# Direct Methylation of Primary and Secondary Alcohols by Trimethyl Phosphate to Prepare Pure Alkyl Methyl Ethers

George Van Dyke Tiers

3M Corporate Research Laboratories, 201-2S-14, PO Box 33221, St. Paul, MN 55133, USA

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Primary and secondary alcohols and diols react autocatalytically with trimethyl phosphate plus small amounts of polyphosphoric acid at 185 °C to give the corresponding methyl ethers. High purity and good yields are achieved when the ether is distilled from the reaction mixture as it is formed. By controlled addition even low-boiling alcohols can be methylated successfully. The reaction mechanism is undetermined. Peroxide formation in ethers is inhibited by storage over 10 molal KOH. Pure isotropic optical crystals are used for refractometer calibration. Improved physical property and NMR data ($^1$H and $^{13}$C) are reported for thirteen methyl ethers. Simple two-point linear extrapolation of NMR shifts (especially $^{13}$C) to infinite dilution produces highly reproducible $\delta°$-values (to 0.01 ppm or better) which uniquely characterize a molecule even when unidentified and/or not isolated from a mixture. This capability appears not to have been recognized in the literature.

Half a century ago Toy[1] reported the direct reaction of trimethyl phosphate (TMP) with primary and secondary alcohols specifically having boiling points above ca. 160 °C to produce alkyl methyl ethers in 50–70% yields, alkoxyphosphoric acids reportedly being the co-product. No information critical as to purity was given; freedom from isomerization was undetermined. Reaction times varied from 2 to almost 30 h; with lower-boiling alcohols 'the reaction proceeds too slowly'. Little or nothing has since been published on the method; there have been about a dozen citations since 1960, but only two apparent examples (undocumented) of its use,[2,3] in both cases to generate 'authentic' comparison samples for gas chromatography.

## Results

As several commercially unavailable $C_5$ and $C_6$ methyl ethers were needed in high purity for polymer-swelling studies,[4] this rather anomalous reaction was modified to make it applicable to the lower alcohols. By trial and error a high reaction temperature, 185–190 °C, was found to be virtually essential. It is best maintained by controlled addition of the low-boiling alcohol, and especially by removal of the even-lower-boiling ether by (crude) fractional distillation. Strong heating is required to balance these heat losses. Although Toy[1] employed a 2:1 or 3:1 molar ratio of alcohol to TMP, it appears much preferable to use ratios from 1:1 to 1.5:1 at most. When no more alcohol remains to be added, the reaction temperature may rise rather quickly to 200–205 °C, with some production of olefins; exothermic decomposition may occur if the temperature is allowed to go much above this range.

It is worth emphasizing that the reactions are fast (2 to 3 h), clean, readily scaled up or down, and require no solvents or highly dangerous reagents such as dimethyl sulfate, a lethal 'irritant vapor'. Work-up consists merely of drying the crude product (some water is evolved) prior to efficient fractional distillation, from which the alkyl methyl ethers are obtained in yields of 50–75%. These distillations have yielded in every case large center cuts of very high purity. No problem is foreseen in extending the procedure to lower-boiling alcohols such as $C_4$. Toy reported[1] that ethylene glycol gave only the monoether, 2-methoxyethanol, b.p. 124.3 °C. By his technique the latter could not be further methylated. Doubtless the refluxing of this product reduced the mixture to well below a practical reaction temperature. In the present work 2-ethoxyethanol, b.p. 135 °C, was readily methylated in good yield. All of the ethers required as polymer swellants[4] have boiling points sufficiently below that of TMP (197 °C) to permit separation by fractional distillation. This was also true of Toy's products.[1] Presumably higher-boiling ethers could be prepared by reaction at 180–190 °C, but it might become

necessary periodically to remove the product (along with unchanged TMP) by solvent extraction or under slight vacuum to avoid eventual olefin formation by acid-catalyzed ether cleavage. Purification would require the removal of the TMP either by chemical means or as a distillation forerun. In the latter case some provision such as addition of, say, calcium carbonate to the distillation flask might be helpful in minimizing decompositions due to traces of acid formed from the TMP upon heating.

## Discussion

*Mechanistic aspects.* While no studies of the mechanism have been done, it is evident from the accelerating rate of evolution of ether products that the reactions are autocatalytic. Mixed methoxyphosphoric acids are formed as the reaction proceeds, while other alkoxy-*P* structures are normally negligible, as shown by $^{31}$P, $^{1}$H, and $^{13}$C NMR analysis of the reaction residues. It is logical to suppose that these behave as acid catalysts, and for this reason up to 2% by weight of polyphosphoric acid (PPA) is added to, and becomes equilibrated with, the TMP upon initial heating to 185 °C. In a single case (methylation of 2-pentanol) the acid was omitted, and 5 h were required to generate an amount of ether usually obtained in the first 40 min (e.g., from cyclopentanol); thereafter the evolution of ether accelerated 'normally'.

Alkylations of reactive nucleophiles by trialkyl phosphates and thiophosphates are well known and have been reviewed.[5,6] Acid-catalyzed carbon-alkylations of phenols are known,[7,8] as are phenol etherifications.[9] Base-catalyzed alkyl exchange between triethyl phosphate and *n*-butanol showed mixed ether formation, but as a minor by-product.[10] Olefin formation by thermal decompositions of trialkyl phosphates[11] and of dialkoxy-phosphoric acids[12] has been reported. A fast 'partial dissociation of the trimethyl phosphate with the charge separation stabilized by a high degree of solvation' has been suggested[13] to explain the kinetics of reaction with strong bases. A presumably related (although obviously more hazardous) etherification of alcohols by dialkyl sulfates has been reported.[14]

*Suggested mechanisms.* None of the mechanistic concepts presented in those references appear usefully applicable to the present work, in which primary alcohols (including neopentyl) and secondary alcohols (including 3-pentyl) are methylated in comparable yields and at similar rates, without rearrangements which would give isomeric ethers as contaminants. Evidently the mechanism does not involve dehydrative protonation of the alcohol. There is also the question as to what is the driving force, since product removal is not required; formation of strongly hydrogen-bonded methoxyphosphoric acids is here proposed. In this view an acidic proton occasionally attacks (hydrogen-bonds to) an ester methoxy group on an adjacent phosphorus atom, which then releases its methyl group to an alcohol as the latter concertedly (in a cyclic

transition state) gives its proton to the 'double-bonded' phosphoric oxygen (to which it may already be hydrogen-bonded). Alternatively, perhaps less plausibly, one might envision a bicyclic transition state involving a single phosphorus atom, in which the alcohol becomes hydrogen-bonded to a donor dimethylphosphoric acid and, upon attack by the ester methyl group, gives its own proton to the adjacent 'double-bonded' oxygen. The present evidence is consistent with either hypothesis; the critical necessity for high reaction temperature is unexplained, but may result from the higher thermal stability of phosphoric acid hydrogen bonds as compared to those of alcohols.

