COMMUNICATION

Reaction of chloride anion with atomic oxygen in aqueous solutions: can cold plasma help in chemistry research?†

Yury Gorbanev, [ID] ⋆[a] Jonas Van der Paal,[a] Wilma Van Boxem,[a] Sylvia Dewilde[b] and Annemie Bogaerts [ID] [a]

Cold atmospheric plasma in contact with solutions has many applications, but its chemistry contains many unknowns such as the undescribed reactions with solutes. By combining experiments and modelling, we report the first direct demonstration of the reaction of chloride with oxygen atoms in aqueous solutions exposed to cold plasma.

Cold atmospheric-pressure plasmas (CAPs) attract interest of researchers from many fields in chemistry, biology, and medicine. The immense potential of CAPs has been shown in green chemistry, materials chemistry, organic chemistry, and many biomedical applications.[1–3] This potential is defined by the large variety of highly reactive oxygen and nitrogen species (RONS), created by plasma.[4] RONS are mostly generated in the gas phase plasma and further interact with targets, which are often represented by liquid solutions.[5] Two main types of cold plasma application are distinguished: (i) direct exposure to CAPs and (ii) indirect treatment, or the use of plasma-treated media (PTM; usually aqueous solutions).[3,6] Depending on the type of treatment, various RONS are responsible for the plasma-induced effects: persistent chemical species as in PTM (H_2O_2, NO_2^-, *etc.*) are combined with short-lived ones (radicals, atoms) during direct plasma application.[7]

Secondary chemistry involving chloride in aqueous solutions exposed to plasma was suggested by several groups.[8–10] The reactions of Cl^- with $^\bullet OH$ or $O_2^{\bullet-}$ radicals leading to ClO^- are known.[11] Very recently, Kondeti *et al.*[12] suggested that in oxygen-containing plasmas, the main reaction leading to ClO^- formation may be a reaction of Cl^- and atomic O (R.1).‡ To the

best of our knowledge, this chemical reaction has not been reported before. Generally, literature on the chemistry of atomic O in liquid phase is limited due to its high reactivity and the absence of simple chemical systems for its generation. The investigation of such process is important for fundamental chemistry purposes, and also has large implications for biomedical plasma research. A direct evidence is required to assess the feasibility of this reaction.

In this work, we studied which RONS can oxidise Cl^- to ClO^- in plasma-treated solutions. We used the COST plasma jet which was created as a 'standard' plasma jet, and its chemistry is well studied both computationally and experimentally.[13] We have previously shown that almost all reactive species are created inside the COST jet, and undergo further reactions in the effluent.[14] Importantly, it was also shown to be an efficient source of O atoms, which were detected in aqueous solutions.[10,15]

The plasma was ignited inside the jet using a feed gas of He with O_2 admixtures operated with two mass flow controllers (MFCs) (Fig. 1), with total flow rate of 1 L min^{-1} (see ESI† for experimental details). We studied the formation of ClO^- in phosphate buffered saline (PBS) exposed to plasma. PBS is often used in biomedical plasma research, especially as PTM.[3,16] Plasma exposure conditions were similar to those we used in our previous works with the COST plasma jet.[3,14]

To assess the interaction of He + O_2 plasma with Cl^- in aqueous media, we measured the concentrations of the

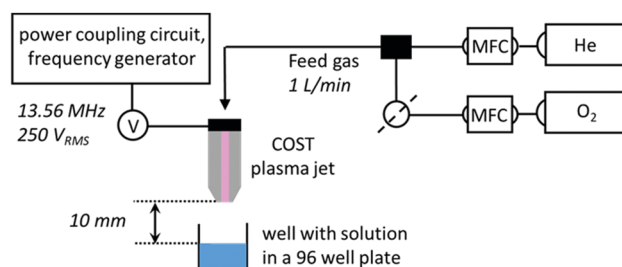[a] *Research Group PLASMANT, Department of Chemistry, University of Antwerp, Universiteitsplein 1, Wilrijk, Antwerpen, BE-2610, Belgium.*
 E-mail: yury.gorbanev@uantwerpen.be
[b] *Protein Chemistry, Proteomics and Epigenetic Signalling,*
 Department of Biomedical Sciences, University of Antwerp, Universiteitsplein 1,
 Wilrijk, Antwerpen, BE-2610, Belgium
† Electronic supplementary information (ESI) available: Detailed description of the chemical kinetics model, materials and the experimental procedures, and further experimental and computational data. See DOI: 10.1039/c8cp07550f
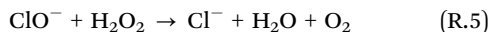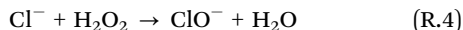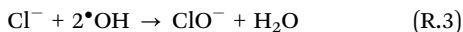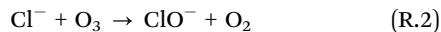

