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Note

Ce(IV) ammonium nitrate catalyzed chemoselective deprotection of acetonides

S Jana & S C Roy*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700 032, India

E-mail: ocscr@iacs.res.in

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Highly chemoselective deprotection of diacetone sugars have been achieved at room temperature in excellent yields using commercially available ceric ammonium nitrate (20 mol%) in moist CH_3CN.

Keywords: Ceric ammonium nitrate, chemoselective, deprotection, acetonide, catalysis

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Selective deprotection of functional groups is an important organic transformation during multi-step total synthesis of many complex natural products and is a crucial challenge in synthetic organic chemistry[1]. Acetonides usually act as masked hydroxyl groups in polyhydroxylated natural products, oligosaccharides and in nucleosides[2]. In the field of total synthesis of natural products or its analogues related to carbohydrate chemistry, it is frequently required to deprotect acetonide moiety selectively[3] leaving the other protecting groups intact. Generally, this transformation is accomplished by aqueous acid hydrolysis which suffers from incompatibility with many other functional groups, longer reaction time and hazardous work-up procedures. To overcome these difficulties, Lewis acid catalyzed/mediated deprotection reactions were developed[4] such as $FeCl_3.6H_2O/SiO_2$, $Zn(NO_3)_2$, $CeCl_3.7H_2O(COOH)_2$, $BiCl_3$, PMA/SiO_2, polymeric $FeCl_3$, lanthanum(III) nitrate *etc*. In continuation of the studies[5] towards developing new methodologies using cheap and commercially available ceric ammonium nitrate (CAN), herein is reported a mild and efficient chemoselective cleavage of the primary acetonide moiety of diacetone glucose derivatives catalyzed by CAN.

Results and Discussion

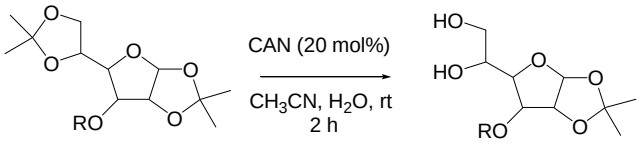
A mixture of diacetonide **1** and CAN (20 mol%)) was stirred at RT for 2 h in moist CH_3CN to afford **2** in excellent yields (**Scheme I**). The crude product was pure enough to characterize without further purification by chromatography. Thus, a series of acetonides **1a-h** were subjected to chemoselective deprotection catalyzed by CAN and the results are summarized in **Table I**.

It is noteworthy that various sensitive functional groups such as OMs, OCH_2Ph, OTBDMS, double bond and triple bonds remained unaffected under the reaction conditions. Not only acetonides but cyclohexyl protected 1,2-diols[6] **1i** and **1j** were also deprotected smoothly under the reaction conditions to furnish **2i** and **2j** in good yields as depicted in **Scheme II**. Primary acetonides are less sterically hindered as compared to the secondary acetonides and cleaved preferentially. The mechanism of this reaction is not fully studied. Since the reaction is catalytic, probably the cleavage *via* formation of a radical cation[7] does not occur in this case. This was further supported by a separate experiment where compound **1a** remained unchanged when treated with 20 mol% of CAN in moist acetonitrile in the presence of 10 equivalents of K_2CO_3 for 2 h. So, it is believed that CAN forms a small amount of HNO_3 in the presence of water which initiates the cleavage of the acetonides. It is noteworthy that the reaction did not proceed at all without the presence of a small amount of water.

In conclusion, a mild and efficient chemoselective deprotection of acetonides of diacetone glucose derivatives and deprotection of cyclohexyl protected diols have been developed using a catalytic amount of ceric ammonium nitrate (CAN) in moist acetonitrile.

