

Radiation Chemistry Symposium: Marie Curie's Heritage
15th -16th November, 2011

*Radiation and Quantum Chemical Study of
Organic Sulphur Compounds*

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Guide : Prof. B. S. M. Rao

Co-guide: Dr. D. K. Maity

Objective

- Investigation of the radiation chemical reactions of oxidizing and reducing radicals ($\cdot\text{OH}$, $\text{Br}_2\cdot^-$, $\text{Cl}_2\cdot^-$, $\text{SO}_4\cdot^-$ and $\cdot\text{H}$, e^-_{aq}) with organic sulphur compounds to elucidate the reaction mechanism.
- Quantum chemical calculations to support the experimental data in the assignment of the structures of the intermediate species.

Why sulphur systems ???

- **Sulphur containing amino acids (cysteine, methionine) are key components of hormones, enzymes and coenzymes.**
- **Sulphur centered radical species, derived from sulphur containing compounds play an important role in the redox chemistry of biological systems.**
- **Due to their free radical scavenging ability sulphur compounds act as radioprotectors.**

Methodology

Pulse Radiolysis

(LINAC at BARC and NCFRR, Energy = 7 MeV, Pulse width = 50 ns)

Theoretical Calculations

Full optimizations on ground state geometry of all the systems studied have been carried out following Density Functional Theory (DFT) using BHHLYP method and 6-31+ G(d,p) set of basis functions.

The gas phase optimized molecular geometries are reoptimized fully including solvent effect following Onsager reaction field model. Time Dependent Density Functional Theory (TDDFT) calculations have been performed to find out excited states.

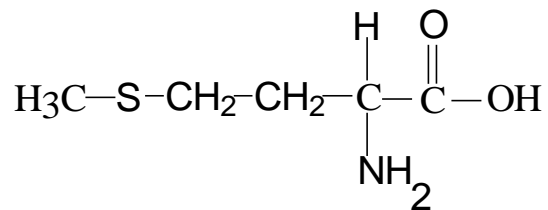
Geometry optimizations ➞ **GAMESS & GAUSSIAN 03 programs**

TDDFT Calculations ➞ **GAUSSIAN 03 programs**

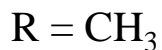
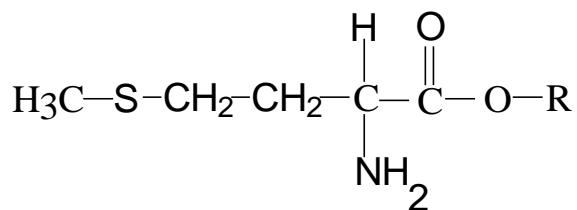
**Visualization of geometry
and molecular orbitals** ➞ **MOLDEN program**

Oxidation Studies of Methionine Derivatives

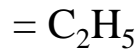
Structures



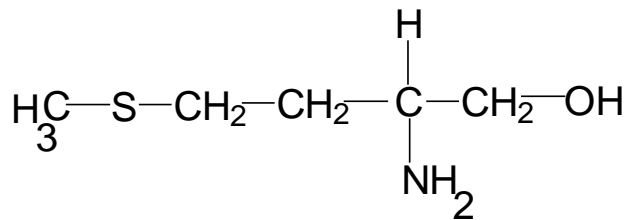
Methionine (Met)



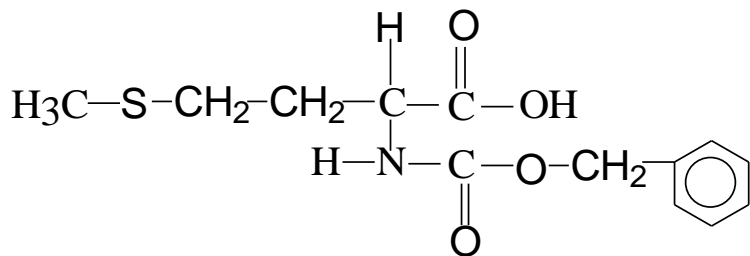
Methionine Methyl Ester (MME)



Methionine Ethyl Ester (MEE)



Methioninol (MOH)

