reference electrode as Cs salts in aqueous 0.1M $NaClO_4$ under Ar at 24 °C with sweep rates of 100 mV s^{-1}. $HClO_4$ was used to adjust the pH.

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Cerium(IV)-Catalyzed Deprotection of Acetals and Ketals under Mildly Basic Conditions**

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Dedicated to Professor Heinz G. Viehe on the occasion of his 70th birthday

The protection – deprotection sequence is probably the most frequently encountered functional-group transformation in organic synthesis.[1] Amongst the plethora of groups typically employed for protecting aldehydes and ketones, cyclic acetals and ketals enjoy a cardinal position, as exemplified by the numerous and ingenious methods devised for their attachment and removal.[2] Unfortunately, these protocols usually require harsh acidic conditions that are unsuitable for sensitive substrates.

A recently investigated example of this transformation is the deprotection of β-hydroxy ketal **1**[3] to give the corresponding highly acid-labile β-hydroxy ketone **2** (Table 1).[4] A variety of Brønsted and Lewis acids were ineffective and provided almost exclusively the α,β-unsaturated ketone **3**.

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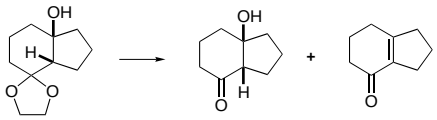
Table 1. Catalytic deprotection of ketal **1** with CAN.



1 **2** **3**

Entry	Conditions	Yield [%][a]	Ratio **2**:**3**[b]
1	3 mol % CAN/1.5 equiv $NaBrO_3$ MeCN/H_2O (1/1), 60 °C	91	100:0
2	3 mol % CAN/borate – HCl buffer (pH 8) MeCN/H_2O (1/1), 60 °C	93	100:0

[a] Yields of pure, isolated compounds. [b] The ratios were measured by NMR spectroscopy, both on the crude reaction product and on the purified material.

During these studies, we discovered that cerium ammonium nitrate (CAN, 2.5 equiv) afforded the desired aldol product **2**, though in a modest yield of 53 %.[5] However, this procedure suffered from serious drawbacks. First, acid-catalyzed epimerization occurred when sensitive substrates were subjected to the deprotection reaction. Second, the large quantities of CAN required for this transformation (2.5 equiv) precluded its application to large scale transformations.

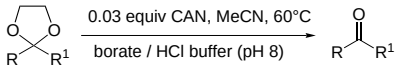
Inspired by reports of the oxidation of a range of functional groups with catalytic amounts of CAN in conjunction with stoichiometric quantities of inexpensive oxidants,[6] we attempted deprotection of ketal **1** with 3 mol % of CAN and 1.5 equivalents of $NaBrO_3$.[7] Gratifyingly, the reaction proceeded smoothly and afforded ketone **2** as the sole product in a much improved yield of 91 % yield (Table 1, entry 1). To our surprise, the diol by-product could also be isolated from the reaction mixture, and this implied that CAN did not act as an oxidant. This unexpected observation prompted us to examine the deprotection of **1** in the absence of $NaBrO_3$. To safeguard our acid-labile product, the oxidant was replaced with a mildly basic aqueous buffer solution. Remarkably, catalytic amounts of CAN (3 mol %) in the presence of a borate – HCl buffer (pH 8) and without any added cooxidant transformed **1** into **2** in excellent yield (Table 1, entry 2).

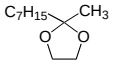
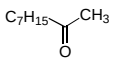
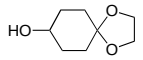
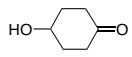
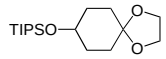
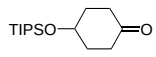
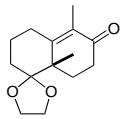
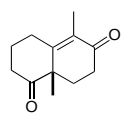
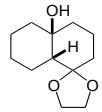
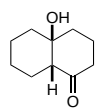
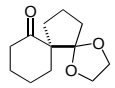
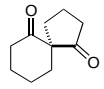
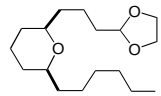
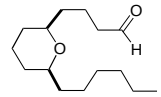
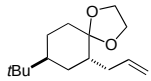
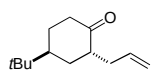
To the best of our knowledge, this is the first report that a simple cyclic ketal could be efficiently removed under neutral or mildly basic conditions with a catalytic amount of a Lewis acid. This novel protocol was applied to a range of acetals and ketals (Table 2).

A variety of cyclic acetals and ketals can be removed efficiently and in high yield. Furthermore, the reaction even tolerates a range of functional groups, including unprotected secondary and tertiary alcohols, ketones, enones, and triisopropylsilyl (TIPS) ethers.[8] It is noteworthy that aldehydes, formed by deprotection of acetals, are stable under these conditions and do not undergo oxidation to the corresponding carboxylic acids.[9] In sharp contrast to the procedure with 2.5 equivalents of CAN,[10] the conditions of this catalytic system are so mild that no epimerization occurs in the case of acid-labile substrates (Table 2, entry 8).

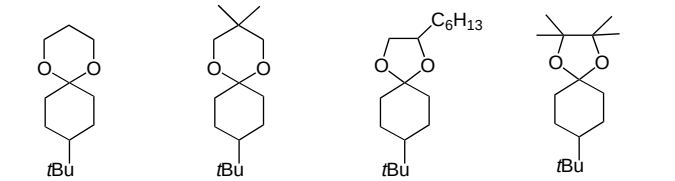
Other cyclic ketals **4** – **6** are also smoothly deprotected.[11] The total inertness of the pinacol-derived ketal **7** under these reaction conditions suggests that the cerium catalyst is highly

Table 2. CAN-catalyzed deprotection reactions with 3 mol % CAN at 60 °C in a 1:1 MeCN/borate – HCl buffer solution (pH 8).



