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Oxidation of Glycylglycine by $KBrO_3$ in Aqueous Acetic Acid Medium and Comparison with Monomer Glycine: A Kinetic and Mechanistic Study

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The kinetics of oxidation reactions of dipeptide glycylglycine (GG) by $KBrO_3$ in aqueous acetic acid medium, under the condition $[KBrO_3] << [GG]$ at different temperatures (313-323 K), to produce formic acid, ammonia, carbon dioxide and water were studied. Study of the kinetic results showed that the first order dependence in $[KBrO_3]$ and fractional order dependence in [GG]. The effect of ionic strength and [AcOH] on rate was studied and thermodynamic parameters were also calculated. Michealis-Menten type mechanism was proposed.

Keywords: Glycylglycine, Glycine, Potassium bromate, Acetic acid.

INTRODUCTION

Bromate is a hypervalent oxyanion of bromine, which is known as a versatile oxidizing agent [1-5] and brominating agent depending on reaction conditions. It oxidizes reducing agents and can be reduced to bromide and bromine. Bromate reactions with natural and synthetic gastric juices have been well documented in literature [6]. In addition, potassium bromate is a strong oxidizing agent with redox potential of 1.44 volts in acid medium [7]. Probably because of this reason bromate [Br(V)] is widely used as an oxidizing agent in synthetic as well as in analytical chemistry. Its oxidizing ability can be compared with reagents such as Ce (IV) [8], potassium iodate [9], sodium periodate [10-12], N-bromoacetamide [13-28] and N-bromosuccinimide [29-31], *etc.* have been earlier used in oxidation of various compounds.

In past several decades, potassium bromate has been widely used for the oxidation of a wide range of compounds [32-34]. Banerji and Negi [35] described the kinetics of oxidation of some aldoses and amino sugars by potassium bromate in hydrochloric acid medium. The reactions appear to proceed through the intermediate formation of bromate esters followed by the decomposition of the esters to give products. Hydrogen ion accelerated the rate of each reaction.

EXPERIMENTAL

Glycylglycine (E. Merck, analytical grade) was purified by column chromatography and used in experiment. Potassium bromate obtained from E. Merck with highest purity and analytical grade used as received, in stock solution. Acetic acid (E. Merck, analytical grade) was purified [36,37] by refluxing over chromium trioxide and acetic anhydride. The solid that separated out was filtered off and the filtrate distilled in an all glass quick fit apparatus and the fraction distilled at 118 °C was collected and used for all experiments. All other chemicals were of analytical grade.

Kinetics and measurements: The kinetic studies were carried out under pseudo-first order conditions with glycylglycine concentrations always greater than the concentration of $KBrO_3$. The progress of the reaction was monitored by estimating the unreacted concentration of $KBrO_3$ by iodometrically using freshly prepared starch as an indicator.

Stoichiometry: Stoichiometry studies were carried out under the conditions $[KBrO_3] >> [GG]$ in the presence of $Hg(OAc)_2$. The reaction was allowed to go to completion and the unreacted $KBrO_3$ was estimated iodometrically. It was found that one mole of glycylglycine required two moles of $KBrO_3$.

$$2HBrO_3 + H_2NCH_2\text{-}CONH\text{-}CH_2COOH \longrightarrow 2HCOOH + 2CO_2 + 2NH_4^+ + Br_2 + H_2O$$

Product analysis: The products of oxidation of glycylglycine were identified as HCOOH, NH_3 and CO_2. Formic acid was detected by conventional spot tests [38], while ammonia was identified by Nessler's reagent [39] and carbon dioxide was detected by gas evolution apparatus.

RESULTS AND DISCUSSION

The kinetics of oxidation of glycylglycine (GG) by $KBrO_3$ was investigated at different concentration of glycylglycine, conducted under the conditions $[KBrO_3] << [GG]$, the reaction was allowed to go for completion. The progress of the reaction was monitored by estimating the unreacted $[KBrO_3]$ at different intervals of time. The plots of $\log\frac{a}{(a-x)}$ [where 'a' and (a-x) corresponds to the concentration of $KBrO_3$ at zero time and at time 't'] *vs.* time were found to be linear passing through the origin Fig. 1 indicating first order dependence of rate in $[KBrO_3]$. From the slops of such plots pseudo-first order rate constants (k′) evaluated were independent of $[KBrO_3]$, conforming the first order dependence in $[KBrO_3]$. The rate increases with increasing in [GG].