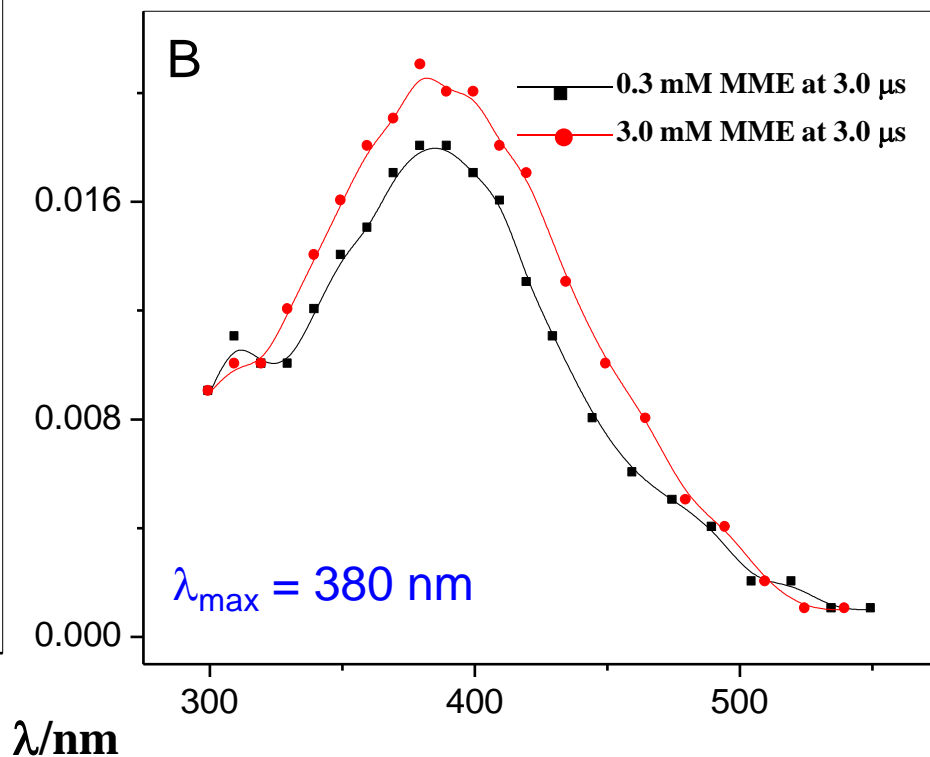
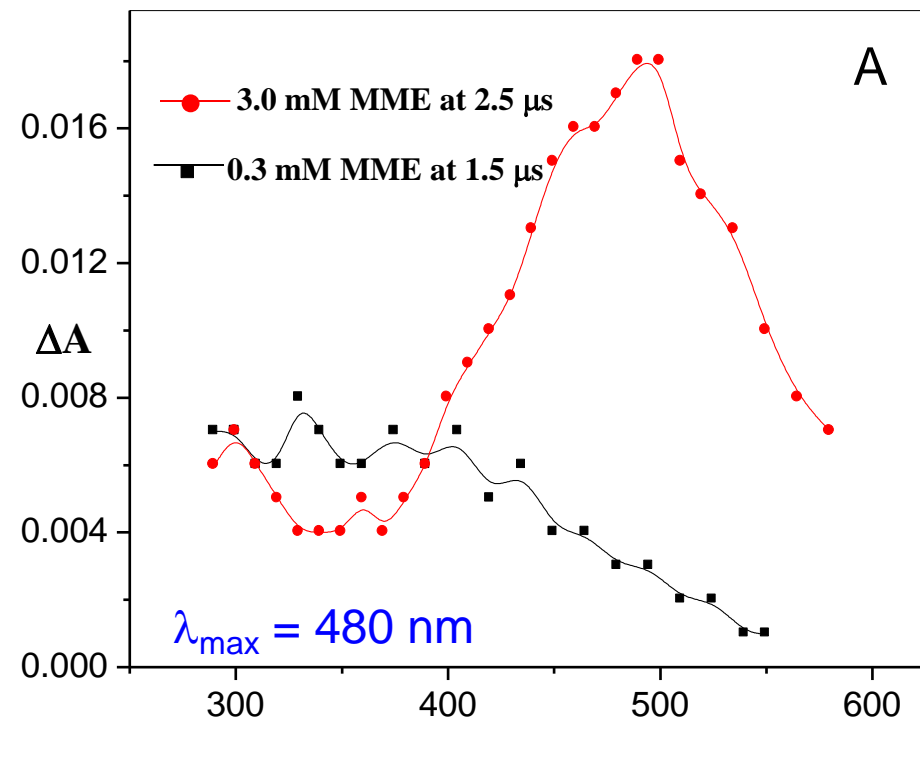


N-Carbobenzyloxy methionine (NCM)

Reaction of OH radical with methionine methylester

pH 1

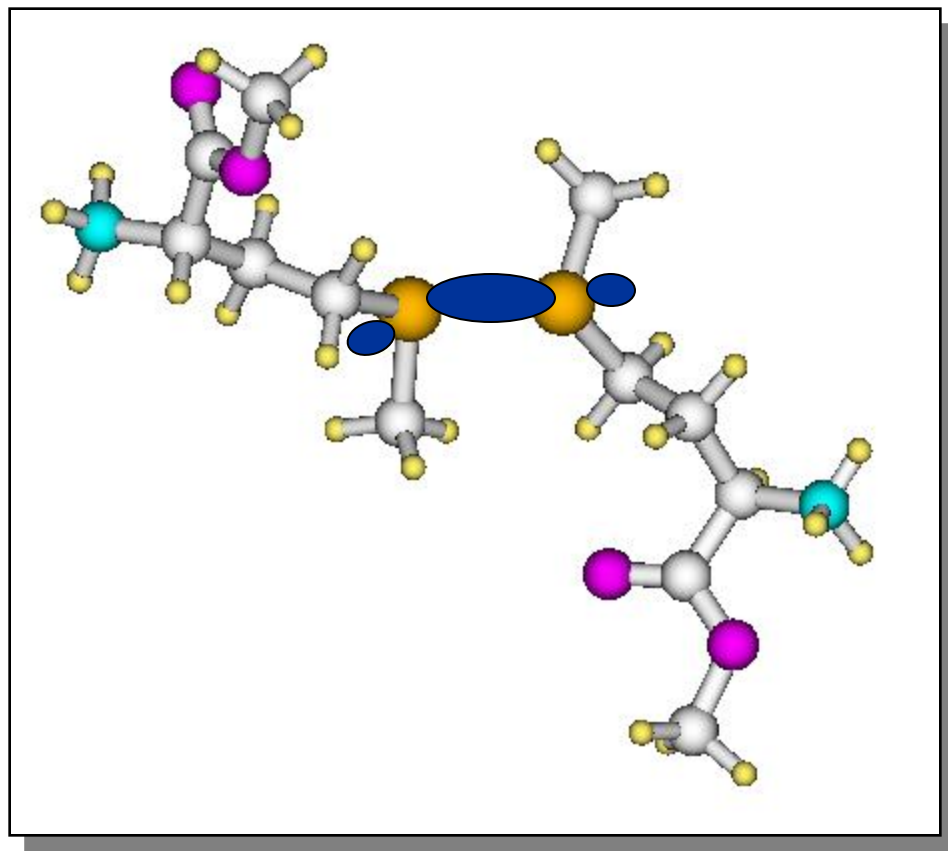
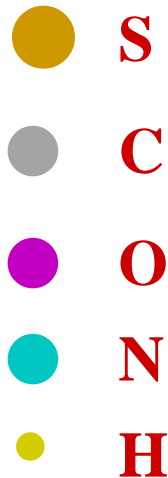
pH 7