Fig. 1 Experimental setup used in the investigation of the reaction of O atoms with Cl^- in aqueous solutions exposed to the COST plasma jet.

plasma-induced RONS in two solutions: PBS and PB (the same as PBS, but without Cl$^-$).

$$Cl^- + O \rightarrow ClO^- \quad \text{(R.1)}$$

$$Cl^- + O_3 \rightarrow ClO^- + O_2 \quad \text{(R.2)}$$

$$Cl^- + 2{}^\bullet OH \rightarrow ClO^- + H_2O \quad \text{(R.3)}$$

$$Cl^- + H_2O_2 \rightarrow ClO^- + H_2O \quad \text{(R.4)}$$

$$ClO^- + H_2O_2 \rightarrow Cl^- + H_2O + O_2 \quad \text{(R.5)}$$

First, we measured the concentration of ROS (O$_3$, ^{1}O$_2$, O) created by CAP. Of these, only the reaction of O$_3$ with Cl$^-$, yielding ClO$^-$ in aqueous solution, is known (R.2).[17] The ROS concentration was measured based on electron paramagnetic resonance (EPR) spectroscopy analysis of the stable nitroxide TEMPO, formed in the reaction of the spin trap TEMP (2,2,6,6-tetramethylpiperidine) with O and ^{1}O$_2$ (Fig. 2a). Although we previously observed oxidation of TEMP by O$_3$,[18] later all formed TEMPO was ascribed to the reaction of TEMP with O (in the absence of ^{1}O$_2$).[19] To investigate this further, the plasma effluent was not exposed to ambient air, but instead propagated inside an air-free reactor[14,20] (Fig. S1, ESI†). Since ^{1}O$_2$ and O are short-lived, the exhaust of the reactor could contain only O$_3$: its presence was confirmed by the oxidation of 3,3′,5,5′-tetramethyl-benzidine (TMB) in PB exposed to the reactor exhaust (Table S1, ESI†). When a solution of TEMP was exposed to the reactor exhaust for 2 min, no formation of TEMPO was observed. This was consistent with the findings by Elg *et al.*, where O$_3$ at CAP-induced concentrations did not oxidise TEMP.[19] Thus, we conclude that all of the formed TEMPO observed under these experimental conditions was due to the oxidation of TEMP by O and ^{1}O$_2$.

Next, the introduction of an ^{1}O$_2$ scavenger (NaN$_3$) enabled distinguishing between TEMPO formed by O and ^{1}O$_2$.[18] The resulting trends of O and ^{1}O$_2$ concentrations in the liquid compared very well with the trends of their gas phase concentrations predicted by a chemical kinetics model (Fig. 3), once again confirming that TEMPO here was formed only by these ROS. The gas phase densities were obtained from a model containing 96 species and 1390 reactions. Our model evaluated the chemistry occurring inside the jet, as well as in the effluent, up to the liquid surface (see ESI,† Fig. S2 and model description). The observed trend of TEMPO concentration was virtually the same in PBS and PB, except that the concentrations were slightly lower in PBS, both with and without added NaN$_3$ (Fig. S3, ESI†). This is probably due to the partial scavenging of O atoms by Cl$^-$. The total concentration of Cl$^-$ in PBS is *ca.* 140 mM,[21] and TEMP was used at 20 mM concentration (see ESI†). Since the concentration of the formed TEMPO changed only marginally in the presence of Cl$^-$, the reaction rate coefficient of O with Cl$^-$ is likely around 2–3 orders of magnitude lower than that of O with TEMP. Further kinetic studies are required for precise evaluation of this reaction.