*Internal consistency of data.* In Tables 1, 2, and 3 are presented the physical properties and NMR spectral data for the methyl ethers. This constitutes a body of self-consistent values measured with the same equipment, the latter having been carefully calibrated by means of well known standards and reference materials. By contrast, the values gathered from the literature, shown in the tables for comparison purposes, are discrepant, imprecise, lack calibration statements, and often lack details of preparation, purification, and measurement.

*Infinite-dilution NMR studies.* Deshielding values (chemical shifts) for $^{13}$C and $^{1}$H are in ppm relative to internal tetramethylsilane (TMS). Simple two-point linear extrapolation to infinite dilution, a 'standard state', provides the most nearly reliable NMR deshielding values;[15] this is valid even though in certain cases a slight correction for nonlinearity might be an improvement. It should be noted here that the extrapolated precisely measured deshielding values (which are not now predictable) characterize a molecule *even in a mixture* more exactly than the melting point identifies a pure compound. This concept has, to my knowledge, never been recognized heretofore in the literature. The symbols $\delta°(CCl_4)$, $\delta°(CDCl_3)$, etc., are proposed for specifying the extrapolated values. The concentration dependence at different sites within a molecule may thus be evaluated; here for $^{13}$C it is mostly positive both in $CCl_4$ and $CDCl_3$, with the exception of methoxy groups in the latter, doubtless as a result of deuterium-bonding to the ether oxygen. (Similar, though lesser, extrapolation effects are seen for the $^{1}$H spectra.) Notably also, chain ends show less dependence [i.e., resemble $^{13}CH_3Si(CH_3)_3$ more] than do interior carbons. For the ethers not so measured, estimates may be made based on the tabulated data. For the solvent the extrapolated deshieldings ideally should be identical for all samples; its variability may be taken as an indication of the quality of measurement.

*Unreliable purity of many reported ethers.* While earlier (literature) NMR data were gathered at lower field strengths and thus were less well discriminated, the data generally agree within their error limits. Such is not the case for refractive indices, where discordance well in

Table 1. Yields and physical properties of methyl ethers.

| Ether[a] | Yield (%) Pure | Yield (%) All[b] | B.p./°C (760 Torr)[a] Found | B.p./°C (760 Torr)[a] Lit. | B.p./°C (760 Torr)[a] Ref. | Coef.[a,d] $10^3 \alpha$ | $n_D$ (°C)[a,e] Found | $n_D$ (°C)[a,e] Lit. | $n_D$ (°C)[a,e] Ref. | Density (°C)[a,e] Found | Density (°C)[a,e] Lit. | Density (°C)[a,e] Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1-Methoxypentane | **55** | (67) | **99.4** | 98–98.5<br>99<br>99–100 | 16<br>17, 18<br>19–22 | **1.228**<br>1.233[f] | **1.3841 (25)**<br>**1.3855 (22)**<br>**1.3864 (20)**<br>**1.3874 (18)** | 1.3862 (22)<br>1.3842 (20)<br>1.3852 (20)<br>1.3865 (20)<br>1.3869 (20)<br>1.3870 (20)<br>1.3873 (20)<br>1.3875 (20)<br>1.3872 (18) | 23<br>21<br>18<br>24<br>16<br>54<br>17<br>25<br>22 | **0.755 (25)**<br>**0.756 (24)**<br>**0.761 (19)** | 0.7552 (25)<br>0.7568 (24)<br>0.767 (19) | 26<br>17<br>20 |
| 1-Methoxy-1-methylbutane (2-Methoxypentane) | **51** | (58) | **89.2** | 88–88.5<br>88–89<br>88.5<br>89–91 | 27<br>28<br>16<br>29 | **1.266** | **1.3800 (25)**<br>**1.3824 (20)** | 1.3827 (20)<br>1.3840 (20)<br>1.3968 (20) | 16<br>27<br>29 | **0.753 (25)**<br>**0.758 (20)** | 0.7564 (20) | 28 |
| 1-Methoxy-1-ethylpropane (3-Methoxypentane) | **31** | (41) | **88.6** | 88–91<br>88.5–89.0 | 36<br>54 | **1.269** | **1.3824 (25)**<br>**1.3848 (20)** | 1.3864 (20) | 54 | **0.700 (25)** | | |
| 1-Methoxy-2-methylbutane | **68** | (75) | **89.9** | 89–90<br>89.5–90.5<br>90; 92 | 30; 35<br>31<br>32; 34 | **1.264** | **1.3825 (25)**<br>**1.3849 (20)** | 1.3832 (25)<br>1.3849 (20)<br>1.385 (20) | 35<br>29<br>33 | **0.754 (25)**<br>**0.759 (20)**<br>**0.761 (18)** | 0.7493 (25)<br>0.753 (20)<br>0.754 (18) | 35<br>33<br>30 |
| 1-Methoxy-3-methylbutane | **62** | (67) | **91.0** | 90–91<br>90.7–91 | 35; 36<br>37; 38 | **1.259**<br>1.269[f] | **1.3810 (25)**<br>**1.3834 (20)** | 1.3830 (20) | 37 | **0.749 (25)**<br>**0.754 (20)** | 0.7490 (25)<br>0.7517 (20) | 26<br>37 |
| 1-Methoxy-2,2-dimethylpropane | **46** | (65) | **71.7** | 71.5–72<br>72<br>72.4 | 39<br>18<br>40 | **1.344** | **1.3703 (30)**<br>**1.3728 (25)**<br>**1.3753 (20)**<br>**1.3778 (15)** | 1.3714 (30)<br>1.3725 (20)<br>1.3762 (20)<br>1.376 (15) | 39<br>29<br>18<br>40 | **0.733 (25)** | | |
| 1-Methoxy-2-ethylbutane | **71** | (79) | **115.6** | 115.5 | 41 | **1.174** | **1.3955 (25)** | | | **0.775 (25)** | | |
| 1-Methoxy-3,3-dimethylbutane | **63** | (74) | **107.7** | | | **1.199** | **1.3905 (25)** | | | **0.761 (25)** | | |
| 1-Methoxy-2-ethoxyethane | **48** | (62) | **103.8** | 101.5–102<br>102.5 | 42<br>41 | **1.212** | **1.3841 (25)**<br>**1.3864 (20)** | 1.3868 (20) | 41 | **0.848 (25)**<br>**0.853 (20)** | 0.8529 (20) | 42 |
| 1,4-Dimethoxybutane | **27** | 35[g] | **131.8** | 131–132<br>131.5<br>132–133 | 43<br>44<br>45–47 | **1.128** | **1.3967 (25)**<br>**1.3989 (20)**<br>**1.4011 (15)** | 1.3966 (25)<br>1.3975 (20)<br>1.4031 (15) | 48<br>43<br>46 | **0.855 (25)**<br>**0.860 (20)**<br>**0.862 (18)**<br>**0.865 (15)** | 0.8529 (25)<br>0.8558 (20)<br>0.859 (18)<br>0.8664 (15) | 48<br>43<br>45<br>46 |
| 1-Methoxy-2-n-butoxyethane | **59** | (73) | **149.0** | 144–146 | 49 | **1.087** | **1.3993 (25)** | 1.3988 (25) | 49 | **0.843 (25)** | 0.8390 (25) | 49 |
| 1,6-Dimethoxyhexane | **12** | (?) | **77 (20t)**<br>**(185.)[c]** | 66/10t.<br>89/35t.<br>180<br>184 | 50<br>46, 51<br>46<br>44 | **1.021** | **1.4116 (25)**<br>**1.4137 (20)**<br>**1.4158 (15)** | 1.4110 (25)<br>1.413 (20)<br>1.4163 (15) | 48<br>50<br>46 | **0.851 (25)**<br>**0.860 (15)** | 0.8518 (25)<br>0.8582 (15)<br>0.8612 (15) | 48<br>46<br>51 |
| Methoxycyclopentane | **63** | (72) | **105.7** | 105<br>105.44 | 52<br>53 | **1.087** | **1.4183 (25)**<br>**1.4206 (20)** | 1.42036 (20)<br>1.4206 (20) | 52<br>53 | **0.861 (25)**<br>**0.866 (20)** | 0.8624 (20)<br>0.8627 (20) | 52<br>53 |