➤ At basic pH the transient spectrum obtained is similar to that obtained at pH 7

pH 1

Optimized geometry of dimer radical cation of MME by DFT method

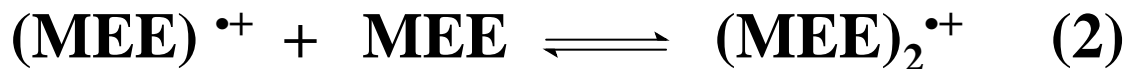
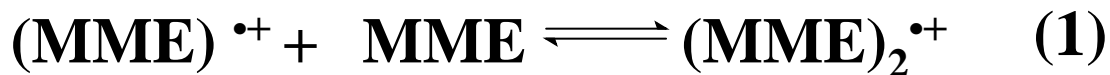


λ_{\max} 480 nm corresponds
to sulphur centered dimer
radical cation

Intermolecular 2c-3e bond between sulphur-sulphur

Binding energy of MME dimer radical cation = 19.4 kcal/ mole

Bond order ($B_{ss} = 0.5$)



❖ Equilibrium Constant (K)

$$\frac{A_0}{A} = 1 + K^{-1} [\text{MME}]^{-1}$$

A_0 and A are the transient absorbance at 480 nm for aqueous solution of MME at pH 1 containing 3 mM and any known concentration from 0.3 mM to 3 mM respectively.

$$K = 1.8 \times 10^3 \text{ M}^{-1} \text{ for Met}$$

$$K = 3.1 \times 10^3 \text{ M}^{-1} \text{ for MME}$$

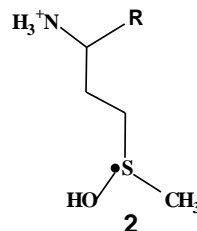
$$K = 2.3 \times 10^3 \text{ M}^{-1} \text{ for MEE}$$

$$K = 1.7 \times 10^3 \text{ M}^{-1} \text{ for MOH}$$

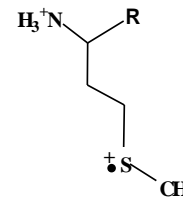
Which transient species corresponds to λ_{\max} 380nm at neutral pH?

Possibilities

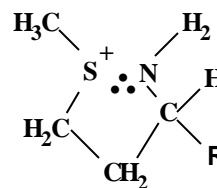
(1) OH-adduct at sulphur atom



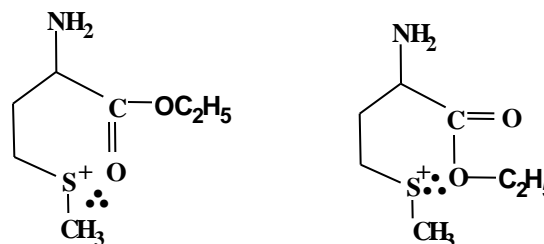
(2) Sulphur centered monomer radical cation

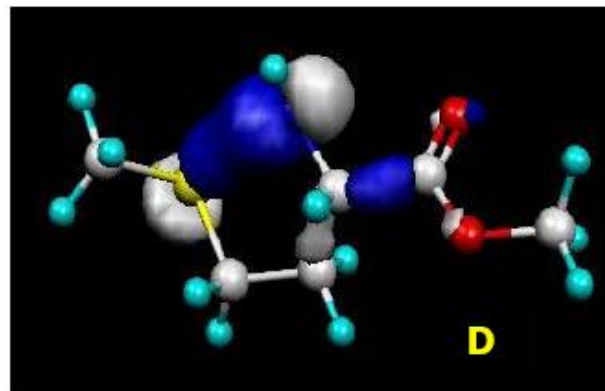
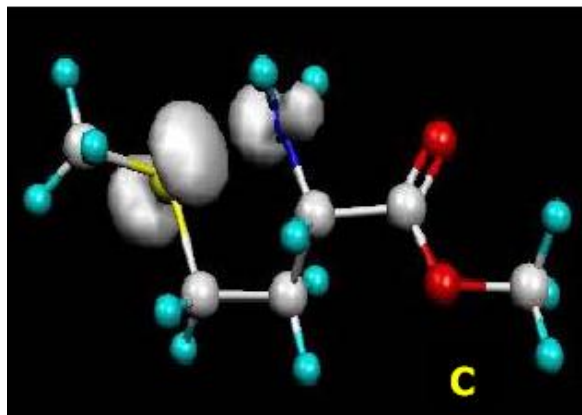
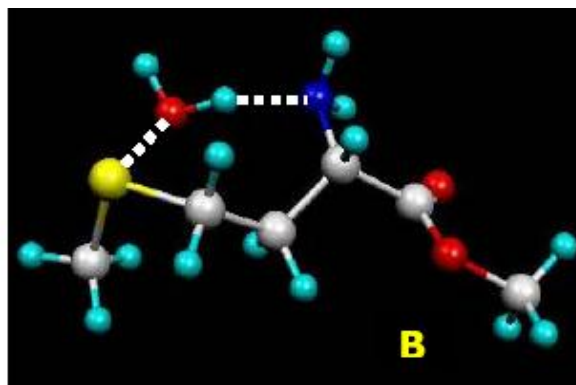
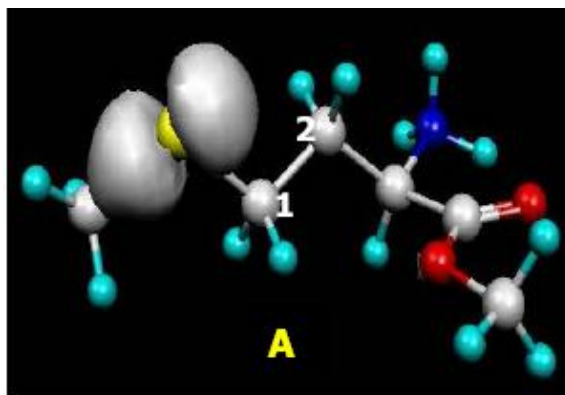


