

Green procedures for the chemoselective synthesis of acylals and their cleavage promoted by recoverable sulfonic acid based nanoporous carbon (CMK-5-SO₃H)

DARYOUSH ZAREYEE*, EHSAN MIRZAJANZADEH and MOHAMMAD ALI KHALILZADEH

Department of Chemistry, Qaemshahr Branch, Islamic Azad University, Qaemshahr, Iran
e-mail: zareyee@gmail.com

MS received 14 January 2015; revised 15 March 2015; accepted 28 March 2015

Abstract. A selective synthesis of gem-diacetates from the reaction of aldehydes and acetic anhydride in the presence of recyclable nanoporous solid sulfonic acid (CMK-5-SO₃H) under solvent-free reaction conditions is reported. The catalyst was also found to be highly active for deprotection of resulting acylals in water.

Keywords. 1,1-Diacetates; acylals; solvent-free; water; CMK-5-SO₃H; heterogeneous sulfonic acid

1. Introduction

From the green chemistry point of view, safety considerations and the simplicity of the process, implementation of methods that avoid the use of harmful organic solvents are fundamental strategies. In this context, with an objective to develop environmentally benign reaction media and conditions for organic reactions with excellent efficiency, solvent-free conditions or using water as the green solvent have aroused considerable attention.^{1–5} Consequently, it is important to investigate new catalysts for organic reactions using less hazardous solvents.

Acylals have often been used as protecting groups for carbonyl compounds because of their stability in neutral and basic conditions and ease of chemoselective preparation in the presence of ketone.^{6,7} Hence, they play an important role for the protection of aldehydes in multi-step organic synthesis. Accordingly, methods for their synthesis have received considerable attention.

Generally, acylals can be prepared from aldehydes by treatment with acetic anhydride and Brønsted acids,^{7–9} Lewis acids,^{10–14} or inorganic heterogeneous catalysts.^{15,16,16–21} However, while acknowledging the pioneering advances in this area, some of these methods suffer from disadvantages such as the use of hazardous organic solvents, harsh reaction conditions, low yields, tedious work-up and effluent pollution. Moreover, some of these procedures are not chemoselective in terms of aldehydes and keto carbonyl functional groups. Additionally, a few of the above

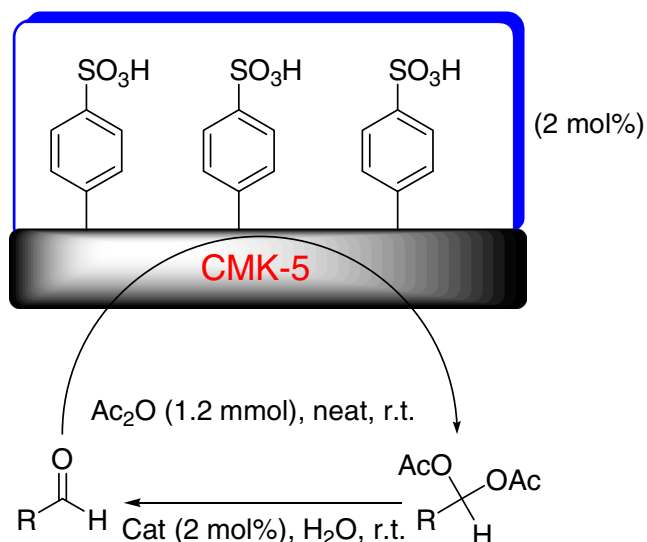
mentioned catalysts are claimed to give protection as well as deprotection. Therefore, the development of efficient, recyclable and environmentally benign catalytic methods for these transformations by using non-polluting reagents and solvents is desirable. Along this line, very recently, we used sulfonic acid nanoreactor SBA-15-Ph-PrSO₃H in the synthesis of gem-diacetates under solvent-free reaction conditions. In continuation of our studies toward the development of new and cleaner methods for organic transformations,^{22–25} we report herein the results of chemoselective preparation of acylals under solvent-free reaction conditions and deprotection of the corresponding acylals in water as green solvent at room temperature using catalytic amounts of heterogeneous recyclable sulfonic acid CMK-5-SO₃H (scheme 1).