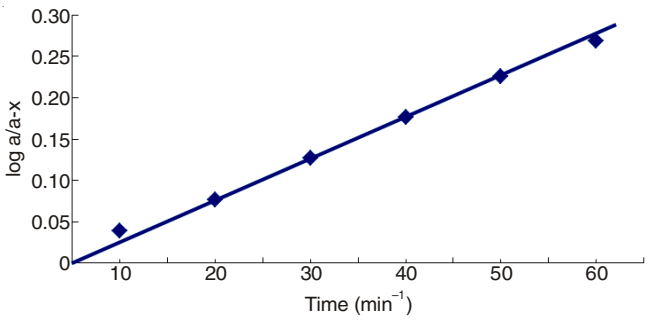


Fig. 1. Oxidation of glycylglycine by $KBrO_3$; $[KBrO_3] = 5 \times 10^{-3}$ mol dm^{-3}; $[GG] = 5 \times 10^{-2}$ mol dm^{-3}; $[Hg(OAc)_2] = 1 \times 10^{-2}$ mol dm^{-3}; [AcOH] = 10 % (v/v); Temp. = 313 K

The plot of log k′ *vs.* log [GG] (Fig. 2) was linear with n = 0.42 (r = 0.97) indicating fractional order dependence of rate on [GG]. No altering of order in glycylglycine further increasing [GG], the reaction obeying the Michealis-Menten kinetics (Table-1). The rate of oxidation of glycylglycine was not altered with the increase in ionic strength (addition of $NaClO_4$). The reaction rate was found to increase with increase in concentration of AcOH content varied by the addition of 10-25 % (v/v) AcOH in the reaction.

Comparison of rates of oxidations of glycylglycine and glycine revealed that the rate of oxidation of glycine is faster than glycylglycine (Table-2).

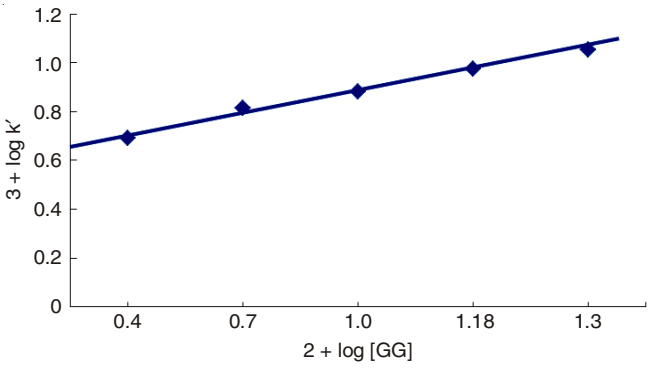


Fig. 2. Effect of [GG] on k_2 in $KBrO_3$-GG reaction; $[KBrO_3] = 5 \times 10^{-3}$ mol dm^{-3}; Temp. = 313 K

TABLE-1
ORDER IN [GG] IN THE OXIDATION OF GLYCYLGLYCINE BY $KBrO_3$ IN AQUEOUS ACETIC ACID MEDIUM
$[KBrO_3] = 5 \times 10^{-3}$ mol dm^{-3}; $[Hg(OAc)_2] = 1 \times 10^{-2}$ mol dm^{-3}; Temp. = 313 K; [AcOH] = 10 % (v/v)

$10^2 \times$ [GG] (mol dm^{-3})	k' $\times 10^3$ min^{-1}	2 + log [GG]	3 + log k'
2.5	4.9	0.40	0.690
5.0	6.5	0.70	0.813
10.0	7.6	1.00	0.881
15.0	9.4	1.18	0.973
20.0	11.2	1.30	1.053

