

## Mechanistic study of oxidation of sulfacetamide by diperiodatocuprate(III) in aqueous alkaline medium

P N Naik, S D Kulkarni, S A Chimatadar &  
S T Nandibewoor\*

PG Department of Studies in Chemistry, Karnatak University,  
Dharwad 580 003, India  
Email: stnandibewoor@yahoo.com

Received 15 July 2008; revised 15 October 2008

The oxidation of sulfacetamide, a sulfonamide drug, by alkaline diperiodatocuprate(III) has been studied at 298 K and at constant ionic strength. The reaction is first order in diperiodatocuprate(III) and has less than unit order in sulfacetamide concentration. The rate constants increase with increase in alkali concentration and decrease with increase in periodate concentration. A mechanism has been proposed wherein monoperiodatocuprate(III) is the active species. The reaction constants involved in the different steps of the mechanism and the activation parameters for the slow step have been computed.

**IPC Code:** Int. Cl.<sup>8</sup> C07B33/00

Sulfonamides are important bacteriostatic agents commonly used in human and veterinary medicine. They are excreted from the human body and animal organisms partially unmetabolized and also as biotransformation products. Expired and unused drugs containing sulfonamides are also introduced into waste water from households. Due to these factors, traces of sulfonamides are most frequently found in almost all kinds of surface water<sup>1-4</sup>. Halling-Sørensen *et al.*<sup>1</sup> have reported that sulfonamides are resistant to biodegradation. They have a long life-time in the environment and can accumulate in various organisms of the food chain<sup>1,2</sup>. Although sulfonamides are present in the environment at low levels, they may cause pathogenic bacteria drug resistance to these compounds. This necessitates development of various advanced oxidation processes for the transformation of sulfonamides in water. Diperiodatocuprate(III) (DPC) is a one-electron oxidant and is used for the oxidation of various organic compounds in alkaline medium<sup>5</sup>. Copper complexes have a major role in oxidation chemistry due to their abundance and relevance in biological chemistry<sup>6-10</sup>. Copper(III) is involved in many biological electron transfer reactions. With the copper(III) periodate complex as oxidant and multiple

equilibria between different copper(III) species, it would be interesting to know which of the species is the active oxidant. Literature survey reveals that there are no reports on the mechanistic studies of sulfacetamide(SUL) oxidation by DPC. The present investigation is aimed to know the kinetics of redox chemistry of Cu(III), reactivity of SUL towards DPC in such media and also to arrive at a plausible mechanism on the basis of kinetic results.

### Experimental

All chemicals used were of AR grade and doubly distilled water was used throughout the work. A solution of sulfacetamide (Yarrow-Chem Products, Mumbai) was prepared by dissolving a known amount of its sodium salt in doubly distilled water. The copper(III) periodate complex was prepared and characterized by standard procedure<sup>11</sup>. The copper(II) solutions were prepared by dissolving known amount of CuSO<sub>4</sub> (BDH) in distilled water. Periodate solution was prepared by weighing out the required amount of sample in hot water and used after 24 h. Its concentration was ascertained iodometrically at neutral pH in phosphate buffer<sup>12</sup>. KOH and KNO<sub>3</sub> (BDH, Analar) were employed to maintain the required alkalinity and ionic strength respectively in reaction solutions.

The kinetics was studied under pseudo-first order conditions ([SUL] >> [DPC]) at 25°C. Varian CARY 50 Bio UV-vis spectrophotometer was used to follow the reaction at 415 nm. It was verified that other constituents of the reaction mixture do not absorb significantly at this wavelength. The application of Beer's law to DPC at 415 nm had been verified ( $\epsilon = 6213 \pm 250 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ). The first order plots were linear up to 75% completion of the reaction (Fig. 1) and the rate constants were reproducible within  $\pm 5\%$ . Oxidation of sulfacetamide by periodate in alkaline medium at 25°C was checked and found to be insignificant. Dissolved oxygen or ubiquitous carbonate in basic solutions had no effect on reaction rate.

