Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
ELSEVIER
Tetrahedron 62 (2006) 2350–2356

Brønsted acidity of ceric ammonium nitrate in anhydrous DMF. The role of salt and solvent in sucrose cleavage

Tonino Caruso,[a] Emiliano Bedini,[b] Cristina De Castro[b] and Michelangelo Parrilli[b,*]

[a]*Department of Chemistry, Università di Salerno, Via S. Allende, Baronissi 84081, Salerno, Italy.*
[b]*Department of Organic Chemistry and Biochemistry, Università Federico II, Complesso Universitario di Monte S. Angelo Via Cintia, 4-80126 Napoli, Italy.*

Received 4 August 2005; revised 8 November 2005; accepted 1 December 2005

Available online 20 December 2005

Dedicated to the memory of Professor Gaspare Barone

Abstract—The generation of an unexpected Brønsted acidity in anhydrous DMF at 50 °C was evidenced by NMR measurements during the investigation on the course of sucrose cleavage by ceric ammonium nitrate (CAN). The formation of a nitrooxy derivative of DMF by reaction with CAN is responsible for this acidity. The reactivity of CAN at 50 °C with several solvents was evaluated by voltammetric and potentiometric measurements. The possible release of protons from these reactions, particularly when aqueous solvent mixtures are used, should always be taken into account in the mechanistic interpretation of CAN synthetic applications.

1. Introduction

Ceric ammonium nitrate is widely utilised to accomplish a variety of oxidative transformations.[1–4] In the carbohydrate field it has been used to perform oxidation reactions under strongly acidic aqueous conditions;[5–8] recently, its ability to induce formation[9] and cleavage[10,11] of ketals on many types of derivatives has also been reported. In addition, the possibility of accomplishing hydrolyses of glycoside linkages with CAN under buffered neutral conditions was reported.[12] Given our interest in the research of new protocols for glycosidic bond cleavage in polysaccharides, we investigated this reaction in-depth. In this regard, we found that ceric ammonium nitrate in anhydrous DMF can be used to cleave selectively the glycosidic linkages of Ko and Kdo in lipopolysaccharides.[13] In that paper, we quoted the development of this method to cleave the glycosidic bond of sucrose: the description of the course of this reaction at 50 °C is now reported. In addition the investigation on the stability at 50 °C of CAN in several solvents, commonly used to perform reactions with CAN, is addressed by NMR analysis and voltammetric and potentiometric measurements.

2. Results and discussion

The first report on sucrose cleavage by CAN was by Ishida,[12] who claimed the glycosidic linkage cleaved at pH = 7 using 5.0 mmol dm^{-3} of CAN with 50 mmol dm^{-3} of Tris buffer at 40–100 °C. In our hands these conditions gave a pH of about 2 instead of 7, on the other hand no disaccharide hydrolysis occurred when, increasing 10-fold the amount of Tris buffer (0.5 mol dm^{-3}), the solution showed a pH of 6.7. Analogously, no reaction occurred when pH = 7 was reached by adding 8 M HCl to a Tris solution of CAN and sucrose. The non-neutral conditions of Ishida reaction was supported by the fact that in no case was reported the precipitation of cerium hydroxide, which occurs under neutral conditions.[14] Accordingly, when we worked under carefully checked neutral conditions, cerium hydroxide precipitated. We think that the deceptive neutral conditions might be due to a deficient buffer concentration, whose amount should not be enough to buffer the acidity determined by CAN hydrolysis. In addition, this acidity should be further increased if it is taken into account that Ishida's reactions are performed at 40–100 °C and that the pH value decreases with the increase of the temperature. Therefore, in our opinion, protic acid hydrolysis is occurring under Ishida's conditions, suggesting a Lewis acid catalysis of Ce(IV) at pH = 2.

However, the possibility that CAN could cleave the sucrose glycoside linkage under non-aqueous conditions was suggested by the finding that in the procedure of

Keywords: Ceric ammonium nitrate; Brønsted acidity; DMF; Sucrose.
* Corresponding author. Tel.: +39 081 674147; fax: +39 081 674393; e-mail: parrilli@unina.it

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.12.001

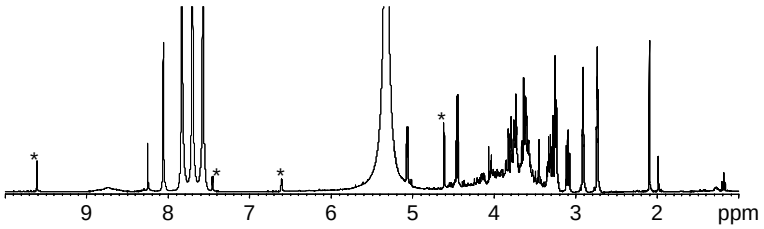


Figure 1. ^{1}H NMR at 400 MHz of the crude CAN sucrose reaction in DMF-d_7 after 2 h at 50 °C (HMF peaks are marked with an asterisk).