TABLE-2
COMPARISON OF RATE OF OXIDATION OF GLYCYLGLYCINE WITH THAT OF GLYCINE
$[KBrO_3] = 5 \times 10^{-3}$ mol dm^{-3}; $[Hg(OAc)_2] = 1 \times 10^{-2}$ mol dm^{-3}; [AcOH] = 10 % (v/v); Temp. = 313 K

$10^2 \times$ [GG] (mol dm^{-3})	$10^3 \times$ k' (min^{-1})	$10^2 \times$ [Glycine] (mol dm^{-3})	$10^3 \times$ k' (min^{-1})
2.5	4.9	2.5	8.6
5.0	6.5	5.0	10.8
10.0	7.6	10.0	11.9
15.0	9.4	15.0	14.5
20.0	11.2	20.0	17.8

The kinetic study of the reaction is studied at different temperature from 313 to 323 K. The substance concentration was changed at each temperature to follow Michealis-Menten kinetics. To determine the activation parameters, the reactions were carried out at different temperatures. Using the Arrhenius equation the activation energies (E_a) were calculated and from these values thermodynamic parameters were evaluated for the rate limiting step have been computed as follows:

Reactive species and mechanism: Potassium bromate exists in following forms in acetic acid solution *viz.*, BrO_3^- and $HBrO_3$. The possibility of BrO_3^- as the reactive species is ruled out in the present investigation as observed, that increasing the ionic strength results no change in the rate of oxidation. As the reaction were conducted in the presence of excess of $Hg(OAc)_2$, which eliminates Br^+ *via* complexation, thus any possible oxidation due to Br_2 is eliminated. Therefore in the present investigation $KBrO_3$ quickly protonated [40-45] to produce $HBrO_3$ is acting as a reactive species in the oxidation of glycylglycine and glycine using $KBrO_3$ in acetic acid medium. It supported by the acetic acid effect data on rate of the oxidation. Increases in the acetic acid content increases in the rate of oxidation increases.

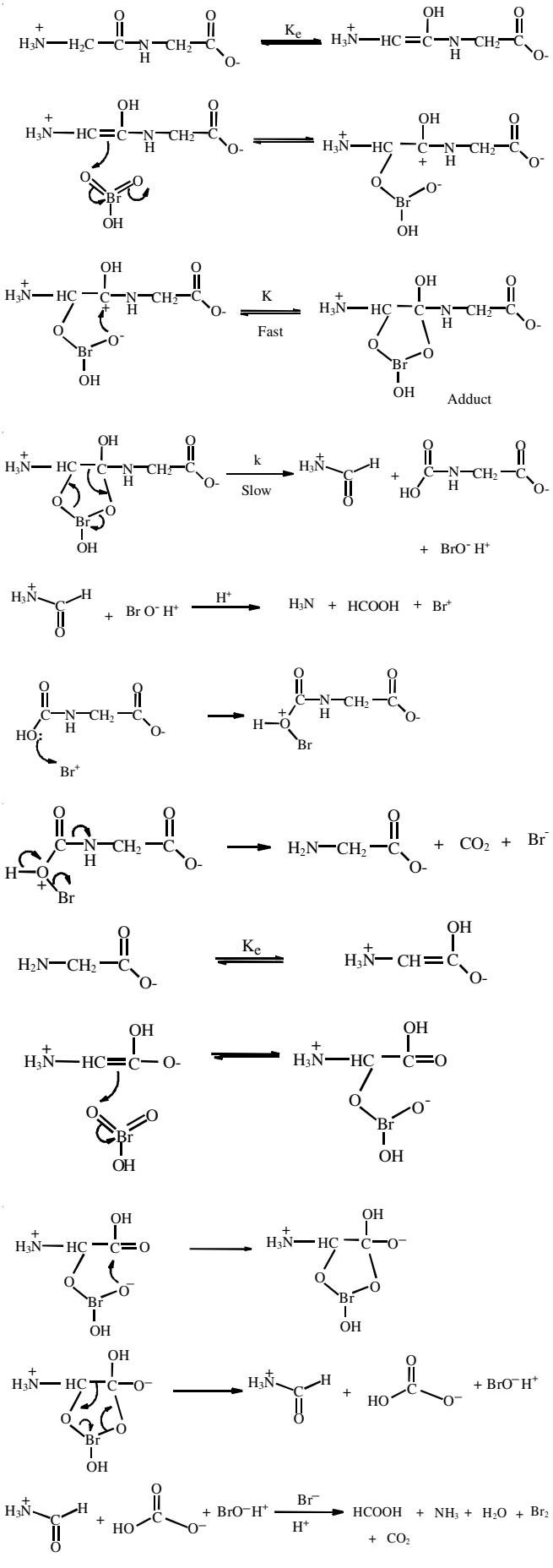
$$H^+ + BrO_3^- \underset{}{\overset{K_P}{\rightleftharpoons}} HBrO_3$$