### Results and discussion

Stoichiometry was determined by varying ratios of DPC to SUL in 0.05 mol dm<sup>-3</sup> OH<sup>-</sup> ion; one mole of

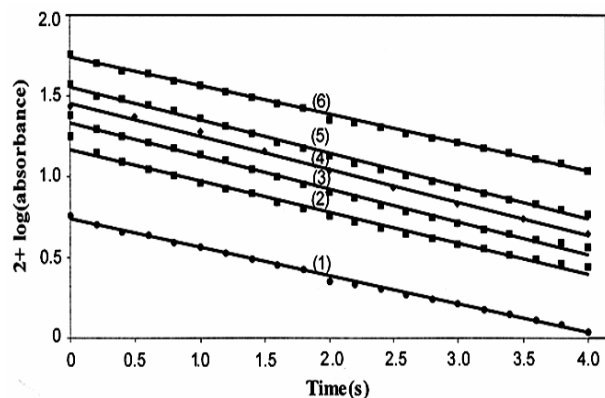
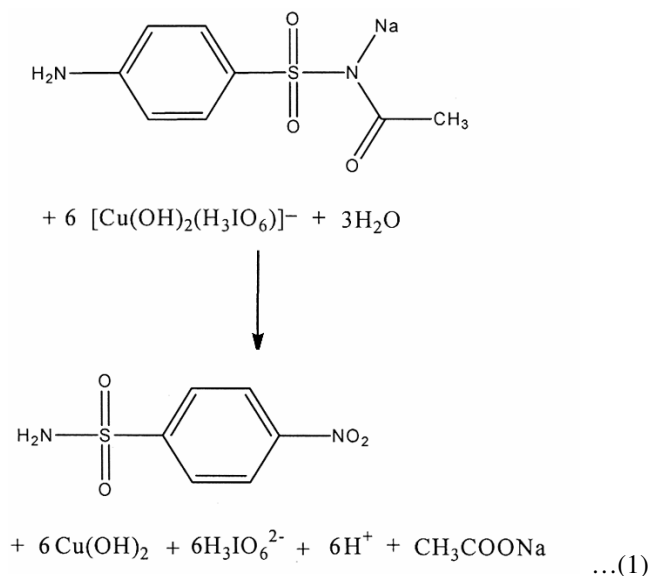


Fig. 1—First order plots on the oxidation of sulfacetamide by diperiodatocuprate(III) in aqueous alkaline medium.  $[\text{DPC}] \times 10^5 \text{ mol dm}^{-3} = 1, 0.8; 2, 3.0; 3, 4.0; 4, 5.0; 5, 6.0; 6, 8.0$ .

sulfacetamide consumes six moles of DPC, as shown in Eq. (1).



After completion of reaction, the reaction mixture was acidified, concentrated and extracted with ether. The ether layer was subjected to column chromatography using a mixture of benzene (65%) and ethylacetate (35%) as mobile phase. From the column the fractions were collected and subjected to spectral investigations. From the IR and NMR spectra, the main oxidation product was identified as *p*-nitrobenzenesulfonamide. The IR spectrum showed ( $-\text{NH}_2$ ) stretch at  $3348 \text{ cm}^{-1}$  (asymmetric) and  $3325 \text{ cm}^{-1}$  (symmetric) while  $-\text{NO}_2$  stretching was

