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β-CD assisted dissolution of quaternary ammonium permanganates in aqueous medium

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ABSTRACT

The non-polar internal cavity of β-cyclodextrin (β-CD) has been exploited for the entrapment of the hydrophobic tails of two water insoluble quaternary ammonium permanganates (QAPs): cetyltrimethylammonium permanganate (CTAP) and tetrabutylammonium permanganate (TBAP), for solubilization in aqueous medium. The solubilization and organizational behavior of the QAPs in aqueous β-CD solution have been determined from the comparison of their rates of self-oxidation in presence and in absence of β-CD. Effect of QAP concentration on their observed rate constants (k_{obs}) at a fixed β-CD concentration, phase solubility analysis in varying β-CD concentration, impact of quaternary ammonium bromides (QABs) on the k_{obs} values of CTAP and TBAP at fixed QAP and β-CD concentrations, and the temperature effect have been reported. A scheme to explain the solvation of QAPs in aqueous β-CD has been proposed based on dynamic light scattering (DLS) analysis of the samples.

1. Introduction

Quaternary ammonium permanganates (QAPs) are an established class of phase transfer oxidants, used for the oxidation of water-insoluble organic compounds of various classes. QAPs are sparingly soluble in water medium; however, they show strong solubility in several organic solvents (Dash & Mishra, 1995). The major problem with these compounds is that they undergo a rapid self-oxidation/dissociation in organic media (Scheme 1); hence choosing a proper medium is generally necessary for their efficient utilization as oxidant for organic substrates. Besides, the compounds are perfectly soluble in organic media only, restricting their utilization for the oxidation of inorganic substrates.

The present communication focuses on a model for the dissolution of some QAP molecules in water medium assisted by β-cyclodextrin (β-CD) from the comparison of their rate constants of self-oxidation in presence and in absence of β-CD. Cyclodextrins are cyclic oligosaccharides composed of glucose units linked by α-1,4-glycosidic bonds. These are of three types: α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, being composed of 6, 7, and 8 α-1,4-glycosidic bonds; each cyclodextrin unit having a hydrophobic cavity, which can act as a host for a hydrophobic guest molecule (Martin Del Valle, 2003). Despite the presence of hydroxyl groups on β-CD, permanganate does not cause any notable oxidation of this host molecule (Manhas, Mohammed, & Khan, 2007).

The most notable feature of cyclodextrins is their ability to form inclusion complexes (host–guest complexes) with a wide range of solid, liquid and gaseous compounds by molecular complexation. The lipophilic cavity of cyclodextrin molecules provides a microenvironment into which appropriately sized non-polar moieties can enter to form inclusion complexes (Loftsson & Brewster, 1996). This property is useful for solubilizing and stabilizing highly hydrophobic molecules in water. No hydrogen bonds are formed or broken during the formation of such host-guest complexes (Singh, Sharma, & Banerjee, 2002). Solubilization may also occur through the formation of micellar types of aggregate in aqueous solutions (Loftsson, Jarho, Masson, & Jarvinen, 2005). The main driving force of complex formation is the release of enthalpy-rich water molecules from the cavity. Water molecules are displaced by more hydrophobic guest molecules present in the solution to attain an apolar–apolar association and decrease the cyclodextrin ring strain resulting in a more stable lower energy state (Szetjli, 1998). The binding of guest molecules within the host cyclodextrin is not fixed or permanent; rather, it is in the state of a dynamic equilibrium.

The ability of cyclodextrin to form an inclusion complex with a guest molecule is a function of two key factors such as steric factor and critical factor. The steric factor depends on the relative size of the cyclodextrin to the size of the guest molecule or certain key functional groups within the guest and the critical factor represents the thermodynamic interactions between the different