Entry	Substrate	Product	Yield [%][a]	Time
1			95	30 min
2			92	25 min
3			91[b]	45 min
4			95	48 h
5			99	1.5 h
6			86[c]	1.5 h
7			95	2.5 h
8	 (96:4 d.r.)	 (96:4 d.r.)	96[b]	20 min

[a] Yields of pure, isolated products. [b] The reaction was carried out in the presence of 1.5 equivalents of $NaBrO_3$. [c] Performed with 4 mol % CAN.



4 (97%; 15 min) **5** (96%; 25 min) **6** (95%; 20 min) **7** (0%; 300 min)

sensitive to steric hindrance in the ketal protecting group and/or in its immediate vicinity.[12] This property is further demonstrated by the prolonged reaction time required for the deprotection of a decalone derivative (Table 2, entry 4).

To gain some insights into the mechanism of this novel catalytic reaction, the deprotection of **1** was monitored by cyclic voltammetry. The only cerium species that was detected throughout the deprotection reaction possesses the Ce^{IV} oxidation state. These experiments clearly confirm that, under our catalytic conditions, CAN acts as a highly selective and efficient Lewis acid that activates the acetal or ketal protect-

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ing group towards hydrolysis but does not behave as a redox catalyst. Such behavior appears to be unique to CAN.[13]

In summary, we have developed a highly efficient, catalytic protocol for the deprotection of acetals and ketals. This is the first time that such deprotections could be carried out under neutral to slightly basic conditions.

Experimental Section

Typical experimental procedure: Deprotection of 1,4-dioxadispiro-[4.0.5.3]tetradecan-7-one (Table 2, entry 6): Solid cerium ammonium nitrate (18 mg, 4 mol %) was added to a stirred solution of 1,4-dioxadispiro[4.0.5.3]tetradecan-7-one (237 mg, 1.13 mmol) in MeCN (3.5 mL) and borate–HCl buffer (Merck, pH 8, 3.5 mL). The faintly yellow solution was heated at 60 °C for 1.5 h. After cooling to room temperature, H_2O (10 mL) was added. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2 (2×15 mL). The combined organic extracts were dried over $MgSO_4$ and filtered, and the solvents were removed in vacuo. The crude product was further purified by column chromatography on silica gel with EtOAc/hexane (3/7; $R_f = 0.58$) as the eluant. Spiro[4.5]decane-1,6-dione was obtained as a colorless liquid (144 mg, 86 %). ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 2.7$ (m, 2H), 2.42 (dt, $J = 14.1$, 5.1 Hz, 1H), 2.31 (dt, $J = 8$, 1.7 Hz, 2H), 2.2 to 1.6 (m, 9H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75.5 MHz): $\delta = 18.9$, 21.0, 26.6, 33.7, 35.9, 38.4, 39.7, 64.3, 207.9, 215.5; IR (film): $\tilde{\nu} =$ 1734, 1700 cm^{-1}; MS (70 eV): *m/z* (%): 166 (92) [M^+], 167 (100) [M^++1].

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[8] So far, we have not been able to find reaction conditions under which unmasking of a dioxolane group could be accomplished chemoselectively in the presence of a *tert*-butyldimethylsilyl (TBDMS) protecting group.
[9] In the presence of $NaBrO_3$, competitive oxidation to give the 2-hydroxyethyl ester derivative takes place.
[10] With 2.5 equivalents of CAN, epimerization takes place, affording a near thermodynamic mixture of axial and equatorial product (60:40).
[11] Deprotection of ketal **6** with 2.5 equivalents of CAN resulted in quantitative formation of *tert*-butylcyclohexanone. However, no 1,2-octanediol could be isolated in this experiment. In contrast, removal of the dioxolane protecting group with 3 mol % CAN in borate buffer (pH 8) afforded not only the desired ketone (95 %) but also 1,2-octanediol (97 %); hence, a different mechanism operates in these two reactions.
[12] Chemoselective deprotections can thus be realized by using dioxolane protecting groups with different steric demands.
[13] Indeed, $Ce(NO_3)_3$, $Ce(OTf)_4$, and other lanthanide salts were inert under our reaction conditions.

Fluorescent Indicators for Imaging Nitric Oxide Production**

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Nitric oxide (NO) is a signal transmitter in vivo.[1] However, many of the functions proposed for NO remain controversial owing to the lack of direct evidence. The use of NO-reactive fluorescent indicators which allow bioimaging of NO with high spatial and temporal resolution in conjunction with fluorescence microscopy should overcome this problem. A reaction that traps NO directly is essential for developing probes for NO, but NO itself shows low reactivity towards organic compounds. Further, a nitroso or nitro group will generally quench fluorescence when dyes react with NO to generate these functional groups. Therefore, few reactions are suitable for this purpose. Recently, fluorescent probes for NO, FNOCTs, were reported.[2] They react with NO to yield nonfluorescent compounds that are reduced by biological compounds, such as ascorbic acid, to afford fluorescent derivatives. However, they have not yet been applied in biological experiments.

We have developed diaminofluoresceins (DAFs), such as DAF-2 (Scheme 1), as fluorescent indicators for NO.[3, 4] The DAFs react not with NO itself but with NO^+ equivalents, such as nitric anhydride (N_2O_3), which are formed by autoxidation of NO. Under aerobic conditions, DAFs can trap NO to yield highly fluorescent triazolofluoresceins (DAF-Ts) by nitrosation and dehydration. This mechanism is convenient because it does not interfere with signal transduction, but is

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