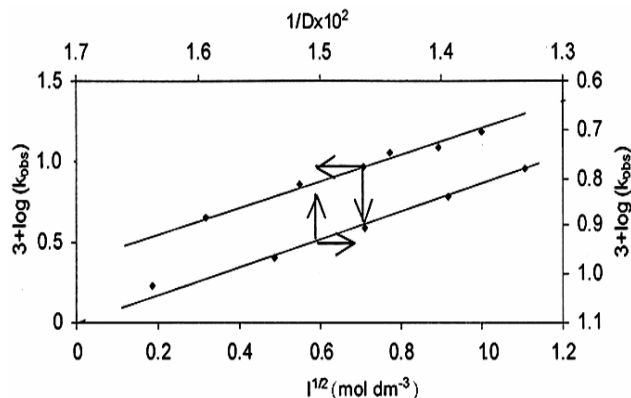


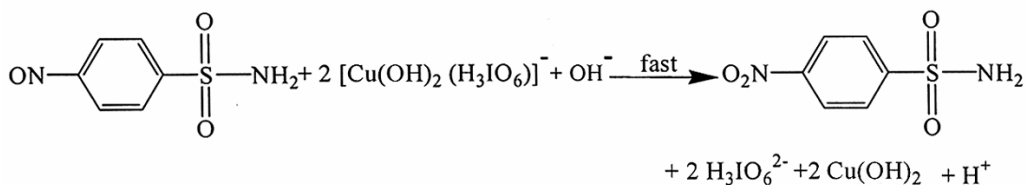
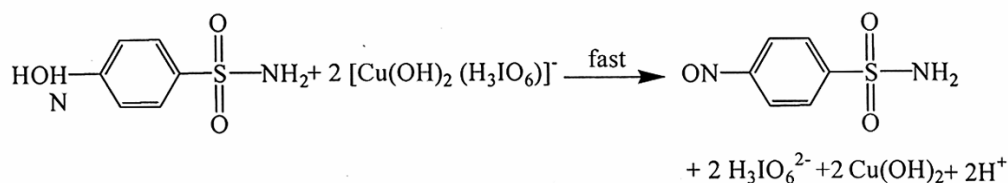
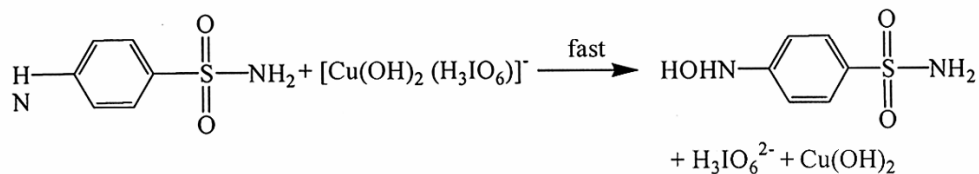
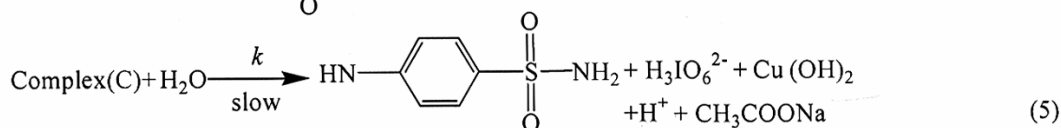
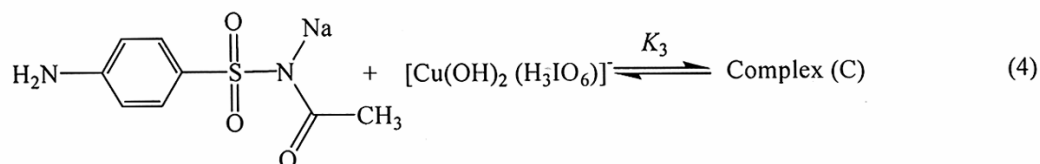
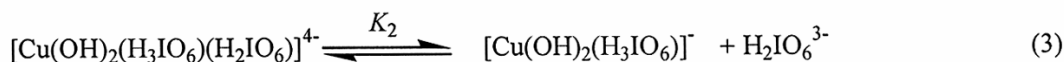
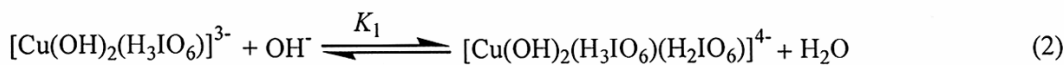
Fig. 2—Effect of ionic strength and dielectric constant of the medium on oxidation of sulfacetamide by diperiodatocuprate(III) at  $25^\circ\text{C}$ .

observed at  $1355 \text{ cm}^{-1}$  (symmetric) and  $1531 \text{ cm}^{-1}$  (asymmetric). Further, *p*-nitrobenzenesulfonamide was characterized by its NMR spectrum ( $\text{CDCl}_3$ );  $\delta$  8.24 ppm (d, Ar-2H (a)),  $\delta$  7.89 ppm (d, Ar-2H (b)),  $\delta$  7.66 ppm (s,  $\text{NH}_2$ ).

The linearity and parallelism of the plots of  $\log$  (absorbance) versus time over 75% completion of the reaction (Fig. 1) indicates unit order with respect to [DPC]. The order with respect to sulfacetamide concentration was found to be less than unity.