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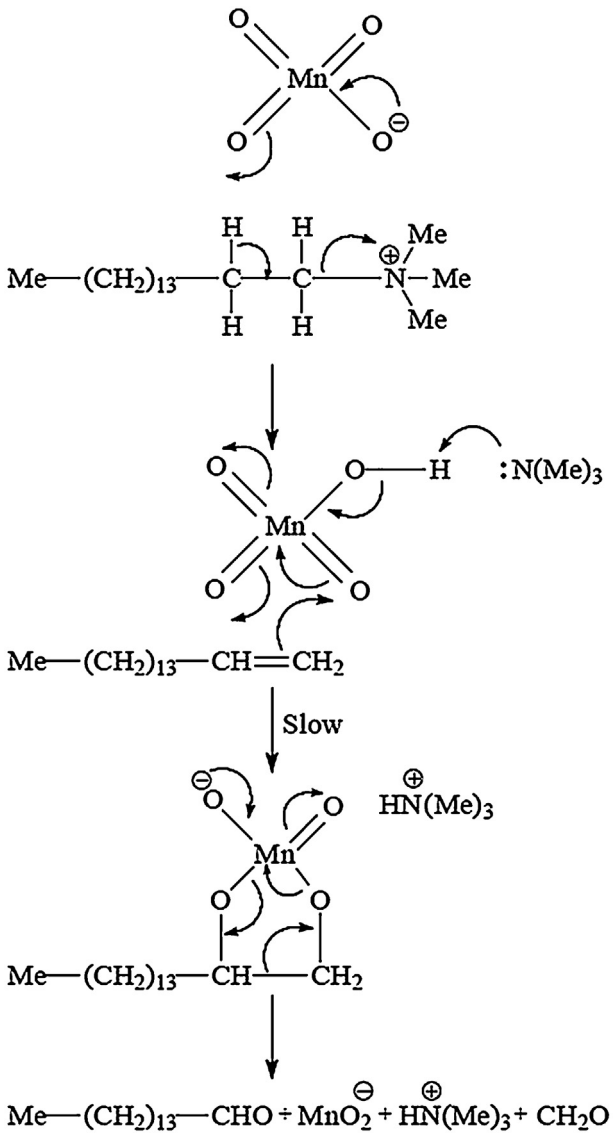


Scheme 1. Self-oxidation of CTAP in chloroform medium.

components of the system (cyclodextrin, guest, solvent) (Martin Del Valle, 2003). For a complex to form there must be a favorable net energetic driving force that pulls the guest into the cyclodextrin. In general, there are four energetically favorable interactions that help shift the equilibrium to form the inclusion complex (Martin Del Valle, 2003): (a) the displacement of polar water molecules from the apolar cyclodextrin cavity, (b) the increased number of hydrogen bonds formed as the displaced water returns to the larger pool, (c) a reduction of the repulsive interactions between the hydrophobic guest and the aqueous environment, and (d) an increase in the hydrophobic interactions as the guest inserts itself into the apolar cyclodextrin cavity. However, host cyclodextrin molecules are also known to form non-inclusion complexes. (Loftsson, Masson, & Brewster, 2004; Loftsson, Magnusdottir, Masson, & Sigurjonsdottir, 2002).

The solution behavior of cetyltrimethylammonium permanganate (CTAP) and tetrabutylammonium permanganate (TBAP) containing C_{16} and C_4 chains respectively in water medium in presence of β-CD have been studied to understand the β-CD-QAP inclusion complexation, their stability and self-oxidation/dissociation properties as well as their oxidizing capabilities of various substrates in that medium. The combination of β-CD and QAPs to create new functionalized oxidant, therefore, will become highly important in the years to come.

2. Materials and methods

2.1. Materials

CTAP and TBAP were synthesized in the laboratory as per the standard procedures (Chidambaram, Sonavane, de la, & Sasson, 2007; Dash et al., 1995). Quaternary ammonium bromides (QAB) such as cetyltrimethylammonium bromide (CTAB) and tetrabutylammonium bromide (TBAB) were procured from Merck, India, and were recrystallized using methanol solution and their purity was checked from physical constants. β-CD (Merck, India) was used as received and triple distilled water was used throughout the experiments.

2.2. Methods

2.2.1. Preparation of solutions

β-CD (8.0 mmol) was dissolved in 500 ml triple distilled water through slight warming, filtered through a cotton plug to prepare the stock solution of 15 mM concentration, which was used for the preparation of a range of solutions of β-CD of concentrations 1.5–15 mM. Freshly prepared solutions of CTAP and TBAP (0.5–0.9 mM) in aqueous β-CD medium maintained within the above concentration range, were prepared and filtered by cotton plug to obtain clear solutions of CTAP and TBAP.

2.2.2. Absorption spectral analysis

Solutions having appropriate concentrations of the QAPs and β-CD were transferred to the sample cuvette of a pair of matched quartz cells to measure the rates of self-oxidation/dissociation of QAPs by a thermostated Hitachi U-3010 double beam UV–vis spectrophotometer at $22.0 \pm 1\,^{\circ}C$ at four different wavelengths (λ_{max}) of 568, 546, 528, and 486 nm. The measurements were done for 40 min in each case with 2 min time interval. All the calculations have been done at a standard λ_{max} of 528 nm and the rate constant values (k_{obs}) have been calculated using Eq. (1) (Dash et al., 1995).

$$k_{obs} = \left(\frac{2.303}{t}\right) \log\left(\frac{OD_o}{OD_t}\right) \quad (1)$$

where OD_o = optical density at '0' time, OD_t = optical density at time 't'.

