[4] Part 4: Burfield, D. R.; Smithers, R. H. *J. Chem. Technol. Biotechnol.* **1980**, *30*, 491.

[5] Part 5: Burfield, D. R.; Smithers, R. H.; Tan, A. S. C. *J. Org. Chem.* **1981**, *46*, 629.

[6] Part 6: Burfield, D. R.; Smithers, R. H. *J. Chem. Educ.* **1982**, *59*, 703.

[7] The use of K_2CO_3 as a desiccant is often considered adequate in these cases. See for example: (a) Calzada, J. G.; Hooz, J. *Org. Synth.* **1974**, *54*, 63. (b) Paul, R.; Riobé, O; Maumy, M. *Ibid.* **1976**, *55*, 62. (c) Vogel, A. I. "Vogel's Textbook of Practical Organic Chemistry"; Longmans: London, 1978; p 270. See also, however: Crandall, J. K.; Rojas, A. C. *Org. Synth.* **1976**, *55*, 1.

[8] See: Weiner, N. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 279. Also relevant are the following quotations. (a) "Yields are poor if the alcohol is not completely dehydrated"; Lycan, W. H.; Puntambeker, S. V.; Marvel, C. S. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 319. (b) "Moisture in the reagents affects the yield seriously": Dox, A. W. "Organic Syntheses"; Wiley: New York, 1941; Collect, Vol. I, p 5. (c) "The use of 98% alcohol results in a lowering of yield by $^1/_3$": Kaufmann, W. E.; Dreger, E. E. *Ibid.*, p 258. (d) "The quality of absolute ethanol used has a very marked effect upon the yield": Adams, R.; Kamm, R. M. *Ibid.*, p 250.

[9] Thus, "Alcohol dried over lime gives very low yields": Ford, S. G.; Marvel, C. S. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 373. "Ethanol dried only by a lime process gives a low yield": Adkins, H.; Gillespie, R. H. *Ibid.*, 1955; Collect. Vol. III, p 672.

[10] For the use of magnesium see: Lund, H; Bjerrum, J. *Ber. Dtsch. Chem. Ges.* **1931**, *64*, 210. For the use of a sodium–alkyl ester combination see: (a) Smith, E. L. *J. Chem. Soc.* **1927**, 1288. (b) Manske, R. H. *J. Am. Chem. Soc.* **1931**, *53*, 1106.

[11] See: (a) Rickert, H.; Schwartz, H. In "Methoden der Organischen Chemie (Houben-Weyl)"; Mueller, E., Georg Thieme Verlag: Stuttgart, 1968; Band I/2, p 873. (b) Loewenthal, H. J. E. "Guide for the Perplexed Organic Experimentalist"; Heyden: London, 1980; p 50. (c) "Drying in the Laboratory"; E. Merck Co.: Darmstadt. (d) Riddick, J. A.; Bunger, W. B. "Organic Solvents", 3rd ed.; Wiley-Interscience: New York, 1970; pp 638–665.

[12] Helferich, B.; Schafer, W. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, p 365.

[13] (a) Murray, J. I. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV. p 744. (b) Baumgarten, H. E.; Petersen, J. M. *Ibid.*, 1973; Collect. Vol. V, p 912.

[14] See ref 6.

[15] See Ref 11d, p 642.

0022-3263/83/1948-2420$01.50/0

Table I. Desiccant Efficiency in Drying[a,b] of Some Common Lower Alcohols[c]

desiccant	residual water content, ppm			
	methanol[d]	ethanol[e]	2-butanol[f]	*tert*-butyl alcohol[g]
3A sieves (bead)	95	99	645 (9)[h]	428 (160)[i]
3A sieves (powder)[j]	940	18	14	13
Mg/I_2[k]	97 (12)[l]	50 (53)[m]		
CaH_2	125	99	17[n]	406 (20)[o]
Na[p]		1800[n]	2400[n]	406 (10)[o]
Na/dicarboxylic acid ester[q]		92[n]	36[n]	
4A sieves (bead)	440	401		406
5A sieves (bead)	475	875		
CaC_2	490	333 (199)[r]	409	430[n] (662)[o]
BaO	1000	*s*		
Ca	1000	*s*		860
K_2CO_3	*s*	*s*		750
CaO	*s*	*s*		770
KOH powder		*s*		
ion exchange resin		*s*		640