The rate constants increased with increasing alkali concentration and the order was found to be less than unity. It was observed that the rate constants decreased by increasing  $[\text{IO}_4^-]$ . The order with respect to periodate concentration was negative and less than unity. Added products, such as Cu(II) had no effect on the rate of reaction. Increasing ionic strength increased the rate of reaction. The plot of  $\log k_{\text{obs}}$  versus  $\sqrt{I}$  is linear (Fig. 2). Decreasing the dielectric constant of the medium increased the rate of reaction. The plot of  $\log k_{\text{obs}}$  versus  $1/D$  (varied by adding *t*-butanol) was linear (Fig. 2). Added acrylonitrile (scavenger) resulted in polymerization, suggesting the participation of free radicals in the reaction. Activation parameters were calculated to be  $\Delta H^\ddagger = 42 \pm 2 \text{ kJ mol}^{-1}$  and  $\Delta S^\ddagger = -81 \pm 3 \text{ J K}^{-1} \text{ mol}^{-1}$ . At the pH employed in this study, the soluble copper(III) periodate complex<sup>13-16</sup> exists as diperiodatocuprate(III),  $[\text{Cu}(\text{H}_3\text{IO}_6)_2(\text{OH})_2]^{3-}$ .

The reaction sequence proposed on the basis of kinetics is given in Scheme 1.



### Scheme 1

According to this sequence,

$$\text{Rate} = \frac{-d[\text{DPC}]}{dt} = k [\text{Complex}] \quad \dots (6)$$

$$= \frac{kK_1K_2K_3 [\text{SUL}] [\text{OH}^-] [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{3-}}{[\text{H}_2\text{IO}_6^{3-}]} \quad \dots (7)$$

The total [DPC] can be written as

$$[\text{DPC}]_T = [\text{DPC}]_f + [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)(\text{H}_2\text{IO}_6)]^{4-} + [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)]^- + \text{Complex (C)}$$

$$= [\text{DPC}]_f \times \frac{\{[\text{H}_2\text{IO}_6^{3-}] + K_1K_2K_3[\text{OH}^-][\text{SUL}] + K_1K_2[\text{OH}^-] + K_1[\text{H}_2\text{IO}_6^{3-}][\text{OH}^-]\}}{[\text{H}_2\text{IO}_6^{3-}]}$$

The free [DPC] is given by,

$$[\text{DPC}]_f = \frac{[\text{DPC}]_T [\text{H}_2\text{IO}_6^{3-}]}{[\text{H}_2\text{IO}_6^{3-}] + K_1K_2K_3[\text{OH}^-][\text{SUL}] + K_1K_2[\text{OH}^-] + K_1[\text{H}_2\text{IO}_6^{3-}][\text{OH}^-]} \quad \dots (8)$$

Similarly, total [OH] can be calculated as,

$$\begin{aligned}
 [\text{OH}^-]_{\text{T}} &= [\text{OH}^-]_{\text{f}} + [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)(\text{H}_2\text{IO}_6)]^{4-} \\
 &+ [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)(\text{H}_2\text{IO}_6)]^{-} + \text{Complex (C)} \\
 &= [\text{OH}^-]_{\text{f}} + \frac{K_1 K_2 [\text{OH}^-] [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{3-}}{[\text{H}_2\text{IO}_6^{3-}]} \\
 &+ K_1 [\text{OH}^-] [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{3-} \\
 &+ \frac{K_1 K_2 K_3 [\text{OH}^-] [\text{Cu}(\text{OH})_2(\text{H}_3\text{IO}_6)_2]^{3-} [\text{SUL}]}{[\text{H}_2\text{IO}_6^{3-}]}
 \end{aligned}$$

In view of the low concentration of DPC used, the second, third and fourth terms in the above equations are neglected, and,

$$[\text{OH}^-]_{\text{T}} \approx [\text{OH}^-]_{\text{f}} \quad \dots (9)$$

and

$$[\text{SUL}]_{\text{T}} \approx [\text{SUL}]_{\text{f}} \quad \dots (10)$$

In the above equations subscripts ‘T’ and ‘f’ refer to total and free concentrations respectively.