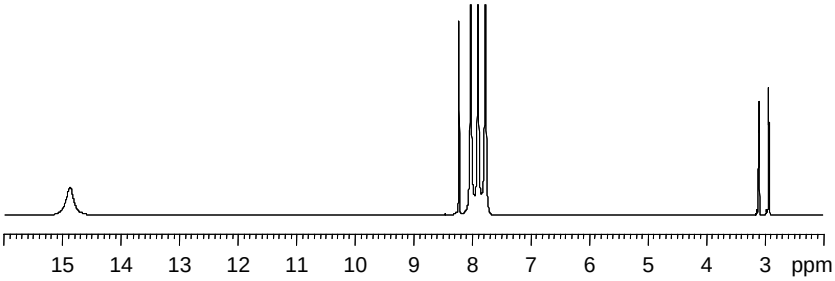


Figure 2. ^{1}H NMR at 400 MHz of the red CAN DMF-d_7 solution at 50 °C.

isopropylidene closure on sucrose at 60 °C by CAN in DMF,[9] the use of a molar ratio of CAN/substrate higher than 0.2 seemed to produce glucose. Actually, we have realized the complete cleavage of the glycosidic linkage of sucrose with CAN in a 1:1 molar ratio in anhydrous DMF under mild temperature conditions (50 °C), obtaining quantitative amounts of glucose and several products arising from the fructose moiety, among which 5-(hydroxymethyl)furfural (HMF) was the most abundant.

In order to gain insight into the course of the reaction we monitored it by NMR measurements. In the first experiment, equimolar solutions of CAN and sucrose in DMF-d_7, both equilibrated at 50 °C, were mixed in a NMR tube and spectra were measured at this temperature every 5 min. The initially red solution of CAN, became colourless after adding sucrose within 15 min. After 2 h the solution appeared slightly yellow and the ^{1}H NMR spectum (Fig. 1) showed the complete disappearance of sucrose signals and the presence of glucose α- and β-anomer signals at 5.04 and 4.43 ppm, respectively, those of HMF at 9.60, 7.50, 6.60 and 4.60 ppm and the triplet signal of the ammonium ion at 7.92 ppm. The ^{13}C NMR spectrum, in addition to glucose and HMF signals, showed in the range between 83–86 ppm at least four minor signals suggesting the presence of several furanic products, among which we were able to identify the 2,6-anhydro-α-D-fructo-furanose and traces of fructose. From a quantitative point of view, HPLC analysis of the crude reaction allowed us to estimate only the amounts of glucose (100% molar yield) and HMF (13% molar yield). A confirmation of HMF molar yield was obtained by integration of its hydroxymethylene signal at 4.60 ppm with respect to the sum of the anomeric glucose signals in the ^{1}H NMR spectrum. The total yield of the other identified minor products was estimated to be about 15%. These results indicated that the fructose moiety of sucrose underwent an extended decomposition whereas the glucose part was stable under the reaction conditions.

When the reaction was performed in the presence of an excess of an acid scavenger (potassium carbonate or pyridine),[15] it did not proceed at all indicating the involvement of an acid reagent in the sucrose degradation. Indeed the ^{1}H NMR spectrum at 50 °C of the red CAN DMF-d_7 solution showed a broad singlet at 14.8 ppm (Fig. 2), suggesting unexpected Brønsted acidity.

An acidic signal at 14.2 ppm was also found in the ^{1}H NMR spectrum of a colourless CAN solution, without sucrose, obtained by standing at 50 °C for about 30 min. This signal was detected even after that the NMR tube was kept at 4 °C for 20 days. The decolourization of the red CAN solution suggested the reduction of Ce(IV) to Ce(III) by DMF. Indeed the oxidation of amides by ceric ion has already been reported, albeit under strongly acidic aqueous conditions.[16,17] Differential pulse voltammetric measures (Fig. 3) confirmed

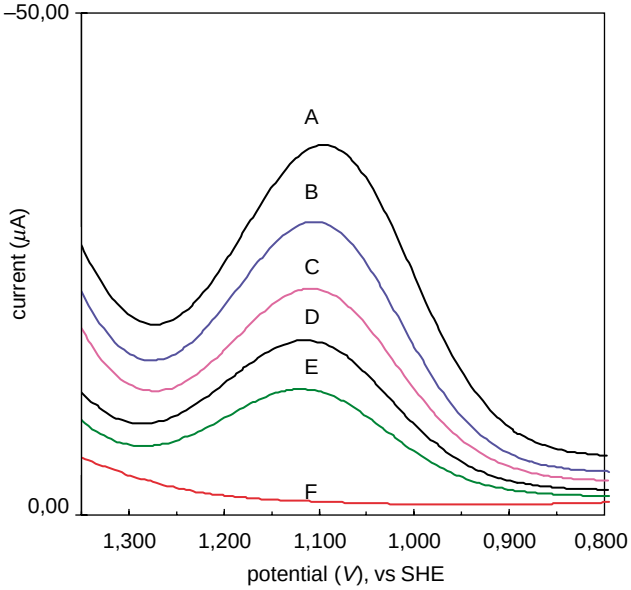


Figure 3. Differential pulse voltammetry for the reduction of CAN at glassy carbon electrode in DMF versus standard hydrogen reference electrode (SHE). The different traces show the decay of Ce(IV) concentration at 20 °C with time: (A) 1 min, (B) 2 min, (C) 4 min, (D) 6 min, (E) 9 min, (F) 20 min.

