$C_{22}H_{16}ClNO_3S$: C, 64.46; H, 3.93; N, 3.42. Found: C, 64.22; H, 3.88; N, 3.46.

3c: 76.5% yield; mp 143–144 °C; mass spectrum, m/e 389 (M^+); ^1H NMR δ 1.09 (3 H, t, J = 7 Hz), 2.62 (2 H, q, J = 7 Hz). Anal. Calcd for $C_{23}H_{19}NO_3S$: C, 70.93; H, 4.92; N, 3.60. Found: C, 70.96; H, 4.83; N, 3.38.

3d: 80.5% yield; mp 139–141 °C; mass spectrum, m/e 425 (M^+ + 2), 423 (M^+); ^1H NMR δ 1.10 (3 H, t, J = 8 Hz), 2.62 (2 H, t, J = 8 Hz). Anal. Calcd for $C_{23}H_{18}ClNO_3S$: C, 65.16; H, 3.80; N, 3.30. Found: C, 65.03; H, 4.07; N, 3.19.

6a: 70.5% yield; mp 159–160 °C; mass spectrum, m/e 376 (M^+); ^1H NMR δ 2.18 (3 H, s). Anal. Calcd for $C_{21}H_{16}N_2O_3S$: C, 67.00; H, 4.28; N, 7.49. Found: C, 66.97; H, 4.18; N, 7.58.

6b: 74.6% yield; mp 161–163 °C; mass spectrum, m/e 390 (M^+); ^1H NMR δ 1.19 (3 H, t, J = 7.5 Hz), 2.74 (2 H, q, J = 7.5 Hz). Anal. Calcd for $C_{22}H_{18}N_2O_3S$: C, 67.67; H, 4.65; N, 7.18. Found: C, 67.48; H, 4.56; N, 7.08.

General Procedure for the Preparation of 4 and 7. To a stirred solution of methylenetriphenylphosphorane [prepared from methyltriphenylphosphonium bromide (5.71 g, 16 mmol) and n-BuLi (10.67 mL of 1.5 M hexane solution, 16 mmol) in THF under ice cooling] was added a solution of **3** (or **6**) (13.6 mmol) in THF (30–60 mL) under ice cooling. The mixture was warmed to room temperature and kept under stirring for 14 h at the same temperature. The mixture was poured into water and extracted with ethyl acetate. The extract was washed with water, dried over Na_2SO_4, and evaporated. A mixture of the remaining residue, 10% NaOH (30 mL), and ethanol (100 mL) was refluxed for 14 h. The solvent was evaporated and the resulting residue was extracted with ethyl acetate. The extract was washed with water, dried over Na_2SO_4, and evaporated to give **4** (or **7**). Yields and physical properties are as follows.

4a: 74.5% yield; mp 73–75 °C; ^1H NMR δ 2.17 (3 H, s), 5.41 (1 H, d, J = 1.6 Hz), 5.59 (1 H, d, J = 1.6 Hz). Anal. Calcd for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.00. Found: C, 87.36; H, 6.31; N, 5.90.

4b: 71.5% yield; mp 102–104 °C; mass spectrum, m/e 269 (M^+ + 2), 267 (M^+); ^1H NMR δ 2.17 (3 H, s), 5.53 (1 H, s), 5.68 (1 H, s). Anal. Calcd for $C_{17}H_{14}ClN$: C, 76.25; H, 5.27; H, 5.27; N, 5.23. Found: C, 76.39; H, 5.39; N, 5.27.

4c: 72% yield; mp 115–117 °C; mass spectrum, m/e 247 (M^+); ^1H NMR δ 1.17 (3 H, t, J = 7 Hz), 2.68 (2 H, q, J = 7 Hz), 5.42 (1 H, d, J = 1.5 Hz), 5.61 (1 H, d, J = 1.5 Hz). Anal. Calcd for $C_{18}H_{17}N$: C, 87.41; H, 6.93; N, 5.66. Found: C, 87.17; H, 6.87; N, 5.90.