[a]Entries in bold-face type are data from the present work; other entries are literature data. [b]Total including summed GC-FID contents of weighed less-pure fractions. ... of Ref. 65. [d]... cubical expansion coefficient calculated from boiling point at 760 Torr; Ref. 71. [e]Measured at 25 °C; corrected to other

*Table 2.* NMR $^{13}C$ spectral data for methyl ethers: deshielding values, $\delta$ and $\delta^\circ$; internal TMS = 0.

| Ether | Methoxy[a] C | $^{13}C$ Chain position relative to methoxy[a] | | | | | | Solvent | Lit. Ref. | Solvent $^{13}C$ |
| | | C(1) | C(2) | C(3) | C(4) | C(5) | C(6) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 1-Methoxypentane | 58.50 | 73.07 | 29.66 | 28.63 | 22.80 | 14.13 | | CDCl$_3$[c] | | 77.484 |
| | 58.534 | 72.946 | 29.345 | 28.317 | 22.558 | 14.042 | | 0%/CDCl$_3$[d] | | 76.978 |
| | 58.09 | 72.64 | 29.56 | 28.61 | 22.71 | 14.12 | | CCl$_4$[c] | | 96.286 |
| | 57.882 | 72.236 | 29.085 | 28.173 | 22.299 | 13.958 | | 0%/CCl$_4$[d] | | 95.887 |
| | 58.3 | 73.0 | 29.6 | 28.6 | 22.7 | 14.0 | | Mix[e] | 55 | |
| | 58.7 | 73.5 | 30.5 | 29.5 | 23.5 | 14.6 | | CCl$_4$[c] | 56 | |
| | 58.84 | 73.27 | 30.10 | 29.21 | 23.28 | 14.99 | | CCl$_4$[f] | 57 | |
| 1-Methoxy-1-methylbutane (2-Methoxypentane) | 55.95 | 76.72 | 38.74 | 19.06 | 14.23 | | 18.77[b] | CDCl$_3$[c] | | 77.270 |
| | 55.422 | 76.075 | 38.698 | 18.563 | 14.168 | | 18.914[b] | CCl$_4$[g] | | 96.095 |
| | 55.284 | 75.847 | 38.438 | 18.349 | 14.076 | | 18.806[b] | 0%/CCl$_4$[h] | | 95.881 |
| | 56.3 | 77.2 | 39.7 | 19.6 | 15.1 | | 20.1[b] | CDCl$_3$ | 58 | |
| | 56.5 | 77.3 | 39.9 | 19.7 | 15.2 | | 20.0[b] | CCl$_4$[c] | 56 | |
| | 56.25 | 76.90 | 39.47 | 19.35 | 15.00 | | 19.76[b] | CCl$_4$[f] | 57 | |
| 1-Methoxy-1-ethylpropane (3-Methoxypentane) | 56.43 | 83.25 | 25.54 | 9.46 | | | | CDCl$_3$[c] | | 77.252 |
| | 55.961 | 82.790 | 25.394 | 9.366 | | | | CCl$_4$[g] | | 96.132 |
| | 55.845 | 82.548 | 25.162 | 9.302 | | | | 0%/CCl$_4$[h] | | 95.914 |
| | 56.1 | 83.1 | 25.2 | 9.2 | | | | CDCl$_3$ | 58 | |
| | 56.3 | 83.5 | 25.8 | 9.5 | | | | CCl$_4$[c] | 55 | |
| | 56.79 | 83.56 | 26.15 | 10.19 | | | | CCl$_4$[f] | 57 | |
| 1-Methoxy-2-methylbutane | 58.72 | 78.35 | 35.10 | 26.38 | 11.38 | | 16.62[b] | CDCl$_3$[c] | | 77.256 |
| | 58.252 | 77.769 | 34.959 | 26.185 | 11.330 | | 16.617[b] | CCl$_4$[g] | | 96.095 |
| | 58.146 | 77.555 | 34.699 | 25.955 | 11.238 | | 16.527[b] | 0%/CCl$_4$[h] | | 95.881 |
| | 59.09 | 78.58 | 35.72 | 26.96 | 12.14 | | 17.45[b] | CCl$_4$ | 57 | |
| 1-Methoxy-3-methylbutane | 58.48 | 71.32 | 38.73 | 25.23 | 22.71 | | | CDCl$_3$[c] | | 77.422 |
| | 58.000 | 70.757 | 38.476 | 24.933 | 22.614 | | | CCl$_4$[g] | | 96.064 |
| | 57.924 | 70.575 | 38.262 | 24.767 | 22.568 | | | 0%/CCl$_4$[h] | | 95.898 |
| | 58.3 | 71.3 | 38.8 | 25.3 | 22.7 | | | Mix[e] | 55 | |
| | 58.87 | 71.61 | 39.29 | 25.78 | 23.49 | | | CCl$_4$ | 57 | |
| 1-Methoxy-2,2-dimethylpropane | 59.19 | 83.74 | 32.04 | 26.75 | | | | CDCl$_3$[c] | | 77.146 |
| | 59.353 | 83.717 | 31.938 | 26.679 | | | | 0%/CDCl$_3$[d] | | 76.984 |
| | 58.699 | 83.252 | 31.952 | 26.702 | | | | CCl$_4$[g] | | 96.042 |
| | 58.659 | 83.112 | 31.862 | 26.650 | | | | 0%/CCl$_4$[h] | | 95.914 |
| | 58.640 | 83.098 | 31.866 | 26.650 | | | | 0%/CCl$_4$[d] | | 95.903 |
| | 59.1 | 83.8 | 32.1 | 26.8 | | | | Mix[e] | 55 | |
| | 59.61 | 84.12 | 32.83 | 27.60 | | | | CCl$_4$[f] | 57 | |
| | 58.82 | 83.32 | 32.24 | 27.04 | | | | CF$_2$Cl$_2$[j] | 59 | |
| 1-Methoxy-2-ethylbutane | 58.78 | 75.50 | 41.47 | 23.60 | 11.21 | | | CDCl$_3$[c] | | 77.325 |
| | 58.371 | 74.911 | 41.381 | 23.513 | 11.200 | | | CCl$_4$[g] | | 96.204 |
| | 58.233 | 74.651 | 41.029 | 23.239 | 11.078 | | | 0%/CCl$_4$[h] | | 95.930 |
| | 58.241 | 74.650 | 41.019 | 23.234 | 11.080 | | | 0%/CCl$_4$[h] | | 95.926 |

