Montmorillonite Clay Catalysis. Part 2.[1] An Efficient and Convenient Procedure for the Preparation of Acetals catalysed by Montmorillonite K-10†

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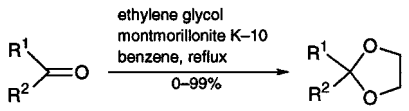
Acetalization of aldehydes and ketones is catalysed by montmorillonite K-10 in refluxing benzene or toluene in excellent yields.

The protection of aldehydes and ketones by the formation of acetals is important in the preparation of a variety of multifunctional organic molecules.[2] Numerous publications have described the formation of acetals under acidic conditions,[3] the main disadvantages of these methods being the use of uncommon reagents and difficult work-up. Clay minerals are known to catalyse a variety of organic reactions in which the clay catalyst acts as a solid Lewis acid or Brønsted acid.[4] Montmorillonite clay is inexpensive and offers several advantages over the classic acid: strong acidity, non-corrosivity, mild reaction conditions, high yield and selectivity, and ease of set-up and work-up.[5] Montmorillonite has also been used to catalyse the acetalization and thioacetalization of carbonyl compounds with trimethyl orthoformate,[6] benzene-1,2-dimethanol,[7] (*Z*)-but-2-ene-1,4-diol[8] and ethane-1,2-dithiol.[9] However, the formation of acetals with ethylene glycol directly catalysed by montmorillonite clays has not been reported. We now describe a direct acetalization of aldehydes and ketones with ethylene glycol catalysed by montmorillonite K-10.

As shown in Table 1 several aldehydes, ketones and steroidal ketones in the presence of montmorillonite K-10 were heated with ethylene glycol in refluxing benzene or toluene, resulting in the corresponding acetals in excellent yields except for benzophenone (entry 7, no reaction) and the two steroidal C-20 ketones (entries 17 and 18). The two aromatic ketones (**1e**,**f**) were not completely converted into the corresponding acetals (**2e**,**f**) after refluxing in benzene for 6 h. Acetals **2k**, **l**, **n**, **p** and **r** are new compounds. The acetal structures were confirmed by comparison with authentic samples (IR, NMR and mass spectra). Hydrolysis of these acetals provided original aldehydes and ketones.

It is worth noting that the steroidal 4-en-3-one system gave the double-bond-migrated products (entries 10 and 13) under these acetalization conditions. However, 4-methylcholest-4-en-3-one (**1l**) provided a mixture of the double-bond-retained product **2k** and the double-bond-migrated product **2l** in a ratio of *ca*. 1:2 as indicated by ^{1}H NMR. The mixture of **2k** and **2l** was inseparable either on silica gel chromatography or on silver nitrate impregnated silica gel chromatography.[10]