The results reported are an average of three runs with an error of (±) 6.0%.

2.2.3. Dynamic light scattering analysis

Dynamic light scattering measurements were made on the fixed scattering angle Zetasizer Nano-ZS system (Malvern, UK) equipped with a He–Ne laser beam at 658 nm. The instrument was used for sizing (dynamic light scattering, DLS) to determine the z-average molecular "size" in terms of the hydrodynamic diameter d_H in solution, a parameter inversely related to the z-average translational diffusion coefficient, D (Eq. (2)) in solution.

$$D = \frac{kBT}{3\pi\eta dH} \quad (2)$$

Samples, filtered through cotton plug, were measured at $22.0 \pm 1\,^{\circ}C$ and the light scattering was detected at 173° and collected in automatic mode, typically requiring a measurement duration of 120 s.

2.2.4. Phase solubility analysis

Phase–solubility analysis of β-CD on the QAPs has been carried out after constructing a phase-solubility diagram by plotting the

total molar concentration of the QAPs on the y-axis and the total molar concentration of β-CD on the x-axis and the profile of the change has been recorded to determine the type of complexation, stability constant ($K_{y:x}$) and the complexation efficiency of β-CD with QAP molecules (Higuchi & Connors, 1965).

For a linear profile of the plot (A_L), which represents a 1:1 complexation (Eq. (3)), the stability constant ($K_{1:1}$) of the complex has been calculated from the slope of the plot, according to Eq. (4).

$$Guest + \beta\text{-CD} = Guest - \beta\text{-CD} \quad (3)$$

$$K_{1:1} = \frac{slope}{S_o(1 - slope)} \quad (4)$$

where S_o = Intrinsic solubility of guest molecules in aqueous complexation medium (i.e. guest molecule solubility when no cyclodextrin is present).

The complexation efficiency (CE) for 1:1 inclusion complex has been calculated from the slope of the plot using Eq. (5).

$$CE = \frac{[Guest - \beta\text{-CD}]}{[\beta\text{-CD}]} = S_o \cdot K_{1:1} = \frac{slope}{(1 - slope)} \quad (5)$$

3. Results and discussion

3.1. Analysis of phase-solubility

Variation of optical density and rate constant of dissociation of QAP with concentration of β-CD has been analyzed to study the phase-solubility analysis of the QAPs. The molar concentration of both CTAP and TBAP have been calculated from their optical densities in their 0.5 mM solution in aqueous β-CD solutions of variable concentrations (1.5–15 mM) using the well-known Beer–Lambart equation (Eq. (6)).

$$OD = \varepsilon.c.l \quad (6)$$

where OD = optical density, ε = extinction coefficient of permanganate (2300 M^{-1} cm^{-1}), c = molar concentration of the substrate, and l = path length of the quartz cell (1 cm).

The plots of molar concentrations of CTAP and TBAP with the concentration of β-CD represent the solution phase-solubility profile for the β-CD induced dissolution of CTAP and TBAP from aqueous medium and are found to be of A_L type (i.e. a linear increase in the solubility of CTAP and TBAP as a function of β-CD concentration), which is indicative of the formation of soluble inclusion complexes (Fig. 1).

The slopes of the phase-solubility profile for CTAP and TBAP are found to be 0.0894 and 0.0483 respectively, which are less than unity, suggesting a probability of formation of 1:1 inclusion complexes, thus enhancing the solubility of the quaternary ammonium ions in aqueous β-CD medium. However, beside the formation of inclusion complexes, formation of some non-inclusion complexes cannot completely be excluded.

Intrinsic solubilities of CTAP ($S_{o\,CTAP}$) and TBAP ($S_{o\,TBAP}$) in aqueous complexation medium (i.e. QAP solubility when no cyclodextrin is present) are found to be 0.9 μg/mL in both the cases. The stability constants ($K_{1:1}$) for CTAP and TBAP are found to be 109.1 and 56.4 M^{-1} indicating the formation of stable inclusion complexes between β-CD and each of the QAP solute (Connors, 1997).