[a] Static drying modes unless specified otherwise. [b] Water content assayed by the Karl Fischer method. [c] Desiccant loading 5% w/v with a drying period of 24 h unless specified otherwise. [d] Initial water content 1010 ppm. [e] Initial water content 1500 ppm. [f] Initial water content 1000 ppm. [g] Initial water content 1030 ppm. [h] 96-h drying period. [i] 168-h drying period. [j] Analysis was performed after settling of desiccant, 3-6 h. [k] Weight of magnesium in accord with general practice, i.e., 0.5% w/v. [l] See text. [m] Weight of magnesium 2% w/v. [n] Distilled sample. [o] Initial water content 1670 ppm, distilled sample. [p] Weight of sodium 3% w/v. See ref 32. [q] Ratio of sodium to 2-butyl succinate for 2-BuOH and to diethyl phthalate for ethanol in accord with general practice (see ref 7c), i.e.; Na, 0.3 mol L^{-1}; dicarboxylic acid ester, 0.14 mol L^{-1}. [r] Stirred sample. [s] No apparent drying.

or oxime type reductions,[17] or as a suitable medium for the preparation of metal ethoxides[18] invariably include warnings as to the lowered yields which are obtained through the use of inadequately dried solvent. Desiccants most frequently prescribed[16–18] include CaO,[19] Mg,[20] Na,[21] or Na in conjuction with a high-boiling ethyl ester such as the phthalic acid derivative. The results (Table I) show that the desiccant *par excellence* both from the viewpoint of residual water levels and convenience is 3A molecular sieve powder.[22] Sieves of larger pore size are again seen to be inappropriate. Of the more traditional siccatives, Mg and CaH_2 are both efficaceous while the performance of the alkaline earth oxides was once more disappointing. The poor result with sodium is not unexpected and is attributable to the equilibrium shown between alkoxide and

$$NaOH + ROH \rightleftharpoons H_2O + RONa$$

hydroxide. On the other hand, the ploy of refluxing the solution obtained after sodium treatment with a high-boiling ethyl ester works well, because saponification of the ester irreversibly removes hydroxide ion.

Butanols. With some notable exceptions,[23] perfectly dry 2-butanol is probably less widely required than the other alcohols in this study but is included for purposes of comparison. In contrast, completely anhydrous *tert*-butyl alcohol is always required for its most common use in the preparation of the potassium derivative. An early source[24] observes that "it is difficult to prepare *t*-BuOH free from water". Later authors recommend tackling drying by refluxing over CaO,[25a,b] Na, or K[25c,d] or more recently by distillation from CaH_2[26] or 3A sieves.[27] The results for both butanols on using most of the absorptive type siccatives under static conditions (Table I) indicate a very much slower rate of water absorption than with methanol or ethanol. It seems likely that this is due to the increased viscosity of the C-4 alcohols compared with their lower homologues, and thus the use of 3A sieves in the *powder* form (which operates as a dispersion) is able to circumvent this difficulty and again appears to be the desiccant of choice.[22] Interestingly, and in striking contrast to 2-butanol, the use of Na alone does efficiently remove water from *tert*-butyl alcohol, and this must mean that the equilibrium shown above lies predominantly to the left, presumably as a consequence of the greater disparity between the acidities of the two protonated species in this case.[28] It should be emphasized, however, that sodium

---

(16) See for example: (a) Croxall, W. J.; Fegley, M. F.; Schneider, H. J. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, p 98. (b) Moffett, R. B. *Ibid.*, p 427. (c) Ford-Moore, A. H.; Perry, B. J. *Ibid.*, p 955. See also ref 8b.

(17) See: Manske, R. H. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 154. See also ref 8a and 9.

(18) See for example: (a) Holmes, H. L.; Trevoy, L. W. "Organic Syntheses"; Wiley: New York, 1955, Collect. Vol. III, p 300. (b) Meyer, K.; Bloch, H. S. *Ibid.*, p 637. (c) Zuidema, G. D.; Van Tamelen, E.; Van Zyl, G. *Ibid.*, 1963; Collect. Vol. IV, p 10. (c) Daeniker, H. U.; Grob, C. A. *Ibid.*, 1973; Collect. Vol. V, p 989. See also ref 8 and 9.

(19) In addition see: (a) Kimball, R. H.; Jefferson, G. D.; Pike, A. B. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 284. (b) Fuson, R. C.; Wojcik, B. H. *Ibid.*, p 260.

(20) In addition see: Lund, H.; Voigt, A. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 594. See also ref 8 and 9.

(21) In addition see: (a) Marvel, C. S.; Hager, F. D. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, p 248. (b) Levene, P. A.; Meyer, G. M. *Ibid.*, 1943; Collect. Vol. II, p 288. See also ref 8.