2. Experimental

2.1 General procedure for the preparation of 1,1-diacetates

To a mixture of aldehyde (1 mmol) and freshly distilled acetic anhydride (1.2 mmol) was added (0.023g, 1 mol%) CMK-5-SO₃H, and the whole mixture was stirred in a round bottomed flask at room temperature for the appropriate time (table 1). The reaction progress was followed by GC and TLC (eluent, n-hexane:ethyl acetate, 4:1). After completion of the reaction, EtOAc was added to the reaction mixture, and the resulting mixture was filtered and then the extracts concentrated

*For correspondence



Scheme 1. Synthesis of gem-diacetates and their deprotection using catalyst CMK-5-SO₃H.

under vacuum. The pure product was isolated following silica gel column chromatography to afford pure acylals. Spectroscopic data for selected examples listed below.

(Entry 1): ¹H NMR (400 MHz; CDCl₃): δ_H = 2.15 (s, 6H), 7.41–7.55 (m, 5H), 7.70 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ_C = 20.9, 89.7, 126.7, 128.6, 129.8, 135.5, 168.8.

(Entry 3): ¹H NMR (400 MHz; CDCl₃): δ_H = 2.14 (s, 6H), 7.33–7.52 (m, 4H), 7.64 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ_C = 20.8, 88.8, 125.0, 126.8, 129.91, 129.97, 134.5, 137.2, 168.7.

(Entry 14): ¹H NMR (400 MHz; CDCl₃): δ_H = 2.17 (s, 6H), 7.70 (s, 1H), 7.73 (d, 2H), 8.28 (d, 2H); ¹³C NMR (100 MHz, CDCl₃): δ_C = 20.8, 88.3, 123.9, 127.9, 141.8, 148.6, 168.6.

(Entry 20): ¹H NMR (400 MHz; CDCl₃): δ_H = 2.12 (s, 6H), δ_H = 2.36 (s, 3H), 7.13–7.15 (d, J = 8.4 Hz, 1H), 7.31–7.34 (t, J = 7.6 Hz, 1H), 7.43–7.47 (t, J = 7.6 Hz, 1H), 7.65–7.67 (d, J = 7.8 Hz, 1H), 7.92 (s, 1H).

2.2 General procedure for deprotection of 1,1-diacetates

To a stirred mixture of aldehyde (1 mmol) and acetic anhydride (1.2 mmol), CMK-5-SO₃H (0.023g, 1 mol%) was added, and the mixture was stirred at room temperature for the appropriate time (table 1). The reaction progress was followed by GC. After completion of the protection reaction, water (3 mL) was added to the reaction mixture to perform the deprotection reaction. After completion of the cleavage reaction, Et₂O (20 mL) was added and the reaction mixture was filtered to separate

the catalyst. The solvent was evaporated under reduced pressure to afford the corresponding aldehydes.

2.3 Preparation of CMK-5

Templated synthesis of CMK-5 has been achieved using known procedure described by Ryoo and co-workers.^{26,27} Initially, Al was incorporated into SBA-15²⁸ (molar ratio Si/Al = 20) by well dispersion of calcined SBA-15 into an aqueous solution of AlCl₃, followed by removal of H₂O by rotary evaporator and calcination in air. Impregnation of Furfuryl alcohol (FA) into Al-SBA-15 was achieved by incipient wetness infiltration at room temperature. The mixture was then heated up at 80°C oven for 16 h for Al-catalyzed polymerization of FA. The obtained composite was recovered by filtration to remove excess and unpolymerized FA, and washed by EtOH and acetone. The composite was heated to 850°C under vacuum at a ramp of 10°C/min, and the carbonization was carried out at the same temperature for 3 h under vacuum. Ordered mesoporous carbon (CMK-5) was obtained by removal of silica template by HF (10% in 1: 1 EtOH – H₂O), washed with copious water and EtOH, and finally dried at 100°C.