1 **2**

Table 1 Formation of acetals catalysed by montmorillonite K-10

Entry	Carbonyl compound	Acetal	Solvent	*t*/h	Yield (%)[a]
1	Benzaldehyde (**1a**)	2-Phenyl-1,3-dioxolane (**2a**)	Benzene	0.5	98
2	2-Furaldehyde (**1b**)	2-(2-Furyl)-1,3-dioxolane (**2b**)	Benzene	1	99
3	Cyclooctanone (**1c**)	1,1-Ethylenedioxyoctane (**2c**)	Benzene	1.5	93
4	Ethyl acetoacetate (**1d**)	Ethyl 3,3-ethylenedioxybutyrate (**2d**)	Benzene	6	98
5	4-Nitroacetophenone (**1e**)	2-Methyl-2-(4-nitrophenyl)-1,3-dioxolane (**2e**)	Benzene	6	99[b]
6	4-Methoxyacetophenone (**1f**)	2-Methyl-2-(4-methoxyphenyl)-1,3-dioxolane (**2f**)	Benzene	6	88
7	Benzophenone (**1g**)	2,2-Diphenyl-1,3-dioxolane (**2g**)	Toluene	6	0[c]
8	5α-Cholestan-3-one (**1h**)	3,3-Ethylenedioxy-5α-cholestane (**2h**)	Benzene	2	98
9	5β-Cholestan-3-one (**1i**)	3,3-Ethylenedioxy-5β-cholestane (**2i**)	Benzene	2	98
10	Cholest-4-en-3-one (**1j**)	3,3-Ethylenedioxycholest-5-ene (**2j**)	Benzene	2	98
11	Cholest-5-en-3-one (**1k**)	**2j**	Benzene	2	98
12	4-Methylcholest-4-en-3-one (**11**)	4-Methyl-3,3-ethylenedioxycholest-4-ene (**2k**, 33%) + 4-methyl-3,3-ethylenedioxycholest-5-ene (**21**, 67%)	Benzene	5	98
13	17β-Propionyloxyandrost-4-en-3-one (**1m**)	17β-Propionyloxy-3,3-ethylenedioxyandrost-5-ene (**2m**)	Benzene	2	99
14	4,4-Dimethylcholest-5-en-3-one (**1n**)	4,4-Dimethyl-3,3-ethylenedioxycholest-5-ene (**2n**)	Benzene Tolune	5 2	96 75
15	3β-Acetoxyandrost-5-en-17-one (**1o**)	3β-Acetoxy-17,17-ethylenedioxyandrost-5-ene (**2o**)	Benzene	7	95
16	Androsta-3,5-dien-17-one (**1p**)	17,17-Ethylenedioxyandrosta-3,5-diene (**2p**)	Benzene Toluene	7 1	97 82
17	3β-Acetoxypregn-5-en-20-one (**1q**)	3β-Acetoxy-20,20-ethylenedioxypregn-5-ene (**2q**)	Toluene	3	12
18	Pregna-3,5-dien-20-one (**1r**)	20,20-Ethylenedioxypregna-3,5-diene (**2r**)	Benzene Toluene	5 4	34 23

[a]Isolated yield. [b]Net yield, conversion rate of **1e** = 65%; conversion rate of **1f** = 96%. [c]100% of **1g** was recovered.

This procedure appears to be efficient for aldehydes, aliphatic ketones and monoaryl ketones but not for diaryl ketones.

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Experimental

Melting points and boiling points are uncorrected. Elemental analyses were performed on a Heraeus CHN-O Rapid instrument. IR spectra were obtained on a Perkin-Elmer 983G spectrometer as films. ^{1}H and ^{13}C NMR spectra were determined on Bruker AC-80 and Bruker AM-400 spectrometers, using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal reference. Mass spectra were performed on a VG 7070E spectrometer, EI, 70 eV.

Caution: Although most of the reactions were carried out in benzene, whenever possible the authors advise the use of toluene as a substitute due to the hazardous nature of benzene.

General Procedure for the Formation of Acetals.—A mixture of carbonyl compound (**1**, 1.00 mmol), ethylene glycol (2.00 mmol), and montmorillonite K-10 (300 mg) in benzene or toluene (20 ml) was stirred at reflux for 0.5–7 h (Table 1) using a Dean-Stark apparatus to remove water. After cooling, the catalyst was removed by filtration and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel to give acetals **2**, yield 0–99% (Table 1).