Table 2. (Continued.)

| Ether | Methoxy[a] C | $^{13}C$ Chain position relative to methoxy[a] | | | | | | Solvent | Lit. Ref. | Solvent $^{13}C$ |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | | C(1) | C(2) | C(3) | C(4) | C(5) | C(6) | | | |
| 1-Methoxy-3,3-dimethylbutane | 58.39 | 70.16 | 43.01 | 29.67 | 29.80 | | | CDCl₃[c] | | 77.300 |
| | 58.516 | 70.151 | 42.859 | 29.588 | 29.704 | | | 0%/CDCl₃[d] | | 76.968 |
| | 57.939 | 69.704 | 42.756 | 29.626 | 29.786 | | | CCl₄[g] | | 96.027 |
| | 57.849 | 69.552 | 42.574 | 29.518 | 29.710 | | | 0%/CCl₄[h] | | 95.873 |
| | 57.869 | 69.559 | 42.589 | 29.529 | 29.721 | | | 0%/CCl₄[d] | | 95.880 |
| | 58.2 | 70.1 | 43.0 | 29.6 | 29.9 | | | Mix[e] | 55 | |
| 1-Methoxy-2-ethoxyethane | 58.97 | 72.10[j] | 69.86[j] | 66.66[j] | 15.19 | | | CDCl₃[c] | | 77.778 |
| | 58.442 | 71.937[j] | 69.751[j] | 66.218[j] | 15.200 | | | CCl₄[g] | | 96.112 |
| | 58.352 | 71.705[j] | 69.519[j] | 66.052[j] | 15.110 | | | 0%/CCl₄[h] | | 95.908 |
| 1,4-Dimethoxybutane | 58.39 | 72.59 | 26.53 | | | | | CDCl₃[c] | | 77.675 |
| | 57.974 | 72.200 | 26.330 | | | | | CCl₄[g] | | 96.112 |
| | 57.884 | 71.982 | 26.092 | | | | | 0%/CCl₄[h] | | 95.908 |
| | 58.25 | 72.65 | 26.89 | | | | | C₆H₆ | 60 | |
| 1-Methoxy-2-n-butoxyethane | 58.99 | 72.10[j] | 70.10[j,k] | 71.27[j] | 31.84 | 19.39 | 13.95 | CDCl₃[c] | | 77.587 |
| | 59.077 | 71.997[j] | 69.975[j,k] | 71.294[j] | 31.669 | 19.274 | 13.931 | 0%CDCl₃[d] | | 76.996 |
| | 58.48 | 72.01[j] | 70.13[j,k] | 70.81[j] | 32.01 | 19.41 | 13.93 | CCl₄[c] | | 96.175 |
| | 58.352 | 71.701[j] | 69.811[j,k] | 70.563[j] | 31.689 | 19.148 | 13.825 | 0%/CCl₄[d] | | 95.899 |
| 1,6-Dimethoxyhexane | 58.43 | 72.81 | 29.76 | 26.18 | | | | CDCl₃[c] | | 77.509 |
| | 58.541 | 72.815 | 29.598 | 26.029 | | | | 0%/CDCl₃[d] | | 76.986 |
| | 58.02 | 72.42 | 29.66 | 26.08 | | | | CCl₄[c] | | 96.120 |
| | 57.905 | 72.192 | 29.398 | 25.834 | | | | 0%/CCl₄[d] | | 95.899 |
| Methoxycyclopentane | 56.29 | 83.06 | 32.13 | 23.73 | | | | CDCl₃[c] | | 77.505 |
| | 56.335 | 82.942 | 31.950 | 23.543 | | | | 0%/CDCl₃[d] | | 76.992 |
| | 55.76 | 82.55 | 31.99 | 23.67 | | | | CCl₄[c] | | 96.244 |
| | 55.581 | 82.209 | 31.676 | 23.380 | | | | 0%/CCl₄[d] | | 95.900 |
| 1-Methoxy-1,1-dimethylpropane[l] | 48.402 | 73.771 | 32.357 | 8.072 | | | 24.384 | CCl₄[g] | | 96.080 |
| ('TAME'; tert- amyl methyl ether) | 48.296 | 73.649 | 32.175 | 8.012 | | | 24.294 | 0%/CCl₄[h] | | 95.882 |

[a] Entries in bold-face type are data from the present work; other entries are literature data. [b] The 'branching' methyl group; the methoxy-bearing carbon atom is numbered '1'. [c] For '50%' solutions. [d] Extrapolated from '50%' and '5%' measurements. [e] The samples were at 50 volume% concentration in a mixture of composition: 50% CDCl₃, 40% CCl₄ and 10% TMS. For best comparison, interpolation of the present data between solvents is necessary. [f] Deshielding values of 1 M solutions, approximately 14 volume% for the C₅ methyl ethers, were measured relative to external dioxane; the conversion to the TMS scale was not described. These values are found to be $0.93 \pm 0.03$ higher than those obtained by interpolation of the present work, thus being in excellent relative agreement. [g] For 20% (by volume) solutions. [h] Extrapolated from 20% and 10% (by volume) measurements. [i] Measured at 110 K; '10%' concentration. [j] Assigned by comparison with reference spectra in the Sadtler NMR database for 2-(2-butoxyethoxy)ethanol and for 2-[2-(2-methoxyethoxy)ethoxy]ethanol, by comparison of spectra of 1-methoxy-2-ethoxyethane and 1-methoxy-2-n-butoxyethane, and further validated by agreement with the computed spectrum (ACD/CNMR). [k] Assigned by heteronuclear multiple quantum coherence (HMQC) from proton signals identified by $^1H$–$^1H$ two-dimensional COSY. [l] From Aldrich, not synthesized in this work; included as a reference for a tertiary methoxy group. Small unidentified impurity peaks were found at $\delta°$ 127.957 and at $\delta(10\%)$ 189.28.