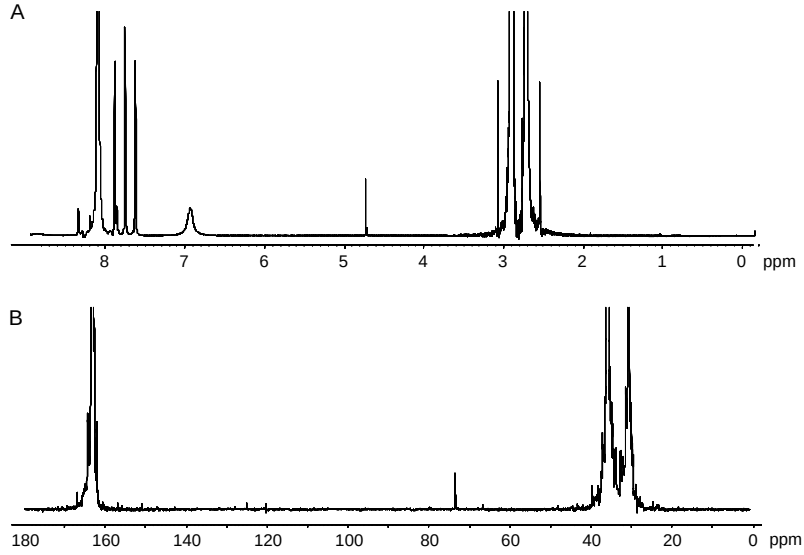


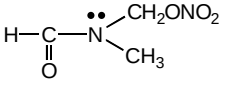
Figure 4. ^{1}H (400 MHz) (A) and ^{13}C NMR (100 MHz) (B) at 50 °C of a 9:1 DMF/DMF-d_7 0.10 M CAN solution.

the reduction of Ce(IV) to Ce(III) in anhydrous DMF within a few minutes at 50 °C, which proceeded in parallel with the decolourization of the solution. When sucrose was added to the colourless CAN solution, the ^{1}H NMR spectrum, measured after 2 h at 50 °C, was very similar to that obtained when sucrose was added to the red CAN solution except for the lack of HMF signals. This suggested that sucrose cleavage was mainly due to the Brønsted acidity and the absence of HMF could be due to the lack of Ce(IV) in the colourless CAN solution.[18]

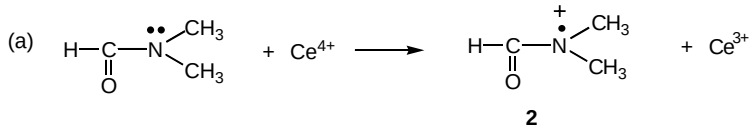
Support for this hypothesis was obtained by observing that a DMF-d_7 solution of sucrose and cereous ammonium nitrate, $Ce(NH_4)_2(NO_3)_5 \cdot 4H_2O$ [CAN(III)], remained unalterated for at least 16 h at 50 °C, confirming that sucrose cleavage in the colourless CAN solution did not depend on Ce(III) ion but, evidently, on the high Brønsted acidity of the solution. In fact, the ^{1}H NMR spectrum of a CAN(III) DMF-d_7 solution at 50 °C showed a singlet signal at 3.8 ppm,[19] indicating a lower acidity than that of colourless CAN solution, salt concentration being equal. In the light of these results the presence of the proton signal at 14.8 ppm in the perdeuterated solvent DMF-d_7 (Fig. 2) must be ascribed to the exchange of deuterium cation with the protons of the ammonium ion of CAN.

To confirm this suggestion we replaced CAN with ceric tetrabutylammonium nitrate (CTAN).[20] When this salt was dissolved in DMF-d_7 at 50 °C, we observed that the red colour of the solution survived longer with respect to the CAN solution and both the red coloured and colourless solution of CTAN showed a ^{1}H NMR spectrum without proton signals excepting the aliphatic ones. However, adding sucrose to the red CTAN solution, the ^{1}H NMR spectrum, after 5 h at 50 °C, was very similar to that obtained from sucrose in the CAN red solution indicating the same product composition in both cases. This strongly suggested that also CTAN produced Brønsted acidity by oxidation of DMF. The main difference was the known slow rate of the CTAN reaction[20] with respect to the CAN one.

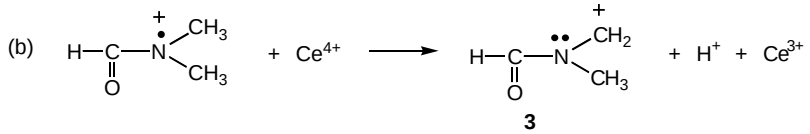
In order to explain the origin of this Brønsted acidity, NMR spectra were measured in a 0.1 M 9:1 DMF/DMF-d_7 CAN solution at 50 °C. Together with the very intense signals due to



1



2



3

$$2Ce^{4+} + H(C{=}O)N(Me)_2 + NO_3^- = 2Ce^{3+} + H(C{=}O)N(Me)CH_2ONO_2 + H^+$$

Scheme 1. Suggested mechanism of oxidation of DMF by CAN.