4d: 69.5% yield; mp 139–140 °C; mass spectrum, m/e 283 (M^+ + 2), 281 (M^+); ^1H NMR δ 1.17 (3 H, t, J = 7 Hz), 2.68 (2 H, q, J = 7 Hz), 5.44 (1 H, d, J = 1.5 Hz), 5.64 (1 H, d, J = 1.5 Hz). Anal. Calcd for $C_{18}H_{16}ClN$: C, 76.72; H, 5.72; N, 4.97. Found: C, 76.56; H, 5.72; N, 4.70.

7a: 68.5% yield; mp 192–194 °C; mass spectrum, m/e 234 (M^+); ^1H NMR δ 2.18 (3 H, s), 5.74 (1 H, s), 5.58 (1 H, s). Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.02; H, 6.02; N, 11.96. Found: C, 82.14; H, 5.96; N, 11.90.

7b: 66.7% yield; mp 140–142 °C; mass spectrum, m/e 248 (M^+); ^1H NMR δ 1.23 (3 H, t, J = 7 Hz), 2.68 (2 H, q, J = 7 Hz), 5.60 (1 H, s), 5.78 (1 H, s). Anal. Calcd for $C_{17}H_{16}N_2$: C, 82.22; H, 6.50; N, 11.28. Found: C, 81.98; H, 6.36; N, 10.99.

6-Methyl-5*H*-benzo[*b*]carbazole (5a). **4a** (100 mg) was heated at 490–510 °C for 3 min and the reaction mixture was purified by preparative TLC on silica gel. Development with 15% ethyl acetate–n-hexane gave **5a** (25.8 mg, 26.0%): mp 210–211 °C; ^1H NMR δ 2.37 (3 H, s); mass spectrum, m/e 231.1032 (M^+) (calcd for $C_{17}H_{13}N$ 231.1047).

9-Chloro-6-methyl-5*H*-benzo[*b*]carbazole (5b). **4b** (100 mg) was heated at 490–500 °C for 3 min and the mixture was purified by preparative TLC on silica gel. Development with 10% ethyl acetate–n-hexane gave **5b** (26.1 mg, 26.3%): mp 150–152 °C; ^1H NMR δ 2.73 (3 H, s); mass spectrum, m/e 265.0635 (M^+) (calcd for $C_{17}H_{12}ClN$ 265.0656).

6,11-Dimethyl-5*H*-benzo[*b*]carbazole (5c). **4c** (100 mg) was heated at 410–420 °C for 5 min. The reaction mixture was purified by preparative TLC on silica gel. Development with 15% ethyl acetate–n-hexane gave **5c** (24.8 mg, 25%): mp 209–211 °C; ^1H NMR δ 2.77 (3 H, s), 3.19 (3 H, s); mass spectrum, m/e 245.1185 (M^+) (calcd for $C_{18}H_{15}N$ 245.1167).

9-Chloro-6,11-dimethyl-5*H*-benzo[*b*]carbazole (5d). **4d** (100 mg) was heated at 400 °C for 5 min and the reaction mixture was purified by preparative TLC on silica gel. Development with 15% ethyl acetate–n-hexane gave **5d** (23.8 mg, 24.0%) as an amorphous solid: ^1H NMR δ 2.77 (3 H, s), 3.14 (3 H, s); mass spectrum, m/e 279.0781 (M^+) (calcd for $C_{18}H_{14}ClN$ 279.0760).

5-Methylpyrido[4,3-*b*]carbazole (1b). **7a** (100 mg) was heated at 500 °C for 3 min and the reaction mixture was purified by preparative TLC on silica gel. Development with 10% methanol–chloroform gave **1b** (59.9 mg, 60.4%): mp 290–291 °C dec (lit.[8] mp 291–292 °C dec); ^1H NMR δ 2.73 (3 H, s); mass spectrum, m/e 232.1020 (M^+) (calcd for $C_{16}H_{12}N_2$ 232.1001).

