Single Electron Transfer Reaction Studies
By ESR

(A CASE STUDY OF N - CHLORO, BROMO & IODO SUCCINIMIDES)

ABSTRACT

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SINGLE ELECTRON TRANSFER (SET) REACTION STUDIES BY ESR SPECTROSCOPY

(A CASE STUDY OF N - CHLORO, BROMO & IODO SUCCINIMIDES).

This thesis describes the results of SET reaction studies involving N - Chloro, Bromo and Iodo succinimides. The major thrust is on the phenomenon of SET chemistry. An extensive application of ESR spectroscopy has been made to study electron transfer processes. The contents of the thesis is distributed over six chapters.

Chapter I presents a brief general introduction pertaining to the work embodied in the thesis. It describes the fundamental aspects of SET chemistry and the various models proposed to describe the SET phenomenon. The methodology used to provide evidences for SET reactions such as :
(i) Detection of radicals by ESR spectroscopy.
(ii) Formation of radical derived secondary products etc.
are listed.

The formation of charge transfer complexes ; precursor in electron transfer reactions through UV study is highlighted. The scope and the basic principles of ESR spectroscopy is described in brief. The direct detection and identification of radicals by ESR is possible only if the radicals are produced in high concentration in situ within the ESR cavity, an indirect method called " Spin Trapping " employed in this work, is described.

<u>Chapter II</u> reviews the work carried out by various researchers in the field of N- Halosuccinimides under different conditions. The N- Halosuccinimides gained recognition when N- Bromosuccinimide was recognised by Karl Ziegler and co - workers as a brominating agent of olefins at allylic positions. Although the reaction became a standard synthetic procedure but the actual chain carriers involved have been the subject of recurrent controversy. Various controversies surrounding succinimidyl chemistry are underscored in this chapter. The work of Eberson is reviewed at the end of this chapter.

<u>Objective</u> This part describes the major objective of the present study. The recent development of the so called Single Electron Transfer (SET) chemistry is gaining ground very fast. The SET reaction is one that is initiated by the transfer of a single - electron from nucleophile to the substrate, producing a radical intermediate. The resulting radical intermediate can than be involved in any number of events. Many organic reactions which were previously classified as polar reactions actually involves radical intermediates formed by

a process initiated by SET from the nucleophile to the substrate. Yet despite the growing evidence that SET processes are far more widespread than originally thought, the relationship between SET and polar pathway remain obscure. Chemical community seems to be coming around to accept SET pathway as a major one but still some reluctance is there. One of the reason could be that their are still some fundamental questions that need to be addressed before SET gains a wider acceptance e.g.,

(i) What are the factors that determine whether a particular reaction proceeds via SET or a polar pathway ?.

(ii) What is the precise relationship between the two ?.

Therefore, one of the objective of the present study would be to answer some of the questions at least to some extent if not in totality.

We feel that in this endeavor ESR spectroscopy (its full potential is yet to be realised) can play an important role. We have made an extensive application of ESR using spin trapping to study the SET aspects of N-Halosuccinimides. The mechanism of N- Halosuccinimide reactions have been the subject of number of investigations however, a definite reaction mechanism could not be established. The controversy over the nature of the chain propagating species have been widely recognised and still continues to attract attention. The areas of disagreement involve both experimental results and their interpretations.

It is an attempt to elucidate the mechanism, the effect of environmental factors and of added substances of potential catalytic / inhibitory action on the reaction mechanism. The suggestion that the succinimidyl radical undergoes ring opening is also investigated. This study is the first of its kind where, nitrones are used in a dual role. The purpose of the nitrone to use for example, as a reductant was to ensure that if at all an electron is donated by it then it will become a cation and the electron captured specie will undergo dissociation and one of the product will be an anion. The probability of anion being trapped by a nitrone cation would be certainly higher then the probability of free radical being trapped by neutral nitrone and thus we may succeed in identifying some of the primary products of ET process. The identification of primary products always imparts some authenticity to the mechanism rather than mechanism derived from end products.