Physical and spectroscopic data. For **2a**: bp 125–127 °C/30 Torr (lit.,[11] 101 °C/10 Torr). For **2b**: bp 118–120 °C/32 Torr (lit.,[12] 60 °C/0.35 Torr). For **2c**: bp 128–130 °C/35 Torr (lit.,[13] 76–77 °C/5 Torr). For **2d**: bp 135–137 °C/30 Torr (lit.,[14] 88 °C/5 Torr). For **2e**: mp 72–74 °C (lit.,[15] 72–73.5 °C). For **2f**: mp 34–36 °C (lit.,[16] 35–36 °C). For **2h**: mp 112–114 °C (lit.,[17] 110–112 °C). For **2i**: mp 76–78 °C (lit.,[17] 77–78.5 °C). For **2j**: mp 133–134 °C (lit.,[18] 129–131 °C). Mixture of **2k** and **2l**, mp 140–145 °C (colourless needles from methanol) (Found: C, 81.71; H, 11.41. $C_{30}H_{50}O_2$ requires C, 81.39; H, 11.38%); δ_H (**2k**) 0.70 (3 H, s, 18-Me), 0.86 (6 H, d, *J* 6.6 Hz, 26,27-di-Me), 0.90 (3 H, d, *J* 6.4 Hz, 21-Me), 1.04 (3 H, s, 19-Me), 1.76 (3 H, s, 4-Me), 3.74 (4 H, m, OCH_2CH_2O); δ_H (**2l**) (400 MHz), 0.678 (3 H, s, 18-Me), 0.863, 0.866 (6 H, 2d, *J* 6.6 Hz, 26,27-di-Me), 0.913 (3 H, d, *J* 6.5 Hz, 21-Me), 0.998 (3 H, d, *J* 6.6 Hz, 4-Me), 1.056 (3 H, s, 19-Me), 3.89–3.99 (4 H, m, OCH_2CH_2O), 5.43 (1 H, m, 6-H); *m*/*z* (mixture of **2k** and **2l**) 442 (10%, M^+), 427 (9), 398 (5), 355 (3), 243 (3), 163 (4), 138 (8), 123 (9), 99 (100). For **2m**: mp 210–212 °C (lit.,[19] 201–202 °C). For **2n**: mp 127–129 °C (colourless needles from methanol) (Found: C, 81.63; H, 11.41. $C_{31}H_{52}O_2$ requires C, 81.52; H, 11.48%); δ_H 0.67 (3 H, s, 18-Me), 0.86 (6 H, d, *J* 6.0 Hz, 26,27-di-Me), 0.91 (3 H, d, *J* 6.0 Hz, 21-Me), 1.05 (3 H, s, 19-Me), 1.13 (3 H, s, 4-Me), 1.24 (3 H, s, 4-Me), 3.94 (4 H, s, OCH_2CH_2O), 5.52 (1 H, m, 6-H); δ_C (100 MHz, number of carbon atoms) 11.87 (18), 18.71 (21), 20.58 (11), 21.71 (4α-Me), 22.40 (19), 22.58 (26), 22.84 (27), 23.85 (15), 24.21 (23), 26.84 (2), 28.02 (25), 28.30 (12), 29.22 (4β-Me), 30.91 (8), 32.36 (7), 35.27 (1), 35.81 (20), 36.16 (10), 36.21 (22), 39.54 (24), 39.76 (16), 42.44 (13), 44.81 (4), 50.57 (9), 56.00 (17), 57.20 (14), 64.86, 65.23 (OCH_2CH_2O), 113.21 (3), 119.91 (6), 149.68 (5); *m*/*z* 456 (2%, M^+), 441 (0.5), 356 (2), 315 (0.6), 243 (0.7), 201 (0.7), 99 (100). For **2o**: mp 142–144 °C (lit.,[20] 135–137 °C). For **2p**: mp 106–108 °C (colourless platelets from methanol) (Found: C, 80.50; H, 9.77. $C_{21}H_{30}O_2$ requires C, 80.21; H, 9.62%); ν_{max}/cm^{-1} (film) 3015, 2935, 2870, 1456, 1375, 1301, 1175, 1040; δ_H 0.88 (3 H, s, 18-Me), 0.95 (3 H, s, 19-Me), 3.87 (4 H, s, OCH_2CH_2O), 5.3–6.0 (3 H, m, 3-H, 4-H, 6-H); δ_C 14.32 (18), 18.80 (19), 20.39 (11), 22.88 (15), 23.03 (2), 30.61 (12), 31.12 (16), 32.08 (7), 33.78 (8), 34.23 (1), 35.78 (10), 42.5 (13), 48.24 (9), 50.85 (14), 64.56, 65.19 (OCH_2CH_2O), 112.6 (17), 122.85 (6), 125.06 (4), 128.95 (3), 141.2 (5); *m*/*z* 314 (46%, M^+), 299 (5), 252 (83), 237 (23), 226 (50), 213 (21), 145 (16), 99 (100). For **2q**: mp 156–158 °C (lit.,[21] 159–161 °C). For **2r**: mp 116–119 °C (colourless needles from methanol) (Found: C, 80.65; H, 10.11. $C_{23}H_{34}O_2$ requires C, 80.65; H, 10.00%); ν_{max}/cm^{-1} (film) 3015, 2940, 2870, 1440, 1370, 1241, 1148, 1050; δ_H 0.80 (3 H, s, 18-Me), 0.95 (3 H, s, 19-Me), 1.29 (3 H, s, 21-Me), 3.90 (4 H, brs, OCH_2CH_2O), 5.3–6.0 (3 H, m, 3-H, 4-H, 6-H); *m*/*z* 342 (3, M^+), 327 (2), 287 (7), 213 (3), 145 (3), 105 (4), 87 (100).

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