Ellipticine (1a). **7a** (100 mg) was heated at 500 °C for 7 min and the reaction mixture was purified by preparative TLC on silica gel. Development with 5% methanol–chloroform afforded ellipticine (49.8 mg, 50.2%): mp 309–312 °C (lit.[9] mp 309–312 °C); ^1H NMR δ 2.71 (3 H, s), 3.22 (3 H, s); mass spectrum, m/e 246.1134 (M^+) (calcd for $C_{17}H_{14}N$ 246.1113).

Registry No. **1a**, 519-23-3; **1b**, 4238-66-8; **2a**, 58550-84-8; **2b**, 77507-52-9; **3a**, 77507-53-0; **3b**, 77507-54-1; **3c**, 77507-55-2; **3d**, 77507-56-3; **4a**, 77507-57-4; **4b**, 77507-58-5; **4c**, 77507-59-6; **4d**, 77507-60-9; **5a**, 77507-61-0; **5b**, 77507-62-1; **5c**, 73326-97-3; **5d**, 77507-63-2; **6a**, 77507-64-3; **6b**, 77507-65-4; **7a**, 77507-66-5; **7b**, 77507-67-6; 3-methylindole, 83-34-1; 3-ethylindole, 1484-19-1; benzoic anhydride, 93-97-0; p-chlorobenzoic anhydride, 790-41-0; isonicotinic anhydride, 7082-71-5.

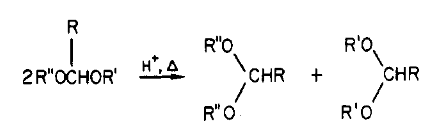
Preparation of Formaldehyde and Acetaldehyde Acetals[1]

Bhalchandra C. Barot and Harold W. Pinnick*

Department of Chemistry, University of Georgia, Athens, Georgia 30602

Received January 22, 1981

Acetals are useful as protecting groups for both carbonyl compounds and alcohols.[2] The preparation of symmetrical acetals derived from formaldehyde or acetaldehyde is not always easy.[3] We report a new method for accomplishing this goal based on an acetal interchange reaction with loss of a volatile symmetrical acetal (eq 1).



(1)

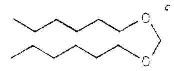
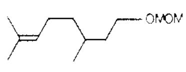
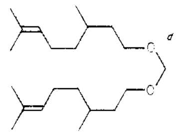
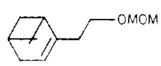
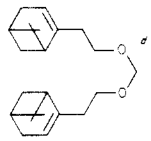
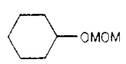
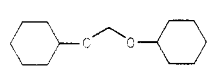
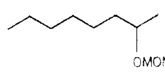
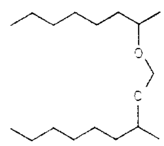
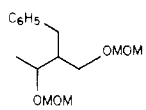
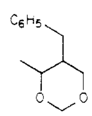
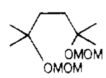
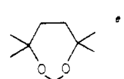
There are many examples of acetal interchange between an alcohol or diol and an acetal;[4a] however, there are few cases of acetal–acetal interchange[4b–d] even though this seems mechanistically straightforward. Consequently, in order to test the viability of the reaction of eq 1, a variety of methoxymethyl (MOM)[5] and ethoxyethyl (EE)[6] ethers were prepared and allowed to react with acid under anhydrous conditions.

Indeed, good yields of formaldehyde[7] and acetaldehyde acetals were obtained from MOM and EE ethers, respectively (see Tables I and II). For example, when the MOM ether of 1-hexanol is allowed to react with a catalytic amount of p-toluenesulfonic acid (p-TsOH) in refluxing benzene for 36 h, a 78% isolated yield of the formaldehyde acetal of 1-hexanol is obtained.[8,9] Even MOM ethers derived from acid-sensitive alcohols such as citronellol and nopol give the formaldehyde acetals but the weaker acid pyridinium p-toluenesulfonate[10] must be used. Ethoxy-

* Address correspondence to this author at the Department of Chemistry, Bucknell University, Lewisburg, PA 17837.