Chapter III deals with the reagents and chemicals used. Their purification and drying etc., is also described. The actual details of the experimental procedures are described. The specifications and limitations of all the instruments used in the present study are mentioned. The calibration and standardisation of the instruments used are also explained. The determination and calculation of various ESR parameters are explained. The computer simulation program developed is given in the appendix of the thesis.

Chapter IV is devoted to the results obtained in electron transfer reaction between N-Chlorosuccinimide (NCS) and nitrones. The formation of charge transfer complex between NCS and nitrone (PBN : N- tert. butyl α - phenylnitrone) is studied. The appearance of an isosbestic point reveals the feasibility of electron transfer. The ESR results obtained under different conditions of concentration, solvent polarities etc., are described. In benzene at 1:1 concentration of NCS and PBN, chloro adduct of PBN with ^{35}Cl and ^{37}Cl isotope signals Fig. 1 along with spectra assigned to benzoyl tert.- butyl nitroxide (PBNOX) were observed. PBNOX was the only signal left after all other signals decayed out. At a concentration of PBN to NCS 4:1, the succinimidyl adduct of PBN was observed. The reaction mechanism formulated in Scheme 1, is proposed. The reaction studied at various concentrations of NCS and PBN reveals that, succinimidyl radical (S·) and chloride ion (Cl^-) are the two species formed from the electron

