

A Practical and Efficient Procedure for Preparation of Diacetals from 2,2-Bis(hydroxymethyl)propane-1,3-diol with Aldehydes and Ketones Catalysed by Anhydrous Ferrous Sulfate†

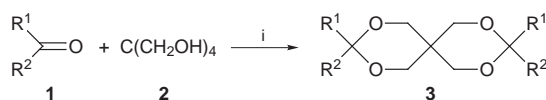
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Synthesis of diacetals in excellent yields from aldehydes and ketones with 2,2-bis(hydroxymethyl)propane-1,3-diol is carried out in refluxing benzene or toluene with anhydrous ferrous sulfate as catalyst.

The synthesis of diacetals of 2,2-bis(hydroxymethyl)propane-1,3-diol with aldehydes and ketones is very useful in preparative organic chemistry and as potential protecting groups for aldehydes and ketones as well as important derivatives of carbonyl compounds, since most of them are crystalline substances and have sharp melting points.¹ They are also applied as plasticizers and vulcanizers of various polymeric materials, as raw materials for production of valuable resins and lacquers, as physiologically active substances,² and as defoamers for detergent solutions containing anionic surfactants.³ Usually, the synthesis of 2,2-bis(hydroxymethyl)propane-1,3-diol diacetals under acidic conditions is described.⁴ Strong protic acids such as sulfuric acid,^{3,5,6} hydrochloric acid,⁷ and *p*-toluenesulfonic acid,^{7–9} and Lewis acids such as zinc chloride¹⁰ and copper sulfate,¹¹ have been employed as catalysts. Some of these methods are not entirely satisfactory, owing to such drawbacks as low yields, long reaction time, problems of corrosivity, tedious workup, effluent pollution and non-recoverable catalysts. Consequently, there is a need to develop alternative methods for the synthesis of 2,2-bis(hydroxymethyl)propane-1,3-diol under mild and environmentally friendly conditions. Montmorillonite clays,¹ cation exchanger KU-2,² 12-tungstophosphoric acid¹² and expansive graphite,¹³ have been employed as catalysts for this purpose to obtain improved results. More recently, microwave irradiation has been applied to accelerate this condensation reaction.¹⁴

Anhydrous ferrous sulfate has been used as a catalyst for organic reactions.^{15–17} Previously we have developed an efficient and convenient method for the preparation and cleavage of 1,1-diacetates using a catalytic quantity of anhydrous ferrous sulfate.^{15,16} Herein we report a mild and efficient procedure for the synthesis of diacetals by condensation of aldehydes and ketones with 2,2-bis(hydroxymethyl)propane-1,3-diol catalysed by anhydrous ferrous sulfate in refluxing benzene or toluene.



Scheme 1 Reagents and conditions: i, anhydrous FeSO₄, benzene or toluene, reflux 0.8–10 h, 0–99%.

When several aldehydes or ketones **1** in the presence of anhydrous ferrous sulfate were heated with 2,2-bis(hydroxymethyl)propane-1,3-diol **2** in refluxing benzene or toluene, the corresponding diacetals **3** are obtained in good to excellent yield (Scheme 1) except for benzophenone (**1s**, no reaction), and results are summarised in Table 1.

The reaction rate is markedly dependent on temperature. We found that the reaction proceeded much slower in refluxing benzene than in refluxing toluene. For example, complete conversion of 4-methoxybenzaldehyde (**1d**) to the corresponding diacetal (**3d**) required 0.8 h in refluxing toluene *cf.* 1.5 h in refluxing benzene in the presence of anhydrous ferrous sulfate as catalyst. Ketones show lower reactivity than aldehydes for this reaction, for example, dibenzal-pentaerythritol (**3b**) was obtained in 98% yield in refluxing toluene for 0.8 h whereas the conversion rate of acetophenone (**1q**) was 87% in refluxing toluene over 8 h in the presence of anhydrous ferrous sulfate. Benzophenone (**1s**) failed to give the corresponding diacetal and the starting materials were quantitatively recovered. It is worth noting that when 4-hydroxybenzaldehyde (**1k**) and 4-(dimethylamino)benzaldehyde (**1m**) were treated with 2,2-bis(hydroxymethyl)propane-1,3-diol in the presence of anhydrous ferrous sulfate, the reactions required longer times even when the reaction mixtures were refluxed in toluene. The explanation for this result may be due to the strong electron donating hydroxy and dimethylamino groups in **1k** and **1m** which will reduce the reactivity. A degree of tautomerisation may occur in **1k** and **1m** with formation of quinoid structure and thus decreased reactivity of the corresponding aldehyde groups. An intramolecular hydrogen bond in **1j** and **1l** would prevent the formation of a quinoid structure.

The catalysts are easily regenerated by washing with dichloromethane and then drying at 180 °C under reduced pressure for 0.5 h. The catalyst could be reused three times for the synthesis of pentaerythritol diacetal **3b** without significant loss of activity.

In conclusion, we have discovered an efficient and convenient method for the preparation of 2,2-bis(hydroxymethyl)propane-1,3-diol diacetals catalysed by anhydrous ferrous sulfate, characterised by operational simplicity, high yields, use of inexpensive materials, as well as being non-corrosive, minimally environmentally pollutive and employing a reusable catalyst. This procedure appears to be efficient for aldehydes, aliphatic ketones and monoaryl ketones but not for diaryl ketones.