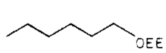
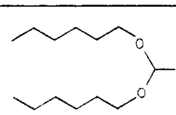
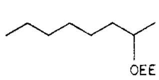
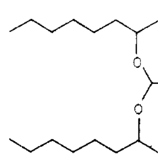
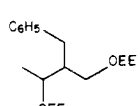
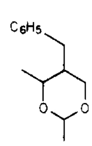
0022-3263/81/1946-2981$01.25/0

Table I. Preparation of Formaldehyde Acetals[a]

MOM ether	acetal	% yield[b]	bp, °C (mm)
	 [c]	78	100 (2.4)
$C_6H_5CH_2OMOM$	$C_6H_5CH_2OCH_2OCH_2C_6H_5$	71	51 (0.65)
	 [d]	56	83 (0.3)
	 [d]	40	86–91 (0.3)
	 [c]	94	75 (0.1)
		60	105–110 (1.0)
		93	66 (0.25)
	 [e]	51	175 (760)

[a] The solvent is toluene unless otherwise indicated. [b] All yields refer to products purified by distillation. [c] Using benzene as the solvent. [d] The catalyst is pyridinium *p*-toluenesulfonate. [e] The solvent is diethyl ether.

Table II. Preparation of Acetaldehyde Acetals[a]

EE ether	acetaldehyde acetal	% yield[b]	bp, °C (mm)
		69	95–100 (2.2)
		65	60–65 (1.5)
		40	100–105 (2.2)

[a] Using a catalytic amount of *p*-toluenesulfonic acid in refluxing toluene. [b] All yields refer to pure, isolated products.

ethyl ethers undergo the reaction also. For example, the EE ether of 1-hexanol gives a 69% yield of the 1-hexanol acetal of acetaldehyde[8] when allowed to react with a catalytic amount of *p*-TsOH in refluxing toluene for 1 h.

(1) Protecting Groups in Organic Synthesis, Part 7. For the earlier parts of this series, see the following: (a) Pinnick, H. W.; Lajis, N. H. *J. Org. Chem.* **1978**, *43*, 371; (b) Anderson, L. C.; Pinnick, H. W. *Ibid.* **1978**, *43*, 3417; (c) Pinnick, H. W.; Lajis, N. H. *Ibid.* **1978**, *43*, 3964; (d) Pinnick, H. W.; Bal, B. S.; Lajis, N. H. *Tetrahedron Lett.* **1978**, *4261*; (e) Pinnick, H. W.; Fernandez, E. *J. Org. Chem.* **1979**, *44*, 2810; (f) Bal, B. S.; Pinnick, H. W. *Ibid.* **1979**, *44*, 3727.

(2) "Protective Groups in Organic Chemistry"; McOmie, J. F. W., Ed.; Plenum: New York, 1973.

(3) The methods for generating these compounds are outlined in ref 1f.

(4) (a) For example, the use of 2,2-dimethoxypropane to prepare acetonides from diols (Tanabe, M.; Bigley, B. J. *J. Am. Chem. Soc.* **1961**, *83*, 756) or the conversion of hydroxy acetals into tetrahydrofurans (Eaton, P. E.; Cooper, G. F.; Johnson, R. C.; Mueller, R. H. *J. Org. Chem.* **1972**, *37*, 1947). (b) There are examples of the conversion of bicyclic acetals into polymeric acetals: Hall, H. K., Jr.; Carr, L. J.; Kellman, R.; DeBlauwe, F. *J. Am. Chem. Soc.* **1974**, *96*, 7265. (c) Acetals react with vinyl ethers in the presence of acid to give *β*-alkoxy acetals: Isler, O.; Lindlar, H.; Montavon, M.; Ruegg, R.; Zeller, P. *Helv. Chim. Acta* **1956**, *39*, 249. (d) Diols can be converted into acetals via intermediate bisacetals: Anteunis, M.; Becu, C. *Synthesis* **1974**, 23.