(3) Intramolecularly stabilized 5-membered ring between oxidized sulphur and nitrogen



(4) Intramolecularly stabilized 6-membered ring between oxidized sulphur and oxygen of either carbonyl or ester group

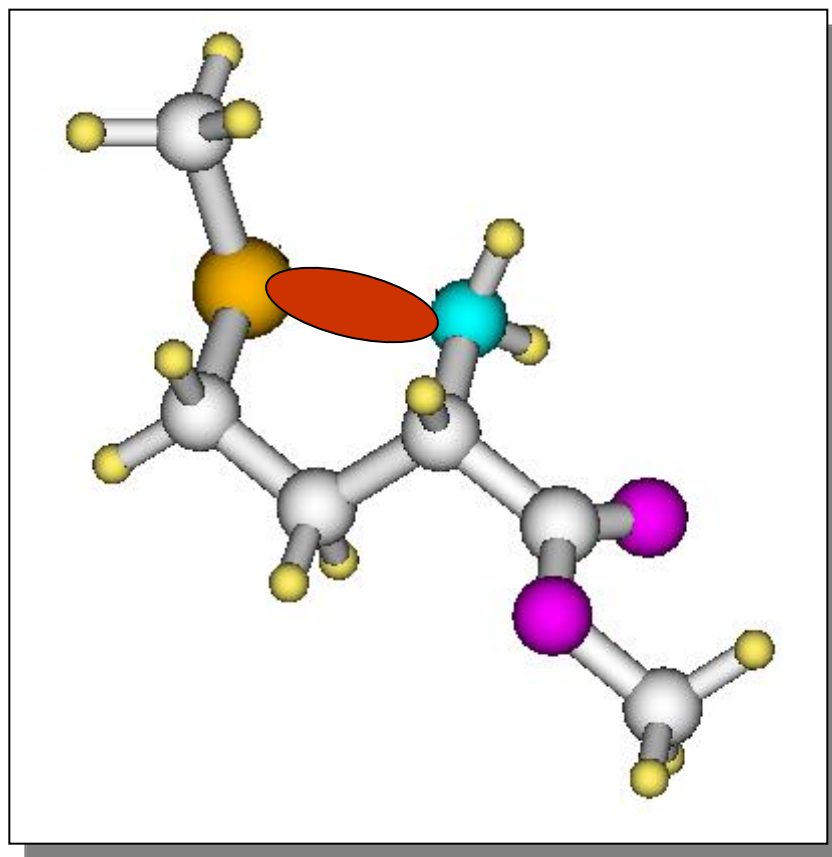
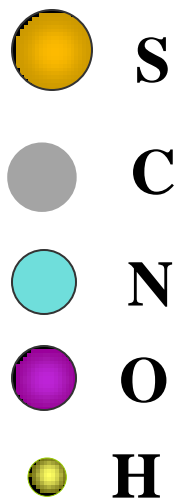




Yellow ball (S atom), ash-grey ball (C atom), blue (N atom), red (O) and sky blue (H atom). The grey lobes refer to the distribution of the atomic spin population of the odd electron.

pH 7

Reaction of $\cdot\text{OH}$ with MME : Formation of 2c-3e –S.:N- bond

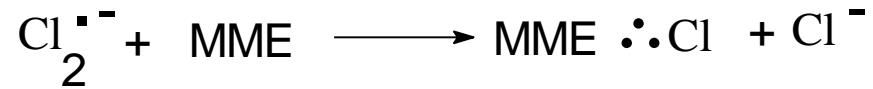
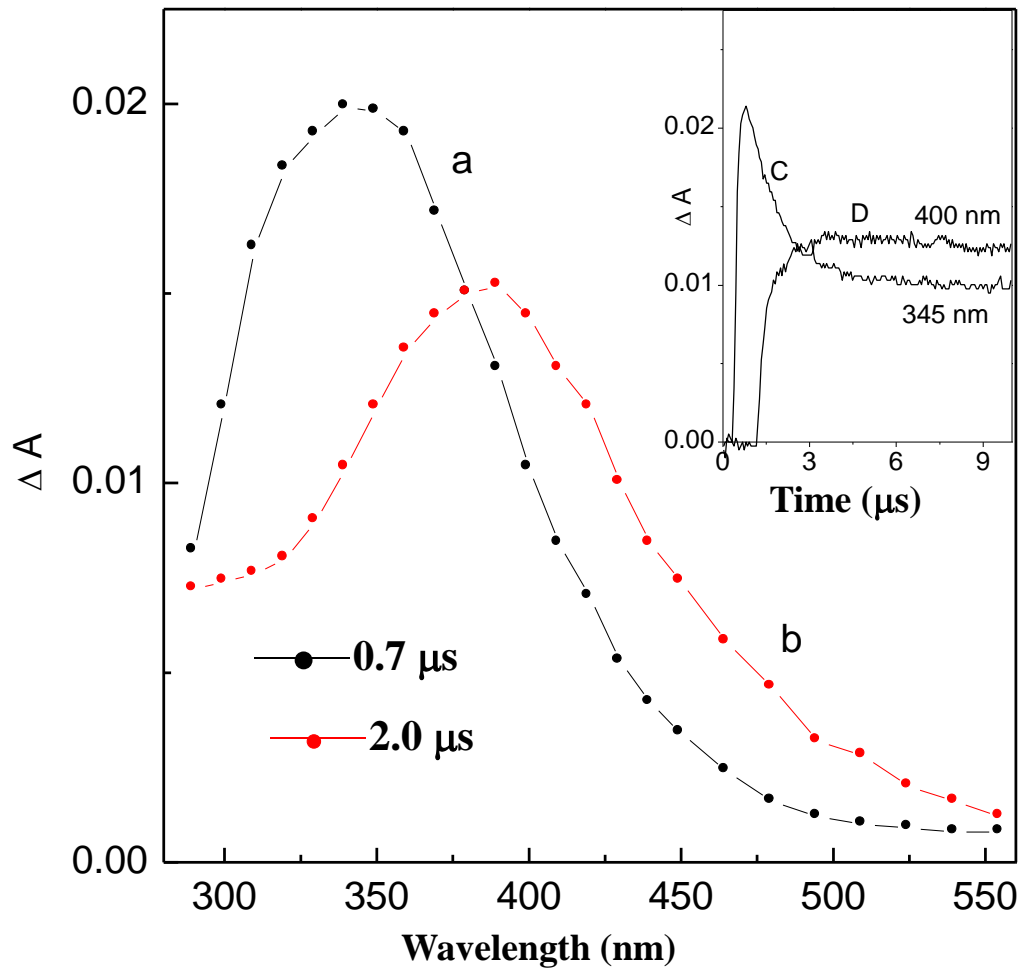