2.4 Preparation of sulfonated ordered mesoporous carbon (CMK-5-SO₃H)

In a typical modification, 1.2 g of CMK-5 was added in a three-necked round bottom flask containing 12.0 g of 4-benzene-diazoniumsulfonate²⁹ in 200 mL of distilled water and 200 mL of ethanol. Subsequently, the mixture was cooled down to 5°C and 200 mL of 50 wt% H₃PO₂ aqueous solution was added. After stirring for 30 min, another 200 mL of H₃PO₂ aqueous solution was added. The mixture was stirred at 5°C for another 30 min. The sulfonic acid functionalized carbon material (denoted as CMK-5-SO₃H) was recovered by filtration, washed thoroughly with distilled water and finally acetone, and dried in an oven at 80°C.

3. Results and Discussion

For our initial protection studies, we carried out the reaction between 1 mmol benzaldehyde, 1 mmol Ac₂O and 1 mol% catalyst at room temperature under solvent free reaction conditions to afford the desired acylal. It was observed that the starting material was consumed after long reaction time (90 min) as indicated by GC analysis. To optimize the reaction conditions, the reaction was performed using 1.2 mmol acetic anhydride in

Table 1. CMK-5-SO₃H catalyzed solvent-free acylal formation, and acylal deprotection in water.

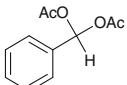
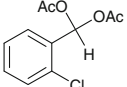
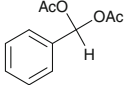
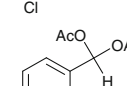
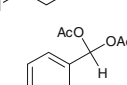
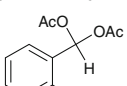
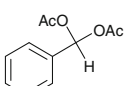
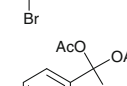
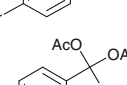
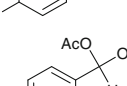
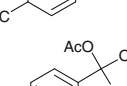
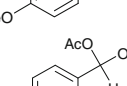
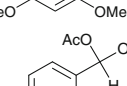
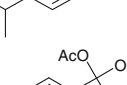
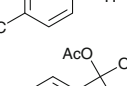
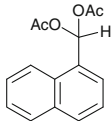
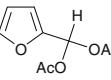
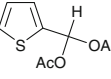
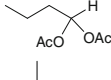
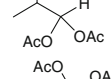
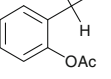
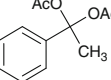
Entry	1,1-Diacetates	Preparation		Deprotection	
		Time (min)	Yield ^{a,b} (%)	Time (min)	Yield ^{a,c} (%)
1		10	97	10	98
2		35	97	15	98
3		20	93	15	96
4		20	94	15	99
5		40	89	25	92
6		35	98	15	92
7		25	98	15	93
8		20	99	15	95
9		20	99	20	96
10		30	99	10	94
11		30	95	10	95
12		40	98	10	90
13		25	95	10	96
14 ^d		45	98	15	90
15 ^d		50	90	20	89

Table 1. continued.

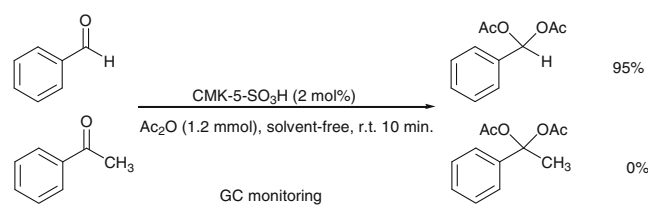
Entry	1,1-Diacetates	Preparation		Deprotection	
		Time (min)	Yield ^{a,b} (%)	Time (min)	Yield ^{a,c} (%)
16		10	98	35	92
17		10	96	15	93
18		15	97	15	94
19		25	94	20	89
20		25	92	20	90
21		30	90	40	92 ^e
22		24h	No reaction	-	-

^aGC Yields. ^bReaction conditions: aldehyde (1 mmol), Ac₂O (1.2 mmol), CMK-5-SO₃H (2 mol%), room temperature, solvent-free. ^cAll deprotection reactions were carried out at room temperature using water as solvent. ^d1.5 mmol Ac₂O was used. ^e2 mmol Ac₂O was used.

the presence of 2 mol% catalyst (scheme 1), and considerable improvement was observed in the yield of product after 10 minute (table 1, entry 1). It is also important to mention that when the same reaction was performed without catalyst and no product was obtained.