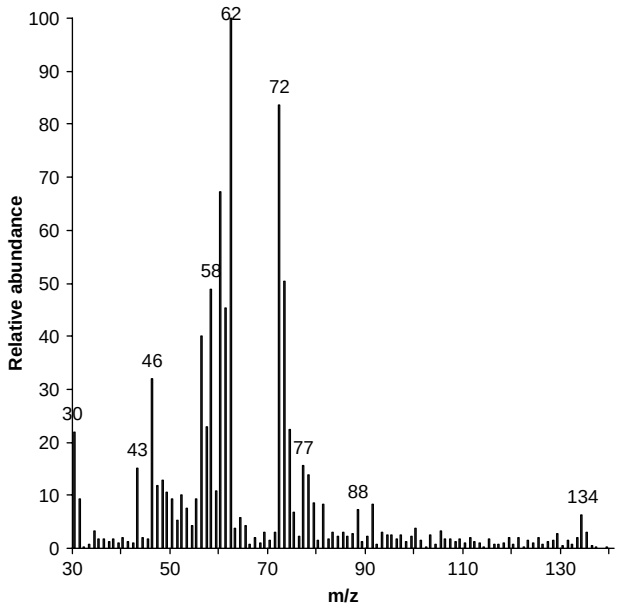


Figure 5. Mass spectrum of **1**, recorded with a ThermoQuest Finnigan ion-trap mass spectrometer Mod. Polaris from 30 to 140 mass units. This MS has been recorded after chromatography carried out on RTX Restek column (30 m×0.25 mmID) mounted in the oven of a ThermoQuest GC Series Trace 2000.

DMF, a strong signal appeared in the ^{1}H NMR spectrum (Fig. 4A) at 4.70 ppm,[21] which was correlated to the carbon signal at 73.4 ppm (Fig.4B), assigned to a methylene carbon on the basis of a DEPT experiment. This signal suggested a product with structure **1** (Scheme 1) by analogy with the mechanism reported for the anodic oxidation of DMF in methanol and acetic acid,[22] or acetonitrile[23] which involves the formation of radical cation **2** in a rate-determining step followed by the formation of cation **3** by loss of another electron and a proton, according to equations (a) and (b) shown in Scheme 1. Finally, cation **3** reacted with the nucleophilic solvent to give an adduct. In our case, **3** should react with the nitrate ion. Unfortunately we were unable to identify the other NMR signals of compound **1**, that is formyl and *N*-methyl protons and the corresponding carbon signals, due to overlap with the corresponding intense signals of DMF. However, confirmatory evidence of the formation of **1** was obtained by GC–MS mass spectrum which showed, in addition to DMF, another product with a molecular ion at *m/z* 134 and fragments at *m/z* 46, 62 and 72, 88 (Fig. 5). The fragment at *m/z* 72 is in agreement with the formation of ion **3**, whereas that one at *m/z* 46 (NO_2^+) is indicative of the nitro-group. This latter is also confirmed by the ion at *m/z* 88, assignable to an ion at M-46. Less immediate is the identification of the ion at *m/z* 62, probably it might correspond to the ion $CH_3N^+(O)OH$, arising from a rearrangement. In agreement with structure **1** was also the IR spectrum, which showed the typical signals of a nitric ester at 1640, 1260 and 870 cm^{-1}. In conclusion, DMF oxidation by CAN involves the production of protons according to the total equation shown in Scheme 1. An acid titration was in a good agreement with a 2:1 Ce ion/H^+ stoichiometry ratio. However, it cannot be excluded that other minor species could be formed, because, when α-2,3-epoxy-5α-cholestane **4** was added to the colourless CAN solution, 2β-formoxy-3α-hydroxy-5α-cholestane **5** was found together with the expected 3α-hydroxy-2β-nitrooxy-5α-cholestane **6** and other unidentified products (Scheme 2).[24] Probably the radical cation **2** can cleave to give a formyl cation,[17] which reacts with the nitrate ion to give a reacting anhydride able to give formates.

On the basis of these results, the involvement of Brønsted acidity in reactions with CAN in anhydrous DMF at 50 °C can be suggested; in particular, in the case of sucrose, the reaction proceeds mainly by protic cleavage of the glycosidic linkage to give glucose and fructofuranosyl cation (Scheme 3) which, in turn, is responsible for all other products. The formation of HMF, which occurs only when Ce(IV) is present, can be ascribed to the strong dehydrating action of Ce(IV) due to its high hardness and oxophilicity. As for 2,6-anhydro-α-D-fructofuranose **7** it arises from the intramolecular cyclization of 6-hydroxymethylene group.