Glycylglycine exists as Zwitterions, cation, anion and neutral molecule depending on the pH of the medium [46-49].

Under the experimental conditions (pH > 3.4) zwitterion form of glycylglycine is supposed to be the reactive species of glycylglycine. Addition of olefinic monomer such as acrylamide or acrylonitrile did not induce polymerization confirming the absence of free radicals in the reaction mixture.

The first order dependence of rate on $[KBrO_3]$ and fractional order dependence on [GG] suggest that the reaction might occur *via* the formation cyclic bromate ester and in the slow rate determining step it dissociate to give final products. On

Proposed mechanism:



the basis of observed kinetics results, products of oxidation and above discussion, the reaction of oxidation of glycylglycine by $KBrO_3$ may be written as:

$$2HBrO_3 + H_2NCH_2\text{-}CONH\text{-}CH_2COOH \longrightarrow 2HCOOH + 2CO_2 + 2NH_4^+ + Br_2 + H_2O$$

The proposed mechanism is also in accordance with the observed stoichiometry, the rate equation in consonance with the mechanism proposed is given as:

$$\text{Rate} = \frac{-d[KBrO_3]}{dt} = \frac{kK[GG][KBrO_3]}{1 + K[GG]} \quad (1)$$

$$\frac{\text{Rate}}{[KBrO_3]} = \frac{kK[GG]}{1 + K[GG]} \quad (2)$$

Reciprocal of eqn. 2 yields:

$$\frac{[KBrO_3]}{\text{Rate}} = \frac{1}{Kk[GG]} + \frac{1}{k} \quad (3)$$

According Lineweaver Burk's plot of $10^{-3}/k_2$ *vs.* 1/[GG] should be linear with positive slope and intercept on Y-axis. This has been observed in the present investigation (Fig. 3), supporting the proposed mechanism. From the intercepts and slopes of $[KBrO_3]$/rate *vs.* 1/[GG] plots at various temperatures activation parameters (Table-3) were calculated.

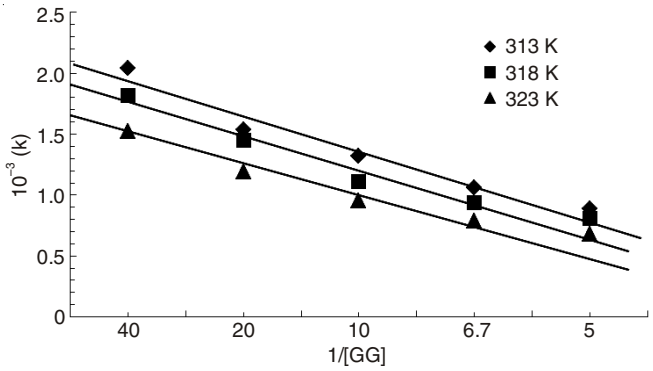


Fig. 3. Lineweaver Burk's plot of $10^{-3}/k_2$ *vs.* 1/[GG]

TABLE-3
ACTIVATION PARAMETERS FOR THE OXIDATION OF GLYCYLGLYCINE BY $KBrO_3$

Substrate	E_a (kJ mol^{-1})	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta G^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (J mol^{-1} K^{-1})
Glycylglycine	99.6	97.1	113.6	-52.7
Glycine	94.7	92.1	122.2	-96.1

