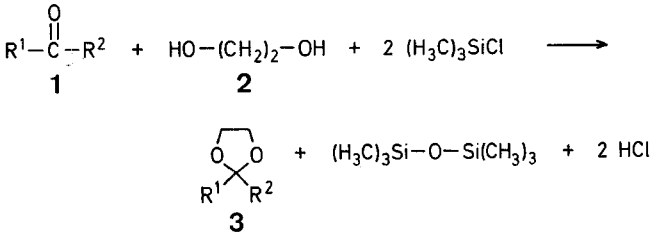


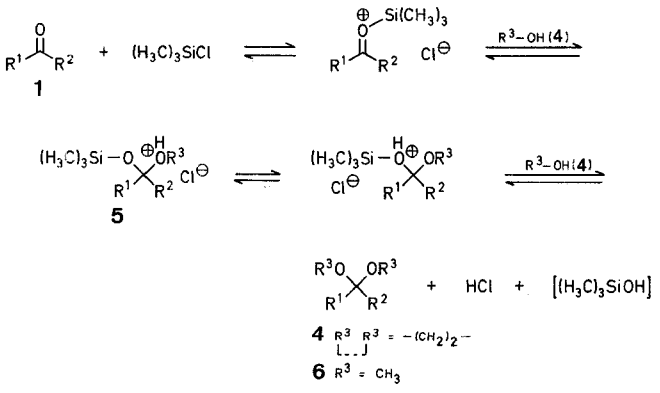
Aldehydes and ketones **1** are converted to the corresponding 1,3-dioxolanes **3** by reaction with a slight excess of ethylene glycol **(2)** in the presence of chlorotrimethylsilane. The reaction can be carried out in methanol as solvent at room temperature (Method A), or in refluxing dichloromethane as solvent (Method B).

With aryl ketones, acetalization was more sluggish; the use of ethylene glycol as solvent and a greater excess of chlorotrimethylsilane (Method C) was necessary to bring about complete acetalization at room temperature. The presence of activating groups α to the carbonyl group, such as chloride, reduced the excess of chlorotrimethylsilane required to a certain extent (see Table 1).

Normal unactivated carbonyl compounds and α-chlorinated aryl ketones are not acetalized by methanol under these conditions. Thus, in Method A, even though the reaction was carried out in methanol as solvent, no significant amount of dimethyl acetal was detected. When the carbonyl group is activated by an α-carbonyl group or by α-halogens, the dimethyl acetal can be formed readily. For α-dicarbonyl compounds, this procedure provides a way to selectively monoacetalize the more activated carbonyl group. Thus, phenylglyoxal (Table 2) was converted to the corresponding dimethyl acetal **6a** in 83% yield simply by stirring in methanol with a slight excess of trimethylchlorosilane overnight (Method D). This is to be compared with the literature procedures[17] for the same transformation which in our hands gave <45% yield.

It should be noted that the acetalization is also successful on a larger scale. For example, 3,3-dimethoxy-2-butanone **(6f)** was prepared on a 50 mmol scale in 91% yield, after fractional distillation.

It is expected that chlorotrimethylsilane is acting both as an acid catalyst and as a dehydrating agent. Nevertheless, the difference in acetalization between ethylene glycol and methanol suggests that the reaction is subject to kinetic factors. When the concentration of the hemiacetal **5** ($R^3 = CH_2CH_2OH$) is low, intramolecular cyclization leading to **4** (R^3, $R^3 = -CH_2CH_2-$) is still occurring sufficiently fast for the reaction to proceed. In the case of methoxy-hemiacetal (**5**, $R^3 = CH_3$), intermolecular acetalization is at a fast enough rate only when the concentration of **5** is substantial, which only occurs when electron-withdrawing groups α to the acetalized carbonyl are present.



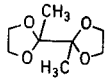
A Simple Procedure for the Acetalization of Carbonyl Compounds

T. H. CHAN*, Michael A. BROOK, T. CHALY

Department of Chemistry, McGill University, Montreal, Quebec, Canada, H3A 2K6

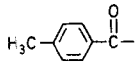
Acetalization of aldehydes and ketones is a commonly encountered reaction in organic synthesis. Many methods are available, most of them involving the removal of water under acid-catalyzed conditions[1]. Recently, the use of alkoxytrimethylsilane and trimethylsilyl triflate has been suggested as a simple method for acetalization[2]. We report here a facile procedure for the acetalization of carbonyl compounds under mild conditions utilizing readily available chemicals. Furthermore, the reaction shows interesting selectivity which may be useful in synthesis.