*Table 3.* NMR ¹H spectral data for methyl ethers: deshielding values, δ and δ°; internal TMS = 0.

| Ether | Methoxy[a] H | ¹H Chain position relative to methoxy[a] | | | | | | Solvent | Lit. Ref. | $CHCl_3$ ¹H |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | | H(1) | H(2) | H(3) | H(4) | H(5) | H(6) | | | |
| 1-Methoxypentane | 3.308 | 3.348 | 1.568 | 1.343 | 1.313 | 0.904 | | $CDCl_3$[c] | | 7.412 |
| | 3.335 | 3.368 | 1.575 | 1.337 | 1.309 | 0.902 | | 0%/$CDCl_3$[d] | | 7.261 |
| | 3.226 | 3.267 | 1.513 | 1.329 | 1.300 | 0.905 | | $CCl_4$c | | |
| | 3.226 | 3.255 | 1.503 | 1.323 | 1.290 | 0.908 | | 0%/$CCl_4$[d] | | |
| 1-Methoxy-1-methylbutane (2-Methoxypentane) | 3.309 | 3.286 | 1.52m/ 1.37m | 1.35m | 0.914 | | 1.117[b] | $CDCl_3$[c] | | |
| | 3.214 | 3.187 | 1.45m/ 1.36m | 1.31m | 0.901 | | 1.056[b] | $CCl_4$[e] | | |
| | 3.215 | 3.181 | 1.44m/ 1.35m | 1.31m | 0.903 | | 1.056[b] | 0%/$CCl_4$[f] | | |
| | 3.3 | 3.1 | 1.4 | 1.4 | 0.90 | | 0.90[b] | $CDCl_3$? | 58 | |
| | 3.4 | 3.4 | 0.7-1.6 | 0.7-1.6 | 0.7-1.6 | | 1.12[b] | $CCl_4$? | 28 | |
| 1-Methoxy-1-ethylpropane (3-Methoxypentane) | 3.324 | 3.018 | 1.509/ 1.483 | 0.892 | | | | $CDCl_3$[c] | | |
| | 3.240 | 2.925 | 1.450/ 1.425 | 0.860 | | | | $CCl_4$[e] | 58 | |
| | 3.239 | 2.920 | 1.445/ 1.420 | 0.858 | | | | 0%/$CCl_4$[f] | | |
| | 3.4 | 3.1 | 1.50 | 0.90 | | | | $CDCl_3$ | | |
| 1-Methoxy-2-methylbutane | 3.315 | 3.224/ 3.142 | 1.632 | 1.448/ 1.134 | 0.896t | | 0.896[b] | $CDCl_3$[c] | | |
| | 3.234 | 3.134/ 3.063 | 1.575 | 1.421/ 1.111 | 0.884t | | 0.866[b] | $CCl_4$[e] | | |
| | 3.238 | 3.129/ 3.057 | 1.570 | 1.413/ 1.107 | 0.886t | | 0.864[b] | 0%/$CCl_4$[f] | | |
| 1-Methoxy-3-methylbutane | 3.305 | 3.379 | 1.459 | 1.704 | 0.905 | | | $CDCl_3$[c] | | |
| | 3.224 | 3.293 | 1.399 | 1.694 | 0.893 | | | $CCl_4$[e] | | |
| | 3.227 | 3.287 | 1.393 | 1.687 | 0.896 | | | 0%/$CCl_4$[f] | | |
| 1-Methoxy-2,2-dimethylpropane | 3.319 | 3.010 | | 0.906 | | | | $CDCl_3$[c] | | 7.349 |
| | 3.346 | 3.032 | | 0.908 | | | | 0%/$CDCl_3$[d] | | 7.260 |
| | 3.266 | 2.938 | | 0.876 | | | | $CCl_4$[e] | | |
| | 3.270 | 2.935 | | 0.872 | | | | 0%/$CCl_4$[f] | | |
| | 3.270 | 2.935 | | 0.873 | | | | 0%/$CCl_4$[d] | | |
| | 3.272 | 2.958 | | 0.897 | | | | $CCl_4$ | 39 | |
| 1-Methoxy-2-ethylbutane | 3.307 | 3.251 | 1.43m/ 1.37m/ | 1.33m | 0.881 | | | $CDCl_3$[c] | | |
| | 3.229 | 3.183 | | | 0.867 | | | $CCl_4$[e] | | |
| | 3.236 | 3.165 | | | 0.866 | | | 0%/$CCl_4$[f] | | |
| | 3.237 | 3.165 | 1.30m/ 1.35m/ | 1.31m | 0.867 | | | 0%/$CCl_4$[d] | | |
| 1-Methoxy-3,3-dimethylbutane | 3.299 | 3.399 | 1.507 | | 0.922 | | | $CDCl_3$[c] | | 7.394 |
| | 3.329 | 3.408 | 1.510 | | 0.919 | | | 0%/$CDCl_3$[d] | | 7.258 |
| | 3.218 | 3.316 | 1.448 | | 0.911 | | | $CCl_4$[e] | | |
| | 3.221 | 3.308 | 1.440 | | 0.911 | | | 0%/$CCl_4$[f] | | |
| | 3.221 | 3.309 | 1.439 | | 0.910 | | | 0%/$CCl_4$[d] | | |
| 1-Methoxy-2-ethoxyethane[g] | 3.375 | 3.530 | 3.570 | 3.521 | 1.213 | | | $CDCl_3$[c] | | |
| | 3.286 | 3.405 | 3.447 | 3.430 | 1.153 | | | $CCl_4$[e] | | |
| | 3.292 | 3.401 | 3.440 | 3.430 | 1.162 | | | 0%/$CCl_4$[f] | | |

Table 3. (Continued.)