(22) Removal of the last traces of this desiccant from a dried solvent probably necessitates distillation or filtration. However, if left to stand for periods of several days, the desiccant usually froms a compacted mass at the bottom of the container, leaving a completely clear solvent layer. In many procedures, the traces of powder remaining in suspension are probably of little consequence, and dried material can be dispensed by simple decantation.

(23) The "alcohol method" for the standardization of alkyllithium solutions requires perfectly dry 2-butanol. See: Watson, S. C.; Eastham, J. F. J. *Organomet. Chem.* **1967**, 165.

(24) Norris, J. F.; Olmsted, A. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, p 144.

(25) (a) Wayne, W.; Adkins, H. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 48. (b) Hauser, C. R.; Hudson, B. E.; Abramovitch, B.; Shivers, J. C. *Ibid.*, p 142. (c) Spassow, A. *Ibid.*, p 145. (d) McElvain, S. M.; Kundiger, D. *Ibid.*, p 506. (e) Johnson, W. S.; Schneider, W. P. *Ibid.*, 1963; Collect. Vol. IV, p 134. (f) Raha, C. *Ibid.*, p 264.

(26) (a) Horning, E. C.; Finelli, A. F. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. IV, p 461. (b) Mikol, G. J.; Russell, G. A. *Ibid.*, 1973; Collect. Vol. V, p 937. (c) Ireland, R. E.; Chaykovsky, M. *Ibid.*, p 171. (d) Crowther, G. P.; Kaiser, E. M.; Woodruff, R. A.; Hauser, C. R. *Org. Synth.* **1971**, *51*, 96. (e) Crockett, G.; Koch, T. H. *Ibid.*, **1979**, *59*, 132.

(27) Itoh, M.; Hagiwara, D.; Kamiya, T. *Org. Synth.* **1979**, *59*, 95.

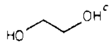
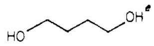
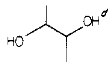
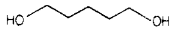
(28) pK_a values for EtOH and *t*-BuOH relative to H_2O have been reported as -1.94 and -2.6, respectively. See: (a) Lee, D. G.; Cameron, R. *J. Am. Chem. Soc.* **1971**, *93*, 4724. (b) Deno, N. C.; Turner, J. O. *J. Org. Chem.* **1966**, *31*, 1969.

Table II. Desiccant Efficiency in Drying[a,b] of 1,2-Ethanediol[c]

desiccant	residual water content, ppm
3A sieves (bead)	1900 (1200,[d] 540[e])
3A sieves (powder)	360[f]
4A sieves (powder)	1900 (2070)[d]
$MgSO_4$	3600
CaC_2	990[g]
B_2O_3	*k*
BaO	*k*
CaO	*k*
distillation[h]	1080
benzene azeotrope	65[h,i] (76)[h,j]
Mg	150 (76)[h,j]
Al	400

[a] Static drying modes unless specified otherwise. [b] Water content assayed by the Karl Fischer method. [c] Dessicant loading 5% w/v with a drying period of 72 h unless specified otherwise; initial water content 2700 ppm. [d] 168-h drying period. [e] 600-h drying period. [f] Analysis was performed after settling of desiccant, ~6 h. [g] Distilled sample, contamination by acetylene. [h] Bp 66–67 °C (0.1 mmHg). [i] Sample contaminated by ~0.02% v/v benzene. [j] Sample size 1 L; benzene azeotroping followed by treatment with Mg/I_2. [k] Little apparent drying.

Table III. Relative Difficulty in Drying[a] of Some Diols[b]

diol	residual water content, ppm	diol	residual water content, ppm
 [c]	360	 [e]	420
 [d]	140	 [f]	220

[a] Drying agent was 3A MS powder at a loading of 5% w/v. [b] Analysis performed by the Karl Fischer method after settling of desiccant, 3–6 h. [c] Initial water content 3600 ppm. [d] Initial water content 4000 ppm. [e] Initial water content 3700 ppm. [f] Initial water content 4200 ppm.

does in fact react with *tert*-butyl alcohol under reflux at an appreciable rate, and, in our opinion, the quite severe solvent losses which can result constitute a drawback serious enough to discourage its use under these conditions.