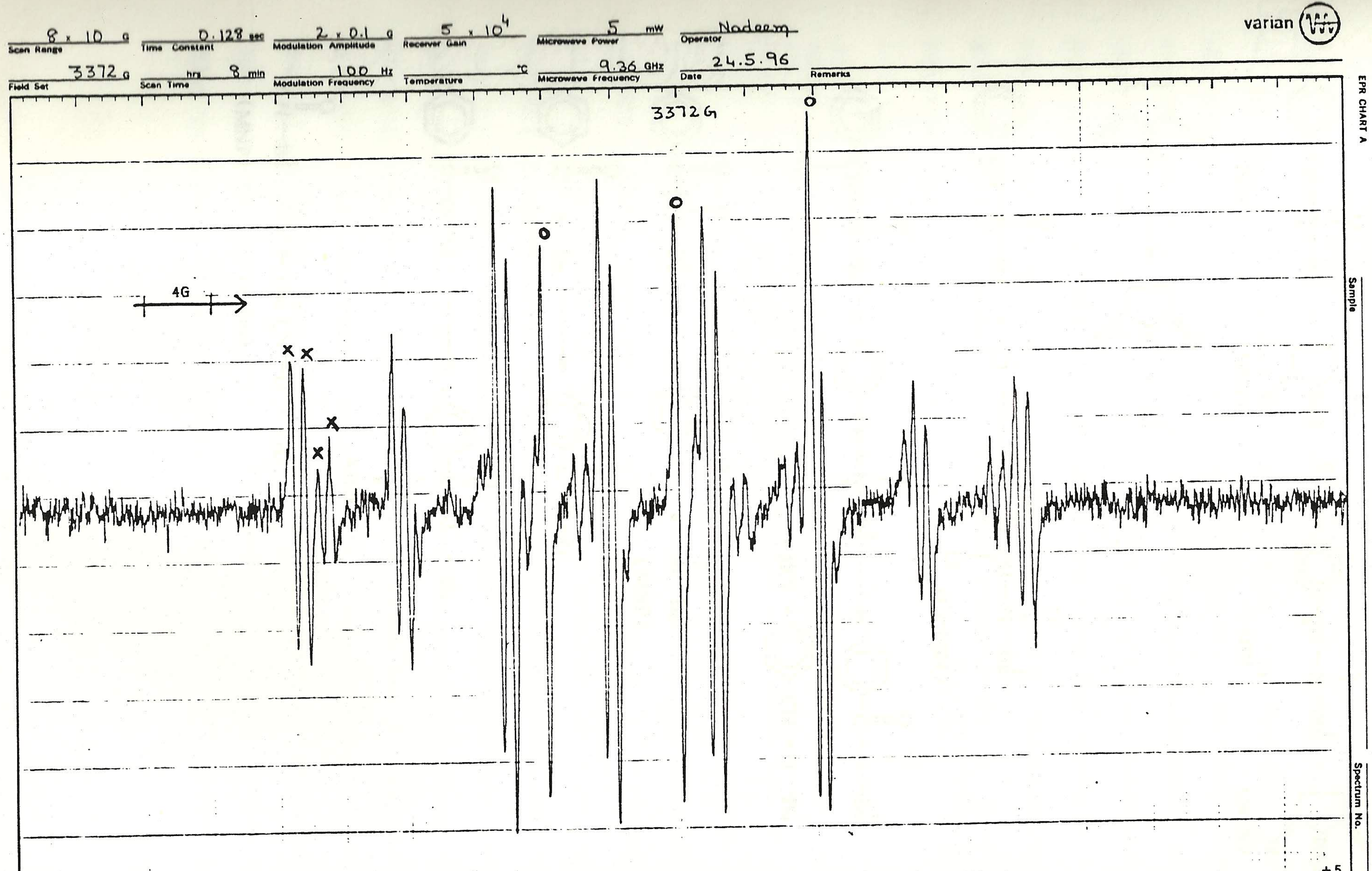

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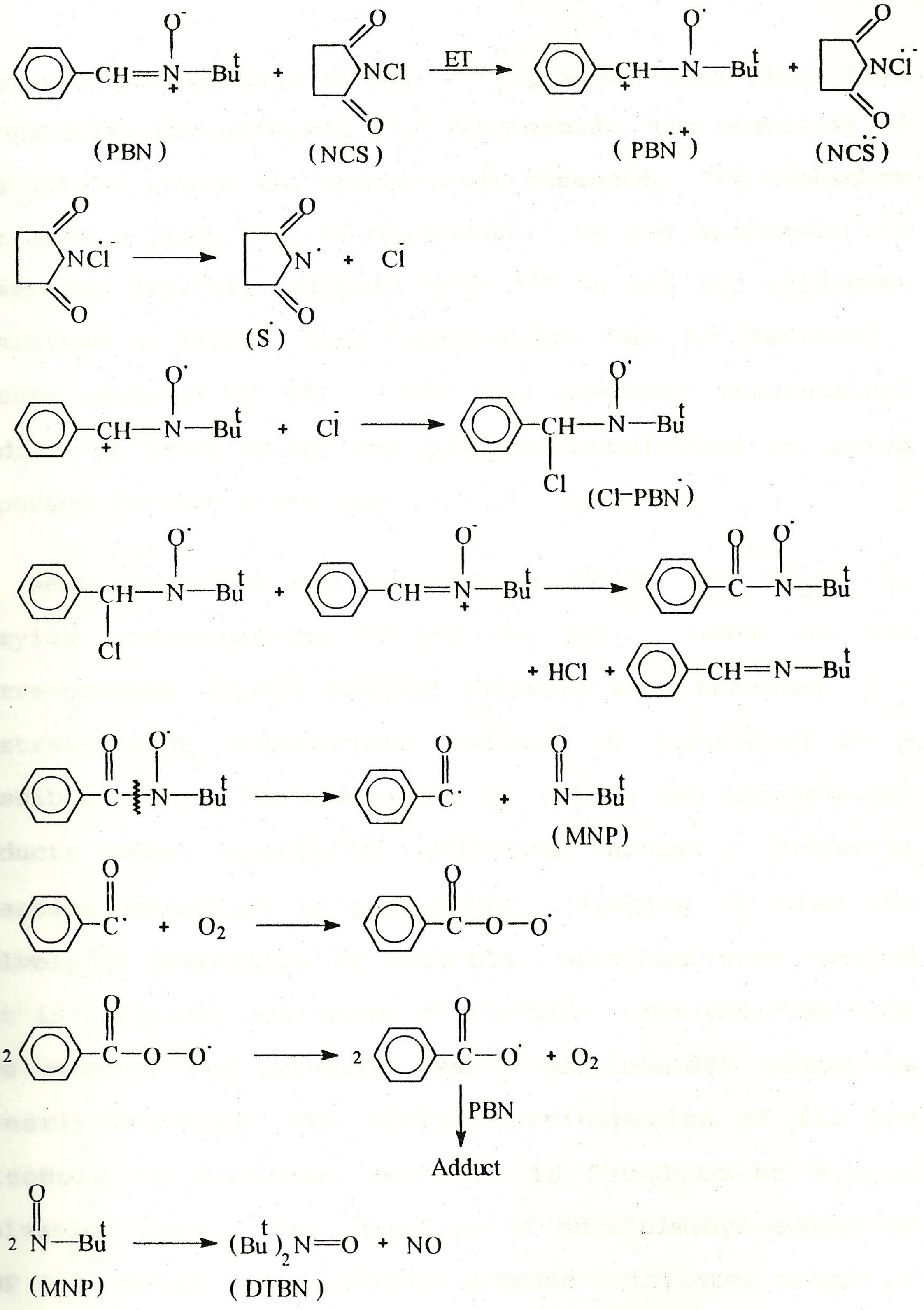
Fig. 1. ESR spectra obtained from PBN and NCS in benzene. **x** , Cl-PBN· adduct ; **o** , PBNOX.