| Ether | Methoxy[a] H | \(^1\)H Chain position relative to methoxy[a] H(1) | H(2) | H(3) | H(4) | H(5) | H(6) | Solvent | Lit. Ref. | CHCl₃ \(^1\)H |
|---|---|---|---|---|---|---|---|---|---|---|
| 1,4-Dimethoxybutane | **3.301** | **3.367** | **1.617** | | | | | CDCl₃ c | | |
| | 3.236 | 3.292 | 1.556 | | | | | CCl₄ e | | |
| | 3.239 | 3.289 | 1.553 | | | | | 0%/CCl₄ | | |
| | 3.1 | 3.2 | 1.5 | | | | | C₆H₆ | 60 | |
| 1-Methoxy-2-n-butoxyethane h | **3.373** | **3.524** | **3.566** | **3.459** | **1.578** | **1.375** | **0.917** | CDCl₃ c | | 7.449 |
| | 3.393 | 3.543 | 3.583 | 3.469 | 1.588 | 1.369 | 0.917 | 0%/CDCl₃ d | | 7.266 |
| | 3.279 | 3.406 | 3.445 | 3.373 | 1.506 | 1.368 | 0.923 | CCl₄ c | | |
| | 3.289 | 3.401 | 3.437 | 3.369 | 1.510 | 1.371 | 0.924 | 0%/CCl₄ d | | |
| 1,6-Dimethoxyhexane | **3.305** | **3.351** | **1.568** | **1.366** | | | | CDCl₃ c | | 7.460 |
| | 3.331 | 3.371 | 1.580 | 1.366 | | | | 0%/CDCl₃ d | | 7.266 |
| | 3.224 | 3.269 | 1.510 | 1.330 | | | | CCl₄ c | | |
| | 3.228 | 3.265 | 1.511 | 1.331 | | | | 0%/CCl₄ d | | |
| | 3.3 | 3.4 | 1.8 | 1.4 | | | | CDCl₃ | 61 | |
| Methoxycyclopentane | **3.255** | **3.779 1.67/** | **1.52** | **1.67** | | | | CDCl₃ c | | 7.425 |
| | 3.281 | 3.799 1.68/ | 1.52 | 1.68 | | | | 0%/CDCl₃ d | | 7.263 |
| | 3.163 | 3.687 1.66/ | 1.48 | 1.621 | | | | CCl₄ c | | |
| | 3.165 | 3.680 1.66/ | 1.48 | 1.605 | | | | 0%/CCl₄ d | | |
| 1-Methoxy-1,1-dimethylpropane i | 3.073 | | 1.426 | 0.832 | | | 1.061 b | CCl₄ e | | |
| (TAME; tert-amyl methyl ether) | 3.072 | | 1.420 | | | | 1.061 b | 0%/CCl₄ | | |

[a] Entries in bold-face type are data from the present work; other entries are literature data. [b] The 'branching' methyl group; the methoxy-bearing carbon atom is numbered '1'. [c] For '50%' solutions. [d] Extrapolated from '50%' and '5%' measurements. [e] For 20% (by volume) solutions. [f] Extrapolated from 20% and 10% measurements. [g] Assigned tentatively by multiplet structure and similarity to the 2-butoxy analog. [h] The assignment of all protons to carbons was made by HMQC; adjacency was identified by COSY. [i] From Aldrich, not synthesized in this work; included as a reference for a tertiary methoxy group.

excess of ten times the combined measurement errors[16,18,21,25,29] testifies to undetected serious contamination of many of the reported samples. And if the present values are accepted as reliable, 'good' samples have been prepared in all periods back to a century ago, while reports of 'poor' substances cluster in the 1960s. No such comparisons of densities are possible, as the polymer-swelling studies[4] required only third-decimal accuracy; agreement with the literature is satisfactory.

Most of the previously reported methyl ethers had been synthesized by Williamson reactions. Contaminated product might arise from incomplete reaction (yields resemble those of the present work) followed by distillation in apparatus of insufficient fractionating efficiency. Base-induced alcohol oxidations may occur. It is especially surprising that the only examples of the phase-transfer-catalyzed modification resulted in similar modest yields, but of quite 'poor' product.[29]

*Inhibition of ether peroxidation.* Peroxidation of ethers is well known; however alcohols, esters, ketones, olefins, and even alkylaromatic hydrocarbons also form 'peroxides' which may be hazardous.[62] The present ethers are stored over liquid 10 molal potassium hydroxide, which interrupts the peroxidation cycle.[63] Tests on other ether samples so stored show zero peroxide, even after 25 years.

## Experimental

*Purification and measurement of properties.* In each case the dried crude product was fractionally distilled and yielded 4–6 consecutive fractions of purest ether having constant boiling point and refractive index; structures, and absence of isomeric or other impurities, were attested to by $^1$H and $^{13}$C NMR spectroscopy (Varian UNITY 500) and by capillary GC (H-P 5890A, 5% phenylsilicone stationary phase, flame-ionization detector) of each fraction, sensitive to contaminants at the 0.1% level.

The vacuum-jacketted 11 mm i.d. distillation column was packed with 60 cm of #2918 Podbielniak 'Heli-Pak',[64] and was measured[65] to provide at least 14 theoretical plates under use conditions. Boiling points were read to 0.1 °C, and barometric pressure corrections to 760 Torr were made;[66] the column's thermometer was calibrated by distillation of $CS_2$, $(CH_3)_2CO$, $CH_3OH$, $CCl_4$, $C_6H_6$, $H_2O$, $n$-$C_7H_{16}$, $C_6H_5CH_3$, $n$-$C_8H_{18}$, and $n$-$C_9H_{20}$, each of 99+% purity. Refractive indices at 25 °C were read to 0.0001 (Abbé refractometer, C. Zeiss); the thermometer was calibrated against a NBS (NIST) certified thermometer checked at the ice point. The index measurements were calibrated by means of pure isotropic crystals of LiF, $CaF_2$, $BaF_2$, NaCl and KBr[67] (flat, polished infrared windows) plus fused silica and glass calibration plates, and water. The accepted[68,69] index values for the distilled calibration liquids (above) were reproduced to 0.0001. Calculation of refractive indices at other temperatures, for comparison with literature values, makes use of the equation $\Delta n = (1 - n)\alpha\Delta T$, based on the Gladstone

and Dale equation[70] and the cubical coefficient of expansion, $\alpha$, the latter being estimated from the boiling point.[71] Densities were measured to 0.001 by means of an electronic Westphal-type balance, it being adequate for the intended use.[4]

*NMR methods; infinite-dilution techniques.* The NMR probe temperature was 22 °C and sample concentrations in $CDCl_3$–1% TMS were ca. 50% by volume, and were diluted with $CDCl_3$ exactly 1 : 10 (to ca. 5%) for linear extrapolation to 0%. Initially the same procedure was used for $CCl_4$ solutions; however, small but uncontrolled amounts of acetone-$d_6$ (for lock) were added, rendering the extrapolation slightly uncertain. A more precise technique was adopted, by which in a 2 mL vial (PTFE-lined cap) 1 mL of a 20% by volume solution of an ether sample in a stock solvent mixture (by volume 95% $CCl_4$, 3% cyclohexane-$d_{12}$, and 2% TMS) was prepared, and from it 0.30 mL was withdrawn (by syringe) and diluted 1 : 1 by 0.30 mL of pure $CCl_4$, for extrapolation. Both solutions contain adequate lock; the high TMS level is needed for $^{13}$C referencing upon dilution. The nonpolar, inert deuteriated cyclohexane is strongly preferred to acetone as a lock substance. This is a fully valid yet simple method to produce reliable $\delta^\circ$-values. Note that the initial solution need not be 20%; any volume percentage (known or unknown) below ca. 35% will yield adequate referencing, and 1 : 1 dilution allows good extrapolation. The results, given in Tables 2 and 3, do not include any spin–spin splittings, as the digital data collection was insufficiently dense to yield good values.

