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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.*

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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

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* Corresponding author. Tel.: +39 081 674147; fax: +39 081 674393; e-mail: parrilli@unina.it

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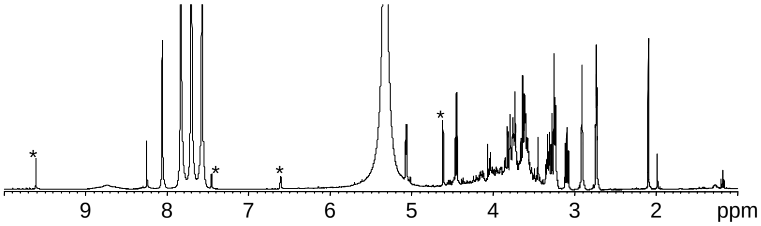

Figure 1. ^{1}H NMR at 400 MHz of the crude CAN sucrose reaction in DMF-d_7 after 2 h at 50 °C (HMF peaks are marked with an asterisk).

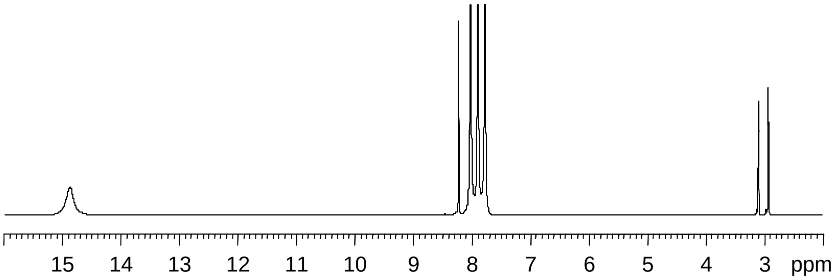

Figure 2. ^{1}H NMR at 400 MHz of the red CAN DMF-d_7 solution at 50 °C.

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-fructofuranose 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

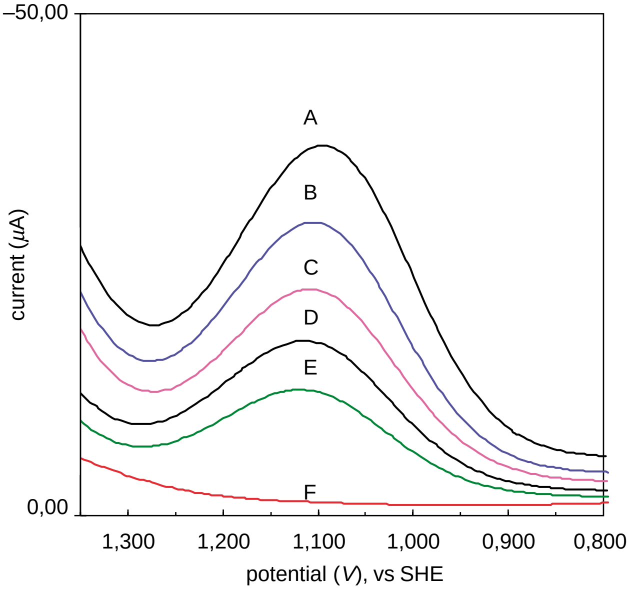

Figure 3. Differential pulse voltammetry for the reduction of CAN at glassy carbon electrode in DMF versus standard hydrogen reference electrode (SHE). The different traces show the decay of Ce(IV) concentration at 20 °C with time: (A) 1 min, (B) 2 min, (C) 4 min, (D) 6 min, (E) 9 min, (F) 20 min.