In conclusion, the detected Brønsted acidity of CAN in anhydrous DMF indicates a low stability of CAN at 50 °C in this solvent, which is confirmed by potentiometric titration. In agreement with the procedure of Torii et al.[25] we reported

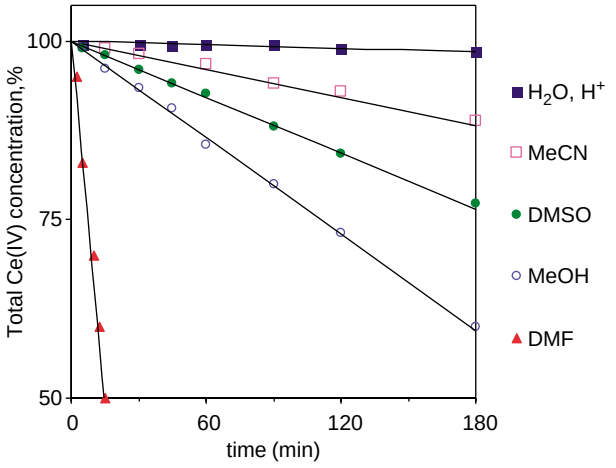
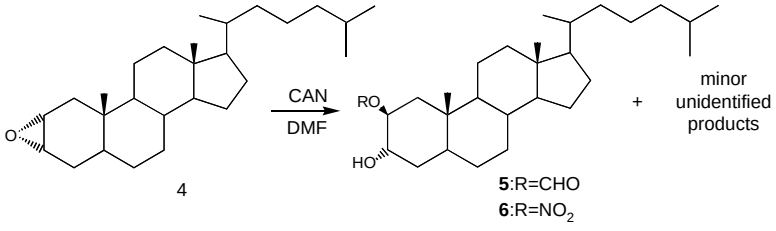
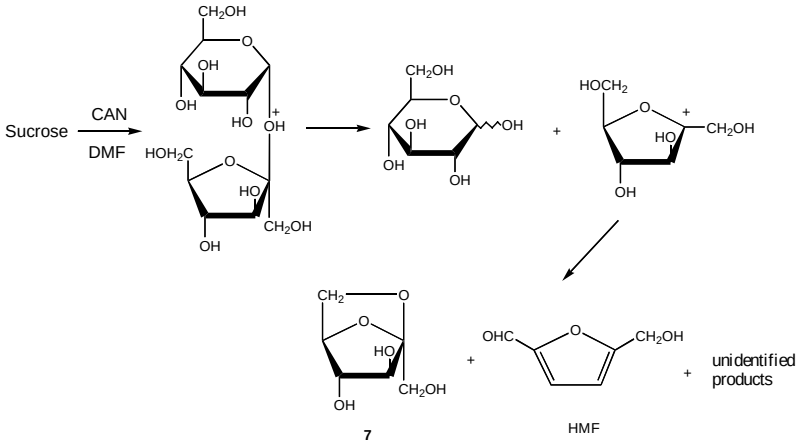


Figure 6. Relationship between the total concentration of Ce(IV) versus time. A 15 mM solution of CAN in different solvents was allowed to stand at 50 °C under N_2 flow. The slope of straight lines is very dependent upon the temperature.



Scheme 2. Cleavage of α-2,3-epoxy-5α-cholestane with CAN in DMF.



Scheme 3. Mechanism of sucrose cleavage by CAN in DMF.

in Figure 6 the relationship between the variation of the total concentration of CAN versus the time indicating the relative CAN stability in several solvents. This figure reports the stability order of CAN in DMF, DMSO, MeOH, MeCN and H_2O. In particular, it is interesting to observe that CAN is very stable[26] only in H_2O/H^+; as for the organic solvents commonly used to perform reactions with CAN, it is rather stable in MeCN but it degrades rather easily in MeOH[27] and DMF.

3. Conclusion

We have shown that, in spite of an expected Lewis acidity, CAN in anhydrous DMF at 50 °C also produces a Brønsted acidity giving Ce(III) ion and a nitrooxy derivative of DMF. This protic acidity is responsible for sucrose cleavage to give quantitative glucose and fructofuranosyl cation, from which arises the formation of HMF, **7**, fructose and other minor unidentified products. A valuable result is that our data stress the high reactivity at 50 °C of CAN with some common solvents (Fig. 6) with possible concomitant release of protons,[27] particularly when aqueous solvent mixtures are used.[10]

4. Experimental

4.1. General methods

^1H and ^{13}C NMR spectra were obtained at 400 and 100 MHz, respectively, with a Bruker AM 400 spectrometer equipped with a reverse probe, in the FT mode at 50 °C. ^{13}C and ^1H chemical shifts are expressed in ppm relative to DMF (^1H 8.02, ^{13}C 162.6 ppm in DMF-d_7) or $CHCl_3$ (^1H 7.26, ^{13}C 77.0 ppm in $CDCl_3$). Two-dimensional spectra (COSY, HSQC and HMBC) were measured using standard Bruker software. HPLC analysis was performed by using a SUPELCO RP-18 column (4×25 mm) with water as eluent at a 0.7 mL/min flow and a double detector (refractive index and $UV_{\lambda=290\ nm}$). Optical rotations were measured on a JASCO P-1010 polarimeter. Melting points were measured on a Reichert Thermovar apparatus. IR spectral measurements were carried out using a Brucker Vector22 FT-IR spectrometer. Elementar analysis were performed on a Carlo Erba 1108 instrument. Positive ESI-MS spectra were recorded on a Finnigan LCQ-DECA ion trap mass spectrometer.