*General procedure for methyl ethers.* A one-liter three-necked flask without stirrer was equipped with a centrally-located thermometer to monitor reaction temperature, a dropping funnel, a short (30 cm × 20 mm i.d.) packed column ('Heli-Pak'; glass helices are usable but inferior) bearing a simple 'total-reflux' take-off head[72] with thermometer, and a heating mantle. (A 30 cm Vigreaux column, used for most of this work, was clearly inferior, as indicated below). In this was placed, except as noted, 280.2 g (2.00 mol) TMP (97%; Acros, Aldrich, Eastman, or Janssen) and 1–5 g PPA (ca. 0.01–0.04 mol P) and the mixture was heated to 185 °C for 15 min to equilibrate. Alcohols, except as noted, were from Aldrich and were stated to be of 98 or 99% purity. The alcohol, 2.00 mol, was added intermittently over a period of 1–3 h, but at a rate to maintain the reaction temperature at 180–190 °C despite strong heating to effect distillation. The head's reflux condenser should be capable of handling moderate surges. Crude product was taken off at temperatures near or below its b.p., as some olefin and water was evolved. In the event that GC monitoring showed substantially incomplete conversion (i.e., 15–30% alcohol, a usual situation with the Vigreaux column) the distillate was recycled to reduce the content to 5% or less. (Overheating to temperatures much above 200–205 °C must be avoided, as vigorous exothermic

decompositions with gas evolution may occur. A sudden temperature rise is to be expected as soon as additions and takeoffs have been completed and little or no cooling reflux is occurring; heating should be reduced or temporarily discontinued. Emergency cooling, such as a compressed air stream, should be available.) The crude product was dried over $CaCl_2$ or, preferably, $K_2CO_3$ and fractionally distilled to provide pure ether; yields and properties are given in Table 1 and NMR spectral data in Tables 2 and 3, along with references to previous work. NMR examinations of the mixed phosphoric acid reaction residues were performed on DMSO-$d_6$ solutions. As the various $^{31}P$ shifts among TMP and the phosphoric acids are somewhat variable in this system and $\delta°$ studies have not been done, the following rough ppm values are given relative to external 85% $H_3PO_4$: $H_3PO_4$ 1.0–1.3, $CH_3OPO_3H_2$ 1.2–1.5, $(CH_3O)_2PO_2H$ 1.9–2.2, TMP 3.6–3.8. Replacing $CH_3O$ by $RCH_2O$ displaces the peak by −1.0 ppm.

*1-Methoxy-2-ethoxyethane.* The 2-ethoxyethanol was added dropwise to a reaction mix containing 3.65 g PPA. The short 'Heli-Pak' column was used and greatly improved the ease of operation and yield, by making recycling unnecessary. (In all but one of the other preparations the Vigreaux column was used and initial product was recycled). Crude product (161.8 g) was collected at ca. 95 °C between 45 min and 2 h after beginning addition of alcohol. Yield and properties (Tables 1–3) come from this sample, purified. As a test of methylation capacity a second 2.00 mol of 2-ethoxyethanol was added dropwise, with takeoff of 144.0 g over the next 45 min; distillation temperature fell to 85 °C and GC showed more side-products. Addition of a third 2.00 mol portion of alcohol produced 144.9 g over 45 min, but this product had, by GC, a much lower ether content. No GC peak was found for ethyl vinyl ether. Subsequent fractionation of the combined later products gave from them a 19% yield of only 99% pure product and a total (by GC) of 43%. The dark amber reaction residue, 342 g, contained by $^{31}P$ NMR spectroscopy no TMP or non-methoxy trialkyl phosphates, or any species having P–O–P bonding; the 'normal' P distribution would be 7–14%, 0%, and 13–25% respectively. Phosphoric, methoxy- and dimethoxy-phosphoric acids were 16%, 8%, and 1% (normal 2–5%, 17–42%, and 30–50%). Mono- and di-alkoxyphosphoric acids with at least one $RCH_2O$– totaled 13% (normal 0–1%) and the bulk of the P, 62%, was 'other POCH$_2$' (normal 0–1%); assignments were by $^1H$ splitting of the $^{31}P$ signals. By $^1H$ NMR spectroscopy the residue appeared to contain substantial amounts of the low-boiling product ether; as that is highly unlikely, the signals may come from the 'other POCH$_2$' or from low oligomers of ethyl vinyl ether. Here the abnormal P distribution and the excess weight resulted from the attempt to utilize all three methyls of the TMP. Except as noted, in all reactions reported below the P distribution was 'normal', as

described above; percentages are of P, generally equivalent to mol%.

*1-Methoxy-2-*n-*butoxyethane.* From 2-butoxyethanol, and using 2.65 g PPA, there was obtained between 0.5 and 2 h a total of 255.6 g of crude product. No butyl vinyl ether was found upon fractionation. The dark brown reaction residue weighed 221 g, and its $^{31}P$ NMR spectrum was normal except for 17% 'other POCH$_2$'.

*1-Methoxypentane.* 1-Pentanol (Matheson, Coleman and Bell) with 1.4 g PPA gave product between 0.5 and 2 h that required recycling for an additional 1.5 h; the resulting crude product, 167.5 g, contained, by GC, less than 1% pentanol. The dark amber reaction residue weighed 253 g. Fractional distillation yielded some 1-pentene and di-$n$-pentyl ether, both identified by NMR spectroscopy.

*2-Methoxypentane.* 2-Pentanol was reacted with TMP without PPA. The product collected slowly, from 3 to 6.5 h, mostly in the last half hour. The necessary recycling took another half hour and gave 169.4 g crude ether having less than 2% pentanol. The reaction residue, 243 g, was colorless. The low-boiling fractions contained (by NMR) pentenes in the rough proportions: 1-pentene 10%, (Z)-2-pentene 35%, and (E)-2-pentene 55%.