1,2-Ethanediol. Although the main thrust of this work was concerned with the lower alcohols, it was thought of interest to investigate 1,2-ethanediol as a comparison. This material does in fact possess a high solvation power for particular ions such as fluoride, and the use of dry diol is prescribed for a general synthesis of primary alkyl fluorides which utilizes this solvent property.[29] It might be anticipated that the effective drying of ethanediol would prove more problematical than the simple monohydric alcohols, and, indeed, the powerfully hydrophilic nature of this material is indicated by a reference in the patent literature[30] where the diol itself is recommended as a dessicant for acetonitrile! There appears to be a paucity of methods used for desiccation, due no doubt to the fact that the use of many effective agents such as CaH_2 is ruled out because of their reaction with this solvent. Most investigators have advocated simple distillation,[31] and, in fact, the results show this to be fairly efficaceous (Table II). With sieves, trends similar to those noted earlier are again observed; thus, due to reasons of slowness of absorption and inappropriate pore size respectively, the 3A bead form and 4A powder form are ineffective, while 3A powder once more demonstrates attributes of powerful desiccant action and simple application. Other noteworthy results were achieved with the use of the benzene azeotrope and with Mg. It would appear that a residual water level of ~70 ppm represents the lower limit for the desiccation of this material under practical conditions.

Other Diols. Finally, it was thought of interest to compare the difficulty of drying 1,2-ethanediol with some selected examples of other diols where factors of a changed positional relationship between the two hydroxyl groups and an increased hydrophobic content might give rise to variations in residual water content. The results (Table III) suggest that 1,2-diols are easier to dry than comparable diols where the hydroxyl groups are situated more remotely (cf. 1,2-ethanediol and 1,4-butanediol), and this seems reasonable from the viewpoint of preferred intramolecular interactions in 1,2-diols rather than the intermolecular alternatives involving water which are presumably more favorable in other cases. Increasing the nonhydrophilic character by the inclusion of more carbon atoms results in an understandably easier drying process (cf. 1,2-ethanediol and 2,3-butanediol; 1,4-butanediol and 1,5-pentanediol). Extension to higher simple diols was precluded by the limit of their liquid ranges.

Experimental Section

Details of the source, activation, and handling of most desiccants have already been described.[1-6] Materials such as CaH_2 and CaC_2 obtained in an aggregate form were crushed rapidly in a mortar and with a hammer, respectively, immediately prior to use. Where drying methods call for procedures other than simple static interaction, e.g., Mg/I_2, the customary directives were followed.[7c]

Water contents were determined throughout by the standard Karl Fischer method with a potentiometrically determined end point.

Alcohols. Chemically pure or AR grades of material were used without further purification. In the normal procedure the water content of a freshly opened Winchester bottle was first determined followed by wetting or by drying and wetting to obtain required water concentrations.

Drying Experiments. Investigations were carried out on 100-ml samples except where stated otherwise in the tables.

Reflux and distillation were carried out under dry nitrogen or argon, and material collected from distillations for analysis was usually a middle cut of 60–75-ml. volume. Where powdered molecular sieves were used as the desiccant, charging of the material into a flask of suitable dimensions was followed by addition of solvent, stoppering of the flask, and vigorous agitation. A clear upper layer suitable for sampling was generally obtained in 3–6 h of standing.

Acknowledgment. We thank the Department of Chemistry and University of Malaya for their support of this work under Vote No. F124/80.

Registry No. Mg, 7439-95-4; I_2, 7553-56-2; CaH_2, 7789-78-8; Na, 7440-23-5; CaC_2, 75-20-7; BaO, 1304-28-5; Ca, 7440-70-2; K_2CO_3, 584-08-7; CaO, 1305-78-8; KOH, 1310-58-3; $MgSO_4$, 7487-88-9; B_2O_3, 1303-86-2; Al, 7429-90-5; methanol, 67-56-1; ethanol, 64-17-5; 2-butanol, 78-92-2; *tert*-butyl alcohol, 75-65-0; 1,2-ethanediol, 107-21-1; 2,3-butanediol, 513-85-9; 1,4-butanediol, 110-63-4; 1,5-pentanediol, 111-29-5; di-2-butyl succinate, 626-31-3; diethyl phthalate, 84-66-2.

---

(29) Vogel, A. I.; Leicester, J.; Macey, W. A. T. "Organic Syntheses"; Wiley: New York, 1963; Collect Vol. IV, p 525.

(30) Derdulla, H. J.; Sommer, M. Ger. (East) 90136 (Cl. C07c), May 20, 1972; Appl. WP C07c/155952, June 21, 1971; *Chem. Abstr.* **1972**, *77*, 151525r.

(31) See for example: Dickinson, C. L.; Melby, L. R. "Organic Syntheses"; Wiley: New York, 1963; Collect, Vol. IV, p 276. See also ref 28.

(32) Monson, R. S. "Advanced Organic Synthesis"; Academic Press: New York, 1971; p 141.