Comparison of rates of glycylglycine-$KBrO_3$ reaction with glycine-$KBrO_3$ reaction revealed that the rate of oxidation is faster in case of glycine (Table-2). The difference of reaction rates may be due to the (i) increased distance between the functional groups, which result in weaker electrostatic effects (ii) glycylglcine (pK_1 3.2 and pK_2 8.2) is weaker both as an acid and a base when compared to glycine (pK_1 2.4 and pK_2 9.8). Thus the oxidation of dipeptide glycylglycine is expected to be slower than the monomer, which is observed in the present study. Similar observations were also made in the oxidation of glycylglycine by other oxidants like, NBS [50], Ce^{4+} [51], PMS [52], CAT [53], BAB [54], Mn(III) [55], BAT [56] and NBP [57].

REFERENCES

1. B. Tamami and M.A.K. Zarchi, *Eur. Polym. J.*, **31**, 715 (1995).
2. P.M. Pujari and P.J. Banerjee, *Chem. Soc. Dalton Trans.*, 1015 (1983).
3. F.S. Burgos, M. del Mar Graciani, E. Munoz, M.L. Moya, M.J. Capitan, M. Galan and C.D. Hubbard, *J. Solution Chem.*, **17**, 653 (1988).
4. S.B. Jonnalagadda and M.N. Shezi, *J. Phys. Chem. A*, **113**, 5540 (2009).
5. C.S. Reddy and P.S. Manjari, *Indian J. Chem.*, **49A**, 418 (2010).
6. J.D. Keith, G.E. Pacey, J.A. Cotruvo and G. Gordon, *Toxicology*, **221**, 225 (2006).
7. W.A. Latimer, Oxidation Potential, Prentice-Hall, New York, edn 2, p. 56 (1952).
8. A.K. Singh and U. Kushwaha, *Flora and Fauna*, **13**, 215 (2007).
9. A.K. Singh and U. Kushwaha, *Flora and Fauna*, **14**, 347 (2008).
10. A.K. Singh and J.P. Pachauria, *Asian J. Chem.*, **5**, 1145 (1993).
11. U. Kushwaha and A.K. Singh, *Rev. Inorg. Chem.*, **2010**, 30- 3.
12. U. Kushwaha, A.K. Singh and A. Singh, *Asian J. Chem.*, **24**, 2373 (2012).
13. B. Shah and K.K. Banerji, *J. Chem. Soc., Perkin Trans. 2*, 33 (1983).
14. B. Singh, A.K. Singh and A. Singh, *Indian J. Chem.*, **50A**, 650 (2011).
15. S. Srivastava, S. Srivastava, S. Singh, Parul and A. Jaiswal, *Bull. Catal. Soc. India*, **6**, 140 (2007).
16. S. Srivastava, K. Singh, M. Shukla and N. Pandey, *Oxid. Commun.*, **24**, 558 (2001).
17. N. Gupta, S. Rahmani and A.K. Singh, *Oxid. Commun.*, **22**, 237 (1999).
18. D.L. Kable and S.T. Nandibewoo, *Oxid. Commun.*, **21**, 396 (1998).
19. N.A. Mohamed Farook and G.A. Seyed Dameem, *E-J. Chem.*, **8**, 479 (2011).
20. R.D. Kaushik, A.K. Chaubey and P. Garg, *Asian J. Chem.*, **15**, 1655 (2003).
21. R.D. Kaushik and R.P. Amrita Dubey, *Asian J. Chem.*, **16**, 831 (2004).
22. H.X. Kong, L.-J. Li, H.G. Wei and L. Yan, J. Juan Guangpy Shi Yanshi, 20, 70 (2003).
23. S. Srivastava, V. Srivastava and A. Awasthi, *Oxid. Commun.*, **26**, 378 (2003).
24. A.K. Singh, A. Singh, R. Gupta, M. Saxena and B. Singh, *Transition Met. Chem.*, **17**, 413 (1992).