Substituting equations (8), (9) and (10) in (7) and omitting T and f we get,

$$\begin{aligned}
 \frac{\text{Rate}}{[\text{DPC}]} &= k_{\text{obs}} = \\
 &\frac{k K_1 K_2 K_3 [\text{SUL}] [\text{OH}^-]}{[\text{H}_2\text{IO}_6^{3-}] + K_1 K_2 K_3 [\text{OH}^-] [\text{SUL}] + K_1 K_2 [\text{OH}^-] + K_1 [\text{H}_2\text{IO}_6^{3-}] [\text{OH}^-]}
 \end{aligned} \quad \dots (11)$$

Equation (11) can be rearranged to Eq.(12).

$$\begin{aligned}
 \frac{1}{k_{\text{obs}}} &= \frac{[\text{H}_2\text{IO}_6^{3-}]}{k K_1 K_2 K_3 [\text{OH}^-] [\text{SUL}]} + \frac{[\text{H}_2\text{IO}_6^{3-}]}{K_2 K_3 [\text{SUL}]} \\
 &+ \frac{1}{k K_3 [\text{SUL}]} + \frac{1}{k}
 \end{aligned} \quad \dots (12)$$

According to Eq. (12), plots of  $1/k_{\text{obs}}$  versus  $1/[\text{SUL}]$ ,  $1/k_{\text{obs}}$  versus  $[\text{H}_2\text{IO}_6^{3-}]$  and  $1/k_{\text{obs}}$  versus  $1/[\text{OH}^-]$  should be linear and are found to be so (Fig. 3). At 298 K, the slopes and intercepts of such plots lead to the values of  $K_1$ ,  $K_2$ ,  $K_3$  and  $k$  as  $12.0 \text{ dm}^3 \text{ mol}^{-1}$ ,  $3.4 \times 10^{-6} \text{ mol dm}^{-3}$ ,  $10.5 \times 10^3 \text{ dm}^3 \text{ mol}^{-1}$  and  $1.7 \times 10^{-2} \text{ s}^{-1}$  respectively. The value of  $K_1$  is in good agreement with its literature value<sup>17</sup>.  $K_1$  is far greater than  $K_2$ . This may be attributed to the greater

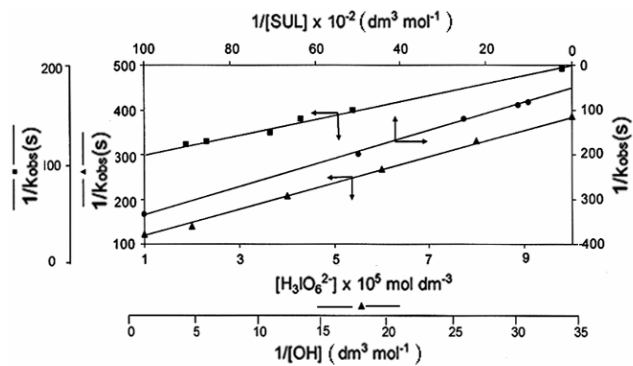


Fig. 3—Plot of verification of rate law (Eq. 11) in the form of Eq. (12).

Table 1—Equilibrium constants and thermodynamic parameters at different temperatures for the oxidation of sulfacetamide by diperiodatocuprate(III) in aqueous alkaline medium

Temp. (K)	$K_1$ ( $\text{dm}^3 \text{ mol}^{-1}$ )	$K_2 \times 10^6$ ( $\text{mol dm}^{-3}$ )	$K_3 \times 10^{-3}$ ( $\text{dm}^3 \text{ mol}^{-1}$ )
288	3.86	0.29	9.95
293	6.03	7.30	10.1
298	11.6	3.36	10.5
303	18.7	1.15	10.9
$\Delta H$ ( $\text{kJ mol}^{-1}$ )	73	-130	4
$\Delta S$ ( $\text{J K}^{-1} \text{ mol}^{-1}$ )	304	-502	129
$\Delta G$ ( $\text{kJ mol}^{-1}$ )	-16	18	-34

tendency of DPC to undergo hydrolysis compared to the dissociation of hydrolysed species in alkaline medium.