Experimental

Anhydrous ferrous sulfate catalyst was prepared according to the literature.^{15,16} Melting points are uncorrected. ¹H NMR spectra were determined on a Varian VXR-300S spectrometer using CDCl₃ as solvent and tetramethylsilane (TMS) as internal reference. IR spectra were

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Table 1 Synthesis of diacetals catalysed by anhydrous ferrous sulfate

Entry	Aldehydes or ketones	Solvent (t/h)	Isolated yield (%)	Mp/°C	
				Found	Reported
1	<i>n</i> -C ₆ H ₁₃ CHO 1a	Benzene (1.2)	93	62–63	63 ⁵
		Toluene (0.8)	95		
2	PhCHO 1b	Benzene (1.5)	97	155–156	155–156 ¹⁴
		Toluene (0.8)	98		
3	4-MeC ₆ H ₄ CHO 1c	Benzene (1.5)	98	211–212	211–213 ¹
		Toluene (1.0)	98		
4	4-MeOC ₆ H ₄ CHO 1d	Benzene (1.5)	98	180–182	177 ⁵
		Toluene (0.8)	99		
5	3,4-(OCH ₂ O)C ₆ H ₃ CHO 1e	Benzene (2.5)	94	190–192	188 ⁵
		Toluene (1.5)	95		
6	3-ClC ₆ H ₄ CHO 1f	Benzene (2.0)	96	121–122	121–122 ¹
		Toluene (1.5)	98		
7	4-ClC ₆ H ₄ CHO 1g	Benzene (3.0)	93	196–197	197–198 ¹⁴
		Toluene (2.0)	95		
8	2-O ₂ NC ₆ H ₄ CHO 1h	Benzene (3.0)	92	162–164	163–164 ¹⁴
		Toluene (2.0)	94		
9	3-O ₂ NC ₆ H ₄ CHO 1i	Benzene (2.5)	90	185–186	185 ⁵
		Toluene (1.5)	92		
10	2-HOC ₆ H ₄ CHO 1j	Benzene (3.5)	90	160–161	160–161 ¹
		Toluene (2.5)	92		
11	4-HOC ₆ H ₄ CHO 1k	Toluene (7.0)	74	108–110	109–110 ¹⁴
12	3-MeO-4-HOC ₆ H ₃ CHO 1l	Benzene (3.0)	95	170–172	170–171 ¹
		Toluene (2.0)	95		
13	4-Me ₂ NC ₆ H ₄ CHO 1m	Toluene (8.0)	84	223–224	223 ¹
14	PhCH=CHCHO 1n	Benzene (3.0)	94	190–192	193 ⁵
		Toluene (2.0)	95		
15	2-Furaldehyde 1o	Benzene (3.0)	92	157–159	158–159 ¹⁴
16	Cyclohexanone 1p	Toluene (6.0)	90	111–113	112–113 ⁶
17	PhCOMe 1q	Toluene (8.0)	87	145–146	147–148 ¹
18	(PhCH ₂)CO 1r	Toluene (10)	89	165–167	166–167 ¹
19	Ph ₂ CO 1s	Toluene (8)	0		

obtained on a Perkin-Elmer 983G spectrometer. The products were also characterised by comparison of their melting points with literature values.

General Procedure for the Preparation of Diacetals.—A mixture of *p*-tolualdehyde **1c** (2.00 mmol), 2,2-bis(hydroxymethyl)propane-1,3-diol **2** (1.25 mmol) and anhydrous ferrous sulfate (100 mg) in benzene (10 ml) was stirred at refluxing temperature for 1.5 h (Table 1) using a Dean–Stark apparatus for water removal. The reaction was monitored by TLC. After cooling, the catalyst was removed by filtration and washed with CH₂Cl₂ (5 ml × 2). The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (light petroleum–dichloromethane as eluent) to give diacetal **3c** in 98% yield; mp 212–213 °C.

For **3c**: $\nu_{\max}/\text{cm}^{-1}$ 2910, 2862, 1600, 1460, 1390, 1050, 805; δ_{H} 2.346 (6H, s, Ar-CH₃), 3.638 (2H d, *J* 11.7 Hz), 3.813 (2H, dd, *J* 11.7, 2.4 Hz), 3.830 (2H, d, *J* 11.7 Hz), 4.853 (2H, d, *J* 11.7 Hz), 5.424 (2H, s, CHO₂), 7.181 (4H, d, *J* 8.0 Hz, 3',5'-Ar-H), 7.370 (4H, d, *J* 8.0 Hz, 2',6'-Ar-H). For **3f**: $\nu_{\max}/\text{cm}^{-1}$ 2986, 2856, 1601, 1578, 1479, 1381, 1335, 1249, 1205, 1160, 1120, 1075, 1035, 966, 896, 877, 796, 750, 703; δ_{H} 3.656 (2H, d, *J* 11.7 Hz), 3.680 (4H, d, *J* 11.7 Hz), 4.829 (2H, d, *J* 11.7 Hz), 5.432 (2H, s, CHO₂), 7.330–7.381 (6H, m, Ar-H), 7.503 (2H, s, 2'-Ar-H). For **3j**: δ_{H} 3.703 (2H, d, *J* 11.7 Hz), 3.903 (2H, dd, *J* 11.7, 2.4 Hz), 3.918 (2H, d, *J* 11.7 Hz), 4.847 (2H, d, *J* 11.7 Hz), 5.655 (2H, s, CHO₂), 6.872–7.284 (8H, A'ABB', Ar-H), 7.565 (2H, s, Ar-OH). For **3q**: δ_{H} 1.502 [6H, s, C(CH₃)O₂], 3.145 (2H, dd, *J* 11.1, 2.4 Hz), 3.255 (2H, d, *J* 11.7 Hz), 3.631 (2H, d, *J* 11.7 Hz), 4.477 (2H, dd, *J* 11.7, 1.8 Hz), 7.313–7.425 (8H, m, Ar-H). For **3r**: δ_{H} 2.878 (8H, s, Ar-CH₂O), 3.589 (8H, s, CHO), 7.142–7.332 (20H, m, Ar-H).

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