Further, we assessed the amounts of other plasma-induced RONS such as NO$_2^-$, H$_2$O$_2$, $^\bullet$OH and $^\bullet$OOH/O$_2^{\bullet-}$ in plasma-treated

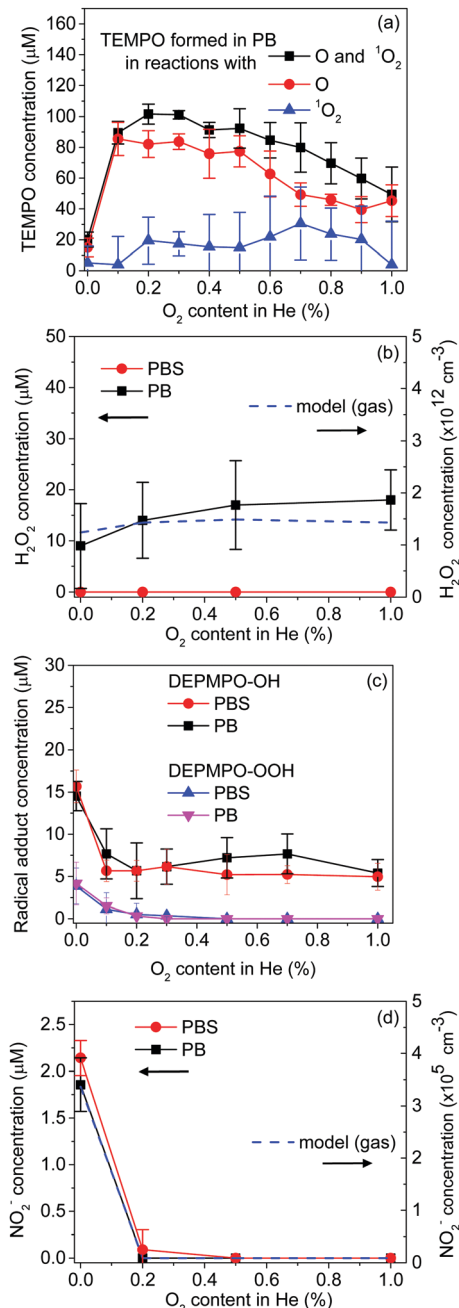Fig. 2 Concentrations of (a) spin trapped O/^{1}O$_2$ in PB by He + O$_2$ plasma; (b) H$_2$O$_2$, (c) spin trapped $^\bullet$OH and O$_2^{\bullet-}$/$^\bullet$OOH radicals, and (d) NO$_2^-$ in both PB and PBS. The error bars are the standard deviations between 3 measurements. The concentrations of ^{1}O$_2$-induced TEMPO were obtained as a difference between the experimental results with and without NaN$_3$; the errors bars are the sum of those obtained in the two conditions. The concentration of TEMPO formed in PBS can be found in Fig. S3 (ESI†). Gas phase modelling data is shown with dashed lines. Additional modelling data is shown in Fig. S4 (ESI†).

PB and PBS (Fig. 2b–d). H$_2$O$_2$ and NO$_2^-$ were detected using colourimetry with Ti(IV) and the Griess reagent, respectively, and the radicals were detected by EPR, as described in our previous works[3,14,18] (see also ESI†).

With the COST jet, H$_2$O$_2$ can be either formed in the liquid from $^\bullet$OH radicals, or delivered into the liquid already in its

4118 | *Phys. Chem. Chem. Phys.*, 2019, 21, 4117–4121
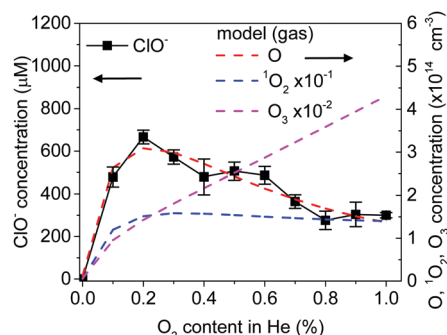
This journal is © the Owner Societies 2019

Fig. 3 Concentration of ClO⁻ in plasma-treated PBS as determined by UV-vis spectrophotometry, and gas phase concentrations of O, $^1O_2$ and O_3 (dashed lines) as predicted by the chemical kinetics model. The error bars are the standard deviations between 3 measurements.

molecular form.[14] However, while low concentrations were detected in PB, no H_2O_2 was detected in PBS (Fig. 2b). This suggests that either •OH or H_2O_2 (or both) were scavenged by Cl⁻ ((R.3) and (R.4)).