$1/k_{\text{obs}}$  versus  $1/[\text{SUL}]$ ,  $1/k_{\text{obs}}$  versus  $[\text{H}_2\text{IO}_6^{3-}]$  and  $1/k_{\text{obs}}$  versus  $1/[\text{OH}^-]$  plots should be linear and were found to be so at different temperatures. From the slopes and intercepts, the values of  $K_1$ ,  $K_2$  and  $K_3$  and  $\Delta H$ ,  $\Delta S$  and  $\Delta G$  for the first, second and third equilibrium steps have been calculated (Table 1). The negative value of  $\Delta S^\ddagger$  indicates that the complex (C) is more ordered than the reactants<sup>18</sup>. The observed modest enthalpy of activation and a relatively low value of the entropy of activation as well as a higher rate constant of the slow step indicate that the oxidation presumably occurs via inner-sphere mechanism<sup>19</sup>. The increase in the rate with increasing ionic strength is in favour of a reaction between same charged species of the reactants, as presented in the proposed sequence. The effect of solvent on the reaction rate is described in detail in the literature<sup>20</sup>. In the present study, the plot of  $\log k_{\text{obs}}$  versus  $1/D$  had

negative slope, which is in the right direction as shown in the proposed sequence.

Among various species of DPC in alkaline medium, monoperiodatocuprate(III) is considered as the active species for the title reaction. In carrying out this reaction, the role of pH in the reaction medium is crucial. The proposed mechanistic sequence described here is consistent with product analysis, mechanistic and kinetic studies.

### References

- Halling-Sørensen B, Nors Nielsen S, Lanzky P F, Ingerslev F, Holten Lu<sup>tz</sup> H C & Jørgensen S E, *Chemosphere*, 36 (1998) 357.
- Ku<sup>m</sup>merer K, *Chemosphere*, 45 (2001) 957.
- (a) Heberer T, *Toxicol Lett*, 131 (2002) 5; (b) Carballa M, Omil F, Lema J M, Llompert M, Garcia-Jares C, Rodriguez I, Gomez M & Ternes T, *Water Res*, 38 (2004) 2918.
- Kolpin D W, Furlong E T, Meyer M T, Thurman E M, Zaugg S D, Barber L B & Buxton H T, *Environ Sci Technol*, 36 (2002) 1202.
- Hiremath D C, Kiran T S & Nandibewoor S T, *Int J Chem Kinet*, 39 (2007) 236.
- Kitajima K N & Moro-oka Y, *Chem Rev*, 94 (1994) 737.
- Karlin K D, Kaderli S & Zuberbuhler A D, *Acc Chem Res*, 30 (1997) 139.
- Piere J L, *Chem. Soc Rev*, 29 (2000) 251.
- Solomon E I, Chen P, Metz M, Lee S K & Palmer A E, *Angew Chem Int Ed Engl*, 40 (2001) 4570.
- Halcrow M A, *Angew Chem Int Ed Engl*, 40 (2001) 816.
- Jeffery G H, Bassett J, Mendham J & Denny R C, *Vogel's Textbook of Quantitative Chemical Analysis*, 5th Ed, (ELBS, Longman, Essex, U K) (1996), p. 370.
- Kiran T S, Hiremath C V, & Nandibewoor S T, *App Cat A: Gen*, 305 (2006) 706.
- Sethuram B, *Some Aspects of Electron Transfer Reactions Involving Organic Molecules*, (Allied Publishers (P) Ltd., New Delhi), (2003) p. 77.
- Lide D R, *CRC Handbook of Chemistry and Physics* (CRC press, London), 73<sup>rd</sup> Edn, (1992) pp. 8-51.
- Bellakki M B, Mahesh R T & Nandibewoor S T, *Proc Nat Acad Sci India*, 75 (2005) 177.
- (a) Hiremath M I & Nandibewoor S T, *Russ J Phys Chem*, 80 (2006) 1029; (b) Shettar R S & Nandibewoor S T, *Int J Chem Sci*, 2 (2004) 419.
- Kiran T S, Hiremath D C & Nandibewoor S T, *Z Phys Chem*, 221 (2007) 501.
- (a) Rangappa K S, Anitha N & Madegouda N M, *Synth React Inorg Met Org Chem*, 31 (2001) 1499; (b) Bugarcic Z D, Nandibewoor S T, Hamza M S A, Heimemann F & Rudi van Eldik, *J Chem Soc, Dalton Trans*, (2006) 2984.
- (a) Hicks K W, *J Inorg Nucl Chem*, 38 (1976) 1381; (b) Farokhi S A & Nandibewoor S T, *Tetrahedron*, 59 (2003) 7595.
- Seregar V, Veeresh T M & Nandibewoor S T, *J Mol Cat : Chem*, 271 (2007) 253.