Complexation efficiency (CE) value for CTAP (CE_{CTAP} = 0.1) is found to be 50% more than that of TBAP (CE_{TBAP} = 0.05). A higher CE value for CTAP than that for TBAP suggest that CTAP is more susceptible for being trapped into the hydrophobic microenvironment of the β-CD since it is hydrophobic due to the presence of long hexadecyl chain. This assumption is also supported by a higher stability constant ($K_{1:1}$) for the CTAP-β-CD inclusion complex than the TBAP-β-CD inclusion complex. Quantification of β-CD molecule

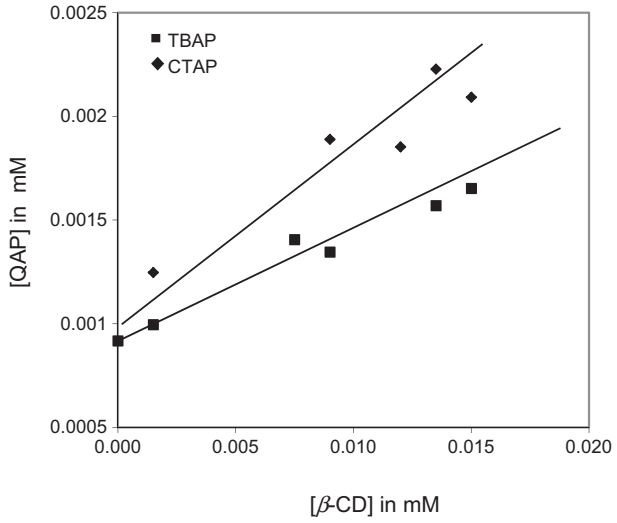


Fig. 1. Variation of [β-CD] in mM with [QAP] in mM in aqueous medium at 22.0 ± 1 °C.

that potentially forms inclusion complex with the number of substrate molecules have been done form the CE value. In case of CTAP, the number of substrate molecules is calculated to be 1 in every 11 number of β-CD molecules, and in case of TBAP, the number of substrate molecules is 1 in every 21 number of β-CD molecules (Loftsson, Hreinsdíottir, & Míasson, 2005).

From the kinetics study it is evident that concentration of cyclodextrin is directly related to the first order rate constant (Fig. 2).

When the number of cyclodextrin molecule increases for a fixed number of guest molecules, the later finds more option to be encapsulated, either due to inclusion and/or non inclusion type complexation and aggregation. Besides, an increase in the rate constant is indicative of the shifting of the equilibrium toward right, thereby leading to the enhanced stability of the guest after complexation. The stability of the 1:1 inclusion complex can also be deciphered from the dissociation constant value. The lower value for the dissociation kinetics indicates the stronger host–guest complexation (Loftsson & Brewster, 2012). The slope for variation of rate constant of CTAP dissociation (Sl_{CTAP} = 4.84)

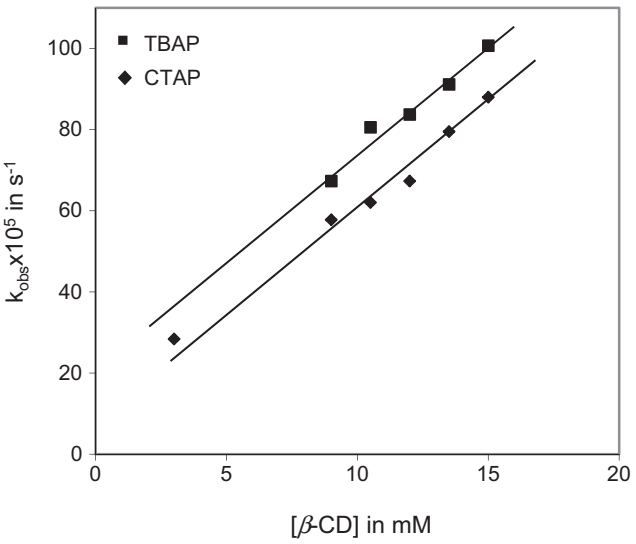


Fig. 2. Variation of [β-CD] in mM with rate constants of self-oxidation/dissociation of QAPs in aqueous medium at 22.0 ± 1 °C.

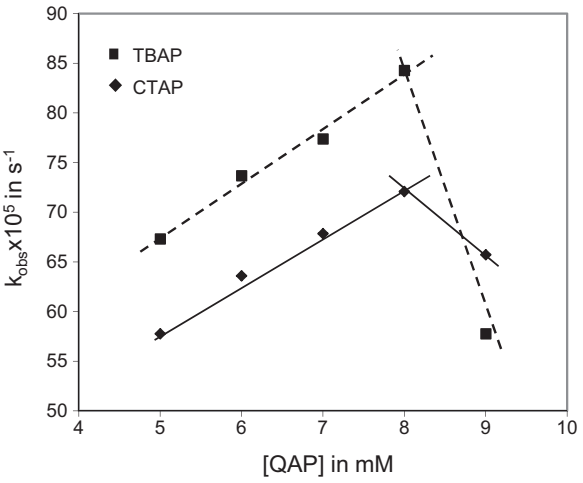


Fig. 3. Variation of [QAP] in mM with rate constants of self-oxidation/dissociation at a fixed β-CD concentration of 9.0 mM in aqueous medium at 22.0 ± 1 °C.

