Pergamon

Tetrahedron Letters, Vol. 38, No. 10, pp. 1733-1736, 1997
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0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00203-7

2,2'-Bipyridinium Chlorochromate/*m*-Chloroperbenzoic Acid-Mediated Cleavage of Cyclic Acetals to Hydroxyesters[1]

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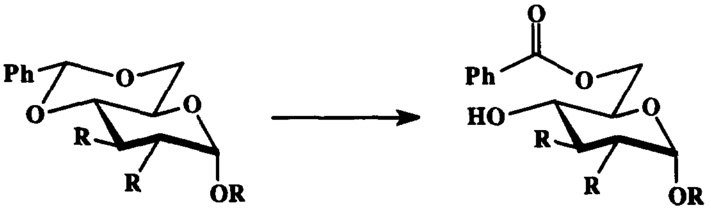
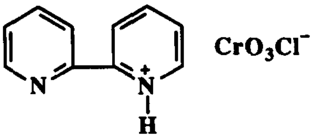
Summary: Benzylidene acetals are cleaved to hydroxyesters by means of a reagent system composed of 2,2'-bipyridinium chlorochromate (BPCC) and *m*-chloroperbenzoic acid. Oxidative cleavage of a 4,6-O-benzylidene glucose derivative affords a 6-O-benzoyl derivative. © 1997 Elsevier Science Ltd. All rights reserved.

The cleavage of cyclic ethers, ketals and acetals has widespread utility in organic synthesis and has many applications in the area of carbohydrate chemistry.[2a-d] Oxidative methods have been utilized in the carbohydrate series where the hydroxyester products of 4,6-O-benzylidene acetal cleavage are obtained regioselectively (**Eq. 1**).[2a,2d] A distinct advantage of the cleavage reaction as applied to carbohydrate chemistry is the preparation of protected glycosyl donors for polysaccharide synthesis. Chandrasekaran has reported the oxochromium(VI)-mediated cleavage reaction[3a] of five and six-membered cyclic acetals to the corresponding hydroxyesters using pyridinium dichromate/*tert*-butylhydroperoxide (PDC/TBHP) under mild conditions.[3b-f] Although the response of a wide range of substrates was examined with the (PDC/TBHP) system, these conditions have yet to be optimized with examples from the carbohydrate series. In accordance with these results we now report our initial findings in the area of benzylidene acetal cleavage utilizing an oxochromium(VI)-amine reagent system coupled with an organic peroxide. 2,2'-Bipyridinium chlorochromate (BPCC, 1), an oxochromium(VI)-amine reagent,[4] was introduced as an



Eq. 1



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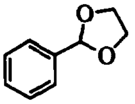
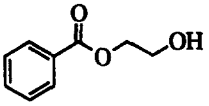
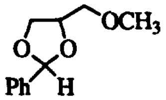
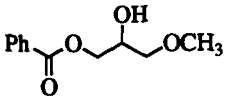
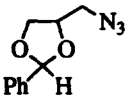
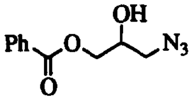
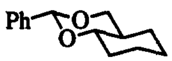
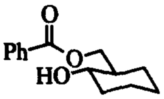
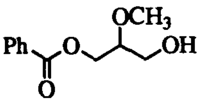
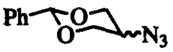
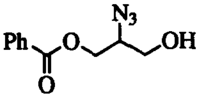
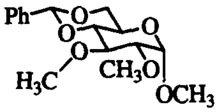
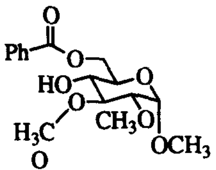
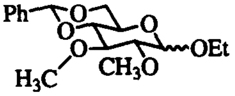
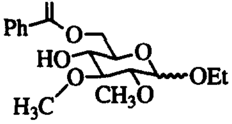
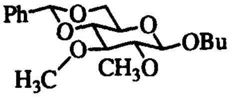
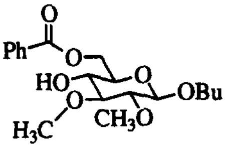
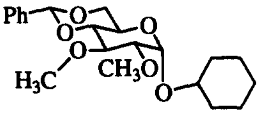
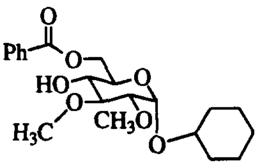
alternative to the Collins reagent, pyridinium dichromate and pyridinium chlorochromate (PCC) reagent systems for the oxidation of alcohols to carbonyl compounds. Since its introduction, BPCC was found to be effective for other types of transformations such as furan cleavage, diol cleavage, sulfide oxidation and benzylic oxidation.[5] A mixture of 2,2'-bipyridinium chlorochromate (2 eq) and *m*-chloroperbenzoic acid (5 eq) in methylene chloride[6] was found to be an optimal system for the oxidative cleavage of simple benzylidene acetal substrates to the corresponding hydroxyesters (**Table 1**). Both five-membered (Entries **1-3**) and six-membered (Entries **4-10**) acetals respond to the oxidizing system. The selectivity of the cleavage favors the primary ester/secondary alcohol product. The possible side reaction involving the oxidation of the released secondary alcohol by any excess chromium reagent is negligible. BPCC was an attractive choice in this regard since its efficiency is markedly less than that of PDC and thus overoxidation does not occur. As typical with many oxidative processes involving oxochromium(VI)-amine reagents there are functionality and protecting groups which preclude their application with certain substrates. The analogs of Entries **7-10** possessing 2,3-O-allyl and 2,3-O-benzyl ether moieties did not tolerate the reaction conditions presumably due to allylic and benzylic oxidation of the protecting groups promoted by the oxochromium(VI)-peroxide system.