Table 1. 1,3-Dioxolanes **3** prepared

Product 3	R^1	R^2	Equiv. $(H_3C)_3SiCl$	Method	Yield [%]	m.p. [°C] or b.p. [°C]/torr	
						found	reported
a	$-(CH_2)_5-$		2.2	A; C	83; 95	—[a]	174–180°/760[4,5,18]
b		H	2.2	A; B	64; 77	—[a]	107–108°/13[6,19]
c		CH_3	6.6	C	71	61° (CH_3OH)	61°[9]
d		$ClCH_2$	4.4	C	99	90° (CH_3OH)	—[10]
e		Cl_2CH	2.2	C	78	58.5–59° (CH_3OH)	59–61°[11]
f	n-C_8H_{17}	H	2.2	A; B	64[a]; 98[b]	117–135°/14[b]	141–142°/40[7]
g	H_3C	$H_3COOC-CH_2$	2.2	B	90	36–38°/0.75	—[c]
h	n-C_5H_{11}	$H_3COOC-CH_2$	2.2	B	88	80–85°/0.5	—[d]
i			2.2	B	95[e]	90°	90°[8]

[a] Purified by flash chromatography: Merck 40–63 mm silica gel (16 g), eluent: ethyl acetate/hexane mixtures.
[b] Kugelrohr distillation.
[c] $C_{17}H_{12}O_4$ (160.2) calc. C 52.49 H 7.55; found 52.38 7.61
^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.46$ (s, 3H); 2.66 (s, 2H); 3.66 (s, 3H); 3.91 ppm (s, 4H).
[d] $C_{11}H_{20}O_4$ (216.3) calc. C 61.09 H 9.32; found 61.13 9.35
^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.1$–1.9 (m, 8H); 2.53 (s, 2H); 3.53 ppm (s, 3H).
[e] Starting material is biacetyl.

Table 2. Dimethyl Acetals **6** prepared by Method D

Product 6	R^1	R^2	Yield [%]	m.p. [°C] or b.p. [°C]/torr	
				found	reported
a		H	83	89°/0.6	101°/4.5[12]
b		H	98	—[a]	108–113°/1[13]
c		H_3COOC	55[b]	—[a]	—[c]
d	H_3C	H_3COOC	92	—[a]	62–63°/12[14]
e	H_3C	Cl_2CH	71[d]	—[a]	—[15]
f		H_3C	91	58°/28	145–146°/760[16]

[a] Purified by flash chromatography: Merck 40–63 mm silica gel (16 g), eluent: ethyl acetate/hexane mixtures.
[b] Yield after correction for recovered starting material: 74%.
[c] $C_{11}H_{14}O_4$ (210.2) calc. C 62.84 H 6.71; found 62.95 6.81
^{1}H-N.M.R. ($CDCl_3$): $\delta = 3.38$ (s, 6H); 4.70 (s, 3H); 7.2–7.7 ppm (m, 5H).
[d] Yield determined by G.L.C.; yield of isolated product: 42% due to high volatility.

The advantages of the described method are as follows; the alcohol need not be silylated[2], low temperatures, option of aqueous or non-aqueous work-up, and the ready availability and low cost of trimethylchlorosilane. In addition, the selectivity of acetalization may allow the protection of a single carbonyl group in a polycarbonyl compound.

1,4-Dioxaspiro[4.5]decane (3a); Typical Procedure for Method A:
To a mixture of dry ethylene glycol (**2**; 3 ml, 54.0 mmol) and dry methanol (20 ml) under a nitrogen atmosphere is added cyclohexanone (**1a**; 0.52 g, 5.2 mmol). Chlorotrimethylsilane (1.4 ml, 11.0 mmol) is added and the mixture is stirred for 16 h at room temperature. The mixture is neutralized to pH 6 by adding a 5% solution of sodium methoxide in methanol and the solvent is removed under reduced pressure. The residue is dissolved in ether (20 ml), filtered through silica gel (5 g), the silica gel is washed with ether (2 × 10 ml), and the ether is removed under reduced pressure. The crude product is submitted to flash chromatography (silica gel, eluent: ethyl acetate/hexane, 1:10, v/v); to give the product as a colourless oil; yield: 0.63 g (83%).

I.R. (neat): $\nu = 2943$, 2865, 1447, 1366, 1102 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.58$ (br. s, 10H); 3.90 ppm (s, 4H).

The methoxide work-up may also be used in Methods C and D when the product is partially water soluble, such as **6e**.

2-Phenyl-1,3-dioxolane (3b); Typical Procedure for Method B:
Benzaldehyde (**1**; 0.53 g, 5.0 mmol) is added to a solution of ethylene glycol (**2**; 0.61 ml, 11.0 mmol) and dry dichloromethane (25 ml) under a nitrogen atmosphere. To the mixture is added chlorotrimethylsilane (2.8 ml, 22.0 mmol) and the mixture is stirred at reflux for 48 h. A 5% aqueous solution of sodium hydrogen carbonate (50 ml) is added and the mixture extracted with ether (2 × 75 ml), washed with brine (2 × 40 ml), and the combined ether extracts are dried with magnesium sulfate. The ether is removed under reduced pressure and the residue is submitted to flash chromatography (silica gel, eluent: hexane/ethyl acetate, 3:1, v/v) to give, after evaporation, the pure acetal as a colourless oil; yield: 0.58 g (77%).