is found to be lower than that for variation of rate constant of TBAP dissociation (Sl_{TBAP} = 5.16) indicating a stronger host–guest complexation in case of CTAP. As the cyclodextrin concentration increases, the cyclodextrin molecules and their complexes self-assemble to form aggregates that often ranges in size between 20 and 100 nm in diameter. The aggregation and the size of the aggregates increase with increasing cyclodextrin concentration (Messner, Kurkov, Jansook, Loftsson, 2010; Jansook, Kurkov, & Loftsson, 2010; Messner, Kurkov, Brewster, Jansook, & Loftsson, 2011; Messner, Kurkov, Flavia-Piera, Brewster, & Loftsson, 2011; Messner, Kurkov, Palazon, et al., 2011; Rao & Geckeler, 2011).

3.2. Variation of CTAP and TBAP concentration in fixed β-CD concentration

Keeping the concentration of β-CD at an optimum value of 9.0 mM within the concentration range of 1.5–15 mM, the inclusion complexation and/or non-inclusion complexation leading to the stability of CTAP and TBAP as well as the possibility of self-oxidation/dissociation of both the QAPs were enumerated. The possible self-oxidation/dissociation of both the QAPs was also compared with the data obtained in absence of β-CD. The pseudo-first order rate constants (k_{obs}) determined from their kinetic study at 22.0 ± 1 °C are found to increase with concentration of both the QAPs up to 0.8 mM, beyond which they decrease. In case of CTAP, the slope of the increasing arm of the plot is 0.472 and that of decreasing arm is −0.636, whereas in case of TBAP, the slope of the increasing arm of the plot is 0.546 and that of decreasing arm is −2.65 (Fig. 3). A sharper change of rate constant in TBAP solutions is indicated from the slopes of both the arms.

With the increase in the concentration of CTAP up to 0.8 mM in aqueous β-CD medium there occurs an increase in the rate constant (k_{obs}) of self-oxidation, a phenomenon which is in sharp contrast with the previous observations during its self oxidation in neat organic solvents, where the rate constant values go on decreasing with concentration rise of CTAP (Dash et al., 1995). The reverse dependence of rate constants on the concentration of CTAP in neat organic medium was proposed to be due to reverse micellization phenomenon of CTAP, which helps in decreasing the self-oxidation of CTAP due to the increase in the extent of aggregation with the rise in the concentration of CTAP (Dash & Mishra, 1997; Dash, Nayak, Sahu, Patel, & Mishra, 2008; Patel & Mishra, 2006). In the present case, the increase in the k_{obs} values for both the QAPs up to a concentration of 8×10^{-4} M, thus indicates the absence of any micellar or reverse micellar aggregation; rather it is an indication of inclusion