25. S. Srivastava, A. Awasthi and V. Srivastava, *Oxid. Commun.*, **26**, 426 (2003).
26. S. Srivastava, A. Awasthi and K. Singh, *Int. J. Chem. Kinet.*, **37**, 275 (2005).
27. S. Srivastava and S. Singh, *Oxid. Commun.*, **29**, 708 (2006).
28. B. Singh, D. Singh and A.K. Singh, *Int. J. Chem. Kinet.*, **20**, 501 (2004).
29. K.S. Mavalangi, Nirmala, N. Halligudi and S.T. Nandibewoor, *React. Kinet. Catal. Lett.*, **72**, 391 (2001).
30. A.K. Singh and D. Chopra, *Oxid. Commun.*, **20**, 450 (1997).
31. A.K. Singh, D. Chopra, S. Rahmani and B. Singh, *Carbohydrate Res.*, **314**, 157 (1998).
32. S. Srivastava and S. Singh, *Oxid. Commun.*, **27**, 463 (2004).
33. S. Srivastava and S. Singh, *J. Indian Chem. Soc.*, **81**, 295 (2004).
34. K.K.S. Gupta, N. Debnath and N. Bhattach, *J. Indian Chem. Soc.*, **77**, 152 (2000).
35. S.C. Negi and K.K. Banerji, *J. Org. Chem.*, **48**, 3329 (1983).
36. R. Filler, *Chem. Rev.*, **63**, 21 (1963).
37. N.K. Mathur and C.K. Narang, Determination of Organic Compounds with N-Bromosuccinimide and Allied Reagents, Academic Press, London (1975).
38. S. Srivastava, A. Kumar and P. Srivastava, *Indian J. Agric. Chem.*, **40**, 107 (2007).
39. V.B. Sharma, S.L. Jain and B. Sain, *J. Mol. Catal.*, **227**, 47 (2005).
40. E. Fagnani, C.B. Melios and L. Pezza, *Talanta*, **60**, 171 (2003).
41. F. Feigl, Spot Tests in Organic Analysis, Elsevier, Amsterdam, p. 341 (1956).
42 A. Indelli, G. Nolan Jr. and E.S. Amis, *J. Am. Chem. Soc.*, **82**, 3233 (1960).
43. M. Anbar and S. Guttmann, *J. Am. Chem. Soc.*, **83**, 4741 (1961).
44. A.F.M. Barton and G.A. Wright, *J. Chem. Soc. A*, 1747 (1968).
45. M.T. Beck, G. Rabai and G. Bazsa, *Int. J. Chem. Kinet.*, **13**, 1277 (1981).
46. M. Clugston and R. Flemming, Advanced Chemistry, Oxford University Press, p. 355 (2000).
47. C.S. Foote and J.S. Valentine, in eds.: J.F. Liebman and A. Greenberg, Active Oxygen in Chemistry, Springer, p. 153 (1995).
48. A.F. Holleman and E. Wiberg, Inorganic Chemistry, Academic Press: San Diego (2001).
49. F.L. Muller, M.S. Lustgarten, Y. Jang, A. Richardson and H. van Remmen, *Free Radic. Biol. Med.*, **43**, 477 (2007).
50. K. Pramila, A. Birla and P. Srinivas, *Asian J. Chem.*, **24**, 4671 (2012).
51. P. Kethavath and P. Srinivas, *Online J. Bio. Sci. Informatics*, **5**, 343 (2013).
52. P. Kethavath, K.N. Reddy and P. Srinivas, *J. Appl. Chem.*, **3**, 683 (2014).
53. P. Kethavath and P. Srinivas, *J. Appl. Chem.*, **2**, 1574 (2013).
54. D.S. Mahadevappa, K.S. Rangappa and N.M.M. Gowda, *Indian J. Chem.*, **20A**, 203 (1981).
55. D.K. Bhat, B.S. Sherigara and B.T. Gowda, *Bull. Chem. Soc. Jpn.*, **69**, 41 (1996).
56. T. Asha Iyengar and D.S. Mahadevappa, *Proc. Indian Acad.*, **63**, 105 (1993).
57. A. Anjum and P. Srinivas, *Asian J. Chem.*, **18**, 1 (2006).