Scheme 1



captured dissociation of NCS$^{\cdot -}$. By using substrates like N- Methylsuccinimide and / or succinimide, the stability of the chloro adduct was considerably enhanced. The mechanism for such a stability is discussed. We are successful in observing satellite signals from ^{13}C in all the different positions of PBNOX. Such examples are rare for conformational studies by ESR. The well resolved succinimidyl adduct of DMPO under the present conditions is being reported for the first time.

Next we studied the reaction in CH_3CN and CH_2Cl_2 in varying concentrations of NCS and PBN. PBNOX and the corresponding solvent derived radicals were observed. H - abstraction by succinimidyl radical is postulated as a possible mode. The observance of chloro and succinimidyl adducts under photolytic conditions through a different reaction mechanism is postulated. Keeping in view the solvolytic properties of alcohols, reactions were carried out in different analogues of alcohols. The chloride ions are removed via solvation while succinimidyl adduct is clearly observed. The active participation of all the alcohols is observed. Methanol is found to be a poor solvating agent. The formation of succinimidyl adduct of MNP (2- Methyl - 2 - nitroso propane) in later stages of the reaction is postulated through β - cleavage of succinimidyl adduct of PBN. The stability of the chloro adduct in CCl_4 is attributed to solvent participation in the reaction mechanism. With 1,4 - Dioxan, we are successful in detecting both the species, chloro and succinimidyl adducts of PBN under different relative concentrations of NCS and PBN, again establishing the formation of only these two species from $NCS^{\cdot -}$. Reaction in DMF as solvent, yielded chloro adduct of PBN and PBNOX in the beginning. At a later stage, spectra due to $(CH_3)_2NCO\text{-}MNP^{\cdot}$ was identified. This points out H-abstraction from the formyl group of DMF. With DMSO as solvent, succinimidylmethyl adduct of MNP is observed. The spectral assignment is confirmed by simulation. A new pathway for the generation of methyl radicals is postulated. The proposed mechanism is supported by other experimental evidences.