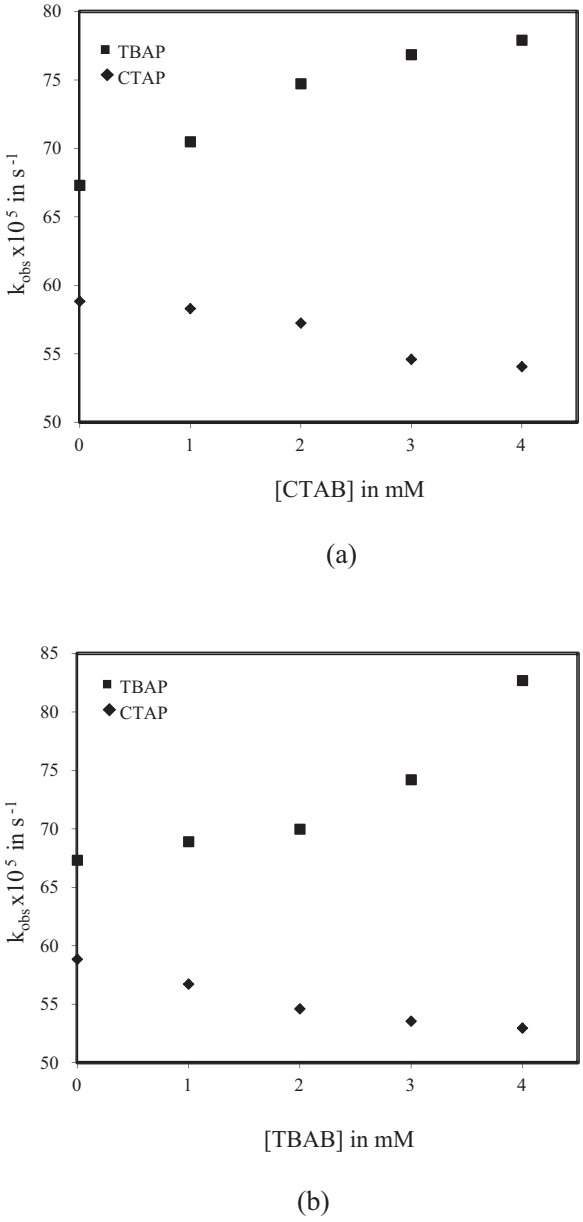


Fig. 4. Effect of [CTAB] in mM (a) and [TBAB] in mM (b) on rate constants of CTAP and TBAP at a fixed β-CD concentration of 9.0 mM in aqueous medium at 22.0 ± 1 °C.

complexation with the inner non-polar cavity of β-CD molecules present in the aqueous medium. In other words, the possibility of micellar aggregation of free QAP molecules up to the above-mentioned concentration in each case are potentially overcome by inclusion complexation with β-CD. Beyond the concentration of 0.8 mM, a sharp decrease in the k_{obs} values for both the QAPs may be due to the aggregation of β-CD inclusion complexes.

3.3. Effect of QAB (CTAB and TBAB)

The effects of CTAB and TBAB have been studied on the self-oxidation/dissociation of CTAP and TBAP at an optimum concentration of 0.5 mM in 9.0 mM β-CD aqueous solution at 22.0 ± 1 °C. The rate constants (k_{obs}) for the self-oxidation of CTAP show a decreasing trend with the increased concentrations of CTAB and TBAB, whereas a reverse trend is observed in case of TBAP (Fig. 4).

Table 1
Size distribution of QAPs and QAP + QABs in aqueous β-CD medium, [β-CD] = 9.0 mM.

Samples[a]	Mean intensity percent at various size range		
	0–100 nm	100–1000 nm	1000–3000 nm
1	13	65	–
2	52	60	–
3	80	62	–
4	07	35	11
5	08	16	05
6	09	11	09

[a] Sample 1: [CTAP] = 0.5–0.9 mM, Sample 2: [TBAB] = 0.0–0.4 mM, [CTAP] = 0.5 mM (Constant), Sample 3: [CTAB] = 0.0–0.4 mM, [CTAP] = 0.5 mM (Constant), Sample 4: [TBAP] = 0.5–0.9 mM, Sample 5: [TBAB] = 0.0–0.4 mM, [TBAP] = 0.5 mM (Constant), Sample 6: [CTAB] = 0.0–0.4 mM, [TBAP] = 0.5 mM (Constant).

Increase in the CTAP and TBAP concentration in the aqueous solution with a constant β-CD concentration increases the rate constant up to a concentration of 0.8 mM of the QAPs, since up to that concentration the inclusion complexes of β-CD–QAP exist in monomeric form. Beyond this concentration, aggregation has been proposed resulting in a decrease in the rate constant values. In the present case, prior to the addition of QABs, the β-CD–QAP inclusion complexes continue to remain in monomeric form; however, addition of QABs change the rate constants of self-oxidation/dissociation of CTAP as well as TBAP.

With CTAP as the substrate, addition of both the QABs decrease the rate constants, which may be due to aggregation of β-CD–CTAP and β-CD–QAB inclusion complexes. However, when TBAP is taken as the substrate, which possesses a shorter hydrophobic cleft, such an aggregation among the inclusion complexes becomes improbable, rather both the inclusion complexes (β-CD–TBAP and β-CD–QAB) may be existing in monomeric forms in the solution, resulting in an increase in the rate constant of self-oxidation/dissociation.

The above outcome was confirmed from the dynamic light scattering experiments of the solution containing CTAP, TBAP, CTAP + TBAB, CTAP + CTAB, TBAP + TBAB, and TBAP + CTAB in 9.0 mM β-CD solution. The mean intensity percent versus size (r) in nm for all the samples have been analyzed within three size ranges (Table 1).

The DLS analyses show that (i) the solutions containing CTAP do not show any peak in the range of 1000–3000 nm, whereas a peak in this range is definitely obtained for all the solutions containing TBAP, (ii) solutions containing only CTAP, as well as those with TBAB and CTAB along with CTAP show much higher intensities at all ranges compared to the solutions with TBAP at comparable size range, (iii) solutions containing CTAP only, CTAP + TBAB, and CTAP + CTAB show clear enhancements of percent intensity in the size range of 0–100 nm in the order, CTAP < CTAP + TBAB < CTAP + CTAB; however, in the size range of 100–1000 the percent intensity remains almost a constant, and (iv) in case of the solutions containing TBAP only, TBAP + TBAB, and TBAP + CTAB, the intensities in each of the size range does not show any remarkable change.