To generalize the scope and versatility of this protocol, different substituted aldehydes were used for the synthesis of substituted acylals. Aldehydes bearing both electron-donating and electron-withdrawing substituents resulted in the corresponding acylals in good to excellent yields (table 1, entries 1–15). The catalyst was also found to be active for the preparation of acylal from sterically hindered aldehyde, 1-naphthaldehyde (table 1, entry 16). Notably, furan-2-carbaldehyde and thiophene-2-carbaldehyde as acid sensitive substrates gave the related 1,1-diacetates in excellent yields (table 1, entries 17–18). Also the present protocol works well for aliphatic aldehydes to give the corresponding geminal diacetates in excellent yields (table 1, entries 19–20). When the reaction was extended towards hydroxybenzaldehydes, the hydroxyl group was also protected as acetate (table 1, entry 21).

Under the selected conditions, acylation of ketones was not successful and the starting material was recovered unchanged even when the reaction mixture was



Scheme 2. Chemoselective acylal formation from benzaldehyde in the presence of acetophenone.

stirred for 24 h (table 1, entry 22). Encouraged by this result, in a competitive experiment, equimolar mixture of benzaldehyde and acetophenone was allowed to react with 1.2 mmol of acetic anhydride under the same reaction condition, gave only 1,1-diacetates of benzaldehyde while the ketone functionality remained unaffected (scheme 2). Hence, chemoselective acylal formation from aldehydes in the presence of ketones could be achieved with this catalytic system.

The feasibility of recyclable properties of the catalyst was examined through a series of sequential synthesis of acylal from benzaldehyde and Ac₂O as model substrates. The catalyst was easily separated by filtration after completion of each run, with addition of ethyl acetate. Interestingly, the recycled catalyst was used for

Table 2. Comparison of various methods for acylal synthesis from 4-nitrobenzaldehyde.

Entry	Catalyst (mol%)	Equiv. of Ac ₂ O	Solvent	T (°C)	Time (min/[h])	Yield (%)
1	CMK-5-SO ₃ H (2)	1.2	Solvent free	rt	50	90 ^a
2	CAN (10)	2	Solvent free	rt	[24]	96 [12] ^{b,c,d}
3	KHSO ₄ (10)	2	Solvent free	rt	90	96 [27] ^{b,c}
4	LiOTf (20)	5–8	Solvent free	rt	[15]	94 [28] ^{b,c,d,e}
5	Cu(OTf) ₂ (2.5)	3	CH ₂ Cl ₂	rt	[4]	94[29] ^{c,d,f}
6	AlPW ₁₂ O ₄₀	1	CH ₂ Cl ₂	rt	45	89 [30] ^{c,f}
7	In(OTf) ₃	1.2–1.5	CH ₂ Cl ₂	rt	15	99[11] ^{c,f}

^aThis work. ^bHigh catalyst loading. ^cNon-recoverable catalyst. ^dLong reaction time. ^eExcess amount of Ac₂O. ^fToxic solvent (CH₂Cl₂).

eight consecutive runs without any appreciable change in catalytic activity.

In order to show the efficiency of the present method, we have compared our results obtained from the acetylation of 4-nitrobenzaldehyde with acetic anhydride catalyzed by CMK-5-SO₃H with other results reported in the literature. As can be seen in table 2, this method avoids some disadvantages of other procedure such as long reaction times^{12,31,32} toxic solvents,³² excess reagents,^{31,32} and non-recoverable catalyst.^{11,12,29–33}

In addition to these results, to evaluate the cleavage of resulting acylals, we also investigated the deprotection procedure by addition of water as a green solvent to the reaction mixture. Indeed, when the formation of 1,1-diacetates were completed, water was added. All reactions were performed at room temperature in good to high yields (scheme 1, table 1).

4. Conclusion

To summarize, we have reported an efficient, green, and chemoselective method for the preparation of gem-diacetates from aldehydes under solvent-free reaction conditions at room temperature using heterogeneous CMK-5-SO₃H. Deprotection of the resulting 1,1-diacetates can also be achieved by addition of water, a green solvent. The elimination of toxic solvents, simple workup procedure, excellent catalytic capacity and outstanding recyclability of catalyst make a valid contribution to the existing methodologies.