Chapter V describes the results of N- Bromosuccinimide (NBS) and N- Iodosuccinimide (NIS) with nitrones. The possibility of charge transfer complex formation through the appearance of an isosbestic point was observed. At 1:1 concentration of NBS and PBN in benzene, intense signals due to PBNOX (with well resolved satellite signals from ^{13}C in different positions along with ^{15}N) and benzoyloxyl adduct of PBN were observed. We could not see any signal due to bromo or succinimidyl adduct of PBN. This suggests that, (i) spin adducts of the primary products are perhaps highly unstable (ii) NBS$^{\cdot -}$ follows a different mode of dissociation. At all other concentrations of NBS and PBN similar results are obtained. The formation of PBNOX is attributed to oxidation of PBN by Br_2 formed by rapid dimerisation of bromine atoms. This was confirmed by the appearance of PBNOX signal when dilute solution of bromine was added to PBN solution. The light yellow colour also suggests the formation of Br_2. The absence of succinimidyl adduct is proposed to be due to oxidation by Br_2. At this stage an opposite cleavage mode of NBS$^{\cdot -}$ appears as compared to NCS$^{\cdot -}$. This conclusion is supported by the observance of well resolved succinimidyl adduct of PBN and very weak PBNOX signals when traces of bicyclopentadiene, a known free radical scavenger was added to the system. This indicate that succinimidyl adduct can only be observed when Br_2 is effectively removed from the system. It would not be out of place to mention that addition of bicyclopentadiene in similar conditions in NCS did not make any qualitative difference in the spectra. This confirms that dissociation of NBS$^{\cdot -}$ gives bromine atoms and succinimidyl anion, while NCS$^{\cdot -}$ gives chloride ions and succinimidyl radicals.

In n- Hexane, major adducts observed at various relative concentrations of NBS and PBN, were PBNOX and benzoyloxyl adducts. The absence of succinimidyl adduct in presence of bicyclopentadiene could be due a higher rate of dimerisation of bromine atoms. Results in solvents such as CH_3CN, CH_2Cl_2 are in line with our postulations of cleavage mode of $NBS^{\cdot -}$. The observance of chloro adduct in CCl_4 is attributed to a different mechanism. The results clearly indicates solvent participation in the reaction. In DMF, $(CH_3)_2NCO^{\cdot}$, $(CH_3)_2N^{\cdot}$ and $BrCH_2CH_3\dot{N}CO$ radical adducts were observed. In alcohols PBNOX, benzoyloxyl and corresponding solvent derived radical adducts were observed. In DMSO, succinimidylmethyl radical adduct of MNP (also observed with NCS) was observed though through a different reaction pathway.

With N- Iodosuccinimide, only PBNOX and benzoyloxyl radical adducts were observed under all the conditions. The electron transfer mechanism and subsequent reactions are identical to that of NBS. The non observance of succinimidyl adduct in the presence of bicyclopentadiene suggests that the rate of dimerisation of iodine atoms is much faster than addition to bicyclopentadiene. This results in the oxidation of PBN to PBNOX as the major pathway.

Last part of the thesis is the concluding chapter. Only some of the salient features are mentioned below :

1. The technique of spin trapping has been very successfuly applied in this system. A new role of nitrone is presented.
2. This work provides another clear example of single electron transfer phenomenon.
3. We are successful in studying electron transfer reaction between N- halosuccinimides and nitrones under
   (i) mildest conditions and
   (ii) At ambient temperatures.
4. We are successful in observing satellite signals from ^{13}C isotope in all the different positions of PBNOX.
5. The observance of succinimidyl adduct of DMPO under the conditions employed is reported first time.
6. The electron capture dissociation of $NCS^{\cdot -}$ leads to succinimidyl radical ($S^{\cdot}$) and chloride ion (Cl^{-}), while $NBS^{\cdot -}$ and $NIS^{\cdot -}$ leads to S^{-} and corresponding halogen atoms.
7. The studied system involves only two major chain carriers succinimidyl and the corresponding halogen moieties with no sign of ring opening of succinimidyl moiety.

8. The role of polar and hydroxylic solvents in solvating the charged species and thus diverting the reaction pathways have been clearly observed.
9. A new route for the generation of methyl radicals from DMSO is postulated.
10. It has been observed that the rate of dimerisation of bromine atoms are relatively slower than iodine atoms.
11. The strong evidence of the charge transfer complexation suggests that the electron transfer proceeds through an " outer - sphere " mechanism.

SCOPE OF THE PRESENT WORK

Since this is a first attempt of this kind at room temperature under mildest conditions, the positive results appears to be quite promising. Therefore, it is certainly worth pursuing with other substituted and structurally similar molecules for example N- Halophthalimides.