Binding energy of MME radical cation = 23.4 kcal/ mole

Bond order (B_{SN}) = 0.42

Optimized geometry of intramolecular bonding between sulphur and nitrogen in MME radical cation by DFT method

Reaction of Cl_2^- with MME at pH 1



➤ $k = 6.1 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$

Time resolved transient optical absorption spectra in the reaction of Cl_2^- with MME Inset: decay and formation traces of the transients at (c) 345 nm (d) 400 nm

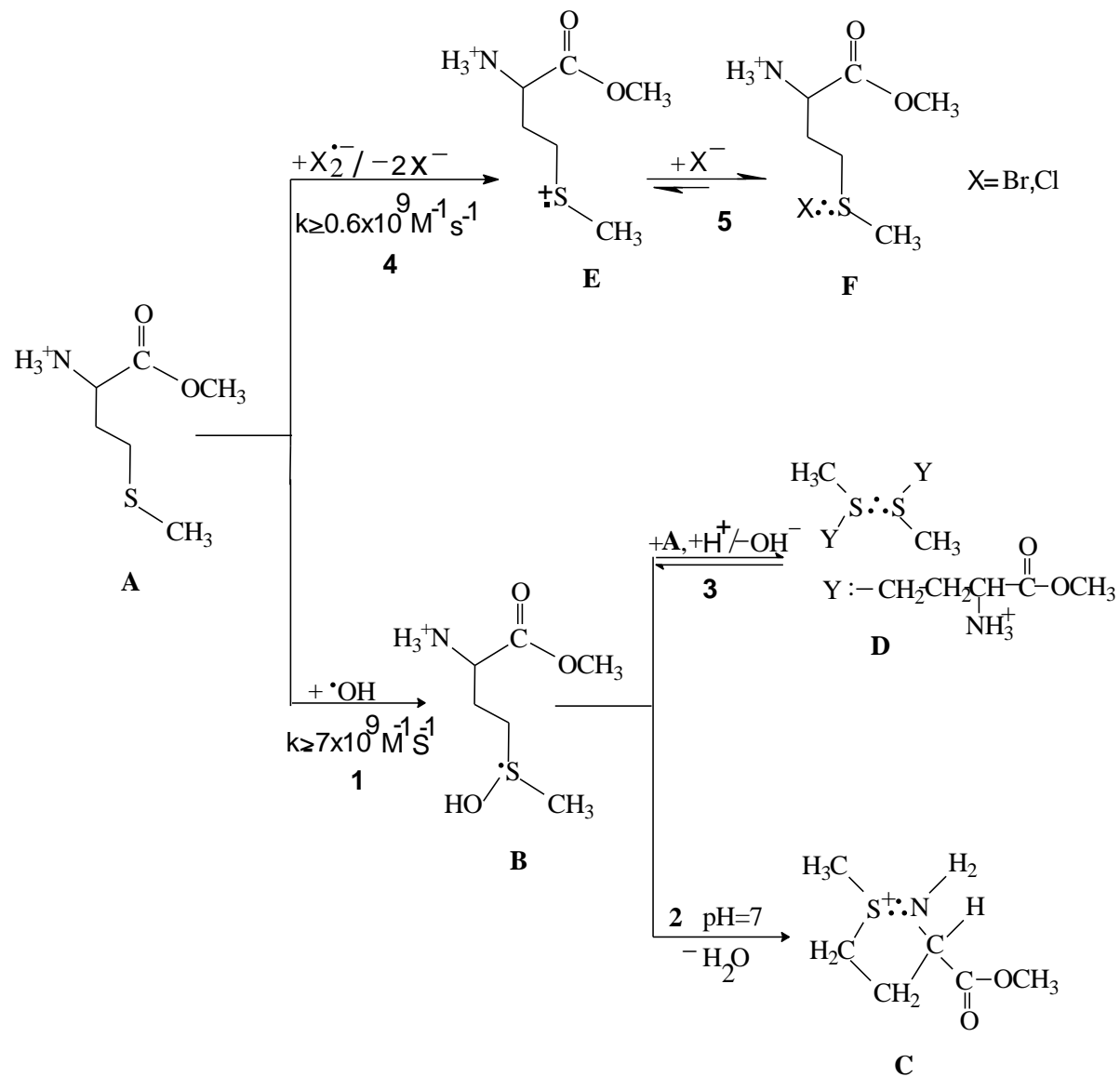
Calculated binding energy and other molecular properties for different systems of methionine methyl ester by theoretical calculations

System	Binding energy (kcal/mol)	Atomic spin population (α - β) in a.u.	Bond order B_{sx} (X=S,O,Cl,Br)	λ_{nm} (nm) Cal/Expt
MME-OH adduct	5.5	S=0.2; O=0.8	0.42	385/380
MME-Cl adduct	17.6	S=0.45; Cl=0.55	0.50	365/390
MME-Br adduct	23.0	S=0.5; Br=0.50	0.50	355/390
MME \cdot^+ (-S...O-)	22.6	S=0.9; O=0.1	0.22	385/380
MME \cdot^+ (-S...N-)	23.4	S=0.6; N=0.4	0.42	380/380
MME dimer radical cation	19.4	$S_1=0.5$; $S_2=0.5$	0.50	465/480

