SHORT PAPER

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An efficient procedure for the synthesis of diacetals from the $InCl_3 \cdot 4H_2O$ catalysed reaction of 2,2-bis (hydroxymethyl)-1,3-propanediol with aldehydes or ketones[†]

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Diacetals of carbonyl compounds are synthesised in good yields by the $InCl_3 \cdot 4H_2O$ catalysed condensation reactions.

Keywords: diacetal, synthesis, $InCl_3 \cdot 4H_2O$

The diacetals of 2,2-bis(hydroxymethyl)-1,3-propanediol (pentaerythritol) as potential protecting groups for aldehydes and ketones as well as important derivatives of carbonyl compounds are practically very useful.[1] They are applied as defoamers for detergent solutions containing anionic surfactants,[2] as plasticisers and vulcanisers of various polymeric materials, as raw materials for the production of valuable resins and lacquers, as physiologically active substances[3] and as insecticides.[4] Many methods for the synthesis of diacetals have been described in the literature. Strong protonic acids such as sulfuric acid,[2,5,6] hydrochloric acid[7] and *p*-toluenesulfonic acid[7-9] and Lewis acids such as zinc chloride,[10] copper sulfate[11] and anhydrous ferrous sulfate[12] have been employed as catalysts. Owing to their drawbacks, such as rather drastic reaction conditions, tedious work up procedures, use of corrosives, effluent pollution or sensitivity to water *etc*., some of these methods are not entirely satisfactory. There is, therefore, a need to develop alternative methods for the synthesis of diacetals from 2,2-bis (hydroxymethyl)-1,3-propanediol under mild and environmentally friendly conditions. For this purpose, montmorillonite clays[1], cation exchanger KU-2[3], 12-tungstophosphoric acid[13] and expansive graphite[14] have been employed as catalysts to obtain improved results.

Recently, indium trichloride has been used in organic synthesis.[15-18] Because of its good characteristics as a catalyst, such as the operational simplicity, usually milder reaction conditions, good yields, high selectivity and inertness to water, $InCl_3$ has aroused interest. Previously we have reported $InCl_3$-catalysed aldol condensation reactions.[18] Herein we report an efficient procedure for the preparation of diacetals from 2,2-bis(hydroxymethyl)-1,3-propanediol with aldehydes and ketones catalysed by $InCl_3 \cdot 4H_2O$ under solvent free conditions in sealed tubes at 120°C (Scheme 1). As shown in Table 1 (entry **3a–3k**), several aldehydes or ketones in the presence of $InCl_3 \cdot 4H_2O$ were heated with 2,2-bis(hydroxymethyl)-1,3-propanediol in sealed tubes at 120°C, resulting in the corresponding diacetals in good to excellent yields except for benzophenone (entry **3k**: no reaction). It is pointed out that the procedures were safe because the reactions were carried out under solvent free conditions.

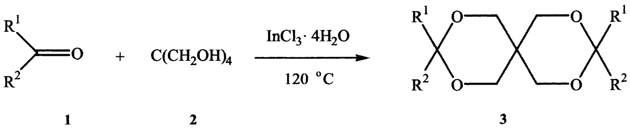
From Table 1 we found that ketones showed less reactivity than aldehydes for this reaction. For example, the diacetal from 2,2-bis(hydroxymethyl)-1,3-propanediol with cyclohexanone was obtained by heating at 120°C for 10h in 80% yield, however, benzophenone failed to give the corresponding diacetal under the same condition, whereas diacetals were obtained in above 80% yields for less than 8h when using aldehydes as substrates. Lower yields and more side-reactions were found when the reaction was carried out in an unsealed tube.