4.2. Electrochemistry: instrumentation and software

Voltammetric experiments were performed using a Metrohm electroanalyser (model 757 VA Computrace) connected to a PC. The system was operated and measurements were recorded using VA Computrace version 2.0 run under Windows 98SE. The three-electrode system consisted of the rotating disk glassy carbon electrode as working electrode, Ag/AgCl/3 M KCl as reference electrode and a platinum wire as auxiliary electrode purchased from Metrohm. All chemicals were electrochemical or spectrophotometric grade. The electrolyte employed in all experiments was potassium perchlorate 0.5 M, while the concentration of CAN was 15 mM. Voltammograms were recorded at room temperature at a scan rate of 50 mV/s. All solutions were degassed with high-purity nitrogen prior to undertake voltammetric experiments. Since there is always a question as to the effect of junction-potential variations on electrochemical measurements, the redox potentials for

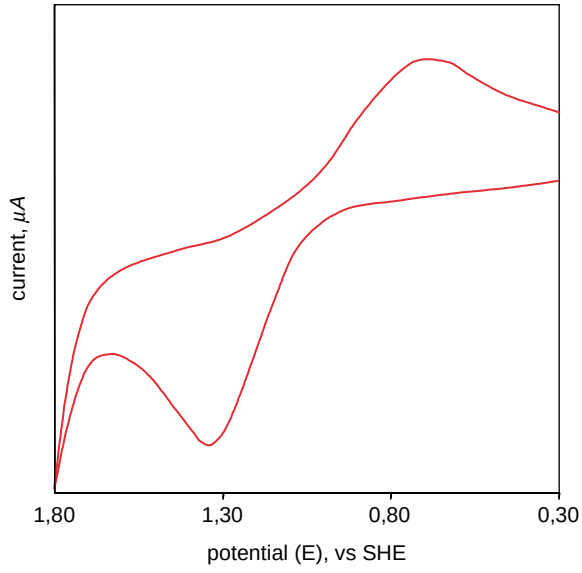


Figure 7. Cyclic voltammetric response of CAN at glassy carbon electrode DMF 0.5 M $KClO_4$ versus standard hydrogen reference electrode (SHE).

the $Fe(CN)_6^{3-}/Fe(CN)_6^{4-}$ couple in the organic solvents have been measured by cyclic voltammetry under the same conditions. Then, the value for the reduction of Ce(IV) to Ce(III) in DMF was determinated to be +0.72 V, while the oxidation peak at about +1.37 V was due to Ce(III) to Ce(IV) oxidation versus standard hydrogen electrode (SHE) (Fig. 7).

4.3. Measure of the stability of Ce(IV)

The stability of the Ce(IV) solutions in the study solvents (DMF, DMSO, MeCN, MeOH, H_2O) was evaluated by measuring at 50 °C during the time the decrease of Ce(IV) total concentration that was determined by titration with a standard solution of Fe(II) ammonium sulfate (FAS). Samples (10 mL) were withdrawn at a recorded time, quenched with an excess of 10 mM FAS in 0.5 M sulphuric acid, and the excess ferrous salt was back-titrated with 10 mM CAN, using *o*-phenanthroline–Fe(II) as indicator. The biamperometric method was used for more accurate determinations with a double platinum sheet electrode (0.2×8×8 mm, Metrohm) in conjunction with an Amel potentiostat (Model 2051). The decay of Ce(IV) concentration was also followed by a potentiometric method. Potentiometric measurements were performed by using two electrodes in conjunction with a high-impedance electrometer (Keithley Model 197A). A platinum wire served as the indicating electrode, and the reference electrode with double junction was used (Ag/AgCl with sleeve diaphragm and bridge electrolyte, purchased from Metrohm).

4.4. Determination of H^+ concentration

The H^+ concentration of a solution in which all Ce(IV) it has been reduced to Ce(III) has been determined by potentiometric titration using a sodium methoxide organic solution as titrant. This solution is standardized against pure benzoic acid. The endpoint has been determined using the Gran plot.[28]

4.5. Hydrolysis of the glycoside linkage of sucrose

(i) Conditions as reported in the literature (Ref. 12): Tris (303 mg, 2.5 mmol) was dissolved in H_2O (43 mL) and 8 M HCl was added up until pH=7 was reached. To this solution CAN (137 mg, 0.25 mmol) was added and the mixture was diluted to 50 mL in order to obtain a final solution, which was 50 mM in Tris and 4.8 mM in CAN. The final pH was 1.9. Sucrose (85 mg, 0.201 mmol) was dissolved in 2 mL of this solution and the mixture was kept at 100 °C. After 30 min the complete hydrolysis of sucrose to glucose and fructose was evidenced by TLC analysis. (ii) Conditions using 10 times of the reported amount of buffer: using identical reagent amounts as above, except for Tris (3.030 g, 25 mmol), the final solution was cloudy and at pH=6.7. Sucrose was found to be unaltered in this solution after 3 h at 100 °C. (iii) Our neutral conditions: Tris (303 mg, 2.5 mmol) and CAN (137 mg, 0.25 mmol) were dissolved in H_2O (43 mL) and 8 M HCl was added until reaching pH=7 and the whole mixture diluted to 50 mL. Also in this case, the solution was cloudy and sucrose was recovered unaltered after 3 h at 100 °C.