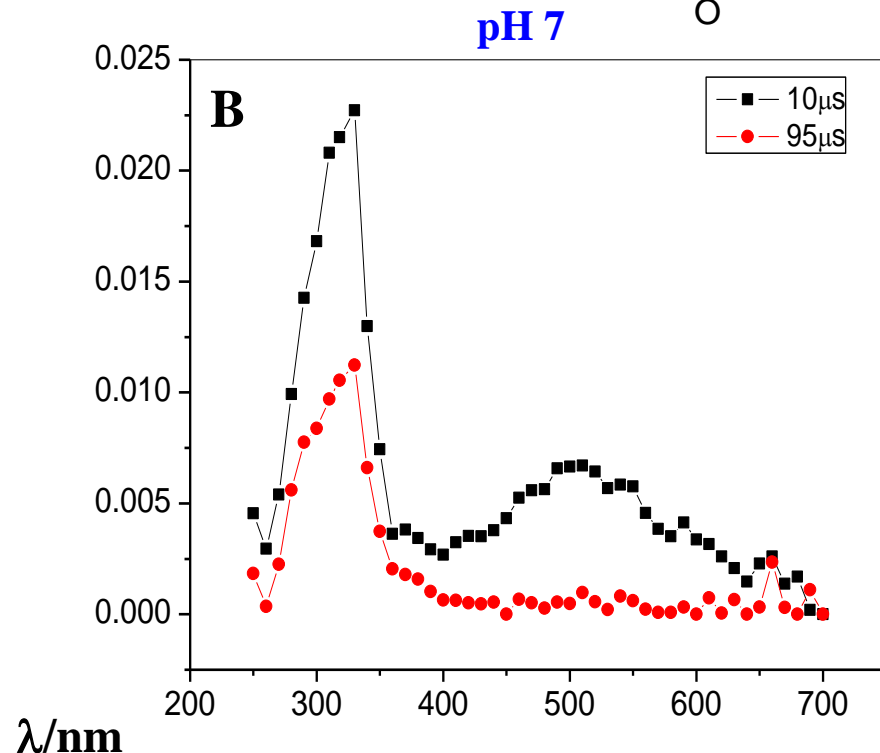
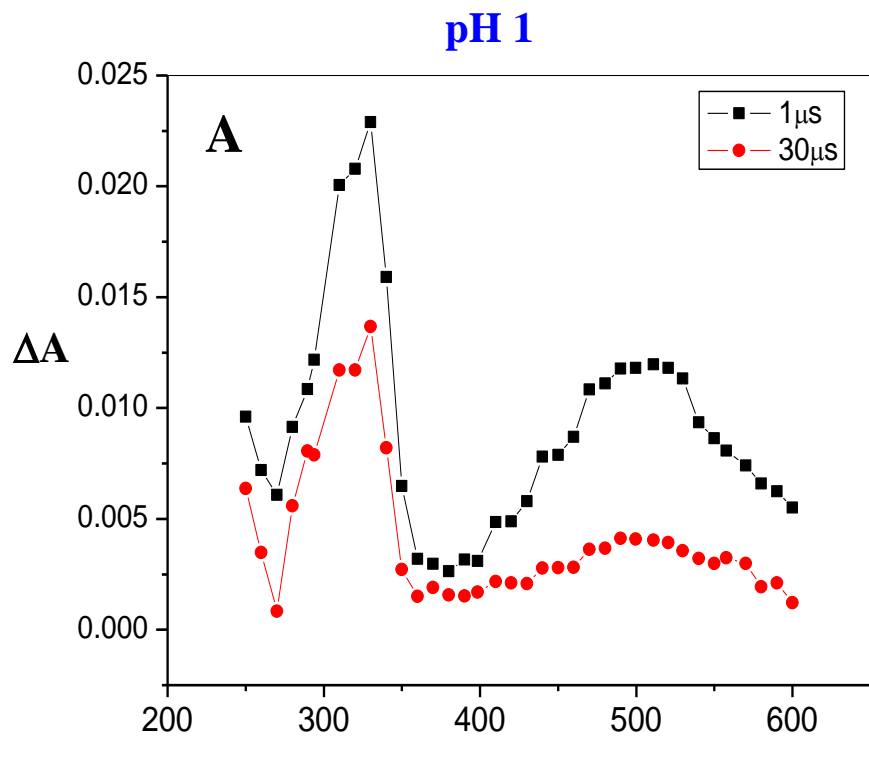
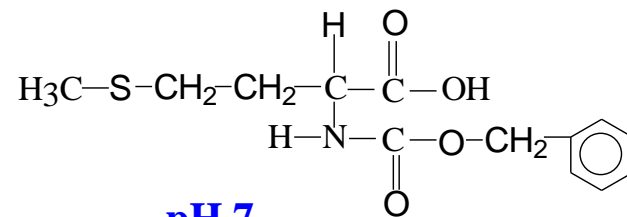
Kinetic and spectral parameters of the transient species formed on reaction of MME, MEE and Methioninol with different radicals.