MOM and EE ethers from diols give cyclic acetals when exposed to catalytic acid in hot solvent. For example, the bisMOM ether of 2-benzyl-1,3-butanediol gives a 93% yield of pure 5-benzyl-4-methyl-1,3-dioxane[8] after 36 h in refluxing toluene containing a catalytic amount of *p*-TsOH. The corresponding bisEE ether gives a 40% yield of 5-benzyl-2,4-dimethyl-1,3-dioxane[8,9] after 36 h in refluxing toluene containing a small amount of *p*-TsOH. Attempts to extend these reactions to bisacetals of diols such as triethylene glycol failed.

Unexpected results were obtained during the preparation of EE ethers using ethyl vinyl ether.[6b] The amount of acid catalyst seems to affect the product. For example, the reaction of 1-hexanol with ethyl vinyl ether in diethyl ether in the presence of 1 mg of *p*-TsOH for 0.5 h at room temperature gives after aqueous sodium bicarbonate workup and distillation, a 66% yield of the desired EE ether. A duplicate reaction which contained 10 mg of acid and which was allowed to stir for 15 h at room temperature gives a 64% yield of the EE ether plus an 18% yield of the 1-hexanol acetal of acetaldehyde after the same workup and distillation. Another curious observation was noted when various reactions of alcohols and ethyl vinyl ether were complete by ^{1}H NMR and TLC and yet only unreacted alcohols were obtained after distillation of the crude material obtained from aqueous sodium bicarbonate workup.[11]

Despite the basic workup routinely used for all reactions, both of these problems are apparently caused by residual acid during the distillation. The use of distillation glassware which had been soaked in alcoholic potassium hydroxide, rinsed with water and acetone, and then oven-dried avoids the difficulty. Alternatively, the crude acetal can be passed through a short column of alumina prior to distillation and only the expected EE ether is obtained. Several pure ethoxyethyl ethers have been deprotected by simple distillation with a trace of *p*-TsOH in the pot. Pyridinium *p*-toluenesulfonate has no effect during the distillation of acetals.

Consequently, it is recommended that the crude product from ethyl vinyl ether reactions be passed through a short alumina column prior to distillation. Alternatively, the product can be used without distillation. All acetals in this study were distilled before use.

In conclusion, MOM and EE ethers give acetals of formaldehyde and acetaldehyde, respectively. Cyclic acetals are obtained from bisMOM and bisEE ethers derived from diols.

Experimental Section

Ether was freshly distilled from calcium hydride, and benzene and toluene were dried over 4-Å molecular sieves. Infrared spectra were recorded on a Perkin-Elmer Model 257 or 297 spectrometer. Proton NMR spectra were obtained with a Varian T-60 spectrometer. Mass spectra were determined with a Finnigan 4023 quadrapole GC/MS. The following procedures are typical.

Preparation of the MOM Ether of 1-Hexanol. 1-Hexanol (2.55 g, 25.0 mmol) was dissolved in 100 mL of methylene chloride, and 18.3 mL (13.6 g, 105 mmol) of diisopropylethylamine and 8.0 g (100 mmol) of chloromethyl methyl ether were added. The reaction mixture was refluxed for 12 h, cooled, and poured into water. The aqueous phase was extracted twice with ether and the organic layers were combined. This was washed with dilute HCl and then water, dried over anhydrous $MgSO_4$, and concentrated to give 2.9 g (79%) of the desired acetal: bp 53–55 °C (0.7 mmHg); ^{1}H NMR (CCl_4) δ 0.9 (t, J = 7 Hz, 3 H), 1.2–1.8 (br s, 8 H), 3.3 (s, 3 H), 3.4 (t, J = 6 Hz, 2 H), 4.5 (s, 2 H); IR (NaCl) 2900, 1480, 1400, 1070, 880, 840, 785, 725, 675 cm^{-1}.