Table 1 Synthesis of diacetals from 2,2-bis(hydroxymethyl)-1,3-propanediol (entries **3a-3k**) and 1, 3 propanediol (entries **4a-4c**) with aldehydes and ketones catalysed by $InCl_3 \cdot 4H_2O$

Entry[a]	Carbonyl compound **1**	Time/h	Yield[b] /%	M.p./°C or B.p./°C/torr	
				Found	Reported
3a	PhCHO	5	83	155–156	155–156[14]
3b	$3\text{-}O_2NC_6H_4CHO$	4	85	184–185	185[5]
3c	$3\text{-}ClC_6H_4CHO$	5	87	120–122	121–122[1]
3d	$4\text{- }ClC_6H_4CHO$	5	82	196–197	197–198[14]
3e	$2\text{- }O_2NC_6H_4CHO$	4	88	163–164	163–164[14]
3f	$4\text{- }O_2NC_6H_4CHO$	4	86	232–234	234[8]
3g	$2,4\text{- }Cl_2C_6H_3CHO$	7	83	178–180	178–180[14]
3h	$4\text{-}CH_3C_6H_4CHO$	10	80	211–212	211–212[12]
3i	$(CH_3)_2CHCHO$	3	89	82–83	82–82.5[13]
3j	Cyclohexanone	7	84	112–113	112–113[5]
3k	Ph_2CO	10	0		
4a[c]	PhCHO	2	84	48–49	47–49[19]
4b[c]	$CH_3CH_2CH_2CHO$	1	87	149–151/728	150–151/722[20]
4c[c]	$CH_3CH_2COCH_3$	1.5	77	147–149/728	148/729[20]

[a] All compounds were confirmed by ^1H NMR and IR. [b] Isolated yield. [c] The condensation reaction of propane-1,3-diol and carbonyl compounds catalysed by $InCl_3 \cdot 4H_2O$ at reflux in benzene.

As shown in Table 1 (entry **4a–4c**), analogous results were obtained when carbonyl compounds in the presence of $InCl_3 \cdot 4H_2O$ were heated with propane-1,3-diol at reflux in benzene. In this case, the reaction was carried out in an unsealable reaction vessel very successfully.



Scheme 1

Experimental

Melting points are uncorrected. ^1H NMR spectra were recorded on Varian Mercury 200 spectrometer, using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal reference. IR spectra were recorded on a Nicolet Instrument Corporation's IR-510P spectrometer.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Typical procedure for the synthesis of compound **3a**: A mixture of benzaldehyde **1a** (1.061 g, 10 mmol), 2,2-bis (hydroxymethyl)-1,3-propanediol **2** (0.68 g, 5 mmol) and $InCl_3 \cdot 4H_2O$ (0.147 g, 0.5 mmol, 5% mol ratio) was placed in a glass tube and sealed. Then the sealed tube was placed in an oil bath and heated at 120°C for 5 h. The sealed tube was opened after cooling to room temperature. The reaction mixture was added to water (20 ml) and the mixture was heated to 90–100°C. The solution was cooled to 0°C and the resultant precipitate was filtered off. The crude product was washed with water and purified by recrystallisation in ethanol to give the title compound **3a** (1.3 g) in 83% yield. m.p.155–156°C (lit[14]. 155–156 °C).

Compound **3a**: IR (KBr) 3034(m), 2959(m), 2857(s), 1720(m), 1603(w), 1497(m), 1387(s), 1204(s), 1163(s), 1076(s), 1022(s), 748(s), 717(m), 698(s) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.35–7.52 (10H, m, Ar-H), 5.46 (2H, s, C-H), 4.85 (2H, d, *J* = 11.6 Hz, H*e*), 3.62–3.88 (6H, m, 2xH*e* and 4xH*a*).

Compound **3b**: IR (KBr) 3082(m), 2984(w), 2905(w), 1618(w), 1533(s), 1471(m), 1354(s), 1201(s), 1078(s,) 1005(s), 711(s), 677(s) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.52–8.37 (8H, m, Ar-H), 5.55 (2H, s, C-H), 4.84 (2H, d, *J* = 11.6 Hz, H*e*), 3.68–3.92 (6 H, m, 2xH*e* and 4xH*a*).

Compound **3c**: IR (KBr) 2986(w), 2856(m), 1601(w), 1578(m), 1479(w), 1381(s), 1335(m), 1249(w), 1204(s), 1159(s), 1074(s), 1036(m), 952(m), 898(m), 877(m), 798(s), 750(s), 704(s) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.50 (2H, s, Ar-H), 7.26–7.36 (6H, m, Ar-H), 5.426 (2H, s, CH), 4.82 (2H, d, *J* = 11.6 Hz), 3.83 (4H, d, *J* = 12.2 Hz), 3.64 (2H, d, *J* =11.6 Hz).