Unlike H_2O_2 which was detected in the liquid after the CAP treatment (and thus was largely affected by further reactions in PBS, involving Cl⁻ and/or ClO⁻), the radicals were spin trapped during the plasma exposure. The EPR analysis with 5-diethoxy-phosphoryl-5-methyl-1-pyrroline N-oxide (DEPMPO) spin trap showed that the concentrations of the radicals decreased dramatically in both PBS and PB when O_2 was added to He (Fig. 2c). The experimentally measured concentrations of H_2O_2 and the radical adducts DEPMPO–OOH and DEPMPO–OH generally agreed with the trends of the concentrations obtained by chemical kinetics modelling (dashed line in Fig. 2b and Fig. S4, ESI†). These data together suggest that H_2O_2 detected in PB was delivered to the solution at least partially in molecular form, and was not detected in PBS due to the reaction with Cl⁻ (leading to ClO⁻)[17] and/or with the formed ClO⁻ [22] ((R.4) and (R.5)).

NO_2^- was formed due to the interaction of the plasma effluent with ambient air. The NO_2^- concentration dropped below the detection limit in both PBS and PB with O_2 in the feed gas (Fig. 2d). This could happen due to the reaction between NO_2^- and the formed ClO⁻ in PBS.[23] However, since the same trend was also observed in PB and was predicted by the model (see dashed line in Fig. 2d), and as the latter did not include Cl⁻ chemistry, we propose that this was due to the further oxidation of NO_2^- to NO_3^-, or of NO_2^- precursors to N_2O_5 (Fig. S4, ESI†).

Most importantly, the results show that the main species present in the system, and which can oxidise Cl⁻ to ClO⁻, is indeed atomic oxygen. This species is delivered to the solutions in high concentrations by the COST jet operated with O_2 admixtures, making this CAP system a unique tool for the selective O induction in liquid.

Finally, we assessed the formation of ClO⁻ in PBS by exposure to plasma. A facile and sensitive measurement of ClO⁻ presents a challenge. Reports on ClO⁻ detection in CAP-exposed water suggest the possible use of L-tyrosine,[24] or describe deep UV spectrophotometry with a high detection limit.[11,12] In this study,

we used a recently reported colourimetric method based on the oxidation of TMB,[25] which allowed us to detect ClO⁻ with a lower limit of 1–2 μM (ESI,† Fig. S5). Since TMB can react with several oxidising species,[25] we investigated the applicability of the method for selective ClO⁻ detection in plasma-treated PBS, i.e. the interference of other possible CAP-induced primary and secondary reactive species. ClO_3^- and ClO_4^- (possible products of further oxidation of ClO⁻) and H_2O_2 did not oxidise TMB in concentrations of up to 1 mM, whereas ClO_2^- did, but only after a long incubation time, in contrast with ClO⁻ (Fig. S6, ESI†). In any case, we did not detect ClO_2^-, ClO_3^- or ClO_4^- in plasma-treated PBS using ion chromatography (see ESI†). NO_2^- (added as $NaNO_2$) used in concentrations detected in plasma-treated PB or PBS did not oxidise TMB either (Fig. S7, ESI†). Furthermore, PB exposed to He + O_2 plasma with any studied O_2 content did not oxidise TMB, clearly indicating the absence of any residual O_3 remaining in solution after plasma treatment. Thus, the presented method is both rather selective and highly sensitive, and can be used for the detection of ClO⁻ in PTM. It also enables the detection of ClO⁻ in a regular plate reader without requiring deep UV spectrophotometers. However, it is not applicable in situ during the treatment, due to the oxidation of TMB by O_3 and possibly other plasma RONS.

The trend of the measured ClO⁻ concentration as a function of the O_2 content in the feed gas is shown in Fig. 3. We also performed ClO⁻ measurements as a function of plasma treatment time, to ascertain that at no experimental time point the ClO⁻ concentration was decreasing (Fig. S8, ESI†). Remarkably, the trend of ClO⁻ concentration coincided with that of the O atom concentration calculated by the computational model (Fig. 3). At the same time, the O_3 concentration in the gas phase increased with higher content of O_2, while the $^1O_2$ concentration stayed nearly the same at 0.2–1% O_2. Additionally, when PBS was first exposed to the O_3-rich exhaust of the air-free reactor (as described above) and then analysed with TMB, no ClO⁻ was detected. Therefore, we conclude that most of the ClO⁻ was formed due to the reactions with atomic O, and not with other RONS created by plasma.

Thus, we were able to confirm the reaction between Cl⁻ and atomic O, which yields ClO⁻, from (i) the similarity of the experimentally obtained trends of the formed ClO⁻ concentration and TEMPO formed by O, (ii) nearly identical trends of formed ClO⁻ and the model-predicted gas phase concentration of atomic O, and (iii) the reduced amounts of TEMPO formed in PBS compared to PB (Fig. 2a, 3 and Fig. S3, ESI†).