Supplementary Information

Schematic preparation of CMK-5-SO₃H (figure S1), TGA (figure S2), BJH (figure S3), N₂ ads-des (figure S4), and XRD diagrams for CMK-5 (figure S5) and CMK-5-SO₃H (figure S6), TEM image for recovered catalyst (figure S7) and copy of ¹H and ¹³C spectra for some products are available at www.ias.ac.in/chemsci.

Acknowledgements

The authors acknowledge the Islamic Azad University of Qaemshahr Research Councils for support of this work.

References

- Martins M A P, Frizzo C P, Moreira D N, Buriol L and Machado P 2009 *Chem. Rev.* **109** 4140
- Walsh P J, Li H and De Parrodi C A 2007 *Chem. Rev.* **107** 2503
- Toda F and Tanaka K 2000 *Chem. Rev.* **100** 1025
- Li C J and Chan T H 1999 *Tetrahedron* **55** 11149
- Li C J 2005 *Chem. Rev.* **105** 3095
- Greene T W and Wuts P G M 1999 In *Protective Groups in Organic Synthesis* 3rd ed. (New York: John Wiley and Sons) p. 306
- Gregory M J 1970 *J. Chem. Soc. B.* 1201
- Jin T S, Sun G, Li Y W and Li T S 2002 *Green Chem.* **4** 255
- Heravi M M, Bakhtiari K and Bamoharram F F 2006 *Catal. Commun.* **7** 499
- Aggen D H, Arnold J N, Hayes P D, Smoter N J and Mohan R S 2004 *Tetrahedron* **60** 3675
- Ghosh R, Maiti S, Chakraborty A and Halder R 2004 *J. Mol. Catal. A: Chem.* **215** 49
- Roy S C and Banerjee B 2002 *Synlett.* 1677
- Zhang X, Li L and Zhang G 2003 *Green Chem.* **5** 464
- Smitha G and Reddy Ch S 2003 *Tetrahedron* **59** 9571
- Olah G A and Mehrotra A K 1982 *Synthesis* 962
- Curini M, Epifano F, Marcotullio M K, Rosati O and Nocchetti M 2002 *Tetrahedron Lett.* **43** 2709
- Kamble V T, Jamode V S, Joshi N S, Biradara A V and Deshmukh R Y 2006 *Tetrahedron Lett.* **47** 5573
- Wu H, Shen Y, Fan L Y, Wan Y and Shi D Q 2006 *Tetrahedron* **62** 7995
- Jermey B R and Pandurangan A 2008 *Catal. Commun.* **9** 577
- Javad Kalbasi R, Massah A R and Shafiei A 2011 *J. Mol. Catal. A: Chem.* **335** 51
- Shirini F, Mamaghani M and Seddighi M 2013 *Catal. Commun.* **36** 31
- Karimi B and Zareyee D 2008 *Org. Lett.* **10** 3989
- Karimi B and Zareyee D 2009 *J. Mater. Chem.* **19** 8665

24. Zareyee D, Asghari R and Khalilzadeh M A 2011 *Chin. J. Catal.* **32** 1864
25. Zareyee D, Moosavi S M and Alaminezhad A 2013 *J. Mol. Catal. A: Chem.* **378** 227
26. Joo S H, Choi J, Oh I, Kwak J, Liu Z, Terasaki O and Ryoo R 2001 *Nature* **412** 169
27. Kurk M, Jaroniec M, Kim T W and Ryoo R 2003 *Chem. Mater.* **15** 2815
28. Yu C, Fan J, Tian B, Zhao D and Stucky G D 2002 *Adv. Mater.* **14** 1742
29. Bouchet M J, Rendon A, Wermuth C G, Goeldner M and Hirth C 1987 *J. Med. Chem.* **30** 2222
30. Heravi M M, Bakhtiari K, Taheri S and Oskooie H A 2005 *Green Chem.* **7** 867
31. Karimi B and Maleki J 2003 *J. Org. Chem.* **68** 4951
32. Chandra K L, Saravanan P and Singh V K 2000 *Synlett* 359
33. Firouzabadi H, Iranpoor N, Nowrouzi F and Amani K 2003 *Tetrahedron Lett.* **44** 3951