Reaction	pH	λ_{\max} (nm)	k (M ⁻¹ s ⁻¹)
·OH + MME	1	480	9.8x 10⁹
	7	380	5.8 x 10⁹
Br₂^{·-} + MME	1	350	2.0 x 10⁹
	7	350	2.4 x 10⁹
Cl₂^{·-} + MME	1	350	6.1 x 10⁹
·OH + MEE	1	480	6.9 x 10⁹
	7	380	7.3 x 10⁹
Cl₂^{·-} + MEE	1	345	2.6 x 10⁹
Br₂^{·-} + MEE	1	350	2.0 x 10⁹
	7	350	1.5 x 10⁹
·OH + MOH	1	490	8.1x 10⁹
	7	390	4.7 x 10⁹
Br₂^{·-} + MOH	1	360	1.5 x 10⁹
	7	400	2.1 x 10⁹
Cl₂^{·-} + MOH	1	345	2.6 x 10⁹

Oxidation mechanism of MME



Reaction of $\cdot\text{OH}$ with N-Carbobenzyloxy methionine (NCM)

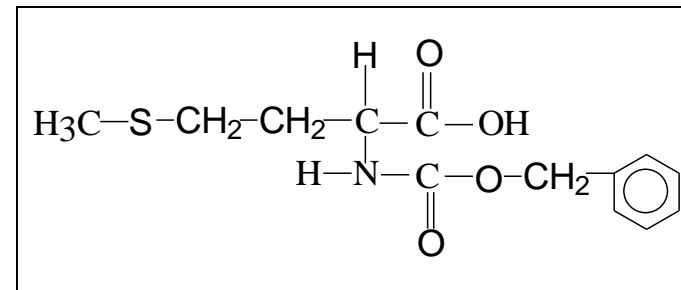
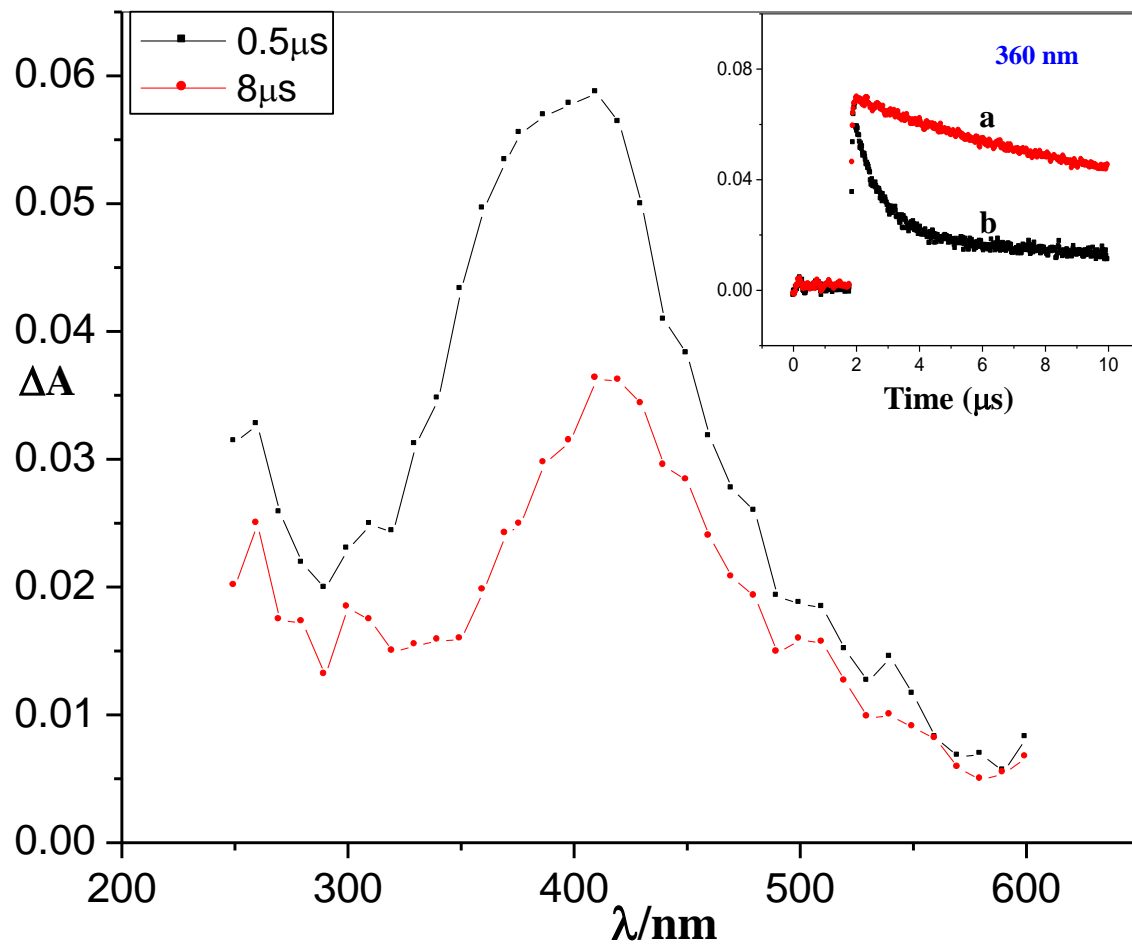


✓ At pH 1, 100% radical cation formation ($\lambda_{\text{max}} = 330, 510 \text{ nm}$) takes place

✓ At pH 7, 320 nm band contributes to the presence of OH adduct (60%) in addition to sulphur centred monomer radical cation (40%)