To evaluate the potential generation of ClO⁻ in PBS treated by other plasma mixtures, we monitored its formation with a He + H_2O plasma. We previously demonstrated that He with 5–20% saturation of H_2O induces large concentrations of •OH and H_2O_2 (in the hundreds of μM range) in PBS.[3] This high concentration of •OH implies possible formation of ClO⁻ [12,17] (R.3). However, we did not detect any ClO⁻ in this case. To understand this discrepancy, we studied the stability of ClO⁻ (added to PBS as NaOCl) in the presence of other RONS, specifically NO_2^- and H_2O_2 which can react with ClO⁻ and thus deplete it. The results showed fast reactions leading to
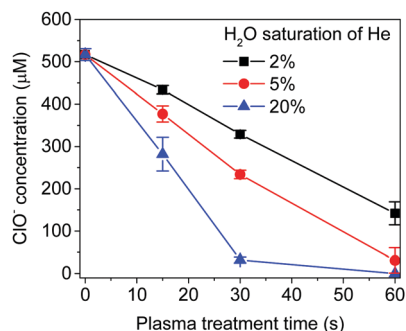
This journal is © the Owner Societies 2019

Phys. Chem. Chem. Phys., 2019, 21, 4117–4121 | 4119

Fig. 4 Decay of ClO⁻ added to PBS upon treatment by He + H₂O plasma.

decay of ClO⁻ up to its complete disappearance, with 1:1 stoichiometries, in agreement with available literature[22,23] (Fig. S9, ESI†). Since He + H₂O plasma generates large amounts of H₂O₂ under the conditions used in this work,[3] it was thus possible that ClO⁻ (formed in the reaction of Cl⁻ with •OH) was consumed in a reaction with H₂O₂ (R.5).

We also treated PBS with the pre-added ClO⁻ (500 µM) by He + H₂O plasma. The concentration of ClO⁻ decreased with higher H₂O vapour saturation of He (Fig. 4). The added ClO⁻ was likely decaying in a reaction with H₂O₂ (R.5), as seen from the stoichiometry of the decay (1:1),[22] in agreement with the data on the CAP-induced H₂O₂ concentrations at various H₂O content in He.[3] Other RONS present in smaller concentrations (such as NO₂⁻₃) could also contribute to degradation of ClO⁻. Since both the pre-added ClO⁻ and the He + O₂ plasma-generated ClO⁻ were stable in PBS (Fig. S10, ESI†) and we did not observe any pH change that could lead to ClO⁻ degradation, we conclude that with He + H₂O plasma ClO⁻ was formed from •OH (R.3), but was also consumed either during the plasma exposure or shortly after (within 1 min). CAPs rarely generate •OH without also creating H₂O₂ in the gas phase. Therefore, although ClO⁻ may be formed from Cl⁻ by •OH radicals, it will be consumed by H₂O₂ (or NO₂⁻ in CAPs operating with air).

In other words, while ClO⁻, possessing high biomedically relevant properties,[12] may potentially be formed in Cl⁻-rich solutions such as PBS by almost all plasmas in situ, its effect on biological or other substrates will depend on the rate of its decay by other CAP-produced RONS.

To summarize, we demonstrate, using a combination of experimental and modelling approaches: (1) a new reaction of Cl⁻ with atomic oxygen yielding ClO⁻; (2) the high dependence of ClO⁻ stability in PTM on other CAP-generated RONS; (3) the virtually absent net production of ClO⁻ in H₂O-vapour saturated plasmas. This emphasises the importance of liquid phase reactions in plasma-exposed solutions. The generation of the secondary reactive species (either short-lived in situ, or persistent in PTM) from solution components could affect biological substrates, similarly to the primary plasma RONS. In addition, we also presented a facile method for ClO⁻ detection in plasma-treated aqueous solutions. Finally and most importantly, we illustrate that cold plasma can serve as a unique tool for generation of short-lived RONS, such as O atoms, much sought-after in chemical applications.

Conflicts of interest

There are no conflicts to declare.

Notes and references

‡ The reaction equations represent the overall chemical reactions.