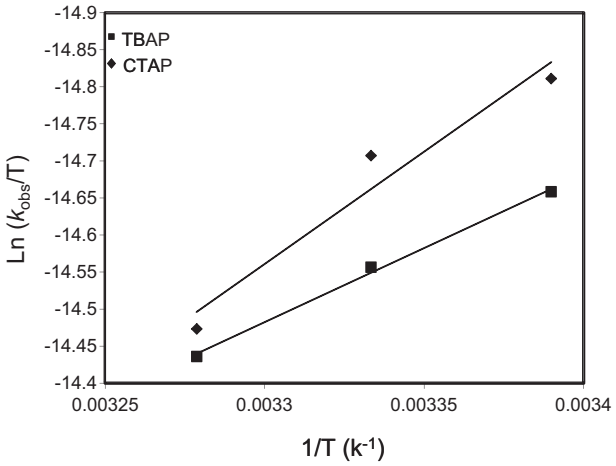


Fig. 5. Plot of ln(k_{obs}/T) versus 1/T at a fixed β-CD concentration of 9.0 mM in aqueous medium.

These observations fully corroborate the explanations from kinetic data: the aggregation of CTAP molecules occurring in the β-CD solution are further enhanced by the addition of quaternary ammonium bromide salts and this enhancement increases in order of the addition of TBAB and CTAB. However, TBAP molecules or any of the quaternary ammonium bromides along with TBAP in the β-CD solution do not trigger the formation of aggregated organizations (Supplementary Fig. 1 (a)–(f)).

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carbpol.2014.05.046.

A model consistent with the above discussions with reference to the impact of QAB concentration on the trend of rate constants of self-oxidation/dissociation of CTAP and TBAP in β-CD aqueous phase has been presented in Scheme 2.