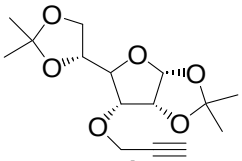
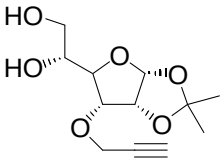
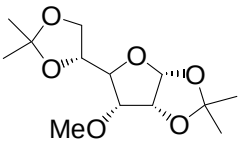
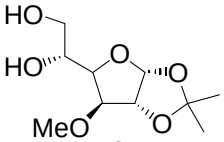
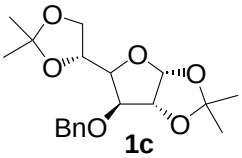
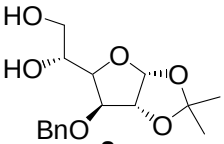
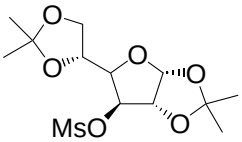
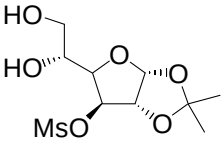
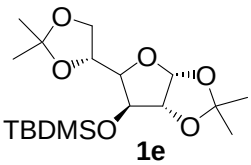
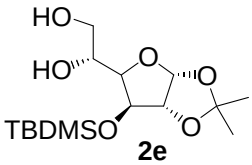
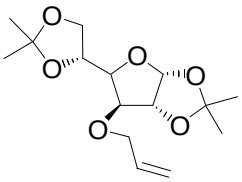
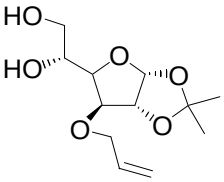
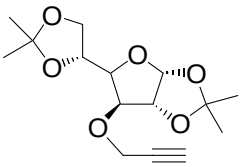
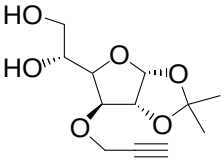
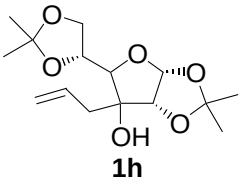
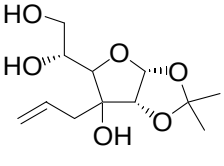
Experimental Section

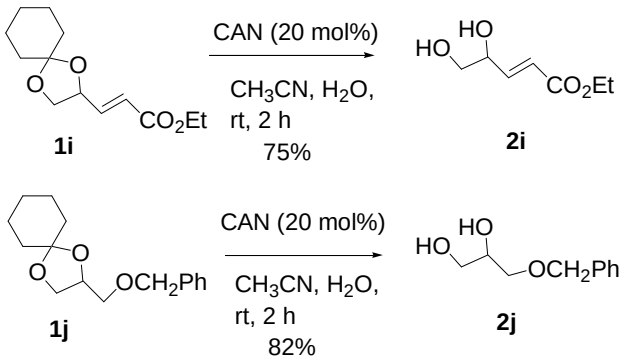
Typical procedure: To a solution of **1d** (170 mg, 0.50 mmol), in acetonitrile (3 mL) at RT, CAN (55 mg, 0.10 mmol) was added in a single lot. Then two drops of water was added and the reaction mixture



Scheme I

Table I — CAN catalysed chemoselective deprotection of acetonides

Entry	Substrate	Product	Yield (%)
1	 **1a**	 **2a**	85
2	 **1b**	 **2b**	88
3	 **1c**	 **2c**	85
4	 **1d**	 **2d**	82
5	 **1e**	 **2e**	75
6	 **1f**	 **2f**	90
7	 **1g**	 **2g**	95
8	 **1h**	 **2h**	70



Scheme II

was allowed to stir at RT for 2 h. Most of the solvent was removed under reduced pressure and the residue obtained was diluted with CH_2Cl_2 (20 mL). The organic layer was thoroughly washed with water (5 mL) followed by brine (5 mL) and finally dried over anhyd. Na_2SO_4. Evaporation of the solvent under reduced pressure afforded pure **2d** (123 mg, 82%). IR (neat): 3400, 2989, 2939, 1635, 1456, 1359 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.51 (s, 3H), 2.09 (brs, OH), 3.15 (s, 3H), 3.77 (t, *J* = 6.1 Hz, 1H), 3.87-3.92 (m, 2H), 4.25 (dd, *J* = 8.7, 2.4 Hz, 1H), 4.75 (d, *J* = 3.6 Hz, 1H), 5.13 (d, *J* = 2.4 Hz, 1H), 5.95 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.9, 26.3, 37.9, 63.7, 68.1, 78.2, 81.8, 83.1, 104.8, 112.5; HRMS calcd for $C_{10}H_{18}O_8S$ (M^++Na): 321.0612; Found 321.0618.

All other compounds were characterized by IR, NMR and HRMS analysis and by comparing the data with authentic samples[4,6].

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