1 J. Harris, A. N. Phan and K. Zhang, *Green Chem.*, 2018, **20**, 2578–2587.
2 Y. Gorbanev, D. Leifert, A. Studer, D. O'Connell and V. Chechik, *Chem. Commun.*, 2017, **53**, 3685–3688.
3 A. Privat-Maldonado, Y. Gorbanev, S. Dewilde, E. Smits and A. Bogaerts, *Cancers*, 2018, **10**, 394.
4 I. Adamovich, S. D. Baalrud, A. Bogaerts, P. J. Bruggeman, M. Cappelli, V. Colombo, U. Czarnetzki, U. Ebert, J. G. Eden and P. Favia, *et al.*, *J. Phys. D: Appl. Phys.*, 2017, **50**, 323001.
5 P. J. Bruggeman, M. J. Kushner, B. R. Locke, J. G. E. Gardeniers, W. G. Graham, D. B. Graves, R. C. H. M. Hofman-Caris, D. Maric, J. P. Reid and E. Ceriani, *et al.*, *Plasma Sources Sci. Technol.*, 2016, **25**, 053002.
6 A. Pankaj, P. Ji Hoon, A. Anser and C. Eun Ha, *Anti-Cancer Agents Med. Chem.*, 2018, **18**, 805–814.
7 Y. Gorbanev, A. Privat-Maldonado and A. Bogaerts, *Anal. Chem.*, 2018, **90**, 13151–13158.
8 M. A. C. Hänsch, M. Mann, K. D. Weltmann and T. von Woedtke, *J. Phys. D: Appl. Phys.*, 2015, **48**, 454001.
9 Z. Ke, Z. Chen and Q. Huang, *Plasma Processes Polym.*, 2017, **15**, 1700153.
10 M. M. Hefny, C. Pattyn, P. Lukes and J. Benedikt, *J. Phys. D: Appl. Phys.*, 2016, **49**, 404002.
11 I. M. Piskarev, *High Energy Chem.*, 2017, **51**, 297–301.
12 V. S. S. K. Kondeti, C. Q. Phan, K. Wende, H. Jablonowski, U. Gangal, J. L. Granick, R. C. Hunter and P. J. Bruggeman, *Free Radical Biol. Med.*, 2018, **124**, 275–287.
13 J. Golda, J. Held, B. Redeker, M. Konkowski, P. Beijer, A. Sobota, G. Kroesen, N. S. J. Braithwaite, S. Reuter and M. M. Turner, *et al.*, *J. Phys. D: Appl. Phys.*, 2016, **49**, 084003.
14 Y. Gorbanev, C. C. W. Verlackt, S. Tinck, E. Tuenter, K. Foubert, P. Cos and A. Bogaerts, *Phys. Chem. Chem. Phys.*, 2018, **20**, 2797–2808.
15 J. Benedikt, M. Mokhtar Hefny, A. Shaw, B. R. Buckley, F. Iza, S. Schäkermann and J. E. Bandow, *Phys. Chem. Chem. Phys.*, 2018, **20**, 12037–12042.
16 W. Van Boxem, J. Van der Paal, Y. Gorbanev, S. Vanuytsel, E. Smits, S. Dewilde and A. Bogaerts, *Sci. Rep.*, 2017, **7**, 16478.

4120 | *Phys. Chem. Chem. Phys.*, 2019, **21**, 4117–4121

This journal is © the Owner Societies 2019

17 Z. C. Liu, L. Guo, D. X. Liu, M. Z. Rong, H. L. Chen and M. G. Kong, *Plasma Processes Polym.*, 2017, **14**, 1600113.

18 Y. Gorbanev, D. O'Connell and V. Chechik, *Chem. – Eur. J.*, 2016, **22**, 3496–3505.

19 D. T. Elg, I. W. Yang and D. B. Graves, *J. Phys. D: Appl. Phys.*, 2017, **50**, 475201.

20 Y. Gorbanev, R. Soriano, D. O'Connell and V. Chechik, *J. Visualized Exp.*, 2016, **117**, e54765.

21 A. A. Green, *J. Am. Chem. Soc.*, 1933, **55**, 2331–2336.

22 A. M. Shams El Din and R. A. Mohammed, *Desalination*, 1998, **115**, 145–153.

23 J. M. Cachaza, J. Casado, A. Castro and M. A. L. Quintela, *Can. J. Chem.*, 1976, **54**, 3401–3406.

24 K. Wende, P. Williams, J. Dalluge, W. Van Gaens, H. Aboubakr, J. Bischof, T. von Woedtke, S. M. Goyal, K.-D. Weltmann and A. Bogaerts, *et al.*, *Biointerphases*, 2015, **10**, 029518.

25 Y. Guo, Q. Ma, F. Cao, Q. Zhao and X. Ji, *Anal. Methods*, 2015, **7**, 4055–4058.