Compound **3d**: IR (KBr) 2980(w), 2864(w), 1601(w), 1578(w), 1493(s), 1383(s), 1335(m), 1249(w), 1204(m), 1163(s), 1076(s), 820(s), 682(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.25–7.45 (8H, m, Ar-H), 5.42 (2H, s, C-H), 4.81 (2H, d, *J* = 11.6 Hz), 3.78–3.85 (4H, m), 3.64 (2H, d, *J* = 11.6 Hz).

Compound **3e**: IR (KBr) 3083(w), 2984(w), 2907(w), 1618(w), 1532(s), 1471(w), 1352(s), 1202(m), 1078(s), 1022(m), 714(m), 679(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.52–8.38 (8H, m, Ar-H), 5.54 (s, 2H, C-H), 4.83 (2H, d, *J* = 11.6 Hz), 3.86–3.93 (4H, m), 3.71 (2H, d, *J* = 11.6 Hz).

Compound **3f**: IR (KBr) 2986(w), 2942(w), 1615(m), 1532(s), 1348(s), 1202(m), 1071(s), 1013(s), 750(m), 698(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 8.06–8.43 (8H, m, Ar-H), 5.54 (2H, s, C-H), 4.82 (2H, d, *J* = 11.6 Hz), 3.85–3.93 (4H, m), 3.71 (2H, d, *J* = 11.6 Hz).

Compound **3g**: IR (KBr) 3076(w), 2945(m), 1593(s), 1568(m), 1460(m), 1381(s), 1204(s), 1163(m), 1074(s), 868(s), 758(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.63 (2H, d, J = 8.2 Hz, Ar-H), 7.25–7.39 (4H, m, Ar-H), 5.72 (2H, s, C-H), 4.85 (2H, d, *J* = 11.6 Hz), 3.79–3.91 (4H, m), 3.68 (2H, d, *J* = 11.6 Hz).

Compound **3h**: IR (KBr) 2917(w), 2862(m), 1618(w), 1454(m), 1383(s), 1117(m), 1078(s), 808(s) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.37 (4H, d, *J* = 8.0 Hz, Ar-H), 7.18 (4H, d, *J* = 8.0 Hz, Ar-H), 5.42 (2H, s, C-H), 4.85 (2H, d, *J* = 11.6 Hz, H*e*), 3.77–3.85 (4H, m, H*a*), 3.62 (2H, d, *J* = 11.6 Hz, H*e*), 2.34 (6H, s, CH_3).

Compound **3i**: IR (KBr) 2986(s), 2876(m), 1473(s), 1387(m), 161(s), 1086(s), 1038(m), 941(m), 720(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 4.55 (2H, d, *J* = 10.2 Hz, H*e*), 4.20 (2H, d, *J* = 4.4 Hz, CH), 3.30–3.61 (6H, m, H*e*, H*a*), 1.76–1.85 (2H, m, CH), 0.93 (12H, d, *J* = 6.8 Hz, CH_3).

Compound **3j**: IR (KBr) 2856(s), 1472(m), 1445(s), 1368(m), 1285(m), 1198(s), 1115(m), 1093(s), 1055(s), 908(s), 825(s), 727(m), 509(m), 499(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 3.73 (8H, s, O-C-H), 1.71 (8H, s, 2,2'-H), 1.48 (12H, s, 3,3', 4-H).

Compound **4a**: IR (CCl_4) 2957(m), 2930(w), 2870(w), 1456(m), 1383(m), 1240(m), 1140(m), 1105(s), 1001(s), 762(s), 702(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 7.24–7,51 (5H, m, Ar-H), 5.50 (1H, s, CH), 4.22–4.31 (2H, m, CH_2), 3.91–4.04 (2H, m, CH_2), 2.10–2.34 (1H, m, H*e*), 1.39–1.49 (1H, m, H*a*).