4.6. Reaction of sucrose with CAN in DMF-d_7

Sucrose (20 mg, 0.058 mmol) was dissolved in DMF-d_7 (250 μL) under stirring at T=50 °C for about 30 min. A CAN (32 mg, 0.058 mmol) solution in DMF-d_7 (500 μL) was then added, after that ^{1}H NMR spectra were recorded at T=50 °C every 5 min. Analogous reactions were conducted in DMF in order to perform HPLC analyses of the mixtures.

4.7. Reaction of sucrose with CAN in DMF-d_7 in presence of acid scavenger

Sucrose (20 mg, 0.058 mmol) was dissolved in DMF-d_7 (250 μL) under stirring at T=50 °C for about 30 min and then K_2CO_3 (40 mg, 0.290 mmol) or pyridine (23 μL, 0.290 mmol) was added. A CAN (32 mg, 0.058 mmol) solution in DMF-d_7 (500 μL) was then added, after that ^{1}H NMR spectra were recorded at T=50 °C every 5 min.

4.8. Reaction of sucrose with $Ce(NH_4)_2(NO_3)_5$ in DMF-d_7

Sucrose (20 mg, 0.058 mmol) was dissolved in DMF-d_7 (250 μL) under stirring at T=50 °C for about 30 min. $Ce(III)(NH_4)_2(NO_3)_5$ was oven-dried at 85 °C for 8 h, then cooled under an argon flow and dissolved in DMF-d_7 (500 μL). The cereous mixture was added to the sucrose solution, after that ^{1}H NMR spectra were recorded at T=50 °C every 5 min.

4.9. Reaction of sucrose with CTAN in DMF-d_7

Sucrose (20 mg, 0.058 mmol) was dissolved in DMF-d_7 (250 μL) with stirring at T=50 °C for about 30 min. A CTAN (58 mg, 0.058 mmol) solution in DMF-d_7 (500 μL) was then added, after that ^{1}H NMR spectra were recorded at T=50 °C every 5 min.

4.10. Reaction of α-2,3-epoxy-5α-cholestane with CAN in DMF

α-2,3-Epoxy-5α-cholestane **4** (30 mg, 0.078 mmol) was dissolved in DMF (700 μL) and then a CAN (47 mg, 0.086 mmol) solution in DMF (300 μL) was added. Additional aliquots (150 μL) of the CAN solution were then added after 2 and 4 h. After 5 h, TLC showed complete disappearance of the starting compound, therefore the reaction was quenched by addition of solid $NaHCO_3$ to reach pH=6. The mixture was filtered and concentrated by co-evaporation with toluene (×5, 1 mL). The residue was then suspended in CH_2Cl_2 (25 mL) and washed with 5 M NaCl (25 mL). The organic layer was collected, dried and concentrated to give a residue, which, after chromatography (3:1 cyclohexane/ethyl acetate) gave several fractions, the main ones being pure 2-β-formoxy-3-α-hydroxy-5α-cholestane **5** (9 mg) as a white solid and pure 3-α-hydroxy-2-β-nitrooxy-5α-cholestane **6** (9 mg) as a white solid.

Compound **5**. $[\alpha]_D$ +32 (*c* 0.3, CH_2Cl_2). Mp=100–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H, *H*CO), 5.02 (br s, 1H, H-2), 3.97 (br s, 1H, H-3), 1.94 (m, 1H, H-1), 1.83 (m, 1H, H-4), 1.70–1.46 (m, 8H), 1.41–1.25 (m, 13H), 1.17–1.05 (m, 7H), 1.02 (s, 3H, H-19), 0.91 (d, 3H, J=6.0 Hz, H-21), 0.88 (2d, 6H, J=6.0 Hz, H-26, H-27), 0.66 (s, 3H,

H-18); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.3 (H*C*O), 72.8 (C-2), 68.8 (C-3), 56.5, 56.4, 55.1, 42.7, 40.7, 40.1, 39.9, 39.6, 36.2, 35.8, 35.4, 34.9, 31.9, 29.7, 28.7, 28.2, 28.0, 24.2, 23.9, 22.8, 22.6, 20.9, 18.7, 14.4, 12.1; IR ($CHCl_3$): 1720 cm^{-1} (formate ester signal). ESI-MS for $C_{28}H_{48}O_3$ (*m*/*z*): M_r (calcd) 432.36, M_r (found) 455.19 $(M+Na)^+$. Anal. Calcd: C 77.72, H 11.18. Found: C 77.40, H 11.09.

Compound **6**. $[\alpha]_D$ +16 (*c* 0.7, CH_2Cl_2). Mp=90–91 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.08 (br s, 1H, H-2), 4.02 (br s, 1H, H-3), 1.92 (m, 1H, H-1), 1.73 (m, 1H, H-4), 1.70–1.47 (m, 8H), 1.45–1.19 (m, 8H), 1.15–0.95 (m, 12H), 0.90 (m, 6H, H-19, H-21), 0.87 (2d, 6H, J=6.0 Hz, H-26, H-27), 0.65 (s, 3H, H-18); ^{13}C NMR (100 MHz, $CDCl_3$): δ 82.0 (C-2), 66.1 (C-3), 56.4, 56.2, 54.8, 42.6, 39.9, 39.5, 38.4, 36.4, 36.2, 35.8, 35.4, 35.0, 32.2, 31.8, 29.7, 28.2, 28.0, 24.1, 23.8, 22.8, 22.5, 20.8, 18.7, 13.4, 12.1; IR ($CHCl_3$): 1629 and 1263 cm^{-1} (nitrate ester signals). ESI-MS for $C_{27}H_{47}NO_4$ (*m*/*z*): M_r (calcd) 449.35, M_r (found) 472.27 $(M+Na)^+$. Anal. Calcd: C 72.12, H 10.54, N 3.11. Found: C 72.17, H 10.51, N 3.08.

