

Per-O-acetylation of Sugars Catalysed by Montmorillonite K-10

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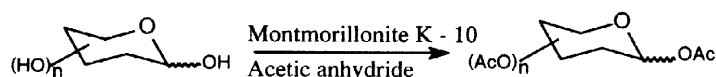
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Abstract: *The inexpensive solid acid, montmorillonite K-10, is shown to be an efficient catalyst for the per-O-acetylation of several mono -, di - and trisaccharides. The pyranose forms accounted for 75 - 100% of the acetylated products.* © 1998 Elsevier Science Ltd. All rights reserved.

The application of inorganic solid acids as heterogeneous catalysts for the organic synthesis is an area of intense research. Montmorillonite clays have been shown to function as effective catalysts for liquid - phase organic transformations.¹ Positive features of these inexpensive clays include stability, ease of handling, lack of corrosion and other environmental hazards and ease of regeneration. Montmorillonite K-10 has been employed in carbohydrate chemistry to catalyse the formation of isopropylidene acetals,^{2a} removal of acetal, silyl and 4,4'-dimethoxytrityl protecting groups,^{2b} O-glycosidation involving trichloroacetimidate donors,^{2c} C-glycosidation of glycals^{2d} and unprotected sugars^{2e} and inter - and intramolecular Ferrier reactions.^{2f,2g}

Per-O-acetylation is most commonly used for the protection of hydroxyl groups in sugars. Fully acetylated sugars are inexpensive and very useful intermediates for the synthesis of many naturally occurring glycosides, oligosaccharides and glycoconjugates. Moreover, structural elucidation of such natural products is often facilitated by transformation to their per-O-acetates. Acetylation of sugars is invariably carried out using acetic anhydride as the reagent and the catalysts^{3a,3b} employed include pyridine, sodium acetate, zinc chloride, ferric chloride, sulphuric acid and ion - exchange resin. Pyridine which functions as both solvent and a nucleophilic catalyst is the most widely used catalyst in spite of its well known acute toxicity and disagreeable odor.⁴ Handling of large volumes of pyridine and other homogeneous catalysts is troublesome and their recovery is also difficult. Large scale acetylation involving sodium acetate requires special modification of the apparatus to keep the reaction under control.⁵ Iodine has recently been shown to be a versatile promoter.⁶ The work - up, however is elaborate and iodine is not recovered. Prompted

by the recent report of montmorillonite K-10 catalysed acetylation of simple alcohols,⁷ we explored the per-O-acetylation of sugars. We report herein that montmorillonite K-10 is an efficient and environment friendly catalyst for the preparation of sugar per-O-acetates (Scheme 1)



Scheme 1

In a typical reaction procedure,⁸ montmorillonite K-10 (1g) was added to a stirred suspension of D-glucose (2 mmol) in acetic anhydride (5 ml) at 0°C. After 15 minutes, the reaction mixture was brought to room temperature and stirring continued for 5 hours and 45 minutes. Completion of reaction was indicated by the disappearance of D-glucose on TLC. The catalyst was then filtered and washed with dichloromethane. The filtrate combined with washings was concentrated to dryness under reduced pressure to obtain a colourless solid.

As shown in Table 1, several monosaccharides (entries 1-8), disaccharides (entries 9-13) and a trisaccharide (entry 14) were acetylated in excellent yields with the exception of cellobiose. The partial conversion of the latter is presumably due to its poor solubility. Use of 0.5 g of the catalyst in the above procedure nearly doubled the reaction time, whereas its exclusion from the reaction mixture did not lead to any per-O-acetate detectable by TLC even after prolonged reaction time (24 h). The successful acetylation of even a trisaccharide shows the generality of the method.

The composition of the per-O-acetylated products was arrived at based on 300 MHz ¹H-NMR spectral analysis.^{3b,9a-f} The pyranose anomers accounted for 75-100% of the products. Formation of α and β-furanose per-O-acetates was observed mostly in the case of monosaccharides. In the case of D-xylose and L-arabinose, a tiny amount of a hexaacetate derivative of the acyclic aldehyde^{3b,9d} was also formed. The composition of per-O-acetates obtained from D-glucose and D-mannose (from the same batch used in the present study) using pyridine and acetic anhydride turns out to be 94% α & 6% β and 79 α & 21% β pyranose forms respectively. As pyridine is known to bring about acetylation without anomerisation,¹⁰ these data represent initial composition of the free sugars. Comparison of these data with those of entry 1 and 4 in Table 1 reveals the partial anomerisation and acetolysis occurring under montmorillonite K-10 catalysed conditions. Methyl-α-D-glucopyranoside, however, was smoothly transformed to its tetra-O-acetate without any ring modification or anomerisation. With the exception of melibiose, all disaccharides examined also underwent smooth conversion to afford only a mixture of pyranose per-O-acetates. Formation of 7% of furanose forms in the case of melibiose may be due to the greater flexibility of 1,6-linkage that lends itself to limited acetolysis. Use of ferric chloride as the acetylating agent for methyl glycosides^{3b,9c} and disaccharides^{3b} has been reported to result in considerable acetolysis of glycosidic linkage. Montmorillonite K-10 proves to be a milder acetylating agent in this regard.

Table 1 : Montmorillonite K-10 Catalysed Reaction of Sugars with Acetic anhydride

Entry	Sugar Substrate	Time (h)	Per-O-acetate yield ^a (%)	Composition ^b				
				Pyranose Form			Furanose Form	
				α	β	$\alpha+\beta$	α	β
1.	D-Glucose	6	94	60	33	93	3	4
2.	Methyl- α -D-glucopyranoside	4	99	100	-	100	-	-
3.	D-Galactose	10	92	55	20	75	8	17
4.	D-Mannose	2	96	60	32	92	5	3
5.	L-Fucose	1	97	58	28	86	5	9
6.	N-Acetyl-D-glucosamine	4	86	30	64	94	4	2
7.	D-Xylose	2	94	53	28	81	9	8 ^c
8.	L-Arabinose	2	99	51	28	79	8	11 ^c
9.	α,α -Trehalose	16	98	100	-	100	-	-
10.	Maltose	12	98	24	76	100	-	-
11.	Cellobiose	48	36	26	74	100	-	-
12.	Lactose	12	98	61	39	100	-	-
13.	Melibiose	36	94	53	40	93	3	4
14.	Raffinose	12	98	-	-	-	-	> 96 ^d

^a Isolated yield; ^b for entries 9-14 anomeric composition refers to the reducing end; ^c in each case 2% of the acyclic hexacetate was also formed; ^d the minor component is not identified.

In conclusion, we have developed an efficient, convenient and environment - friendly method for the acetylation of sugars using the inexpensive montmorillonite K-10 as the heterogeneous catalyst.

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