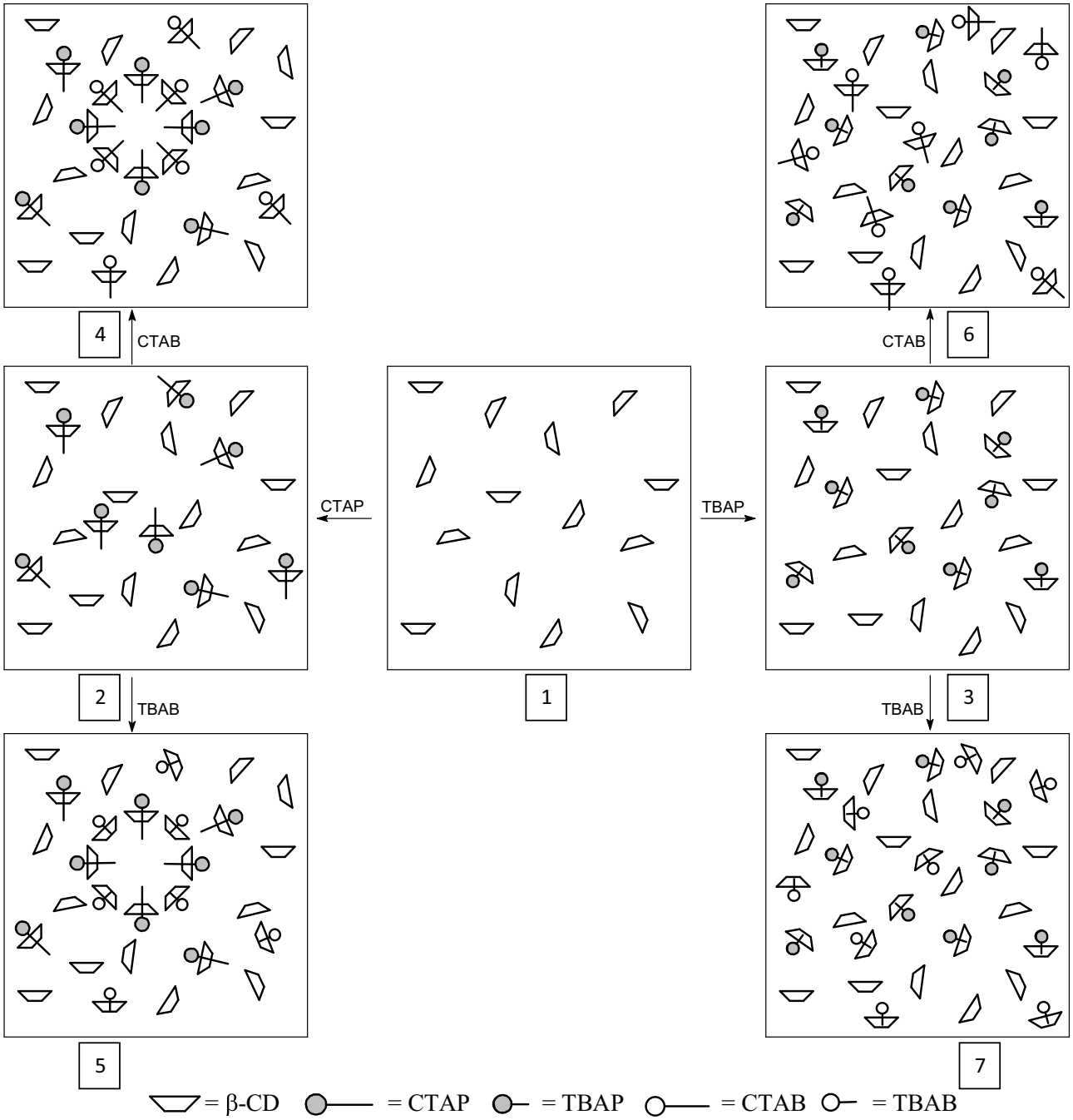
3.4. Temperature effect

Activation parameters for self-oxidation/dissociation of the QAPs in β-CD aqueous phase were calculated from the plots of ln (k_{obs}/T) versus 1/T, which are found to be linear (Fig. 5) and the data are presented in Table 2.

The thermodynamic parameters are dependent not only on the extent of self-oxidation/dissociation of QAPs, but also on the impact of complexation induced by β-CD. $\Delta H^{\#}$ values are found to be significantly higher than the $T\Delta S^{\#}$ values, indicating the complexation process to be enthalpy driven. Besides, the higher $\Delta H^{\#}$ value of CTAP compared to TBAP shows a better inclusion complexation of the former, due to its longer hydrophobic cleft. The $\Delta G^{\#}$ values in both the QAPs increase with temperature, which indicate better complexation with the β-CD host molecules at a lower temperature condition. The negative values of $\Delta S^{\#}$ for both the QAPs show lower randomness and higher stabilization of the systems in the aqueous β-CD medium.

Table 2
Thermodynamic parameters of pseudo-first order kinetics of self- oxidation/dissociation of QAPs in aqueous medium, [QAP] = 0.5 mM, [β-CD] = 9.0 mM.

QAP	$k_{obs} \times 10^5$ (s^{-1})	T (K)	$\Delta G^{\#}$ (kJ/mol)	$\Delta H^{\#}$ (kJ/mol)	$-\Delta S^{\#}$ (J/mol/K)
CTAP	57.8	295	94.6	25.2	235.3
	65.2	300	95.8		
	83.7	305	97.0		
TBAP	67.3	295	94.2	16.6	263.0
	75.8	300	95.5		
	86.9	305	96.8		



Scheme 2. Impact of CTAB and TBAB on CTAP and TBAP dissolved in β-CD aqueous phase (1: β-CD aqueous phase, 2: CTAP dissolved in β-CD aqueous phase, 3: TBAP dissolved in β-CD aqueous phase, 4: partitioning of CTAP to CTAP-CTAB micellar submicro phase, 5: partitioning of CTAP to CTAP-TBAB micellar submicro phase, 6: CTAB-enhanced inclusion complexation of TBAP, 7: TBAB-enhanced inclusion complexation of TBAP).

4. Conclusion

An attempt has been initiated to solubilize QAP molecules in water medium for their further oxidizing applications. β-CD has been found to enhance the solubilization and stabilization of these molecules in water medium through inclusion-complex formation. The impact of chain-length of CTAP and TBAP are the chief deciding factor in their solubilization and stabilization. The reverse micellization phenomenon observed during the oxidation of substrates by QAP molecules in neat organic media during the course of several previous works does not exist in the β-CD aqueous phase. Dynamic light scattering experiments show that with an increase in the concentration of CTAP, a competition seems to occur between β-CD-CTAP complexation and micellar aggregation of CTAP molecules, whereas, with an increase in the concentration of TBAP, an increased β-CD-TBAP complexation might be occurring. The work will stem further research on the oxidation of various water-soluble inorganic and organic substrates using quaternary ammonium permanganate oxidants.

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