References and notes

1. Ho, T.-L. In Paquette, L. A., Ed.; Encyclopaedia of Reagents for Organic Synthesis; Wiley: New York, 1995; Vol. 2, pp 1025–1029.
2. Molander, G. A. *Chem. Rev.* **1992**, *92*, 29–68.
3. Nair, V.; Balagopal, L.; Rajan, R.; Matthew, J. *Acc. Chem. Res.* **2004**, *37*, 21–30.
4. Hwu, J. R.; King, K. Y. *Curr. Sci.* **2001**, *81*, 1043–1053.
5. Pottenger, C. R.; Johnson, D. C. *J. Polym. Sci.* **1970**, *8*, 301–318.
6. Mehrotra, R. N.; Amis, E. S. *J. Org. Chem.* **1974**, *39*, 1788–1791.
7. Virtanen, P. O. I.; Lindroos, R.; Oikarinen, E.; Vaskuri *J. Carbohydr. Res.* **1987**, *167*, 29–37.
8. Sen Gupta, K. K.; Sen Gupta, S.; Mahapatra, A. *J. Carbohydr. Chem.* **1989**, *8*, 713–722.
9. Manzo, E.; Barone, G.; Parrilli, M. *Synlett* **2000**, 887–889.
10. Manzo, E.; Barone, G.; Bedini, E.; Iadonisi, A.; Mangoni, L.; Parrilli, M. *Tetrahedron* **2002**, *58*, 129–133.
11. Barone, G.; Bedini, E.; Iadonisi, A.; Manzo, E.; Parrilli, M. *Synlett* **2002**, 1645–1648.
12. Ishida, H.; Seri, K. *Chem. Lett.* **1997**, 379–380.
13. Manzo, E.; Molinaro, A.; Bedini, E.; De Castro, C.; Parrilli, M. *Carbohydr. Res.* **2001**, *333*, 339–342.
14. Kajimura, A.; Sumaoka, J.; Komiyama, M. *Carbohydr. Res.* **1998**, *309*, 345–351.
15. The excess of acid scavenger was evaluated respect to the total concentration of H^+ of the solution, measured by titrimetry.
16. Krishnamurthy, S. S.; Soundararajan, S. 1st Proc. Chem. Symp., Chemistry and Metallurgy Comm. of the Dep. of Atomic Energy, Bombay, 1970; Book of Abstracts, pp 261–264.
17. Sondu, S.; Sethuram, B.; Rao, N. T. *Oxid. Commun.* **1984**, *7*, 223–233.
18. As suggested by a referee, the inclusion of an acid scavenger (potassium carbonate or pyridine) might be expected to attenuate also the Lewis acidity of the Ce(IV), and suppress an eventual Lewis-acid mediated glycolysis pathway; nevertheless the hard character of this Lewis acid means that any reduction in Lewis acidity would be minimal with these additives used.
19. The attempt to see an acidic proton signal in the CAN(III) DMF-d_7 solution was initially unsuccessful, probably due to the presence of water of crystallization, which was then removed by oven drying the salt sample and adding powdered 4 Å molecular sieves to the NMR tube.
20. Zhang, Y.; Flowers, R. A., II *J. Org. Chem.* **2003**, *68*, 4560–4562.
21. The appearance of a single resonance at 4.70 ppm rather than two signals, as could be expected taking into account the possibility of a slow interconversion of the two rotamers, typical for tertiary amides, might be explained suggesting the presence of a very predominant rotamer. Actually molecular models obtained by MM2 force field calculations suggested the presence of an electrostatic attraction between the carboxylic oxygen and the positive-charged nitrogen of nitrate, for only one rotamer, which should be the predominant one.
22. Rudd, E. J.; Finkelstein, M.; Ross, S. D. *J. Org. Chem.* **1972**, *37*, 1763–1767.
23. Genies, M. *Bull. Soc. Chim. Fr.* **1975**, 389–392.
24. Iranpoor, N.; Salehi, P. *Tetrahedron* **1995**, *51*, 900–912.
25. Torii, S.; Tanaka, H.; Ioukuchi, T.; Nakane, S.; Akada, M.; Saito, N.; Sirakawa, T. *J. Org. Chem.* **1982**, *47*, 1647–1652 and references therein.
26. Baes, C. F.; Mesmer, R. E. *The Hydrolysis of Cations*; Wiley: New York, 1976; pp 129–146 and references therein.
27. Chapuzet, J.-M.; Beauchemin, S.; Daoust, B.; Lessard, J. *Tetrahedron* **1996**, *52*, 4175–4180.
28. Gran, G. *Analyst* **1952**, *77*, 661–671.