*3-Methoxypentane.* 3-Pentanol similarly gave no product after 45 min, so 1.1 g PPA was added. After 4 h the entire product was recycled (1.5 h) to give 150.0 g crude product. The reaction residue, 234 g, was colorless. Only 2-pentene, about 2:3 $E$, was found by NMR spectroscopy in the low boilers.

*1-Methoxy-2-methylbutane.* From 2-methyl-1-butanol and 0.81 g PPA there were obtained after 4 h (including recycling) 183.6 g crude product and 239 g colorless reaction residue. The pentene fraction was, by NMR spectroscopy, ca. 85% trimethylethylene, 10% 1,1- and 5% 1,2-disubstituted ethylene.

*1-Methoxy-3-methylbutane.* The reaction of isoamyl alcohol, 3.00 mol, with 2.00 mol TMP containing 0.20 g PPA produced a little ether after 1.5 h at 165 °C. On raising the temperature to 175 °C, ca. 1 g per min of crude ether boiling around 95 °C was formed, and at 185 °C about 2 g per min. After recycling, 251.9 g crude product were collected. The pale straw colored reaction residue weighed 269 g. From the fractional distillation very little olefinic material was collected; the distillation residue contained about 1 g diisoamyl ether.

*2,2-Dimethyl-1-methoxypropane.* Neopentyl alcohol, 2.00 mol, was liquefied by 0.40 mol TMP for dropwise addition to 1.60 mol TMP containing 1.0 g PPA. Product was collected from 1.5 to 3.5 h and recycled (0.5 h) to give 168.5 g crude ether. The reaction residue weighed 241 g; the theoretical weight is 252 g for loss of one methyl group. Distillation gave (by GC) no 1,1-dimethyl-1-methoxypropane in any fraction; the early cuts contained (by GC) at least 5 g of trimethylethylene.

*Methoxycyclopentane.* Cyclopentanol (2.00 mol) was added to TMP containing 3.0 g PPA; product collection began after 0.5 h and was complete in less than 2 h. The short 'Heli-Pak' column (instead of the Vigreaux) was used, which by more efficient return of alcohol to the reaction mixture resulted (without recycling) in 176.1 g crude ether with (by GC) less than 3% cyclopentanol. An additional 1.00 mol of cyclopentanol was then added and in 0.5 h 87.1 g similar product were obtained. The amber reaction residue weighed 245 g. Fractional distillation recovered ca. 70 g cyclopentene and 7 g cyclopentanol, and a total 72% yield of ether (63% highly pure).

*2-Ethyl-1-methoxybutane.* From 2-ethyl-1-butanol and 1.0 g PPA, product was collected from 1 to 2.5 h and recycled for 1 h to give 225.8 g crude ether; the colorless reaction residue weighed 222 g. The hexene fractions contained (by NMR) ca. 10 g 3-methyl-2-pentene, 1 g each of 1,1- and 1,2-dialkylethylene, and a small amount of monosubstituted ethylene.

*3,3-Dimethyl-1-methoxybutane.* 3,3-Dimethyl-1-butanol (1.47 mol) was reacted with 1.50 mol TMP containing 1.9 g PPA. Crude ether was collected from 0.5–2 h and recycled (1 h) to give 147.1 g product; the pale amber reaction residue weighed 185 g. The hexene fractions contained (by GC and NMR) ca. 4 g 3,3-dimethyl-1-butene, 2 g 2,3-dimethyl-2-butene, and 1 g 2,3-dimethyl-1-butene.

*1,4-Dimethoxybutane.* 1,4-Butanediol, 1.00 mol, was added to 2.00 mol TMP containing 1.0 g PPA. Between 20 min and 1 h 102.2 g crude product were collected, which by GC was diether–tetrahydrofuran–methanol in a ca. 3 : 2 : 1 ratio. A second mol of butanediol was added and in the next half hour gave 85.4 g product, but in a ratio of 1 : 4 : 1. A third mol of butanediol gave, in 0.5 h 89.7 g, but in the ratio 1 : 20 : 30. The reaction residue (240 g) was dark amber, and was by $^{31}$P NMR spectroscopy normal except for 14% 'other POCH$_2$' and only 1% TMP. From the first two products the yield of pure ether by fractional distillation was 27%, and of tetrahydrofuran 49%. By GC estimation the yield from the first mol would have been ca. 40%. It appears that the build-up of methoxyphosphoric acids catalyzes cyclization preferentially to methylation, especially as 'free' TMP disappears.

*1,6-Dimethoxyhexane.* This was the initial experiment and generally followed Toy's[1] procedure. The 1,6-hexanediol, 2.50 mol, TMP, 2.58 mol, and 0.5 g PPA were mixed and heated to 150 °C for two days. Crude product (115.6 g) was then distilled off; however, the temperature of the viscous reaction mixture was not monitored, and at this point there began an exothermic reaction with evolution of gases and volatiles which flooded and overflowed the condenser, effectively ending the experiment. The reddish-amber residue weighed 416 g and by $^{1}$H NMR spectroscopy had virtually no organic species except methoxy groups; hexanedioxy structures were

detected by FAB-MS. It was normal by $^{31}$P NMR spectroscopy except for having 45% phosphoric acid, only 1% TMP, and 6% dimethoxyphosphoric acid. From vacuum fractional distillation of the crude product 50 g (12%) of relatively pure diether (ca. 99% by GC) were obtained. Earlier fractions contained unsaturated components and some oxepane. In view of the high boiling point (185 °C/760 Torr) of the desired product, it would be preferable to follow the present procedure but with half the diol, and at a slightly reduced pressure.

*High-boiling methyl ethers.* In an early probe experiment on a 0.01 mol scale, a sample of polyethylene glycol monomethyl ether (Aldrich, av. MW 350) was heated to the reflux temperature of TMP, ca. 200 °C, for 100 h (without PPA), and gave (by GC) the dimethyl ethers $CH_3(OCH_2CH_2)_nOCH_3$ having $n$ from 1 to 12, plus substantial amounts of dioxane and small to trace amounts of unchanged monomethyl ethers having $n$ from 5 to 9 (no NMR work was done). This strongly indicates yield-reducing side-reactions that are minimized when the desired product can be removed quickly by distillation.

*Inhibition of ether peroxidation.* Potassium hydroxide, 10 molal (56%), results from making a 66 wt% solution of reagent (85%) KOH pellets, and is nearly saturated at room temperature. A 5–10 mm layer in the bottom of an ether bottle eliminates peroxides already present over a period of several days, and maintains freedom thereafter. Discoloration indicates prior build-up of peroxidation products which are easily removed by passage through a short column of neutral activated alumina when pure, dry, ether is required. Very little water is taken up, even by water-miscible ethers.

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