✓ No increase in absorbance with NCM concentration is observed

Reaction of $\text{Br}_2^{\cdot-}$ radicals with NCM

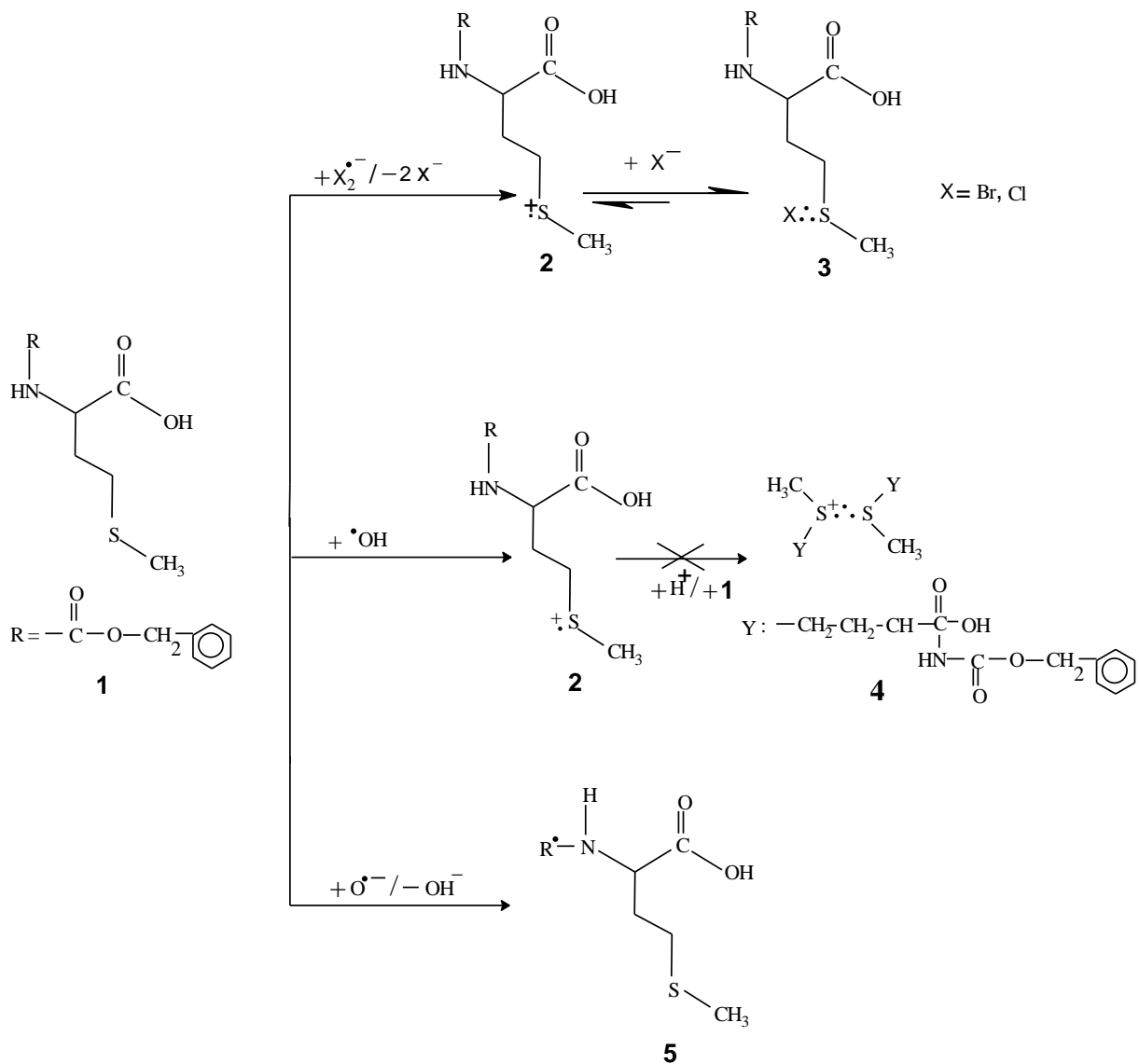


λ_{max} at 410 nm corresponds to -S: \cdot X- adduct

Same results are obtained in the reaction of $\text{Cl}_2^{\cdot-}$ with NCM

$$k = 1.7 \pm 0.1 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$$

Transient absorption spectra obtained after the reaction of $\text{Br}_2^{\cdot-}$ radicals with NCM at pH 7 Dose:16.3 Gy /pulse Inset: decay traces of the transients at 360nm (a) only $\text{Br}_2^{\cdot-}$ (b) $\text{Br}_2^{\cdot-}$ + NCM



Oxidation reaction mechanism of NCM in neutral, acidic and basic solutions

Conclusions



- ❖ **·OH radical reaction with MME, MEE and MOH depends strongly on pH.**
In acidic conditions - dimer radical cation formation takes place
Theoretical studies - intermolecular 2c-3e bond between sulphur-sulphur

In neutral conditions – monomer radical cation formation takes place
Theoretical studies - intramolecular 2c-3e bond is formed between oxidised sulphur and nitrogen
- ❖ **The reaction of ·OH with NCM at pH1 shows formation of sulphur centred monomer radical cation ($\lambda_{\text{max}} = 330, 510 \text{ nm}$). Its contribution only 40% at pH 7. No dimer formation was seen.**
- ❖ **Reactions of $\text{Br}_2^{\cdot-}$ and $\text{Cl}_2^{\cdot-}$ radicals with MME, MEE, MOH and NCM proceed *via* adduct formation - Independent of pH.**
Theoretical studies - support adduct formation

Publications

- 1. Oxidation of methionine methyl ester in aqueous solution: A combined pulse radiolysis and quantum chemical study, M. Shirdhonkar, D. K. Maity, H. Mohan and B. S. M. Rao, *Chem. Phys. Letters*, 417, 116, 2006.**
- 2. Pulse radiolysis: Pune University LINAC facility, B. S. M. Rao, P. Yadav, M. S. Kulkarni, M. B. Shirdhonkar, *Current Science*, 92, 599, 2007.**
- 3. Oxidation of phenyl trifluoromethyl sulphide: A pulse radiolysis and theoretical study, M. Shirdhonkar, H. Mohan, D. K. Maity and B.S.M. Rao, *J. Photochem. Photobiol. A: Chem*, 195, 277-283 , 2008.**
- 4. Oxidation of phenyl vinyl sulphide and phenyl vinyl sulphoxide in aqueous solution: A pulse radiolysis and theoretical study, M. Shirdhonkar, H. Mohan, D. K. Maity and B. S. M. Rao, *Chem. Phys. Letters*, 478, 2009, 155.**
- 5. Pulse Radiolysis and Theoretical Study of Oxidation of Methionine Derivatives, M. Shirdhonkar, H. Mohan, D. K. Maity and B.S.M. Rao (Under preparation).**

ACKNOWLEDGEMENT

➤ *Prof. B.S.M. Rao*

➤ *Late Dr. Hari Mohan*
Dr. D.K. Maity

➤ *Head, Department of Chemistry, Pune University*

➤ *Labmates & Friends*

➤ *DAE-BARC :Financial Support*

Thank You