Preparation of the Formaldehyde Acetal of 1-Hexanol. The MOM ether of 1-hexanol (2.48 g, 17.0 mmol) was stirred with 0.19 g (1.0 mmol) of *p*-TsOH·H_2O in 100 mL of refluxing toluene for 36 h.[9] The reaction was cooled and quenched with aqueous $NaHCO_3$. The aqueous phase was extracted three times with ether, and all organic layers were combined, dried, and distilled to give 1.44 g (78%) of a colorless liquid: bp 50–60 °C (0.9 mm); ^{1}H NMR (CCl_4) δ 0.9 (t, J = 7 Hz, 6 H), 1.2–1.8 (br s, 16 H), 3.5 (t, J = 6 Hz, 4 H), 4.6 (s, 2 H).

Registry No. 1-(Methoxymethoxy)hexane, 66675-06-7; [(methoxymethoxy)methyl]benzene, 31600-55-2; 8-(methoxymethoxy)-2,6-dimethyl-2-octene, 77661-65-5; 2-[2-(methoxymethoxy)ethyl]-6,6-dimethylbicyclo[3.1.1]hept-2-ene, 77661-66-6; (methoxymethoxy)-cyclohexane, 42604-09-1; 2-(methoxymethoxy)octane, 77661-67-7; [2-[(methoxymethoxy)methyl]-3-(methoxymethoxy)butyl]benzene, 77661-68-8; 2,5-bis(methoxymethoxy)-2,5-dimethylhexane, 77661-69-9; 7,9-dioxapentadecane, 54815-12-2; 1,1′-[methylenebis(oxymethylene)]bisbenzene, 2749-70-4; 2,6,14,18-tetramethyl-9,11-dioxanonadeca-2,17-diene, 71316-96-6; 2,2′-[methylenebis(oxy-2,1-ethanediyl)]bis[6,6-dimethylbicyclo[3.1.1]hept-2-ene], 77679-99-3; 1,1′-[methylenebis(oxy)]bis[cyclohexane], 1453-21-0; 7,11-dimethyl-8,10-dioxaheptadecane, 71316-97-7; 4-methyl-5-benzyl-1,3-dioxane, 77661-70-2; 4,4,7,7-tetramethyl-1,3-dioxepane, 77661-71-3; 1-(ethoxyethoxy)hexane, 59184-44-0; 2-(ethoxyethoxy)octane, 77661-72-4; [2-[(ethoxyethoxy)methyl]-3-(ethoxyethoxy)butyl]benzene, 77661-73-5; 7,9-dioxa-8-methylpentadecane, 5405-58-3; 7,9,11-trimethyl-8,10-dioxaheptadecane, 77680-00-3; 2,4-dimethyl-5-benzyl-1,3-dioxane, 77661-74-6; 1-hexanol, 111-27-3; chloromethyl methyl ether, 107-30-2; formaldehyde, 50-00-0; acetaldehyde, 75-07-0.

(5) These were prepared from the alcohols with chloromethyl methyl ether; for example, see: Auerbach, J.; Weinreb, S. M. *J. Chem. Soc., Chem. Commun.* **1974**, 298.

(6) These are available from the reaction of alcohols with (a) α-chloroethyl ethyl ether (for example, see: Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481) or (b) ethyl vinyl ether (Chladek, S.; Smrt, J. *Chem. Ind.* **1964**, 1719).

(7) For another preparation of formaldehyde acetals see ref 1f.

(8) All products give satisfactory ^{1}H NMR and IR spectra as well as the expected mass spectral fragmentation.

(9) The conditions for none of the reactions in this paper have been optimized. Many of the reactions are certainly complete in much shorter times than that indicated.

(10) (a) Miyashita, N.; Yoshikoshi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772. (b) Pinnick, H. W.; Bal, B. S.; Lajis, N. H. *Tetrahedron Lett.* **1978**, 4261.

(11) For example, 1-hexanol and ethyl vinyl ether after 12 h in the presence of *p*-TsOH in ether showed some unreacted alcohol after $NaHCO_3$ workup but distillation gave only unreacted alcohol in 72% yield. An identical reaction whose crude product was passed through alumina before distillation gave a 45% yield of the EE ether.