Compound **4b**: IR (CCl_4) 2963(s), 2851(s), 1468(m), 1406(m), 1379(m), 1242(m), 1147(s), 1107(s), 1074(m), 973(s), 935(m), 823(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 4.49 (1H, t, *J* = 7 Hz, CH), 4.06–4.14 (2H, m, CH_2), 3.69–3.86 (2H, m, CH_2), 1.98–2.17 (2H, m, CH_2) 1.19–1.62 (4H, m, CH_2), 0.88–0.97 (3H, t, *J* = 7 Hz, CH_3).

Compound **4c**: IR (CCl_4) 2973(s), 29469(s), 2868(s), 1466(w), 1383(m), 171(m), 1248(s), 1181(s), 1130(m), 1099(s), 968(m), 862(m) cm^{-1}; ^{1}H NMR (200MHz, $CDCl_3$, TMS) δ 3.87–3.94 (4H, m, CH_2), 1.66–1.80 (4H, m, CH_2), 1.37 (3H, s, CH_3), 0.88–0.96 (3H, t, *J* = 7Hz, CH_3).

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References

1 Z. -H. Zhang, T. -S. Jin, T. -S. Li and J. -T. Li, *J. Chem. Res. (S)*, 1998, 640.
2 J. Perner, K. Syork, F. Merger and K. Oppenlaender, *Ger. Offen.*, 1978, 2707875 (*Chem. Abstr.*, 1978, **89**, 181503x).
3 T.N. Shakhtakhtinskii and L.V. Andreev, *Dokl. Akad. Nauk. Azerb. SSR.*, 1962, **18**, 17 (*Chem. Abstr* .1963, **59**, 3762g).
4 E.L. Mager, R.H. Nelson and C.E. Robertson, *US Dept. Agric. Bur Entomol. Plant Quarantine*, 1951, E-833.
5 J. Read, *J. Chem. Soc.*, 1912, **101**, 2090 (*Chem. Abstr.*, 1913, **7**, 968).
6 N.P. Klyushnik, *Ukr. Khim. Zh.*, 1964, **30**, 965 (*Chem, Abstr.*, 1965, **62**, 2717a)
7 D. Callejas, M. Echemique and H. Seeboth, *Res. Cubana. Quim.*, 1988, **4**, 73 (*Chem. Abstr.*, 1989, **111**, 77927a).
8 E. Bograchov, *J. Am. Chem. Soc.*, 1950, **72**, 2268.
9 V.G. Mkhitaryan, *J. Gen. Chem.*, 1939, **9**, 1923 (*Chem. Abstr.*, 1940, **34**, 4381).
10 H.J. Backer and H.B. Schurink, *Rec. Trav. Chim.*, 1931, **50**, 1066 (*Chem. Abstr.*, 1932, **26**, 964).
11 L. Orthner, *Ber.*, 1928, **61B**, 116.
12 T.S. Jin, Y.R. Ma, T.S .Li and J.X. Wang, *J. Chem. Res.(S).*, 1999, 268.
13. X. Chen, Y.T. Xu and C. -X. Jin, *Hecheng Huaxue*, 1997, **5**, 212.
14. C.-D. Wang, X.-Z. Shi and. R.-J. Xie, *Synth.Commum.*, 1997, **27**, 2517.
15. Y.-F. Yuan, Z. Cao, A.-G. Hu and J.-T. Wang, *Chin. J. Org. Chem.*, 2000, **20**, 269.
16. T. Mukaiyama, T. Ohno, T. Nishimura, J.S. Han and S. Kobayashi, *Chem. Lett.*, 1990, 2239.
17. T. Mukaiyama, T. Ohno, T. Nishimura, S. Suda and S. Kobayashi, *Chem. Lett.*, 1991, 949.
18. G.-S. Deng and T.-G. Ren, *Chin. Chem. Lett.*, 2001, **12**, 859.
19. R.M. Munamu, H.H. Szmant, *Tetrahedron Lett.*, 1975, **16**, 4543.
20. W. Kantlehner, H.-D. Gutbrod, *Liebigs Ann. Chem.*, 1979, 1362.