Although the cleavage may involve oxochromium(VI)-promoted benzylic hydrogen abstraction followed by oxygenation of the radical center to a hemiorthoester, alkylbenzenes are not oxidized by the BPCC/MCPBA reagent system to an appreciable extent. For example, treatment of ethylbenzene under the same conditions as the examples detailed in **Table 1** resulted in less than 1% conversion to acetophenone (48 hr.) as detected by gas chromatographic analysis. Furthermore treatment of indan with the BPCC/MCPBA[7] reagent system under similar conditions as ethylbenzene resulted in a 15% isolated yield of 1-indanone as the major product. Further studies involving application of the BPCC/MCPBA to complex carbohydrate synthesis are in progress and will be the topic of future reports from our laboratory in the area of oxochromium(VI)-amine reagents.[8]

REFERENCES AND NOTES

1. Presented at the 212th National Meeting of the American Chemical Society, Orlando, Florida, August 28, 1996; ORGN 394.
2. a) Zhang, Z.; Magnusson, G. *J. Org. Chem.*, **1996**, *61*, 2394-2400. b) Arasappan, A.; Fuchs, P. L. *J. Am. Chem. Soc.*, **1995**, *117*, 177-183 and references cited therein. For a related transformation see: c) Binkley, R. W.; Goewey, G. S.; Johnston, J. C. *J. Org. Chem.*, **1984**, *49*, 992-996. d) Sato, K.; Igarashi, T.; Yanagisawa, Y.; Kawauchi, N.; Hashimoto, H.; Yoshimura, J. *Chem. Lett.*, **1988**, 1699-1702.

Table 1. Oxidative Cleavage of Benzylidene Acetals.

Entry	Substrate	Product[2]	% Yield[1]
1			72
2			71
3			70
4			67
5			69
6			73
7			70
8			79 (α) 25 (β)
9			48
10			69

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[1] Yields are of isolated pure compounds.

[2] Satisfactory spectral data were obtained for all products.

3. a) Chidambaram, N.; Bhat, S.; Chandrasekaran, S. *J. Org. Chem.*, **1992**, *57*, 5013-5015. For related transformations see: b) Huang, N. J.; Xu, L. *Synth. Commun.*, **1990**, *20*, 1563-1567. c) Hosokawa, T.; Imada, Y.; Murahashi, S. I. *J. Chem. Soc. Chem. Commun.*, **1983**, 1245-1246. d) Delongchamps, P.; Atlani, P.; Frehel, D.; Malaral, A.; Moreau, C. *Can. J. Chem.*, **1974**, 3651-3664. e) Prugh, J. D.; McCarthy, W. C. *Tetrahedron Lett.*, **1966**, 1351-1356. f) Huyser, E. S.; Garcini, Z. *J. Org. Chem.*, **1962**, *27*, 2716-2719.
4. Guziec, F. S., Jr.; Luzzio, F. A. *Synthesis*, **1980**, 691-694.
5. Luzzio, F. A.; Guziec, F. S., Jr. *Org. Prep. and Proc. Int.*, **1988**, *20*, 533-584.

6. Typical procedure for preparing hydroxyesters. (+)-6-O-Benzoyl-1,2,3-trimethyl-α-*D*-glucopyranoside: (+)-4,6-O-Benzylidene-1,2,3-trimethyl-a-*D*-glucopyranoside (200 mg, 0.64 mmol) was dissolved in methylene chloride (5 mL). To this solution was added *m*-chloroperoxybenzoic acid (0.55 g, 3.2 mmol) followed by 2,2'-bipyridinium chlorochromate (0.37 g, 1.29 mmol). The resulting red-orange suspension was stirred at room temperature during which time formation of the product was monitored by thin-layer chromatography (hexanes/ethyl acetate, 3:1; R_f=0.12. After 36 hrs the reaction mixture was diluted with ethyl acetate (15 mL) and the red-brown chromium reduction products were removed by filtration through silica gel while washing with ethyl acetate. Concentration of the filtrate and silica gel column chromatography (hexanes/ethyl acetate, 3:1) of the resulting crude residue gave the product hydroxyester 0.14 g, 0.44 mmol, (70%). ^{1}H NMR ($CDCl_3$)d: 8.04-8.02 (d, 2H); 7.55-7.53 (m, 1H); 7.43-7.40 (m, 2H); 4.85 (d, 1H); 4.66-4.63 (dd, 1H); 4.53-4.50 (dd, 1H); 3.9 (m, 1H); 3.63 (s, 3H); 3.48 (s, 3H); 3.47-3.45 (m, 2H); 3.43 (s, 3H); 3.24-3.21 (m, 1H). ^{13}C NMR ($CDCl_3$) d: 166.87; 133.2; 129.75; 128.40; 126.1; 97.50; 82.59; 70.13; 63.71; 61.37; 58.60; 55.27. IR (KBr) (cm^{-1}): 1719. $[\alpha]^{20}D$: +75.3 (*c* 0.17, CH_2Cl_2).
7. Commercially available 2,2'-bipyridinium chlorochromate (Aldrich Chemical Co.) was used for all reactions.
8. This research was assisted financially by a Fulbright-LASPAU Fellowship to RAB. An instrument grant from Glaxo-Wellcome is gratefully acknowledged.

(*Received in USA* 7 *October* 1996; *revised* 23 *January* 1997; *accepted* 26 *January* 1997)