I.R. (neat): $\nu = 2900$, 1455, 1390, 1314, 1221 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 4.0$ (m, 4H); 5.77 (s, 1H); 7.1–7.6 ppm (m, 5H).

2-Chloromethyl-2-phenyl-1,3-dioxolane (3d); Typical Procedure for Method C:
To a solution of α-chloroacetophenone (**1d**; 0.83 g, 5.4 mmol) in dry

ethylene glycol (**2**; 25 ml) under a nitrogen atmosphere is added chlorotrimethylsilane (2.8 ml, 22.0 mmol). The reaction is stirred for 16 h at room temperature. A 5% aqueous sodium hydrogen carbonate solution (50 ml) is added, the mixture is extracted with ether (2 × 75 ml), and the extracts washed with brine (2 × 50 ml). The combined ether extracts are dried with magnesium sulfate and the solvent removed under reduced pressure. Recrystallization of the residue from methanol gives the product as white crystals; yield: 1.05 g (99%); purity ≥97% by G.L.C. (5% OV 101 on Chromosorb W, 6 ft column); m.p. 90 °C.

I.R. (Nujol): $\nu = 1449, 1227, 1181, 1027, 729\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 3.75$ (s, 2H); 3.8–4.2 (m, 4H); 7.2–7.6 ppm (m, 5H).

M.S.: $m/e = 149$ ($M^+ - CH_2Cl$); 105 ($C_6H_5CO^+$).

Benzoyldimethoxymethane (6a); Typical Procedure for Method D:
Freshly distilled phenyl glyoxal (8.26 g, 62.2 mmol) is added to dry methanol (75 ml) under a nitrogen atmosphere. The yellow solution becomes colourless after the addition of chlorotrimethylsilane (18 ml, 143 mmol). The mixture is stirred for 18 h at room temperature. The solvents are removed under reduced pressure and the residue distilled to give the pure acetal **6a**; yield: 9.16 g (83%); colourless oil; b.p. 89 °C/0.6 torr.

I.R. ($CHCl_3$): $\nu = 2945, 2842, 1695$ (C=O), 1603, 1583, 1454, 1288 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 3.48$ (s, 6H); 5.23 (s, 1H); 7.4–7.6 and 8.0–8.2 ppm (m, 5H).

Financial support by NSERC and the Ministry of Education, Government of Quebec is gratefully acknowledged. The award of a NSERC scholarship to MAB is also greatly appreciated.

Received: June 15, 1982
(Revised form: August 31, 1982)

* Author to whom correspondence should be addressed.

1 For a recent review see: F. A. J. Meskens, *Synthesis* **1981**, 501.
2 T. Tsunoda, M. Suzuki, R. Noyori, *Tetrahedron Lett.* **21**, 1357 (1980).
3 W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **43**, 2923 (1978).
4 V. M. Thuy, P. Maitte, *Bull. Soc. Chim. Fr.* **1975**, 2558.
5 H. E. Audier, M. Fetizon, J.-C. Tabet, *Organ. Mass Spectrom.* **10**, 178 (1975).
6 G. Dousse, H. Lavayssière, J. Satgé, *Helv. Chim. Acta* **58**, 2610 (1975).
7 I. Rosenthal, D. Elad, *J. Org. Chem.* **33**, 805 (1968).
8 H. Baganz, L. Domaschke, *Chem. Ber.* **91**, 650 (1958).
9 F. Alderweireldt, M. Anteunis, *Bull. Soc. Chim. Belg.* **74**, 488 (1965).
10 E. N. Gutierrez, R. C. Reardon, *U. S. Patent* 3944568 (1970), Lever Bros. Corp.
11 D. C. Mueller, D. Seyferth, *J. Am. Chem. Soc.* **91**, 1754 (1969).
12 D. W. Griffiths, C. D. Gutsche, *J. Org. Chem.* **36**, 2184 (1971).
13 D. Papillon-Jegou, B. Bariou, M. Kerfanto, *C. R. Acad. Sci. Ser. C* **279**, 221 (1974).
14 N. E. Hoffman, T. V. Kandathil, *J. Org. Chem.* **32**, 1615 (1967).
15 E. N. Gutierrez, R. C. Reardon, *U. S. Patent* 3918328 (1975), Lever Bros. Corp.; *C. A.* **84**, 30436 (1976).
16 L. Brodsley, W. C. Agosta, *J. Org. Chem.* **39**, 2928 (1974).
17 B. M. Trost, E. Keinan, *J. Org. Chem.* **45**, 2741 (1980).
18 *Dictionary of Organic Compounds*, R. Stevens, Ed., Eyre and Spottiswood and E. F. Spon, London, 1971.
19 F. Nerdel, J. Buddrus, G. Scherowsky, D. Klamann, M. Fligge, *Liebigs Ann. Chem.* **710**, 85 (1967).